Aqueous oxidation of bisphenol analogues by ozone: Relevance of substituents on reactivity

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ABSTRACT

In recent years, bisphenol A has been progressively replaced by other bisphenol analogues, leading to an increase of their occurrence in aquatic environments. However, limited data is available regarding their removal through oxidation treatments, such as ozonation. In this work, the reactivity of ozone with seven novel bisphenol A substitutes (bisphenol E, bisphenol B, bisphenol AF, bisphenol C, bisphenol AP, bisphenol Z and bisphenol C-Cl) was studied over a wide range of pH by competition kinetics. The second-order rate constants of ozone were determined for their protonated species (k_1, k_2 and k_3), together with their pH-dependent reactivity profile. High and similar reactivity of ozone with all bisphenols was distinguished at basic pH ($k_3 = 8.83 \times 10^8$ - 1.39×10^9 M^{-1} s^{-1}). This reactivity decreased at neutral pH, although it remained comparable for all bisphenols ($k_{app} = 2 \times 10^6$ - 5×10^6 M^{-1} s^{-1}). In contrast, the even lower reactivity observed at acidic pH exhibited significant variations between them ($k_1 = 1.54 \times 10^2$ - 1.22×10^5 M^{-1} s^{-1}), due to the influence of the different functional groups, as their behaviour as electron-donating or electron-withdrawing moieties strongly govern their reactivity with ozone. Additionally, the oxidation products resulting from the reaction of ozone with bisphenols at neutral pH were also assessed. The generation of catechol derivatives was suggested as the primary degradation pathway for the majority of bisphenols. Other oxidation products were also commonly detected, such as *ortho*-quinone derivatives, ring opening products and simple phenolic fragments.

1. Introduction

Bisphenol A (BPA) is one of the most produced chemicals, extensively used to manufacture polycarbonate plastics and epoxy resins [1, 2], incorporated in many consumer products, such as feeding bottles, plastic food containers and cash register receipts [3]. Due to its endocrine-disrupting behaviour, especially as estrogenic compound [4] BPA was demonstrated to be responsible for several adverse effects for both human health and environment [5,6]. As a result, its production and use are being regulated in many countries [7]. To face restrictions, bisphenol A has been progressively replaced by other bisphenols with similar chemical structure, called bisphenol A analogues or substitutes, such as, bisphenol F (BPF), bisphenol S (BPS), bisphenol AF (BPAF), bisphenol B (BPB), bisphenol E (BPE), bisphenol C (BPC), bisphenol Z (BPZ), bisphenol C-Cl (BPC-Cl), and bisphenol AP (BPAP), among others [8]. Physicochemical properties such as, molecular weight and octanol/water partition coefficient (K_{OW}) of bisphenol analogues, as well as their CAS number and chemical structure are exhibited in Table 1.

Most of these bisphenols are also employed in the manufacturing process of epoxy resins and polycarbonate plastics [8,12], where the resulting commercial products are labelled as "BPA free" [13]. Currently, BPF and BPS, and more recently BPAF, are the most widely employed BPA substitutes [8,14]. BPF, BPS, BPE and BPB can be found in beverage containers, paper products and food packaging items [13, 15–17]. BPAF is used in fluoroelastomers, fluoropolymers, phenolic resins and in electronics and optical fibers [8,16]. BPAP is employed as flame retardant and in synthesizing plastic and rubber, among other industrial products [18]. BPC is also used as a flame retardant [19] and BPZ is employed to cure heat-resistant plastic materials [20], among other uses. Finally, BPC-Cl is used in polymers and plastics to provide fire-resistance and thermal stability [21]. Several studies already proved that some bisphenol A analogues exhibit similar endocrine-disrupting activity to that of BPA [13,22], or even greater, as happens in the case of BPAF [12]. As well as for BPA, most of these bisphenols have been detected in different surface waters and in effluents of wastewater treatment plants (WWTPs), predominantly at concentrations of a few ng L^{-1} [3,23,24]. The occurrence of the bisphenol A substitutes is expected to increase even more in the following years, evidencing the need to
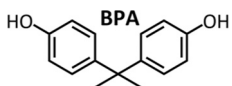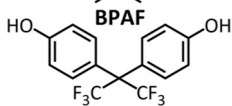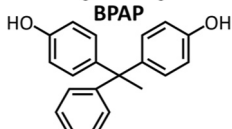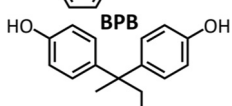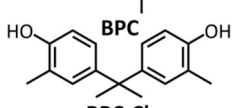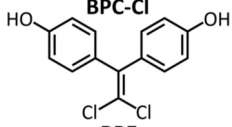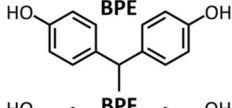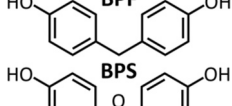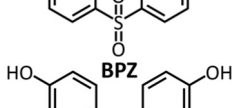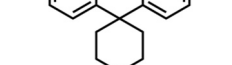
Table 1

Physicochemical properties, CAS number and chemical structure of the different bisphenol analogues, including bisphenol A.

