Computational consideration on advanced oxidation degradation of phenolic preservative, methylparaben, in water: mechanisms, kinetics, and toxicity assessments

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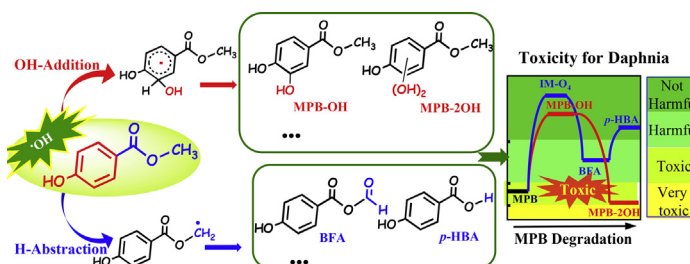
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HIGHLIGHTS

- Computational approach is effective to reveal the transformation mechanism of MPB.
- MPB degradation was more dependent on the [$^\bullet$OH] than temperature during AOPs.
- O_2 could enhance MPB degradation, but more harmful products were formed.
- The risks of MPB products in natural waters should be considered seriously.
- The risks of MPB products can be overlooked in AOPs due to short half-time.

GRAPHICAL ABSTRACT

ABSTRACT

Hydroxyl radicals ($^\bullet$OH) are strong oxidants that can degrade organic pollutants in advanced oxidation processes (AOPs). The mechanisms, kinetics, and toxicity assessment of the $^\bullet$OH-initiated oxidative degradation of the phenolic preservative, methylparaben (MPB), were systematically investigated using a computational approach, as the supplementary information for experimental data. Results showed that MPB can be initially attacked by $^\bullet$OH via OH-addition and H-abstraction routes. Among these routes, the $^\bullet$OH addition to the C atom at the *ortho*-position of phenolic hydroxyl group was the most significant route. However, the methyl-H-abstraction route also cannot be neglected. Further, the formed transient intermediates, OH-adduct ($^\bullet$MPB-OH$_1$) and dehydrogenated radical ($^\bullet$MPB(-H)α), could be easily transformed to several stable degradation products in the presence of O_2 and $^\bullet$OH. To better understand the potential toxicity of MPB and its products to aquatic organisms, both acute and chronic toxicities were assessed computationally at three trophic levels. Both MPB and its products, particularly the OH-addition products, are harmful to aquatic organisms. Therefore, the application of AOPs to remove MPB should be carefully performed for safe water treatment.

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1. Introduction

Pharmaceuticals and personal care products (PPCPs) have raised increasing global concern because of the potential threat to

drinking water safety and aquatic ecosystems [1]. Parabens, a group of important PPCPs with antimicrobial and preservative properties, are widely used in toothpastes, cosmetics, textiles, and beverages [2–4], resulting in approximately 8000 tons of parabens consumed annually globally [5]. Among these parabens, methylparaben (MPB) has the highest concentration in various cosmetic products [6,7]. MPB is continuously released into aquatic environment through domestic wastewater because of daily consumption. Consequently, MPB is ubiquitously detected in various aquatic environments [8–10], thus creating potential risks to aquatic organisms [7,11]. Moreover, MPB could potentially contribute to the incidence of breast cancer [12–14] and has been classified as an emerging contaminant (EC) by U.S. Environmental Protection Agency. Nevertheless, the conventional wastewater treatment technologies are inadequate to remove these ECs [15,16]. Therefore, advanced oxidation processes (AOPs), as the alternatives to traditional water treatment technologies, have attracted global attention in this field.

Over past few years, various AOPs including photocatalysis [17,18], ozone oxidation [19], UV irradiation [20] with the *in situ* production of highly reactive hydroxyl radicals (•OH), as the main oxidants, have been frequently employed to degrade MPB experimentally. However, some studies only optimized experimental conditions without considering MPB degradation mechanism [18,20,21]. Some proposed that •OH can attack both the alkyl chain and benzene ring of MPB based on experimental determination of intermediates [17,19]. However, the specific reaction sites in MPB and pathways involved are still unclear. For example, a tentative reaction pathway reported that MPB is mainly attacked by •OH at –CH$_3$ and –H in the aromatic ring [17], hydroxylation at the aromatic ring and hydrogen abstraction were the degradation mechanism of MPB in ozonation [19]. Nevertheless, these studies on quantitative distribution and potential toxicities of products during MPB degradation using AOPs have not yet been concerned, even though this information is very important for environmental protection. Therefore, the mechanisms, kinetics, and toxicity assessments of MPB degradation during AOPs still deserve to be investigated systematically. At this point, the computational results are expected to interpret the experimental findings and provide theoretical support for the conclusions of the experimental MPB degradation results. In addition, as a approach of cost-effective, convenient, and avoiding the use of animals for toxicological study [22,23], computational approach is frequently adopted to investigate the molecular basis of environmental, chemical, and biological processes [24,25]. To date, no computational study has been reported on the mechanisms and kinetics of MPB degradation using AOPs, as well as the toxicity assessment of its degradation products.

In this study, the mechanisms and kinetics of •OH-initiated degradation of MPB were systemically elucidated by quantum chemical calculations. All the possible MPB degradation mechanisms were considered, and the intermediates formed in these processes were quantified according to the ratio of different routes determined from kinetics results. Furthermore, the acute and chronic toxicities of MPB as well as its degradation products were evaluated using "ecological structure–activity relationships" (ECOSAR) program to better understand the potential risks to aquatic organisms during MPB degradation using AOPs.

2. Computational methods

2.1. Mechanism and kinetics computations

All the quantum chemical calculations were performed using the Gaussian 03 program [26]. The geometries of all stationary points were optimized using the hybrid density functional B3LYP

method with the 6-31G(d,p) basis set. At the same level, the theoretical harmonic vibrational frequencies were calculated to identify these stationary points, as either minima (with zero imaginary frequency) or transition state (*TS*, with one and only one imaginary frequency), and the thermodynamic contributions. The intrinsic reaction coordinate (IRC) calculations were conducted to confirm that each *TS* connected the corresponding reactants (*RC*) to products (*PC*). The single-point energy calculations, including solvent effect, were performed to establish potential energy surface (PES) at B3LYP/6-311++G(d,p) level based on the above optimized structures, and the conductive polarizable continuum model (CPCM) [27] was employed to consider solvent effect. Based on the above PES information, the reaction kinetics were calculated using conventional transition-state theory (TST), solvent cage effects [28], and diffusion-limited effects [29], as shown in supporting information (SI). The half-life ($t_{1/2}$) of the •OH-initiated reaction of MPB was calculated using the formula, $t_{1/2} = \ln 2/(k_{total} \times [•OH])$, where [•OH] denotes the •OH concentration in aqueous phase.

2.2. Ecotoxicity assessment

The acute and chronic toxicities of MPB and its degradation products during AOPs were assessed using ECOSAR program [30] to estimate their risk to three trophic levels of aquatic organisms, namely, green algae, daphnia, and fish. Herein, the acute toxicity is expressed by EC$_{50}$ values (the tested pollutant concentration for 50% growth inhibition of green algae after 96 h) and LC$_{50}$ values (the tested pollutant concentration for 50% dead fish and daphnia after 96 and 48 exposures, respectively). For conservative consideration, the lowest toxicity concentration was chosen. The risk of target chemicals on aquatic organisms was also assessed by hazard quotient (HQ) method [31]; the detail description is given in SI.

