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(Article begins on next page)
**Influence of electron acceptors on the kinetics of metoprolol photocatalytic degradation in TiO$_2$ suspension. A combined experimental and theoretical study.**

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Metoprolol (MET) belongs to a group of frequently used β$_1$-blockers, which often occur in waste waters. The objective of this work was to employ liquid chromatography (LC) and total organic carbon methods to study the photocatalytic degradation of MET in UV irradiated aqueous suspensions of TiO$_2$ (Wackherr’s “Oxyde de titane standard” and Degussa P25), in the presence of different electron acceptors such as molecular oxygen, hydrogen peroxide, potassium bromate, and ammonium persulfate. The degradation rates were found to be strongly influenced by the kind of electron acceptor and the type of catalyst. The optimal amount of hydrogen peroxide and potassium bromate was investigated as well. MET photocatalytic degradation was fastest in the presence of O$_2$ and potassium bromate with TiO$_2$ Degussa P25, while mineralization was most efficient in the presence of molecular oxygen alone. In all investigated cases, degradation followed a pseudo-first order kinetics. Reaction intermediates of MET degradation in the presence of different electron acceptors with both catalysts were studied in detail and a number of them were indentified using LC–ESI–MS/MS. The interactions with MET of reactive radical species relevant to this study (O$_2^•$, 'OH, BrO$_2^−$, and SO$_4^{2−}$) were theoretically investigated by means of density functional theory (DFT) computations.

1. Introduction

Studies dating more than 30 years ago dealt with photocatalytic reactions, which irrupted into the scientific literature when they were proposed as a suitable tool to promote separation of molecular H$_2$ and molecular O$_2$ from water using solar irradiation. Heterogeneous photocatalysis using TiO$_2$ powders has become a subject of increasing interest during the past twenty years, mainly in the field of environmental protection and wastewater decontamination. Photocatalysis in the presence of semiconductors is triggered by the interaction of electrons and holes, generated in a photochemically activated solid, with the surrounding medium. Activation is the consequence of light absorption: the irradiation of the photocatalytic material with sufficient energy leads to the formation of holes (h$^+$) in the valence band and electrons (e$^−$) in the conduction band.

The two species can either recombine or participate in reductive and oxidative reactions that lead to the decomposition of contaminants. The h$^+$ can either directly oxidize pollutants, or oxidize water (preferably the OH$^−$ groups adsorbed on the solid surface) to produce ‘OH. In contrast, e$^−$ reduces surface-adsorbed O$_2$. The oxidative and reductive reaction steps taking place with the irradiated photocatalyst (TiO$_2$) are expressed as follows:

(1) $\text{TiO}_2 + \text{hv} \rightarrow e^− + h^+$
(2) $h^+ + \text{organic compound} \rightarrow \text{CO}_2 + \text{H}_2\text{O} + \text{inorganic ions}$
(3) $2\text{H}_2\text{O} + h^+ \rightarrow '\text{OH} + \text{H}^+$
(4) $2\text{O}_2 + e^− \rightarrow \text{O}_2^2^−$

A practical problem in using TiO$_2$ as a photocatalyst is the energy waste due to the e$^−$–h$^+$ recombination, which results in lower degradation efficiency. The prevention of recombination is thus very important, and it can be achieved by adding proper electron acceptors. In the simplest systems, in aerated solution, molecular O$_2$ acts as electron acceptor to prevent e$^−$–h$^+$ recombination. Additional oxidants, such as H$_2$O$_2$, SO$_4^{2−}$, and BrO$_2^−$, can act as electron acceptors to enhance the photodegradation efficiency. These electron acceptors can have several effects including: (I) avoidance of e$^−$–h$^+$ recombination because of scavenging of conduction-band electrons; (II) increase of the concentration of ‘OH and (III) production of other oxidizing species that can enhance the oxidation rate of the substrate and of its intermediate compounds.