compound	CAS number	MW (g mol^{-1})	K_{OW}	chemical structure
bisphenol A	80–05–7	228.29	3.32[a]	BPA
bisphenol AF	1478–61–1	336.23	4.77[b]	BPAF
bisphenol AP	1571–75–1	290.36	5.18[b]	BPAP
bisphenol B	77–40–7	242.31	4.49[b]	BPB
bisphenol C	79–97–0	256.34	4.74[b]	BPC
bisphenol C-Cl	14868–03–2	281.13	4.29[c]	BPC-Cl
bisphenol E	2081–08–5	214.26	3.74[b]	BPE
bisphenol F	620–92–8	200.23	3.46[b]	BPF
bisphenol S	80–09–1	250.27	2.32[b]	BPS
bisphenol Z	843–55–0	268.35	4.91[b]	BPZ

[a] [9],
[b] [10],
[c] [11]

study the performance of applied strategies for their abatement from drinking waters and WWTPs effluents.

Currently, ozonation is one of the most efficient and technologically mature process to that purpose [25]. However, even though ozone is able to oxidize a wide range of organic contaminants, it is also a selective oxidant whose reactivity strongly depends on the different functional groups in the target molecules. There is scarce information about the abatement of bisphenol analogues with ozone. Previous studies revealed high reactivity of ozone with BPA, BPF and BPS, under basic conditions, while lower reactivity was distinguished at acidic pH, especially for BPS [26,27]. Thus, the objective of this work was to evaluate the reactivity of ozone with seven novel bisphenols A substitutes (BPE, BPB, BPC, BPAF, BPC-Cl, BPAP and BPZ) over a wide range of pH. To do that, determination of the second-order rate constants of ozone with their protonated species was conducted through a competition kinetics approach, allowing the establishment of a reactivity model in relation to pH. Additionally, the main transformation products resulting from their reaction with ozone at neutral pH were also assessed using Liquid Chromatography coupled with High-Resolution Mass Spectrometry

(LC-HRMS). The chemical structures of the identified TPs were suggested based on experimental masses and MS^2 spectra. Through this data, a mechanism for the generation of the different detected TPs was proposed. The obtained results from both kinetic and transformation products studies were compared with the previous reported data from the reaction of BPA, BPF and BPS with ozone [26–28].

2. Materials and methods

2.1. Chemicals and reagents

Bisphenol A (BPA) (purity $\geq$ 99%), bisphenol AF (BPAF) (purity $\geq$ 99%), bisphenol AP (BPAP) (purity $\geq$ 99%), bisphenol B (BPB) (purity $\geq$ 98%), bisphenol C (BPC) (2,2-Bis(4-hydroxy-3-methylphenyl)propane, 4,4′-Isopropylidenedi-*o*-cresol) (purity $\geq$ 99%), bisphenol C-Cl (BPC-Cl) (Bis(4-hydroxyphenyl)− 2,2-dichloroethylene) (purity $\geq$ 98%), bisphenol E (BPE) (purity $\geq$ 98%), bisphenol Z (BPZ) (purity $\geq$ 99%), phenol (purity $\geq$ 99%) and *tert*-butanol (purity $\geq$ 99.7%) were analytical grade, provided by Merck. H$_2$SO$_4$ (95–98%), NaOH, KH$_2$PO$_4$, K$_2$HPO$_4$, CH$_3$COOH (purity $\geq$ 99.7%), CH$_3$COONa·3 H$_2$O, NaHCO$_3$, Na$_2$CO$_3$ and H$_3$PO$_4$ (85%), were pharma grade, supplied by Panreac, as well as acetonitrile (for UHPLC, super gradient grade). All aqueous solutions were prepared in ultrapure water.

2.2. Kinetic method: determination of second-order rate constants and reactivity model

Second-order rate constants for ozone reactions with the selected bisphenols were established by competition kinetics. As a result of the expected variation of ozone reactivity with the three protonated species of these bisphenols, these experiments were performed in a wide range of pH conditions. The integrated Eq. (1) considers the simultaneous reaction of ozone with both the bisphenol and competitor and the resulting slope is equal to the division of the apparent rate constant of the corresponding bisphenol (k$_{app(BP)}$) with the apparent rate constant of the selected competitor (k$_{app(C)}$). The apparent rate constant of the corresponding bisphenol includes the contribution of the three protonated species (k$_1$, k$_2$ and k$_3$) in the reaction with ozone, as specified in Eq. (2), while Eq. (3) is similarly employed for compounds with just two protonated species, such as phenol, one of the selected competitors.

$$-\ln\left(\frac{[BP]_{T,t}}{[BP]_{T,0}}\right) = \frac{k_{app(BP)}}{k_{app(C)}} \left(-\ln\left(\frac{[C]_{T,t}}{[C]_{T,0}}\right)\right) \tag{1}$$

$$k_{app(A)} = \frac{k_1 \quad [H^+]^2 + k_2 \quad [H^+] \quad K_{a1,A} + k_3 \quad K_{a1,A} \quad K_{a2,A}}{[H^+]^2 + [H^+] \quad K_{a1,A} + K_{a1,A} \quad K_{a2,A}} \tag{2}$$

$$k_{app(B)} = \frac{k_1 \quad [H^+] + k_2 \quad K_{a,B}}{[H^+] + K_{a,B}} \tag{3}$$

Further details, regarding the establishment of the second-order rate constants of ozone with the different protonated species of these bisphenols can be found in Text S1 of supplementary information. Once the values of k$_1$, k$_2$ and k$_3$ are established, k$_{app}$ can be calculated for all pH conditions using Eq. 2, allowing a model representation of the ozone reactivity with bisphenols in front of pH.