3. Results and discussion

3.1. Structure and aquatic toxicity of MPB

The optimized MPB structure and the description of its carbon atom number are shown in Fig. 1. MPB contains a methyl ester and phenolic hydroxyl (OH) group, which is structurally similar to natural 17β-estradiol. This structure may be responsible for the estrogenic activity of MPB in breast cancer [32]. In addition, the octanol–water partitioning coefficient ($\log K_{ow}$) of MPB was calculated to be 2.00, which agrees well with the experimental value 1.98 [33]. Thus, MPB may have potential toxicity to aquatic organisms according to previous reports that chemicals with $\log K_{ow}$ below 6.0 could exert aquatic toxicity [34,35]. To validate this supposition, the acute and chronic toxicities of MPB at three trophic levels were calculated (Table S1). For acute
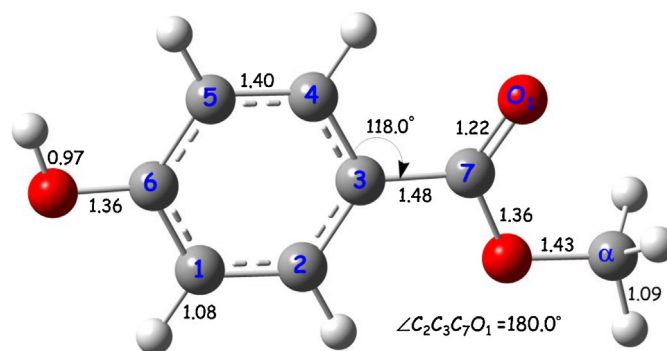

Fig. 1. Optimized geometries of MPB at the B3LYP/6-31G(d,p) level; bond lengths are in angstroms (Å); Herein, ●, C; ●, H; ●, O.

toxicity, daphnia LC_{50} was $7.99\,mg\,L^{-1}$, indicating that MPB was acutely toxic ($1.0 < LC_{50} < 10.0\,mg\,L^{-1}$) for daphnia, according to the EU criteria [23]. However, for fish and green algae, MPB was classified as harmful ($10.0 < LC_{50} < 100.0\,mg\,L^{-1}$), owing to the LC_{50} of $20.43\,mg\,L^{-1}$ for fish and EC_{50} of $18.09\,mg\,L^{-1}$ for green algae. For chronic toxicity, all chronic toxicity values (ChV) of MPB were predicted in the range 1.0–$10.0\,mg\,L^{-1}$, indicating that MPB is chronically harmful for all three tested organisms according to the guidelines for the hazard evaluation of new chemical substances of China (HJ/T 154-2004). Moreover, the calculated toxicity values such as ChV for daphnia was $1.52\,mg\,L^{-1}$, which well agreed with experimental values of $1.50\,mg\,L^{-1}$ [36]. This indicates that the ECOSAR program is suitable to assess the toxicities of MPB and its transformational products. Generally, MPB was a harmful substance with adverse effects on aquatic organisms, particularly for daphnia. It is therefore very deserved to investigate the elimination mechanisms and kinetics of MPB from water environment using AOPs.

3.2. Initial reaction of MPB with $^{\bullet}OH$

Mechanism. In the aqueous-phase AOPs, MPB degradation was mainly initiated by $^{\bullet}OH$ [17]. Thus, all the possible routes for MPB $+\,^{\bullet}OH$ reaction were thoroughly considered and summarized in Fig. 2. These routes can be divided into three types: (i) OH-addition: either onto the C atom of benzene ring ($R_{add}1$–6) or carbonyl group ($R_{add}7$); (ii) H-abstraction by $^{\bullet}OH$: either from methyl ($R_{abs}\alpha$), phenolic hydroxyl ($R_{abs}OH$), or the benzene ring ($R_{abs}1,2,4,5$); and (iii) single-electron transfer: from MPB by $^{\bullet}OH$ (R_{set}). The geometries of all stationary points, such as TSs and PCs, involved in these routes are shown in Figs. S1–2, and the PES profile of all the above-mentioned routes is shown in Fig. 2. Herein, the energies were calculated relative to the reactants, MPB and $^{\bullet}OH$, and $\Delta G^{\neq}$ values were defined as the free energy barrier ($\Delta G^{\neq} = G_{TS} - G_{RC}$). ΔG is the reaction energy ($\Delta G = G_{PC} - G_{RC}$).

For OH-addition routes (Fig. 2), five routes ($R_{add}1,2,4,5,6$) were found to be exothermic ($\Delta G < 0$), except that routes $R_{add}3$ and $R_{add}7$ were endothermic with ΔG of 2.36 and $23.35\,kcal\,mol^{-1}$, respectively, indicating that $R_{add}3$ and $R_{add}7$ routes could not contribute to MPB degradation during AOPs. In the five exothermic routes, the lowest $\Delta G^{\neq}$ of $7.53\,kcal\,mol^{-1}$ was located in $R_{add}1$ route, which was 2.55–$4.12\,kcal\,mol^{-1}$ lower than the $\Delta G^{\neq}$ of the others ($R_{add}2,4,5,6$), indicating that $R_{add}1$ route is the most favorable OH-addition route. However, the contribution of other four routes ($R_{add}2,4,5,6$) may not be ascertained easily because of the small differences in $\Delta G^{\neq}$, e.g., the $\Delta G^{\neq}$ were 10.40 ($R_{add}2$), 10.08 ($R_{add}4$), 11.65 ($R_{add}5$), and 11.59 ($R_{add}6$) $kcal\,mol^{-1}$, respectively. Thus, the kinetic calculation is very important for further understanding.

For H-abstraction routes (Fig. 2), the $\Delta G^{\neq}$ of methyl-H-abstraction ($R_{abs}\alpha$) and phenolic-H-abstraction ($R_{abs}OH$) routes were calculated to be 9.74 and $10.63\,kcal\,mol^{-1}$, respectively, which were lower by ~ 2.6–$6.3\,kcal\,mol^{-1}$ than those of benzene-H-abstraction routes ($R_{abs}1,2,4,5$). Furthermore, the latter four routes were at least $14\,kcal\,mol^{-1}$ less exothermic than those of the former two routes. These results indicate that $R_{abs}\alpha$ and $R_{abs}OH$ routes are significant; however, other H-abstraction routes should be neglected. Because of the small difference in $\Delta G^{\neq}$ between $R_{abs}\alpha$ and $R_{abs}OH$, their contributions were unlikely to be identified only from mechanism aspect; therefore, further kinetics calculations were needed to distinguish their detailed contributions.

For single-electron transfer route (R_{set}) (Fig. 2), the $\Delta G^{\neq}$ was $13.30\,kcal\,mol^{-1}$ and higher by at least $5\,kcal\,mol^{-1}$ than that of the most favorable OH-addition route ($R_{add}1$). More importantly, R_{set}

route was the endothermic route, and the reaction energy was less by $\sim 34\,kcal\,mol^{-1}$ than that of the most significant H-abstraction route ($R_{abs}\alpha$). Therefore, R_{set} route was less spontaneous than other exothermic routes and could be difficult to occur in the initial step of MPB degradation, indicating a very low probability for the electron-transfer reactivity of parabens with $^{\bullet}OH$. The finding also explains the previous experimental results, i.e., the transient spectrum of the single-electron transfer product, the radical cation of propylparaben ($PPB^{+\bullet}$), was not observed during the degradation of propylparaben using AOPs [37].