By employing computer simulations within the framework of the density functional theory (DFT), it is possible to gain insight into the changes of the investigated structures as a
consequence of the presence of other molecules in the system.\textsuperscript{11,22} The information thus obtained is very important to further understand the degradation mechanisms of the investigated compounds.\textsuperscript{13,14}

Fukui functions and Fukui indices are often used as local quantum-molecular descriptors. Fukui functions describe the changes in the molecular electron density as a consequence of the addition or removal of charge, while Fukui indices represent scalar values for each atom. Fukui functions are visualized as iso-surfaces, and larger Fukui values indicate higher reactivity.\textsuperscript{15,16} It should be emphasized that values of Fukui functions are sensitive to changes in basis sets and population analysis. Therefore, one shouldn’t use these values as absolute but rather as comparative parameters.

The molecular electrostatic potential (MEP) is related to the charge distribution and it is a very useful descriptor to determine potential sites prone to electrophilic attack and nucleophilic reactions.\textsuperscript{14,17,18} In the field of pollutant degradation, MEP enables the localization of parts of a molecule that are prone to various types of attacks, also giving information on how molecules interact with other molecules or radicals. The MEP (hereafter indicated as $V(r)$), when neglecting polarization and nuclear rearrangement effects due to the presence of a unit test charge at the distance $r$, is given as follows:

$$V(r) = \sum Z_i \rho(r) d\tau$$

where the summation runs over all nuclei $A$ with charge $Z_A$ and coordinate $R_A$, while $\rho(r)$ is the electron density of the molecule. $V(r)$ represents the potential exerted at the coordinate $r$ by the nuclei and the electrons. The sign of $V(r)$ at any point depends on whether the effects of the nuclei or the electrons are dominant.\textsuperscript{19,20}

Natural bond order (NBO) can be used for efficient investigation of intra- and inter-molecular bonding and interactions. It is a convenient basis for the investigation of charge transfer or conjugative interactions in molecular systems.\textsuperscript{21–23} NBO analysis is carried out by examining all possible interactions between ‘filled’ (donor) NBOs and ‘empty’ (acceptor) NBOs, estimating their energetic importance by 2nd-order perturbation theory. In this way one obtains the energies of delocalization of electrons from filled NBOs into empty NBOs, e.g. stabilization energies gained by donation from the donor NBO to the acceptor NBO. For each donor NBO ($i$) and acceptor NBO ($j$), the stabilization energy associated with $i \rightarrow j$ delocalization can be estimated on the basis of the second-order perturbation theory:\textsuperscript{24–26}

$$E(2) = A_{ij} = q_i f(i,j)^2 / \epsilon_{ij}$$

where $q_i$ is the donor orbital occupancy, $\epsilon_i$, $\epsilon_j$ are diagonal elements (orbital energies) and $F_{ij}$ is the off-diagonal NBO Fock matrix element.

Metoprolol (MET) is a selective $\beta_1$-blocker of the cardiac adrenergic receptors.\textsuperscript{27} Due to the frequent use, MET is present in sewage waters, in rivers from Netherlands (25–100 ng L$^{-1}$),\textsuperscript{28} Poland (51–155 ng L$^{-1}$),\textsuperscript{29} UK (7–11 ng L$^{-1}$),\textsuperscript{30} Sweden (60–70 ng L$^{-1}$),\textsuperscript{30} and Germany (exceeding 1000 ng L$^{-1}$).\textsuperscript{31}

Previous work has shown that the rate of MET photocatalytic degradation tended to a plateau at about 0.5–1.0 mM initial concentration of the substrate, and that photodegradation was most efficient at a photocatalyst loading of 1.0 mg mL$^{-1}$.\textsuperscript{13} The aim of this work was to compare the kinetics of photodegradation of MET, sensitized by TiO$_2$ Wackherr or Degussa P25 in aqueous suspension under the same experimental conditions, in the presence of different electron acceptors ($O_2$, H$_2$O$_2$, SO$_4^{2-}$, and BrO$_4^-$). To monitor MET removal and mineralization, liquid chromatography (LC) and total organic carbon (TOC) analysis were used, respectively. An attempt has also been made to identify the intermediates formed during the photooxidation of MET in the presence of different electron acceptors with both catalysts, and a number of them were indentified using LC–ESI–MS/MS. Employing DFT computations, the interactions of radical species ($O_2^+$, $OH^-$, BrO$_4^-$, and SO$_4^{2-}$) with MET and their possible effects on its degradation were investigated from the aspect of structural considerations, charge distribution, NBO analysis, Fukui functions and Fukui indices.