2.3. Kinetic experiments

Kinetic experiments were performed in a series of vials of 30 mL. Based on the experimental solubility, aqueous mother solutions of 50 mg L^{-1} were prepared for BPC, BPE, BPB and BPAF, 5 mg L^{-1} for BPC-Cl and 2.5 mg L^{-1} for BPZ and BPAP. Thus, the experimental concentration employed for BPC, BPE, BPB and BPAF was 50 μM, while it was decreased to 3 μM for BPZ, BPAP and BPC-Cl. These experiments were performed in triplicate in a wide range of pH (0−12) and/or

(2−12), depending on the compound, by the addition of different buffer solutions. The competitors used were phenol and BPA, both at the same concentration as the target bisphenol. The buffers and competitors employed for each bisphenol and pH condition are presented in Tables S1 and S2 of the Supplementary Information (SI), respectively. Additionally, the pK$_a$ values of the competitors, and the second-order rate constants of their protonated species with ozone, can be found in Table S3 and Table S4 of the SI, respectively. To prevent the presence and interference of hydroxyl radicals (·OH) in the kinetic experiments, *tert*-butanol (TBA) was used as a scavenger at a concentration of 50 mM. Ozone was generated through a 301.19 lab ozoniser (Sander, Germany) from pure oxygen ($\geq$ 99.999%) provided by Abelló Linde (Spain). A thermostatic bath (Huber, Germany) was employed to keep the temperature of the ozoniser at 5 °C. The flow rate of ozone in its gas phase was established at 1 L min^{-1}, with an ozone concentration of approximately 100 mg L^{-1} for BPC, BPE, BPB and BPAF, and 20 mg L^{-1} for BPZ, BPAP and BPC-Cl, quantified by the ozone analyser BMT 964 (BMT Messtechnik, Germany). Ozone was introduced into a 250 mL Erlenmeyer flask filled with Milli-Q water and placed in ice, by a stainless-steel porous diffuser. Ozone stock solutions about 45 mg L^{-1} were employed in experiments with bisphenols presenting higher solubility (BPC, BPE, BPB and BPAF), while for those bisphenols presenting lower solubility (BPZ, BPAP and BPC-Cl), the ozone stock solutions used were about 5 mg L^{-1}. The ozone concentration of the stock solutions was measured by a DR6000 UV-Vis spectrophotometer (Hach, USA) at 260 nm (ε O$_3$ = 3200 M^{-1} cm^{-1}) [29]. Then, different ozone aliquots were added into the corresponding vials and shaken for a few seconds. For BPC, BPE, BPB and BPAF, the initial concentrations of ozone in the multiple set of vials ranged from 0.5 to 3 mg L^{-1}, approximately, while for BPZ, BPAP and BPC-Cl, the ozone concentration varied from 0.020 to 0.20 mg L^{-1}, approximately. Afterwards, the reaction vials were left in the dark for approximately 16 h to ensure the completely consumption of ozone.

2.4. Transformation products study

The main transformation products formed from the reaction of ozone with selected bisphenols were identified by Liquid Chromatography-Mass Spectrometry (LC-MS). This study was performed at pH 7, employing 5 mM phosphate buffer (KH$_2$PO$_4$/K$_2$HPO$_4$). The concentrations of bisphenols were 50 μM for those with higher solubility (BPC, BPE, BPB and BPAF) and 5 μM for the rest, which presented lower solubility (BPZ, BPAP and BPC-Cl). Again, hydroxyl radical was scavenged with 50 mM of *tert*-butanol. The ozone production and addition methodology were identical to that of the kinetic experiments. In this case, the employed concentrations of ozone ranged from 1.9 to 9 mg L^{-1} for BPC, BPE, BPB and BPAF and from 0.2 to 1.2 mg L^{-1} for BPZ, BPAP and BPC-Cl. The reaction vials were left 15 h under dark conditions. Samples

presenting around 80% of degradation of the parent compound were used for the MS^2 analyses. The proposed chemical structures of the different TPs were assisted by the acquired data from MS and MS^2 analyses, displayed in the Section 2 of the SI, simultaneously with their peak intensities and retention times of the different TPs, as well as their experimental mass, formula and proposed chemical structures. Additionally, the evolution of the detected TPs over the reaction with ozone of some selected bisphenols (i.e., those presenting higher solubility) was followed by min-max normalization. This is exhibited in Fig. S1 of the SI.