Based on the above discussion, the single-electron transfer route (R_{set}) and two OH-addition routes ($R_{add}3$ and $R_{add}7$) can be ruled out during MPB degradation using AOPs because of the endothermic processes. Therefore, following discussion on the kinetics and toxicity assessments of degradation products will be focused on the five OH-addition ($R_{add}1,2,4,5,6$) and two H-abstraction ($R_{abs}\alpha$ and $R_{abs}OH$) routes.

Kinetics. To quantitatively evaluate the contribution of each route and better insight into the fate of MPB in aquatic environment, the reaction kinetics were studied at 273–$313\,K$ [38]. The second-order rate constants for each route and total reaction (k_{total}, the sum of rate constants of each route) were calculated (Table S2). At $298\,K$ (room temperature), the calculated k_{total} was $5.01 \times 10^9\,M^{-1}\,s^{-1}$, which agreed well with the available experimental value $6.8 \times 10^9\,M^{-1}\,s^{-1}$ [19]. This indicates that our calculation values are reliable and particularly very important for those routes without experimental data. As the temperature increased from 273 to $313\,K$, the k_{total} increased from 2.61×10^9 to $7.31 \times 10^9\,M^{-1}\,s^{-1}$. These data are close to the estimated diffusion limit ($4 \times 10^9\,M^{-1}\,s^{-1}$) [39], indicating that MPB could be rapidly degraded by $^{\bullet}OH$ by a diffusion-controlled process within the entire temperature range investigated. In addition, the rate constant of each route also increased with increasing temperature, e.g., the rate constant of $R_{add}1$ route increased from 1.97×10^9 to $2.51 \times 10^9\,M^{-1}\,s^{-1}$ as temperature increased from 273 to $313\,K$, indicating that increasing temperature can promote $^{\bullet}OH$-initiated degradation of MPB during AOPs. However, this slight increase in the rate constant with temperature indicates that the reaction was in fact dependent on diffusion-controlled processes and independent of chemical-reaction-controlled processes.

The Arrhenius formulas were established from the rate constants data at 273–$313\,K$ (Table S3). The pre-exponential factor, activation energy, and the second-order rate constants in specific experimental temperatures can be obtained from these formulas. It was found that within the investigated temperature range, the activation energy was only $4.39\,kcal\,mol^{-1}$, further implying that MPB can be readily degraded by $^{\bullet}OH$ in AOPs.

The $t_{1/2}$ is a simple index to assess the degradation feasibility of organics and often used to predict the organics fate in water environment and degradation systems. Thus, the $t_{1/2}$ was calculated to estimate the degradation feasibility of $^{\bullet}OH$-initiated MPB degradation at 273–$313\,K$ (Table S4). At a certain $^{\bullet}OH$ concentration, [$^{\bullet}OH$], the $t_{1/2}$ decreased with increasing temperature. For most AOPs used in wastewater treatment, [$^{\bullet}OH$] of 10^{-11}–$10^{-9}\,mol\,L^{-1}$ can be typically found [40]. At the highest [$^{\bullet}OH$] of $10^{-9}\,mol\,L^{-1}$, the $t_{1/2}$ decreased from 0.25 to $0.08\,s$ as temperature increased from 273 to $313\,K$. At a fixed temperature, the $t_{1/2}$ also decreased with increasing [$^{\bullet}OH$], e.g., at $298\,K$, when [$^{\bullet}OH$] decreased from 10^{-9} to $10^{-11}\,mol\,L^{-1}$, the $t_{1/2}$ increased from 0.12 to $12.38\,s$. From these results, it can be concluded that the increase in both temperature and [$^{\bullet}OH$] will benefit the MPB degradation during AOPs, and $t_{1/2}$ was more dependent on [$^{\bullet}OH$] than temperature. Anyway, these very short half-lives indicated that MPB can be easily eliminated from wastewater during AOPs.

To better understand the effect of temperature on the degradation intermediates and contribution of each route on entire initial
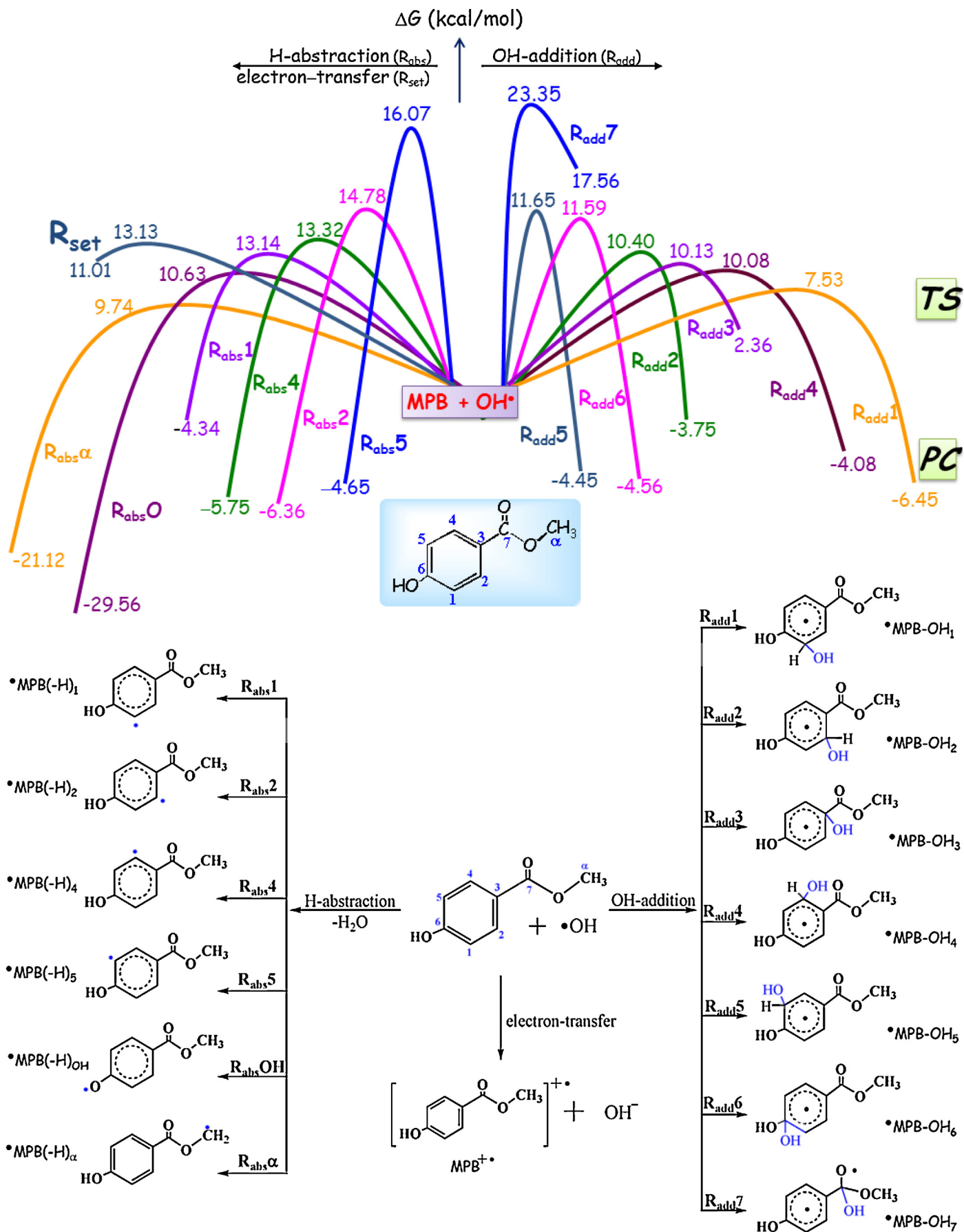
Fig. 2. Schematic diagram of free energy for the reaction of MPB with •OH at the B3LYP/6-311++G(d,p)//B3LYP/6-31G(d,p) level, and all possible routes for the reactions of MPB with •OH.
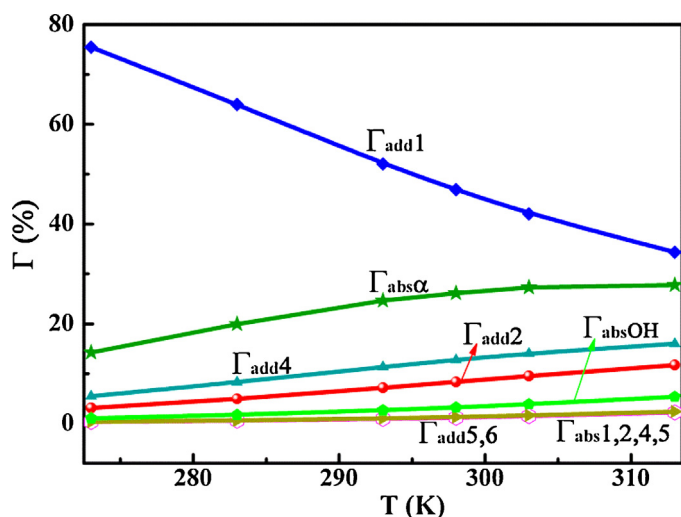
Fig. 3. Calculated branching ratio (Γ) of each route in the reaction of MPB with •OH at 273–313 K.