2. Materials and methods

2.1. Chemicals and solutions

All chemicals were of reagent grade and were used without further purification. The drug (±)-Metoprolol (+)-tartrate salt (Sigma-Aldrich) was used as received (≥99% purity); 85% H$_2$PO$_4$ was purchased from Lachema, Neratovice; acetonitrile (ACN) was a product of J.T. Baker. Other chemicals were as follows: 30% H$_2$O$_2$ from Sigma-Aldrich; KBrO$_3$ and (NH$_4$)$_2$S$_2$O$_8$ from Merck. All solutions were made using doubly distilled water. The used catalysts were TiO$_2$ Degussa P25 (75% anatase and 25% rutile, surface area 50 ± 1.0 m$^2$ g$^{-1}$, crystallite size about 20 nm, non-porous) and TiO$_2$, Wackherr’s “Oxyde de titane standard” (100% anatase, surface area 8.5±1.0 m$^2$ g$^{-1}$, crystallite size 300 nm, hereafter “TiO$_2$, Wackherr”), produced by the sulfate process.\textsuperscript{32}

2.2. Photodegradation procedures

Photocatalytic degradation was carried out in a cell made of Pyrex glass (total volume of ca. 40 mL, liquid layer thickness 35 mm), with a plain window on which the light beam was focused. The cell was equipped with a magnetic stirring bar and a water circulating jacket. A 125 W high-pressure mercury lamp (Phillips, HPL-N, emission bands in the UV region at 304, 314, 335 and 365 nm, with maximum emission at 365 nm) together with an appropriate concave mirror was used as the radiation source. The output of the mercury lamp was calculated to be $8.8 \times 10^9$ Einstein mL$^{-1}$ min$^{-1}$ (potassium ferrioxalate actinometry).

Experiments were performed using 20 mL of 0.05 mM MET containing 1.0 mg mL$^{-1}$ of TiO$_2$ (Wackherr or Degussa P25), except for the study of direct photolysis. The aqueous suspension of TiO$_2$ was sonicated (50 Hz) in the dark for 15 min before irradiation, in order to uniformly disperse the photocatalyst particles and to attain adsorption equilibrium. Before irradiation, the suspension thus obtained was thermostatted at 25±0.5 °C in a stream of O$_2$ (3.0 mL min$^{-1}$), except for a control run in the absence of electron acceptors when N$_2$ was bubbled (3.0 mL min$^{-1}$) to remove dissolved oxygen. During irradiation, the mixture was stirred at a constant rate under continuous gas flow. All experiments were performed at the natural pH which changed during the photodegradation, from pH 7 to pH 4 in the case of TiO$_2$
Wackherr and from pH 7 to pH 5 in the case of Degussa P25. In the investigation of the influence of electron acceptors, apart from constant O₂ bubbling, solutions of H₂O₂, KBrO₃ or (NH₄)₈S₂O₇ (at typical 3.0 mM initial concentration) were added to the MET solution.

### 2.3. Analytical procedures

The photodegradation of MET was monitored by liquid chromatography–photodiode array detection (LC–PDA). To do so, aliquots of 0.30 mL were taken from the reaction mixture at the beginning of the experiment and at regular time intervals. Aliquot sampling caused a maximum volume variation of ca. 10% in the reaction mixture. The suspensions were filtered through Millipore (Millex-GV, 0.22 µm) membrane filters to eliminate the photocatalyst. Lack of adsorption of MET on the filters was preliminarily checked. Afterwards, a 10-µL sample was injected and analyzed using a Shimadzu UFLC–PDA, equipped with an Eclipse XDB-C18 column (150 mm × 4.6 mm i.d., particle size 5 µm, 25 °C). The UV/vis PDA detector was set at 225 nm (wavelength of MET maximum absorption), as well as at 210, 260, 270 and 280 nm for the monitoring of the intermediates. The mobile phase (flow rate 0.8 mL min⁻¹) was a mixture of ACN and water (the latter acidified with 0.1% H₃PO₄), with the following gradient: 15% ACN at 0 min, which was increased to 30% ACN in 5 min, after which 30% ACN was constant for 5 min; post time was 3 min. The retention time for MET was 6.0 ± 0.1 min. Reproducibility of repeated runs was around 3–10%.