2.5. Analytical methods

For the kinetic study, an Infinity 1260 HPLC provided by Agilent Technologies (USA), was used to quantify the abatement of the selected bisphenols and competitors. The employed HPLC column was a Mediterranea Sea18 column (250 mm x 4.6 mm and a particle size of 5 μm), supplied by Teknokroma (Spain). The chromatographic conditions for the various mixtures of compounds (bisphenols and their competitors) are detailed in Table S5 of the SI. The transformation products were identified using LC-HRMS, which involved a 1200RR HPLC (Agilent Technologies) and a QSTAR Elite hybrid Quadrupole-Time of Flight (Q-ToF) mass spectrometer (Sciex, Germany). The software Analyst QS 2.0 was used to process the obtained data. All TPs were identified in negative electrospray ionization mode (ESI (−)) and collected in a scan range of 70–600 *m/z*. A collision energy of − 30 eV was applied for MS^2 scans. For the chromatographic separation, the injection volume was set to 25 μL, while the column temperature was set to 30 °C. A gradient of Milli-Q water and acetonitrile was used with a flow rate of 1 mL min^{-1} for 30 min, as shown in Table S6 of the SI. To prevent the introduction of salts from the phosphate buffer into the mass spectrometer, the eluate from the first 2 min was discarded.

3. Results and discussion

3.1. Ozone kinetics with bisphenol analogues

3.1.1. Influence of pH on the reactivity of ozone with bisphenol analogues
The selected bisphenols present three different species according to their acid-base speciation (di-protonated, mono-protonated and deprotonated). The pK$_a$ values are shown in Table 2. Some of these pK$_a$ values were recalculated employing the experimental data and the theoretical pH reactivity profile, modelled in this work, as initially the obtained model did not fit with the experimental results. The protonated species of studied bisphenols present different electron density in their phenol rings. The di-protonated species is the one with the lowest electron density, while the deprotonated presents the highest one. Thus, a variation of the reactivity of ozone with these compounds over different pH values is expected since ozone is electrophilic and, therefore, more

Table 2

Values of pKa$_1$ and pKa$_2$ of the different bisphenol analogues and second-order rate constants of ozone with the different protonated species of the studied bisphenol analogues, and also with the protonated species of BPA, BPF and BPS.

Compound	pK$_{a,1}$	pK$_{a,2}$	k$_1$ (M^{-1} s^{-1})	k$_2$ (M^{-1} s^{-1})	k$_3$ (M^{-1} s^{-1})
bisphenol C	9.8[a]	10.4[a]	1.22 ($\pm$ 0.01) x 10^5	1.11$\times$10^9	1.39 ($\pm$ 0.01) x 10^9
bisphenol F	9.8[c]	10.5[c]	2.38$\times$10^4[d]	1.31$\times$10^9[d]	1.43$\times$10^9[d]
bisphenol E	9.8[c]	10.4[c]	1.90 ($\pm$ 0.01) x 10^4	1.34$\times$10^9	1.39 ($\pm$ 0.05) x 10^9
bisphenol B	9.8[c]	10.4[c]	2.00 ($\pm$ 0.15) x 10^4	1.23$\times$10^9	1.24 ($\pm$ 0.08) x 10^9
bisphenol A	9.6[b]	10.2[b]	1.68$\times$10^4[b]	1.06$\times$10^9[b]	1.11$\times$10^9[b]
bisphenol Z	9.6[a]	10.4[c]	1.98 ($\pm$ 0.09) x 10^4	8.80$\times$10^8	8.93 ($\pm$ 0.79) x 10^8
bisphenol AP	9.3[a]	10.3[c]	9.15 ($\pm$ 1.20) x 10^3	8.11$\times$10^8	8.83 ($\pm$ 0.54) x 10^8
bisphenol C-Cl	9.1[a]	9.7[a]	2.67 ($\pm$ 0.39) x 10^3	6.19$\times$10^8	1.15 ($\pm$ 0.06) x 10^9
bisphenol AF	8.9[a]	9.7[c]	1.54 ($\pm$ 0.18) x 10^2	3.87$\times$10^8	1.31 ($\pm$ 0.03) x 10^9
bisphenol S	7.6[d]	9.7[d]	5.01[d]	2.82$\times$10^7[d]	1.09$\times$10^9[d]

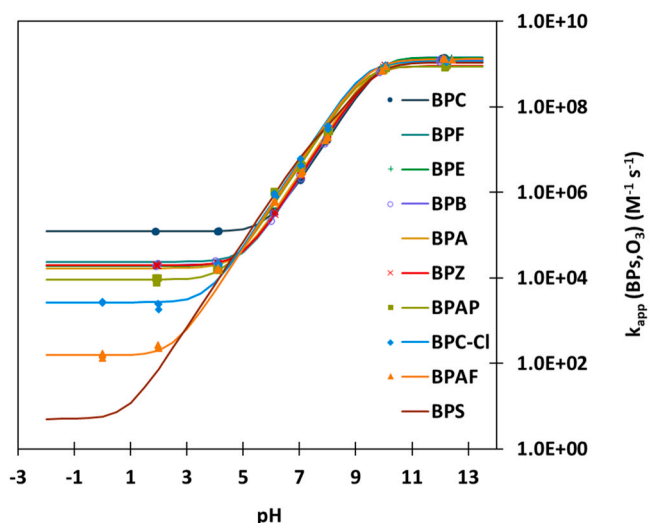[a] (This work),
[b] [26],
[c] [10],
[d] [27]