reaction, the temperature dependence of branching ratio (Γ) was calculated at 273–313 K (Fig. 3). The Γ of each route was determined according the following equation:

$$\Gamma_i = \frac{k_i}{k_{total}}$$

where k_i is the reaction rate constant of the ith route. Except for the $R_{add}1$ route, the Γ of other routes increased with increasing temperature. For the OH-addition routes, the $R_{add}1$ route was the predominant route, particularly the Γ up to 75.5% at 273 K. With increasing temperature, although $\Gamma_{add}1$ decreased to 34.3% at 313 K, it was still higher than those of other OH-addition routes by at least ~18.0%. As for H-abstraction routes, it was clearly found that $\Gamma_{abs}1,2,4,5$ values were not more than 0.01% in the entire temperature range, indicating that these four benzene-H-abstraction routes ($R_{abs}1,2,4,5$) are completely negligible. At 273 K, the $\Gamma_{abs}\alpha$ and $\Gamma_{abs}OH$ were 14.3% and 1.0%, respectively, while they increased to 27.8% and 5.1% when temperature reached to 313 K. These results indicate that $R_{abs}\alpha$ was the main H-abstraction route in the entire temperature range investigated.

In summary, AOPs are very effective and promising technologies to eliminate MPB from water environment. The degradation efficiency closely depend on [•OH] and temperature, and particularly, increasing [•OH] will benefit MPB degradation. It can help people to optimize AOPs system with minimizing the operating cost [41]. Two major transient intermediates, •MPB-OH$_1$ and •MPB(-H)α, can be produced in the initial step of the MPB reaction with •OH, which agrees well with the mechanism discussed above. Therefore, •MPB-OH$_1$ and •MPB(-H)α were tracked as two examples to investigate the following degradation reaction in AOPs.

3.3. Subsequent reactions of OH-addition and H-abstraction intermediates

The subsequent routes for the radical intermediates, •MPB-OH$_1$ and •MPB(-H)α, of OH-addition and H-abstraction routes are shown in Fig. 4a–c. If the supply of •OH is insufficient in certain AOPs (Fig. 4a), the intramolecular reactions could be observed for both OH-addition and H-abstraction intermediates. For OH-addition intermediate (•MPB-OH$_1$), the H-transfer route was more difficult to occur than the direct dehydrogenation route, because of large $\Delta G^{\neq}$ difference of 16.62 kcal mol^{-1}. For H-abstraction intermediate (•MPB(-H)α), the de-formaldehyde route could occur through energy barrier of 26.92 kcal mol^{-1}. However, •OH could

be continuously generated in AOPs. Therefore, with enough •OH (Fig. 4b), •OH further attack on the benzene ring of •MPB-OH$_1$ was more favored than the single-electron transfer, thereby forming di-hydroxylated MPB (MPB-2OH). This is because the former route was a barrierless radical–radical reaction with an exothermic energy of −47.02 kcal mol^{-1}, while the latter needed to overcome a high $\Delta G^{\neq}$ of 19.80 kcal mol^{-1}. Furthermore, if enough •OH was still continuously produced, MPB-2OH could be attacked by •OH because of a very low $\Delta G^{\neq}$ of 4.43 kcal mol^{-1}, followed by benzene ring opening to MPB final mineralization. Otherwise, mono-hydroxylated MPB (MPB-OH) should be rapidly produced because the high released energy, −47.02 kcal mol^{-1}, could completely overcome $\Delta G^{\neq}$ of 45.44 kcal mol^{-1} to achieve dehydration reaction. For •MPB(-H)α, •OH attack on the methylene group of •MPB(-H)α was a barrierless reaction with exothermic energy up to −78.65 kcal mol^{-1}, to produce hydroxymethyl-MPB (MPB-OHα). This exothermic energy was larger by at least 56 kcal mol^{-1} than that of single-electron transfer by •OH. These indicate that MPB-OHα was the dominant degradation product, which could be further decomposed to para-hydroxybenzoic acid (p-HBA).

On the other hand, most AOPs, such as photocatalysis [42–44] and Fenton reactions [45], are generally carried out in aerated aquatic environments, indicating that O$_2$ might participate in the subsequent reaction as a mild oxidant. Therefore, the presence of O$_2$ was also considered in this study to better understand the subsequent fate of MPB in AOPs (Fig. 4c). For OH-addition intermediate (•MPB-OH$_1$), O$_2$ addition to the benzene ring of •MPB-OH$_1$ was an endothermic process with a ΔG of 5.44 kcal mol^{-1}, whereas H-abstraction reaction by O$_2$ was a strongly exothermic process with a ΔG of −34.80 kcal mol^{-1}. The latter route was easier to occur than the former in the presence of O$_2$, and the degradation products were HOO• and MPB-OH, in line with the experimental results [17,19]. This theoretical finding can further explain the experimental results as to why the O atom of O$_2$ cannot be incorporated into the degradation product through direct coupling between molecular O$_2$ and substrate-based radicals during AOPs [42]. As for H-abstraction intermediate (•MPB(-H)α) (Fig. 4c), O$_2$ could attack the methene group of •MPB(-H)α to form peroxyl radical (R–OO•); this was a barrierless process with an exothermic energy of −20.86 kcal mol^{-1}. Further, R–OO• could easily combine with each other via oxygen-to-oxygen coupling reaction to form a tetroxide intermediates (IM-O$_4$). This route was also a barrierless process and more likely to occur than direct decomposition of R–OO• with a $\Delta G^{\neq}$ of 59.17 kcal mol^{-1}. Furthermore, IM-O$_4$ could readily undergo a simultaneous O–O bond fission and H-transfer process to generate para-hydroxybenzoic formic anhydride (BFA). This route was a strongly exothermic process with a release energy of −115.04 kcal mol^{-1} to produce p-HBA easily. With prolonging degradation time, this intermediate could be further decomposed into low-molecular-weight products [45,46].