Concerning TOC analysis, 10 mL aliquots of the reaction mixture were taken at regular time intervals, diluted to 25 mL and analyzed after filtration on an Elementar Liqui TOC II analyzer, according to Standard US 120 EPA Method 9060A. For the LC–ESI–MS/MS evaluation of intermediates after 10 min irradiations, 100-µL samples were analyzed on an Agilent Technologies 1200 series LC with Agilent Technologies 6410A series electrospray ionization triple-quadrupole MS/MS, using Agilent Technologies Zorbax XDB-C18 column (50 × 4.6 mm i.d., particle size 1.8 µm, 40°C). The mobile phase (flow rate 0.5 mL min⁻¹) consisted of 0.05% aqueous formic acid and MeOH (gradient, 0 min 20% MeOH, 10 min 60% MeOH, 12 min 100% MeOH, post-time 3 min). Analytes were ionized using the electrospray ion source, a capillary voltage of 4.0 kV and with nitrogen as the drying gas (temperature 350°C, flow 10 L min⁻¹) and nebulizer gas (45 psi). High-purity nitrogen was used as the collision gas. Full scan mode (m/z range 50–800, scan time 100 ms, fragmentor voltage 100 V) in positive ion mode was used to select precursor ions for the starting compound and each degradation intermediate, as well as to examine isotopic peak distribution. Then, the product ion scan MS² mode (fragmentor voltage 135 V, scan time 200 ms, collision energy 10–40 V in increments of 10 V) was used to elucidate the structure of each degradation intermediate.

### 2.4. Computational details

All DFT calculations were carried out using the Gaussian 03 software package, except for Fukui functions and Fukui indices that were calculated at the same level of theory using Jaguar, version 8.4, as implemented in the Schrödinger Materials Suite, release 2014-2. For the purpose of NBO analysis, it was used the NBO 3.0 program as implemented in Gaussian 03. For all systems, calculations were performed employing the B3LYP exchange and correlation functional with 6-31 G+(d) basis set. Two stages took place for all configurations. Firstly, equilibrium geometry of the investigated systems was located using default convergence criteria and, secondly, the harmonic vibrational spectrum was checked to assure that the true minimum of potential energy, characterized by positive frequencies, was located.

In this work we investigated five systems: MET, MET/O₂⁻, MET/O₂⁻/PHO, MET/O₂⁻/BrO₃⁻, and MET/O₂⁻/SO₄²⁻. To make the simulations more realistic, solvent effects of water were taken into account using the default Polarizable Continuum Model (PCM). Initially, in all cases O₂⁻ was placed above the hydroxyl group located at the tail of MET, while OH, BrO₃⁻ and SO₄²⁻ were placed above the aromatic ring. Interesting sites containing a significant amount of charges were located through MEP surfaces, which were obtained using Molekel after geometry optimization and frequency check.

### 3. Results and discussion

#### 3.1. Effect of electron acceptors

Apart from O₂, which is the most frequently applied electron acceptor, in this work we also investigated the influence of H₂O₂, BrO₃⁻, and S₂O₆²⁻. These compounds operate as e⁻ scavengers and should be able to prevent e⁻–h⁺ recombination, thereby enhancing the formation of *OH and other reactive species. However, compounds such as H₂O₂ are also able to scavenge the photogenerated transients.

Fig. 1 and Table 1 show the time trend and degradation kinetics of MET, upon irradiation in the presence of TiO₂ (Wackherr, 1a, and Degussa P25, 1b) and several electron acceptors. In all investigated cases, the degradation process followed a pseudo-first order kinetics. Note that the role of O₂ as electron acceptor was investigated by comparing the system in air (blue triangles) with the one in which oxygen was bubbled to create an O₂ atmosphere (purple stars; in such a system, the concentration of both gas-phase and dissolved O₂ is expected to be ~5 times higher than in the case of air equilibrium). For further comparison, the behaviour of the deoxygenated system (N₂ bubbling, pink triangles) was also studied.

As expected, all the studied electron acceptors increased the efficiency of MET photocatalytic removal. It was determined that the influence of electron acceptors on the efficiency of degradation followed the order: O₂/H₂O₂ > O₂/H₂O; O₂/S₂O₆²⁻ > O₂/BrO₃⁻ using TiO₂ Wackherr, and O₂/BrO₃⁻ > O₂/H₂O₂ > O₂/S₂O₆²⁻ > O₂ using Degussa P25 (Fig. 1, Table 1). The added oxidants (H₂O₂, BrO₃⁻, S₂O₆²⁻) did not cause MET transformation in the dark.