Fig. 1. Experimental values of the apparent rate constant for the corresponding pH (symbols) and the resulting model in front of pH for the different bisphenol analogues, including the previous established models for BPA, BPF and BPS (lines).

reactive with compounds containing high electron density sites. For this reason, in this work, the evaluation of the reactivity of ozone with the different bisphenol analogues was studied in a wide range of pH with the establishment of the apparent rate constants, involving the contribution of the different protonated species, as well as the determination of the species-specific second-order rate constants. Data obtained from the different replicates conducted for each bisphenol is given in the SI, from Table S7 to Table S13. In Fig. 1 is displayed the values of the apparent rate constants experimentally determined and the resulting theoretical model as a function of pH. Additionally, the established values of the second-order rate constants of ozone with the protonated states of the studied bisphenols are also exhibited in Table 2. For comparison purposes, the kinetic model and the values of the second-order rate constants of ozone with bisphenol A (BPA) [26], bisphenol F (BPF) and bisphenol S (BPS) [27], determined in previous studies, are also presented in both Fig. 1 and Table 2, respectively.

At strong basic conditions, the apparent rate constant is equal to the second-order rate constant of the deprotonated species (k_3), when the value of this constant remains invariable. This trend is perceived approximately between pH 10 and pH 12 for all bisphenols, including BPA, BPF and BPS, previously studied. At these pH conditions, their reactivity with ozone is very similar, as observed in Fig. 1 and Table 2 (values of k_3 from 8.83×10^8 to 1.43×10^9 M^{-1} s^{-1}). These values are comparable to the second-order rate constant of ozone with the deprotonated species of phenol (1.4×10^9 M^{-1} s^{-1}) [30].

From basic to neutral pH conditions (pH 10 to pH 6) a decrease of the reactivity of ozone with these compounds is observed. This is the result of the increase of the contribution of the di-protonated species to the overall reactivity, containing less electron density in the phenol rings. However, their reactivity with ozone is still mainly influenced by the deprotonated and mono-protonated species, observed in the resulting values of their apparent rate constants, which persisted considerably high and similar for all bisphenols, as occurred at strong basic pH. The reactivity of ozone with the mono-protonated species is close to that of the deprotonated species (see Table 2), probably because of the available, electron-rich, non-protonated phenol ring, that is, a preferential reaction site for ozone. At pH 7, the experimental values of the apparent second-order rate constants of the studied bisphenols range from 2×10^6 M^{-1} s^{-1} to 5×10^6 M^{-1} s^{-1} (see Tables S7 to S13 of the SI), similar to that observed for BPA [26], BPF and BPS [27]. This is in agreement with that found in previous works investigating the reactivity of simple phenolic

compounds with ozone at pH 7, where no significant difference of reactivity was observed regardless of the ring substituents [31].

Kinetics display greater differences at strong acidic conditions, where the apparent rate constant equals the second-order rate constant of the di-protonated species (k_1) at pH < 4 for most cases (see Fig. 1). Under such conditions, all bisphenols, including BPA, BPS and BPF, present the lowest reactivity with ozone compared to other pH values (values of k_1 from 5.01×10^0 to 1.22×10^5 M^{-1} s^{-1}), see Table 2. This is the result of the exclusive contribution of the di-protonated species to their reaction with ozone, presenting the lowest electron density in the phenol rings (see Table 2). Additionally, in strong acidic medium, the reactivity of ozone with the different bisphenols is strongly influenced by the different substituents which are present in such compounds, a trend not perceived at other pH conditions.

3.1.2. Role of substituents on ozone reactivity with di-protonated species of bisphenol analogues

Under strong acidic conditions, the resulting reactivity of ozone with the di-protonated species of these bisphenols, depends on the role of their different substituents. Functional groups with electron donating behaviour increase the electron density in the phenol rings of bisphenols, and thus the reactivity with ozone. On the contrary, bisphenols with electron withdrawing groups decrease the electron density of the phenolic ring, resulting in lower reactivity with ozone. The variation of the electron density of the different bisphenol analogues, including BPA, BPF and BPS, under acidic conditions, is exhibited in Fig. 2.

At these acidic conditions, bisphenol C is the one presenting the highest reactivity with O$_3$ among the studied bisphenols ($k_1 = 1.22\times10^5$ M^{-1} s^{-1}). This value, about 10 times higher than that for BPA ($k_1 = 1.68\times10^4$ M^{-1} s^{-1}) [26], is the result of the hyperconjugation effect exerted by the methyl groups into the *ortho* position of the phenolic ring [32]. This also justifies the increase of reactivity about 1 order of magnitude observed in 2-cresol (1.2×10^4 M^{-1} s^{-1}) compared to phenol (1.3×10^3 M^{-1} s^{-1}) [30].