In short, for both intermediates (•MPB-OH$_1$ and •MPB(-H)α) from OH-addition and H-abstraction routes, the intramolecular reactions probably did not occur in AOPs because of the presence of enough reactive species like •OH and O$_2$. Although the subsequent reactions with •OH were more easy to occur than with O$_2$, the further degradation products with O$_2$ cannot be neglected because [•OH] was lower by at least 5 orders of magnitude than the concentration of O$_2$ (2.6×10^{-4}–1.3×10^{-3} mol L^{-1}) in AOPs [47]. Therefore, the transformation of initial intermediates (•MPB-OH$_1$ and •MPB(-H)α) with •OH and O$_2$ were calculated, respectively (see SI). Results showed that the transformations with O$_2$ were much larger than that with •OH by at least 524 times for •MPB-OH$_1$, and 6 orders of magnitude for •MPB(-H)α. Therefore, the presence of O$_2$ (i.e., in aerated aquatic environments) could significantly enhance MPB degradation. In the subsequent reaction with O$_2$, MPB-OH would be produced first followed by MPB-2OH.
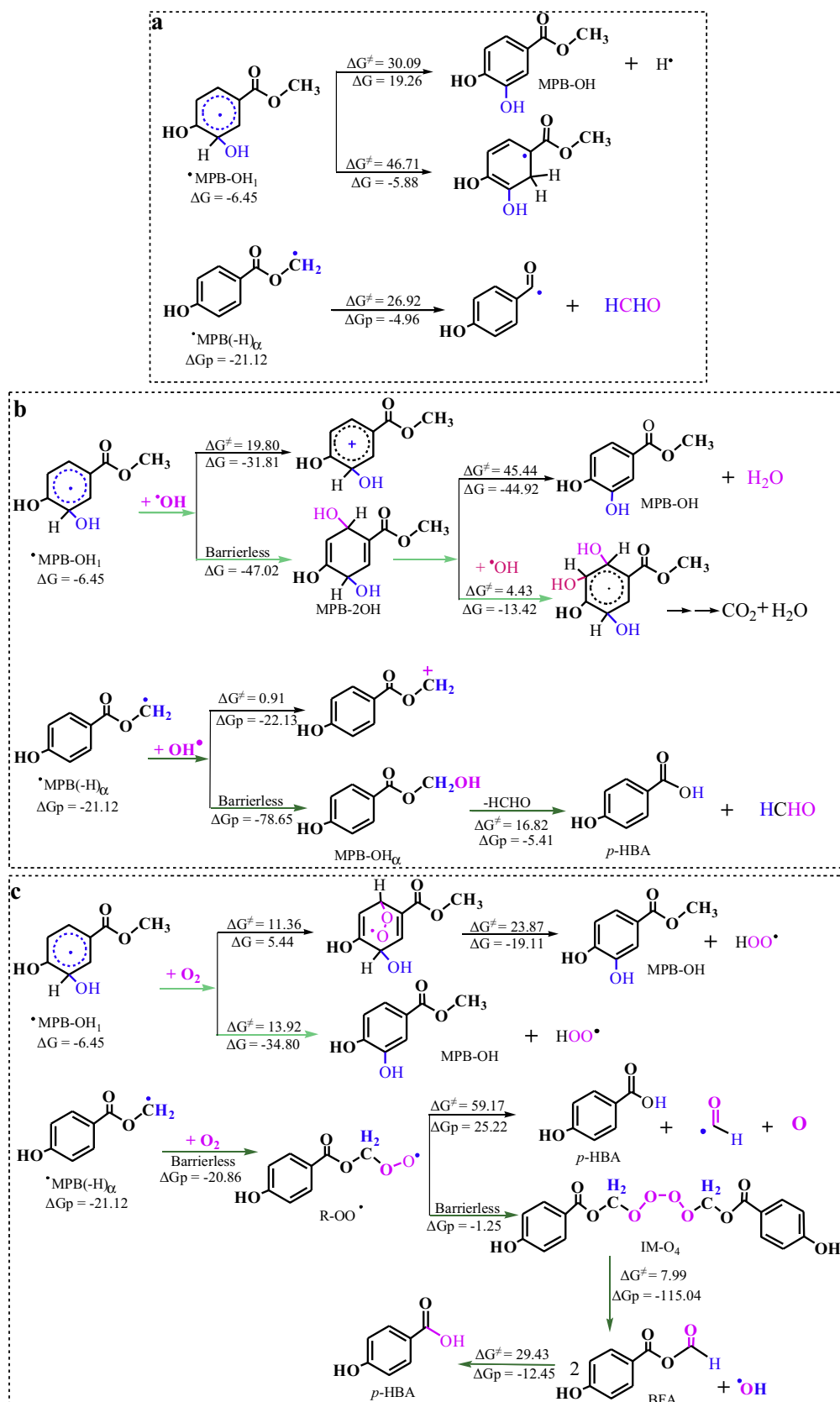
Fig. 4. Schematic diagram of the subsequent routes of •MPB-OH$_1$ and •MPB(-H)α. (a) With insufficient •OH; (b) with enough •OH; (c) with enough O$_2$.
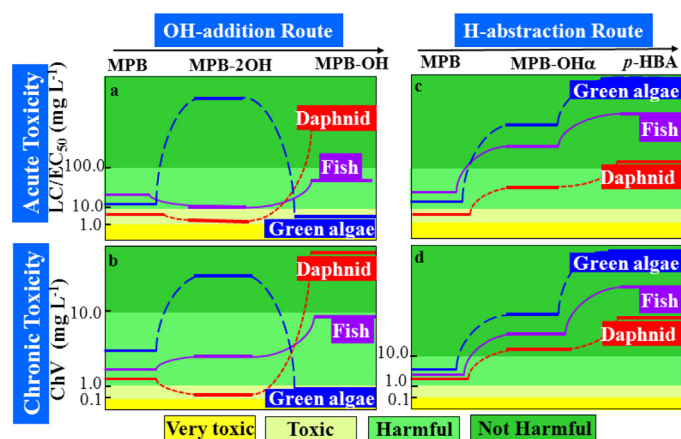
Fig. 5. Acute and chronic toxicity evolution of the OH-addition and H-abstraction routes toward three tested aquatic organisms in the presence of •OH.

However, opposite result was observed in the subsequent reaction with •OH. This can well explain experimental results as to why mono-hydroxylated paraben was first observed and then converted into highly hydroxylated products in the aerated aquatic environments [37].