In the case of bisphenol E, bisphenol B and bisphenol Z, the established values of k_1 resulted similar to those previously determined for BPA and BPF [26,27], with values ranging from 1.68×10^4 to 2.38×10^4 M^{-1} s^{-1} for these 5 bisphenols. These results prove that the electron density in the phenol rings is barely altered by the different alkyl variations attached to the central carbon of these bisphenols, resulting in similar reactivity with ozone. On the other hand, the reactivity of ozone with bisphenol AP is observed to be approximately 2 times lower than that with BPE, BPB, BPZ, BPA and BPF, with a value of k_1 of 9.15×10^3 M^{-1} s^{-1}. This may occur as a result of the inductive effect of the phenyl group in BPAP, which contains sp^2 hybridized carbon atoms that are more electronegative than hydrogen and sp^3 hybridized carbon atoms, such as methyl or ethyl groups [33]. Thus, the electron cloud around the phenol groups of BPAP is slightly attracted to the phenyl group, resulting in moderate lower electron density and lower reactivity with ozone.

Regarding bisphenol C-Cl and bisphenol AF, the corresponding k_1 values are even lower, as a result of the decrease of the electron density in the phenol rings through the stronger electron withdrawal effect exerted by the alkyl halides groups, particularly (CCl$_2$) for BPC-Cl and (2CF$_3$) in the case of BPAF [32]. This drop in ozone reactivity is much more noticeable in the case of BPAF (100 times lower reactivity than BPA, compared to 6 times less in the case of BPC-Cl), since the electron withdrawing effect of the alkyl fluoride group is more powerful than that exerted by the alkyl chloride group. The stronger inductive effect of BPC-Cl and BPAF is also in accordance with the observed lower values of pK$_{a,1}$, these being 9.1 for BPC-Cl and 8.9 for BPAF, compared to the value of 9.8 for the previous compounds (see Table 2).

Furthermore, the reactivity of ozone with BPAF is about 30 times higher than with BPS (5.01 M^{-1} s^{-1}), previously reported [27], as BPS presents both inductive and mesomeric effects by the sulfonyl group [32]. This reduces even more the electron density in both phenol rings, resulting in the lowest reactivity among all these bisphenol analogues.
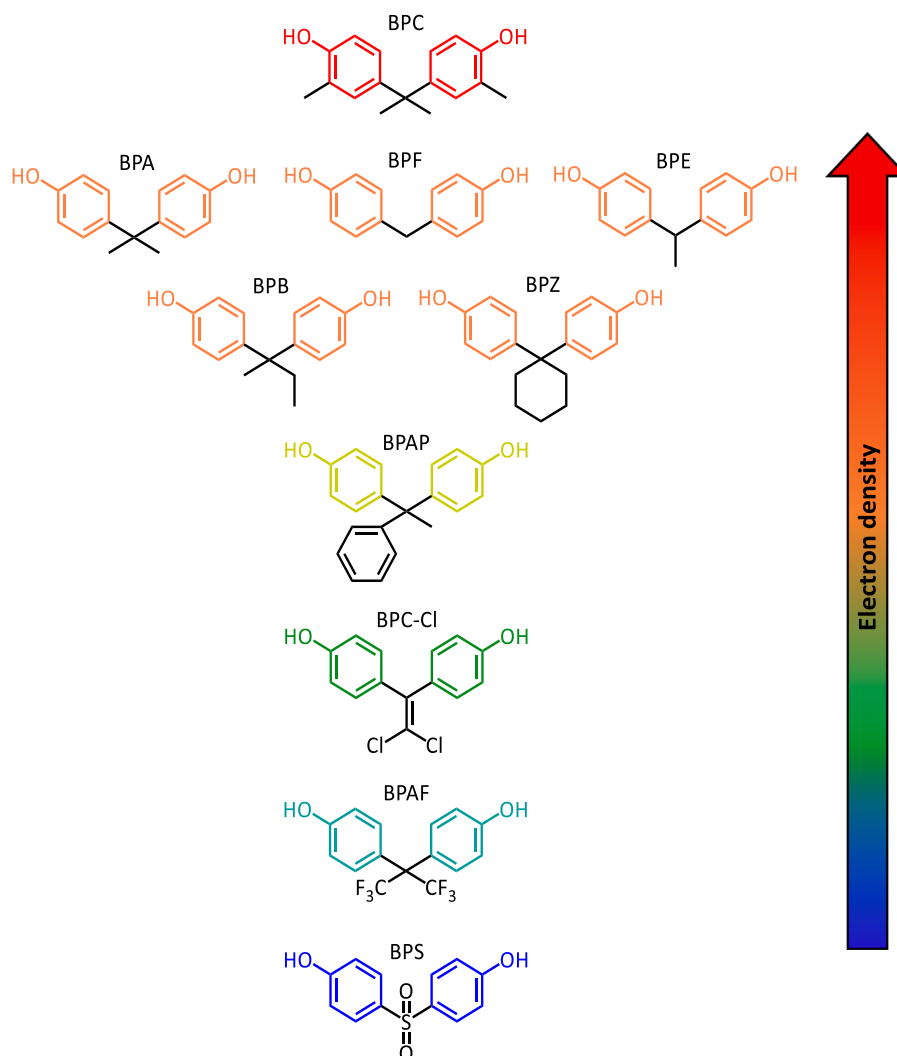
Fig. 2. Variation of the electron density for the different bisphenol analogues (neutral species).

The case is comparable to the reactivity of ozone with 4-nitrophenol [30].

3.2. Transformation products from the reaction of ozone with the different bisphenol analogues

Through the obtained MS and MS^2 data and the relative evolution of the detected intermediates presented in Section 2 of the SI and Fig. S1 of the SI, respectively, a general mechanism was proposed for the formation of TPs during ozone oxidation of selected bisphenols. It is exhibited in Fig. 3, where the main TPs from the reaction of ozone with BPA, BPF and BPS, previously studied [27,28], were also included for comparison purposes.

At neutral pH conditions, the main reaction pathway for ozone with most of the selected bisphenols is proposed to be the hydroxylation of the phenol rings in the *ortho* position, as noticed for BPA, BPF and BPS in previous studies [27,28]. This pathway leads to the formation of catechol derivatives (TP1), which was found to be a common TP for all compounds. Additionally, TP1 is one of the oxidation products to reach its maximum concentration earlier (see Fig. S1 of SI), thus it is suggested to be one of the primary TPs produced during the reaction with ozone. In most of the cases, the direct oxidation of the corresponding bisphenol and/or the oxidation of this catechol derivative resulted in the generation of the *ortho*-quinone derivative (TP2). Similar to what occurs with TP1, TP2 is also produced in the early stages of the reaction of

bisphenols with ozone, also exhibited in Fig. S1 of supplementary information. Therefore, TP2 is also suggested to be one of the main oxidation products for most of the bisphenols. On the other hand, from TP1, a second hydroxylation was observed in the *ortho* position of the other phenol ring for several of these bisphenols (BPE, BPB, BPAF and BPZ), leading to the generation of another catechol derivative (TP3). Then, the formation of the quinone derivative (TP4) from the oxidation of TP2 and/or TP3 was also detected, in this case for BPE and BPB.

Several ring opening products, containing two carboxylic groups, were detected for some of the studied bisphenols. The first one is TP5, which could be formed by the direct oxidation of the corresponding bisphenol and/or from the catechol derivative TP1. This TP was not detected for the seven selected bisphenols of this work. However, it was detected in earlier studies for BPA and BPS [27,28]. Additionally, TP6 was identified for BPAF, which suggests the formation of the ring opening product (TP5) as a previous step.

Bisphenol C is suggested to present an alternative primary hydroxylation pathway at the *para*-position of the phenol ring, leading to the formation of a 4-hydroxy-4-alkylcyclohexadien-1-one derivative (TP7). In fact, its detected intensity was even higher than that corresponding to the catechol derivative (TP1) (see Fig. S2 of the SI, where the intensity of both TP1 and TP7 are compared). The hydroxylation in the *para* position for simple *para*-substituted phenols was observed in previous works [31]. However, this *para*-hydroxylation was not clearly distinguished for the rest of the bisphenol analogues. Thus, the *ortho*-alkyl substitution of
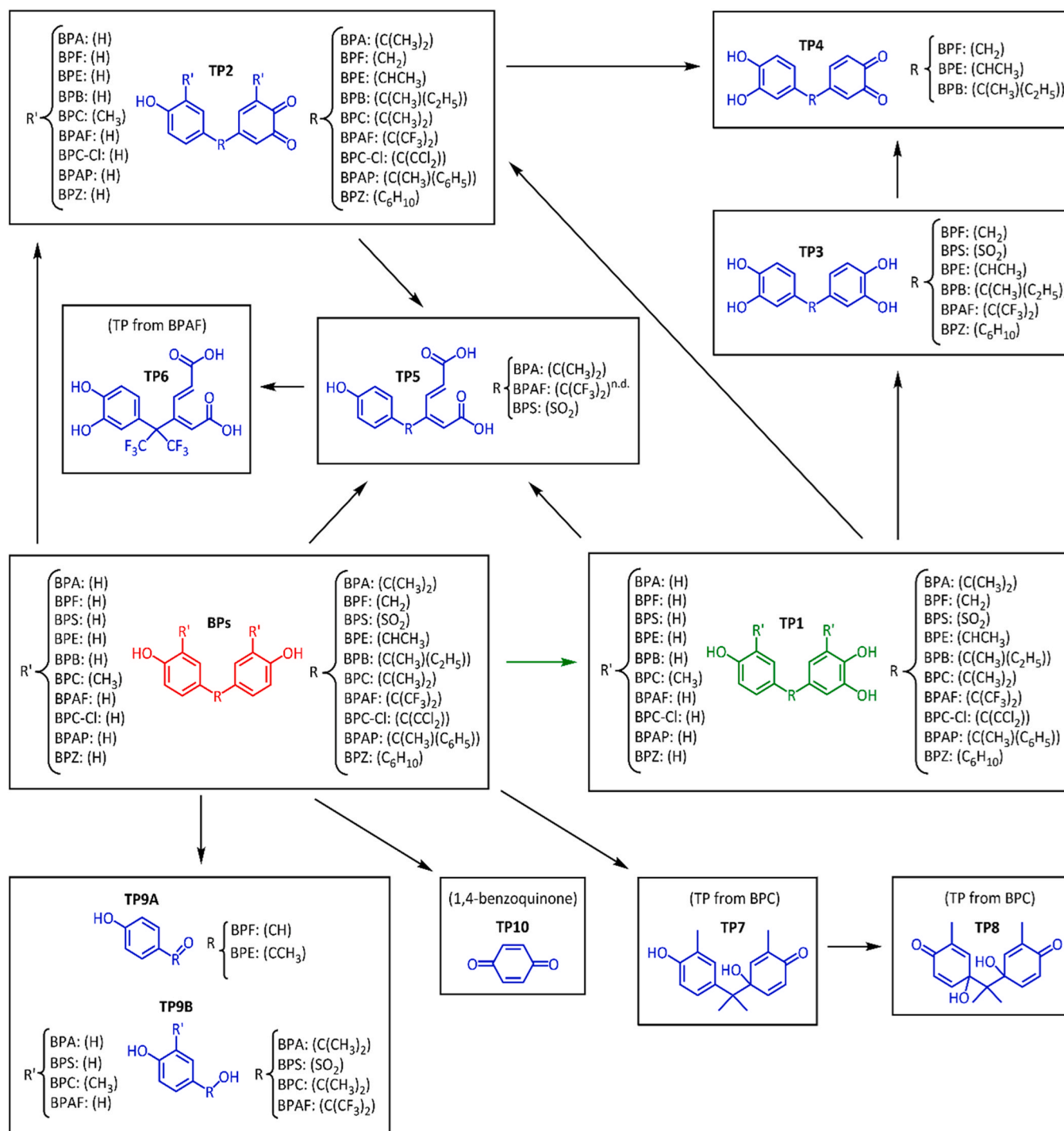
Fig. 3. Proposed mechanism for the formation of the transformation products during the reaction of ozone with bisphenol analogues, including the previously studied BPA, BPF and BPS, at pH 7. Red colour: parent compounds (BPs); green colour: the catechol derivative (TP1) common for all BPs; blue colour: the rest of the TPs. [n.d.] TP5 is proposed but not detected for BPAF.