3.4. Toxicity assessment

In the presence of •OH. The schematic representation of the acute and chronic toxicity evolutions in the presence of enough •OH are shown in Fig. 5a–d and Table S1. For OH-addition route (Fig. 5a), the acute toxicity to green algae decreased firstly, and then increased; however, the opposite trend was observed for fish and daphnia. As shown in Fig. 5b, the trends of chronic toxicity to green algae and daphnia are similar to those of the corresponding acute toxicity, whereas for fish, the chronic toxicity decreased during MPB degradation. As shown in Table S1, according to the abovementioned toxicity criteria, MPB-2OH was non-harmful for green algae because both EC_{50} and ChV are above $100.0 \, mg \, L^{-1}$. However, the LC_{50} and ChV were 1.17 and $0.23 \, mg \, L^{-1}$ for daphnia, and 10.91 and $2.69 \, mg \, L^{-1}$ for fish, respectively, indicating that MPB-2OH was toxic for daphnia and harmful for fish. MPB-OH, the subsequent product from MPB-2OH, was toxic to both green algae and fish; however, non-harmful for daphnia, e.g., the LC_{50} and ChV were 8.51 and $0.96 \, mg \, L^{-1}$ for green algae, making it toxic (Fig. 5a and b). However, both acute and chronic toxicities for H-abstraction route decreased during AOPs (Fig. 5c and d). However, harmful products could be still generated, e.g., the LC_{50} of MPB-OHα was calculated to be $59.73 \, mg \, L^{-1}$ and termed harmful for daphnia (Fig. 5c).

In the presence of O_2. The acute and chronic toxicity evolutions of byproducts during MPB degradation process in the presence of O_2 are shown in Fig. S3a–d and Table S1. MPB-OH was obtained as the first product and then transformed to MPB-2OH for OH-addition route. This order is opposite to that in the presence of •OH. Therefore, the trends of acute and chronic toxicities for OH-addition route would be opposite in the presence of •OH, e.g., acute and chronic toxicities to green algae increased initially and then decreased, whereas those for daphnia and fish decreased initially and then increased (Fig. S3a). Overall, the intermediates could still adversely affect aquatic organisms. For H-abstraction route (Fig. S3c), acute toxicities decreased for both green algae and fish, whereas a complex trend of initial decrease, then increase, and then again a slight decrease was observed for daphnia regardless of acute (Fig. S3c) and chronic toxicities (Fig. 3d). The same trend of chronic toxicity for fish and daphnia was observed. However, to green algae, chronic toxicity increased initially, and then decreased. The EC_{50} and ChV of

$IM-O_4$ were calculated to be 23.94 and $2.58 \, mg \, L^{-1}$ for green algae, and the LC_{50} of BFA was calculated to be $61.61 \, mg \, L^{-1}$ for daphnia (Table S1), indicating that both $IM-O_4$ and BFA are harmful.

In summary, hazardous products are produced during MPB degradation using AOPs, although the intermediates can be detoxified finally with sufficient treated time. Particularly, OH-addition products may have higher toxicity to different aqueous organisms than MPB, such as toxic MPB-OH for green algae and MPB-2OH for daphnia. OH-addition products are more harmful than H-abstraction products for all tested aquatic organisms. Although the presence of O_2 could enhance MPB degradation during AOPs, more harmful products were produced in the aerated aquatic environment.

3.5. Fate prediction of MPB in natural waters

In fact, various reactive species, like •OH, are also persistent in natural waters with low concentration [48]. Therefore, •OH may play an important role in parabens degradation in natural waters, and •OH-initiated photochemical degradation of MPB may occur [49]. Generally, [•OH] in natural waters is 10^{-15}–$10^{-18} \, mol \, L^{-1}$ [50] and much lower than that in AOPs by 5–9 orders of magnitude. Thus, the fate of MPB in natural waters might be different from AOPs; the $t_{1/2}$ of MPB degradation was measured by varying the [•OH] and water temperature (Table S4 and Fig. S4). At 298 K, the $t_{1/2}$ increased from 1.43 d to 3.98 y with decreasing [•OH] from 10^{-15} to $10^{-18} \, mol \, L^{-1}$. At fixed [•OH], $t_{1/2}$ decreased with increasing temperature, e.g., at the highest [•OH] of $10^{-15} \, mol \, L^{-1}$, $t_{1/2}$ decreased from 2.93 to 0.95 d with increasing temperature from 273 to 313 K. These findings indicate that $t_{1/2}$ of the •OH-initiated MPB transformation not only mainly depends on [•OH], but also slightly depends on the water temperature. According to the screening criteria used by the Stockholm Convention [51], organics with a $t_{1/2}$ of more than 60 d in aquatic environment are classed as persistent organic pollutants (POPs). Therefore, in this study, when $t_{1/2}$ was selected as ∼60 d for •OH-initiated MPB transformation (Fig. S4), [•OH] was deduced to be $2.39 \times 10^{-17} \, mol \, L^{-1}$ at 298 K. This indicate that MPB could be considered as a potential POP when [•OH] is below this value in aquatic environment.

To further provide a quantitative assessment of the potential hazards of MPB and its products to aquatic organisms, the threshold environmental concentrations (TEC) in natural waters were obtained by the hazard quotient (HQ) method [52] (see SI). Daphnia, as the sensitive species to MPB and its intermediates, and fish, as food source for human beings, were chosen as models to assess potential hazards of MPB and its intermediates. According to the common criteria for risk level [31], the TEC of MPB and MPB-2OH were conservatively deduced to be 79.9 and $11.7 \, ng \, L^{-1}$ for daphnia, and 204.3 and $109.1 \, ng \, L^{-1}$ for fish (Table S5), respectively. This indicates that both compounds may have potential ecological risk to aquatic organisms, particularly when their concentrations are above any of these relevant values in natural waters. Especially, when the concentration of MPB and MPB-2OH were above 204.3 and $109.1 \, ng \, L^{-1}$ in aquaculture water, the potential hazard to fish should be considered.

As mentioned, MPB is ubiquitously detected in various aquatic environments, e.g., MPB concentration was detected up to $1062 \, ng \, L^{-1}$ in urban streams of Guangzhou, South China [9]. From the combined results of the kinetics and subsequent reactions, the concentration of MPB-2OH product was conservatively estimated to be $499 \, ng \, L^{-1}$ (detail discussion in SI). In this case, the MPB concentration was 13 and 5 times higher than the calculated TEC for daphnia ($79.9 \, ng \, L^{-1}$) and fish ($204.3 \, ng \, L^{-1}$), respectively. Further, the MPB-2OH concentration was larger by 43 and 5 times than the calculated TEC of $11.7 \, ng \, L^{-1}$ for daphnia and $109.1 \, ng \, L^{-1}$ for fish, respectively. These suggest that in the urban streams of Guangzhou,

China, MPB might exhibit a risk to aquatic organisms, and its degradation products may be more harmful, i.e., the toxicity on aquatic ecosystems may be significantly underestimated if only the effect of MPB is considered. Thus, the risks of the original PPCPs and their byproducts in natural waters should not be overlooked in the future experimental studies.