the phenol rings of BPC may favour the attack of ozone in the *para*-position instead. Subsequently, a second hydroxylation from TP7 was also detected, suggested to be in the second phenol ring, again in the *para*-position, resulting in the formation of TP8.

Furthermore, some simple phenolic byproducts were also detected from the reaction of ozone with several of the selected bisphenols. The cleavage of one of the phenolic rings resulted in the formation of TP9A for BPE, containing one aldehyde moiety, as well as the generation of one alkyl alcohol derivative (TP9B), for BPC and BPAF. Finally, the generation of *para*-benzoquinone was not clearly detected by mass

spectrometry, presumably because its concentration was near or below the detection limit. Thus, a standard solution of *p*-benzoquinone was prepared and analysed by liquid chromatography-mass spectrometry and the observed retention time of the corresponding peak was compared with the chromatogram of the selected bisphenols, observing a small peak for some of them (e.g., BPE, see Fig. S3 of the SI). Thus, the generation of *para*-benzoquinone from the reaction of ozone with the different bisphenol analogues is suggested, as well as it was for BPA in previous works [28]. In addition, most of the detected TPs are observed to accumulate over the reaction with ozone, even for the main TPs firstly

produced, see Fig. S1 of SI.

4. Conclusions

The reactivity of ozone with bisphenol analogues is pH dependent due to the variation of the electron density of their protonated species. Under strong basic conditions, their reactivity with ozone is relatively high because of the contribution of the deprotonated species to the overall reactivity (higher electron density), while it significantly decreases at acidic pH due to the increase of contribution of the di-protonated species (lower electron density). Additionally, at these acidic conditions, the reactivity of bisphenols with ozone is governed by the role of their different functional groups as electron donors or acceptors. Electron donating groups increase the reactivity with ozone, as observed with bisphenol C, while electron withdrawing moieties decrease it (e.g., bisphenol AP, bisphenol C-Cl and bisphenol AF).

Under neutral pH conditions, the formation of catechol and *ortho*-quinone derivatives was proposed as the main degradation pathway. For degradations of bisphenols around 90%, most of the generated TPs are close to their maximum concentration, and therefore they accumulate during the ozone oxidation. Some of the generated TPs are expected to present endocrine-disrupting activity, as estrogenic compounds, such as the catechol derivatives. Thus, further studies are required to evaluate the evolution of their endocrine-disrupting activity during ozone-based treatments.

CRediT authorship contribution statement

Oriol Porcar-Santos: Conceptualization, Methodology, Investigation, Formal analysis, Writing – original draft, **Alberto Cruz-Alcalde:** Conceptualization, Supervision, Methodology, Validation, Writing – review and editing, **Carmen Sans:** Conceptualization, Supervision, Validation, Writing – review and editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

Acknowledgements

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jece.2023.110849.

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