4. Conclusions

A computational approach was developed to study the degradation process of MPB in aquatic AOPs and to evaluate the toxicity of intermediates to aquatic organisms. The major findings were:

(1) MPB can be easily degraded by $^\bullet$OH in AOPs, and the activation energy of this reaction was only 4.39 kcal mol^{-1}. At 298 K, when [$^\bullet$OH] was up to 10^9 mol L^{-1}, the half-life of MPB degradation was only 0.12 s in AOPs.
(2) The increase temperature and [$^\bullet$OH] will benefit MPB degradation during AOPs without affecting the optimal experimental conditions, and the half-life was more dependent on the [$^\bullet$OH] than temperature.
(3) MPB can be degraded by $^\bullet$OH via OH-addition and H-abstraction routes in AOPs. In particular, the contribution of OH-addition routes was more important than H-abstraction routes, and thus, more OH-addition products would be formed relative to H-abstraction products. Remarkably, OH-addition products are more harmful than H-abstraction products for all tested aquatic organisms.
(4) Although the presence of O_2 in AOPs could enhance MPB degradation, more harmful byproducts were produced in the aerated aquatic environment.
(5) In natural waters, the toxicity on aquatic ecosystems may be significantly underestimated if only the effect of MPB is considered. Thus, the risks of the original PPCPs and their intermediates in natural waters should not be overlooked in the future experimental studies.

Acknowledgments

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jhazmat.2014.05.081.

References

[1] T. Brodin, J. Fick, M. Jonsson, J. Klaminder, Dilute concentrations of a psychiatric drug alter behavior of fish from natural populations, Science 339 (2013) 814–815.
[2] J.D. Meeker, D.E. Cantonwine, L.O. Rivera-González, K.K. Ferguson, B. Mukherjee, A.M. Calafat, X. Ye, L.V. Anzalota Del Toro, N. Crespo-Hernández, B. Jiménez-Vélez, A.N. Alshawabkeh, J.F. Cordero, Distribution, variability, and predictors of urinary concentrations of phenols and parabens among pregnant women in Puerto Rico, Environ. Sci. Technol. 47 (2013) 3439–3447.
[3] A.M. Calafat, X.Y. Ye, L.Y. Wong, A.M. Bishop, L.L. Needham, Urinary concentrations of four parabens in the US population: NHANES 2005-2006, Environ. Health Perspect. 118 (2010) 679–685.
[4] P. Canosa, I. Rodríguez, E. Rubí, R. Cela, Determination of parabens and triclosan in indoor dust using matrix solid-phase dispersion and gas chromatography with tandem mass spectrometry, Anal. Chem. 79 (2007) 1675–1681.
[5] B.R. Ramaswamy, J.W. Kim, T. Isobe, K.H. Chang, A. Amano, T.W. Miller, F.P. Siringan, S. Tanabe, Determination of preservative and antimicrobial compounds in fish from Manila Bay, Philippines using ultra high performance liquid chromatography tandem mass spectrometry, and assessment of human dietary exposure, J. Hazard. Mater. 192 (2011) 1739–1745.
[6] I. Marquez-Sillero, E. Aguilera-Herrador, S. Cardenas, M. Valcarcel, Determination of parabens in cosmetic products using multi-walled carbon nanotubes as solid phase extraction sorbent and corona-charged aerosol detection system, J. Chromatogr. A 1217 (2010) 1–6.
[7] H. Yamamoto, I. Tamura, Y. Hirata, J. Kato, K. Kagota, S. Katsuki, A. Yamamoto, Y. Kagami, N. Tatarazako, Aquatic toxicity and ecological risk assessment of seven parabens: individual and additive approach, Sci. Total Environ. 410 (2011) 102–111.
[8] B. Kasprzyk-Hordern, R.M. Dinsdale, A.J. Guwy, The occurrence of pharmaceuticals, personal care products, endocrine disruptors and illicit drugs in surface water in South Wales, UK, Water Res. 42 (2008) 3498–3518.
[9] X.Z. Peng, Y.J. Yu, C.M. Tang, J.H. Tan, Q.X. Huang, Z.D. Wang, Occurrence of steroid estrogens, endocrine-disrupting phenols, and acid pharmaceutical residues in urban riverine water of the Pearl River Delta, South China, Sci. Total Environ. 397 (2008) 158–166.
[10] T. Benijts, W. Lambert, A. De Leenheer, Analysis of multiple endocrine disruptors in environmental waters via wide-spectrum solid-phase extraction and dual-polarity ionization LC-ion trap-MS/MS, Anal. Chem. 76 (2004) 704–711.
[11] M. Terasaki, M. Makino, N. Tatarazako, Acute toxicity of parabens and their chlorinated by-products with Daphnia magna and Vibrio fischeri bioassays, J. Appl. Toxicol. 29 (2009) 242–247.
[12] L. Barr, G. Metaxas, C.A.J. Harbach, L.A. Savoy, P.D. Darbre, Measurement of paraben concentrations in human breast tissue at serial locations across the breast from axilla to sternum, J. Appl. Toxicol. 32 (2012) 219–232.
[13] P.D. Darbre, P.W. Harvey, Paraben esters: review of recent studies of endocrine toxicity, absorption, esterase and human exposure, and discussion of potential human health risks, J. Appl. Toxicol. 28 (2008) 561–578.
[14] N. Kus, S.H. Bayarı, R. Fausto, Methylparaben isolated in solid argon: structural characterization and UV-induced conversion into methylparaben radical and isomeric ketenes, J. Phys. Chem. B 117 (2013) 13543–13555.
[15] B. Albero, R.A. Perez, C. Sanchez-Brunete, J.L. Tadeo, Occurrence and analysis of parabens in municipal sewage sludge from wastewater treatment plants in Madrid (Spain), J. Hazard. Mater. 239 (2012) 48–55.
[16] L.H. Leal, N. Vieno, H. Temmink, G. Zeeman, C.J.N. Buisman, Occurrence of xenobiotics in gray water and removal in three biological treatment systems, Environ. Sci. Technol. 44 (2010) 6835–6842.
[17] Y.X. Lin, C. Ferronato, N.S. Deng, F. Wu, J.M. Chovelon, Photocatalytic degradation of methylparaben by TiO$_2$: multivariable experimental design and mechanism, Appl. Catal. B: Environ. 88 (2009) 32–41.
[18] S.M. Lam, J.C. Sin, A.Z. Abdullah, A.R. Mohamed, Green hydrothermal synthesis of ZnO nanotubes for photocatalytic degradation of methylparaben, Mater. Lett. 93 (2013) 423–426.
[19] K.S. Tay, N.A. Rahman, M.R. Bin Abas, Ozonation of parabens in aqueous solution: Kinetics and mechanism of degradation, Chemosphere 81 (2010) 1446–1453.
[20] J. Sánchez-Martín, J. Beltrán-Heredia, J.R. Domínguez, Advanced photochemical degradation of emerging pollutants: methylparaben, Water Air Soil Pollut. 224 (2013) 1483–1494.
[21] K.S. Tay, N.A. Rahman, M.R.B. Abas, Kinetic studies of the degradation of parabens in aqueous solution by ozone oxidation, Environ. Chem. Lett. 8 (2010) 331–337.
[22] F.S. Collins, G.M. Gray, J.R. Bucher, Toxicology – transforming environmental health protection, Science 319 (2008) 906–907.
[23] Y.P. Gao, Y.M. Ji, G.Y. Li, T.C. An, Mechanism, kinetics and toxicity assessment of OH-initiated transformation of triclosan in aquatic environments, Water Res. 49 (2014) 360–370.
[24] A. Perez-Gonzalez, A. Galano, OH radical scavenging activity of edaravone: mechanism and kinetics, J. Phys. Chem. B 115 (2011) 1306–1314.
[25] A. Galano, M. Francisco-Marquez, Reactions of OOH radical with beta-carotene, lycopene, and torulene: hydrogen atom transfer and adduct formation mechanisms, J. Phys. Chem. B 113 (2009) 11338–11345.
[26] M.J. Frisch, G.W. Truck, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, J.R.E. Stratmann, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, A.G. Baboul, B.B. Stefnov, G. Liu, A. Liaschenko, P. Piskorz, L. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, J.A. Pople, GAUSSIAN 03, Guassian, Inc., Pittsburgh, PA, 2003.
[27] V. Barone, M. Cossi, Quantum calculation of molecular energies and energy gradients in solution by a conductor solvent model, J. Phys. Chem. A 102 (1998) 1995–2001.
[28] Y. Okuno, Theoretical investigation of the mechanism of the Baeyer–Villiger reaction in nonpolar solvents, Chem. Eur. J. 3 (1997) 212–218.
[29] F.C. Collins, G.E. Kimball, Diffusion-controlled reaction rates, J. Colloid Sci. 4 (1949) 425–437.
[30] ECOSAR, http://www.epa.gov/oppt/newchems/tools/21ecosar.htm, 2014.

[31] M.D. Hernando, M. Mezcua, A.R. Fernandez-Alba, D. Barcelo, Environmental risk assessment of pharmaceutical residues in wastewater effluents, surface waters and sediments, Talanta 69 (2006) 334–342.

[32] P. Guadarrama, S. Fomine, R. Salcedo, A. Martínez, Construction of simplified models to simulate estrogenic disruptions by esters of 4-hydroxy benzoic acid (parabens), Biophys. Chem. 137 (2008) 1–6.

[33] D. Casoni, C. Sarbu, The lipophilicity of parabens estimated on reverse phases chemically bonded and oil-impregnated plates and calculated using different computation methods, J. Sep. Sci. 32 (2009) 2377–2384.

[34] P. Mayer, F. Reichenberg, Can highly hydrophobic organic substances cause aquatic baseline toxicity and can they contribute to mixture toxicity? Environ. Toxicol. Chem. 25 (2006) 2639–2644.

[35] H. Konemann, Quantitative structure–activity-relationships in fish toxicity studies. 1. Relationship for 50 industrial pollutants, Toxicology 19 (1981) 209–221.

[36] L.L. Dobbins, S. Usenko, R.A. Brain, B.W. Brooks, Probabilistic ecological hazard assessment of parabens using daphnia magna and pimephales promelas, Environ. Toxicol. Chem. 28 (2009) 2744–2753.

[37] H.S. Fang, Y.P. Gao, G.Y. Li, J.B. An, P.K. Wong, H.Y. Fu, S.D. Yao, X.P. Nie, T.C. An, Advanced oxidation kinetics and mechanism of preservative propylparaben degradation in aqueous suspension of TiO₂ and risk assessment of its degradation products, Environ. Sci. Technol. 47 (2013) 2704–2710.

[38] K.L. Swancutt, M.K. Dail, S.P. Mezyk, K.P. Ishida, Absolute kinetics and reaction efficiencies of hydroxyl-radical-induced degradation of methyl isothiocyanate (MITC) in different quality waters, Chemosphere 81 (2010) 339–344.

[39] C.J. Cramer, D.G. Truhlar, Implicit solvation models: equilibria, structure, spectra, and dynamics, Chem. Rev. 99 (1999) 2161–2200.

[40] A.S. Gong, C.A. Lanzl, D.M. Cwiertny, S.L. Walker, Lack of influence of extracellular polymeric substances (EPS) level on hydroxyl radical mediated disinfection of Escherichia coli, Environ. Sci. Technol. 46 (2011) 241–249.

[41] G.L. Puma, P.L. Yue, Comparison of the effectiveness of photon-based oxidation processes in a pilot falling film photoreactor, Environ. Sci. Technol. 33 (1999) 3210–3216.

[42] Y. Li, B. Wen, C.L. Yu, C.C. Chen, H.W. Ji, W.H. Ma, J.C. Zhao, Pathway of oxygen incorporation from O₂ in TiO₂ photocatalytic hydroxylation of aromatics: oxygen isotope labeling studies, Chem. Eur. J. 18 (2012) 2030–2039.

[43] T.C. An, H. Yang, W.H. Song, G.Y. Li, H.Y. Luo, W.J. Cooper, Mechanistic considerations for the advanced oxidation treatment of fluoroquinolone pharmaceutical compounds using TiO₂ heterogeneous catalysis, J. Phys. Chem. A 114 (2010) 2569–2575.

[44] T.C. An, G.Y. Li, X.H. Zhu, J.M. Fu, G.Y. Sheng, Z. Zhu, Photoelectrocatalytic degradation of oxalic acid in aqueous phase with a novel three-dimensional electrode-hollow quartz tube photoelectrocatalytic reactor, Appl. Catal. A: Gen. 279 (2005) 247–256.

[45] C.K. Duesteberg, T.D. Waite, Kinetic modeling of the oxidation of p-hydroxybenzoic acid by Fenton's reagent: implications of the role of quinones in the redox cycling of iron, Environ. Sci. Technol. 41 (2007) 4103–4110.

[46] F.J. Rivas, F.J. Beltran, J. Frades, P. Buxeda, Oxidation of p-hydroxybenzoic acid by Fenton's reagent, Water Res. 35 (2001) 387–396.

[47] S. Halladja, A. ter Halle, J.P. Aguer, A. Boulkamh, C. Richard, Inhibition of humic substances mediated photooxygenation of furfuryl alcohol by 2,4,6-trimethylphenol. Evidence for reactivity of the phenol with humic triplet excited states, Environ. Sci. Technol. 41 (2007) 6066–6073.

[48] M.M. Dong, F.L. Rosario-Ortiz, Photochemical formation of hydroxyl radical from effluent organic matter, Environ. Sci. Technol. 46 (2012) 3788–3794.

[49] D. Bledzka, D. Gryglik, J.S. Miller, Photodegradation of butylparaben in aqueous solutions by 254 nm irradiation, J. Photochem. Photobiol. A 203 (2009) 131–136.

[50] J.M. Burns, W.J. Cooper, J.L. Ferry, D.W. King, B.P. DiMento, K. McNeill, C.J. Miller, W.L. Miller, B.M. Peake, S.A. Rusak, A.L. Rose, T.D. Waite, Methods for reactive oxygen species (ROS) detection in aqueous environments, Aquat. Sci. 74 (2012) 683–734.

[51] J. Klasmeier, M. Matthies, M. Macleod, K. Fenner, M. Scheringer, M. Stroebe, A.C. Le Gall, T. McKone, D. Van De Meent, F. Wania, Application of multimedia models for screening assessment of long-range transport potential and overall persistence, Environ. Sci. Technol. 40 (2005) 53–60.

[52] Y. Liang, M.H. Wong, R.B.E. Shutes, D.M. Revitt, Ecological risk assessment of polychlorinated biphenyl contamination in the Mai Po marshes nature reserve, Hong Kong, Water Res. 33 (1999) 1337–1346.