Moreover, MET degradation using TiO₂ under N₂ atmosphere was very slow, and only marginally faster compared to the direct photolysis (MET irradiation in air without TiO₂). As reported in Fig. 1 and Table 1, a considerable enhancement of MET degradation was observed, with irradiated TiO₂ in air compared to N₂ atmosphere: the increase of the pseudo-first order rate constant k' was around 7 times with TiO₂ Wackherr and around 12 times with Degussa P25.
was observed with TiO₂. Wackherr, it appears that O₂ bubbling already brought the reaction to its optimum and that any further enhancement was difficult. The situation was very different for Degussa P25. As far as the role of O₂ as electron acceptor is concerned, photoelectrons can be captured by O₂ to produce O₂•−, H₂O₂ (reactions 4, 7, and 8) and then eventually hydroxyl radicals (reactions 9-11):8,10,38

\[
O_2^•− + H^+ \rightarrow HO_2^• \quad (7)
\]

\[
2HO_2^• \rightarrow H_2O_2 + O_2 \quad (8)
\]

\[
H_2O_2 + hν \rightarrow 2OH \quad (9)
\]

\[
H_2O_2 + e^- \rightarrow OH^- + OH^- \quad (10)
\]

\[
H_2O_2 + O_2•− \rightarrow *OH + OH^- + O_2 \quad (11)
\]

When comparing the systems O₂ and O₂/H₂O₂ (oxygen bubbling in both cases, reported as purple stars and red circles, respectively, in Fig. 1), one can notice a small acceleration (by a factor of 1.2) caused by H₂O₂ addition in the case of TiO₂ Wackherr, and a more marked H₂O₂ effect (2.2 times) with Degussa P25. Despite the more important role of H₂O₂ in the MET degradation with Degussa P25 and O₂/H₂O₂ was still a bit slower compared to TiO₂ Wackherr with otherwise identical conditions. The fact that a photocatalyst with lower surface area (TiO₂ Wackherr) could induce faster MET degradation compared with Degussa P25 is most likely accounted for by lower radiation scattering, which allows a better use of the incoming photons.13

The increase of MET degradation rate upon addition of H₂O₂ to Degussa P25 (Table 1) was likely due to increased generation of *OH. Indeed, H₂O₂ can enhance *OH production through the following pathways: (I) direct photolysis of H₂O₂ under UV irradiation (reaction 9); (II) reaction between H₂O₂ and e−: H₂O₂ is a more effective electron acceptor than oxygen because its reaction with e− yields *OH and OH− (reaction 10), while the corresponding process with O₂ produces the weaker oxidant O₂•− (reaction 4); (III) reaction with O₂•−, also yielding *OH (reaction 11).8,10,38

In the presence of Degussa P25, the O₂/BrO₃⁻ system was the most efficient for the degradation of MET. In contrast, the addition of BrO₃⁻ did not have an important effect on MET degradation with TiO₂ Wackherr. When operational, the enhancement of photodegradation efficiency would likely be a consequence of the reaction between BrO₃⁻ and conduction-band electrons. A first effect is the inhibition of e−−h⁺ recombination, which prolongs the life time of the photogenerated holes. One should additionally consider the formation of the reactive species BrO₅²⁻ (reaction 12).38,39 The possible role of BrO₅²⁻ in MET degradation was investigated with DFT methods (vide infra).

\[
BrO_3^- + 2 H^+ + 2 e^- \rightarrow BrO_5^{2-} + H_2O \quad (12)
\]

Moreover, while MET degradation with Degussa P25 was little influenced by a further increase of the oxygen concentration (compare the runs with and without bubbled O₂), a further significant increase of the MET rate constant (over three times) was observed with TiO₂ Wackherr. Interestingly, in the case of TiO₂ Wackherr the degradation of MET did not undergo a further important enhancement upon addition of other e− scavengers. In contrast, with Degussa P25 the additional effect of the scavengers was substantial. The differences between the two photocatalysts may be connected with the different surface area (much larger for Degussa P25) and different crystal structure (presence of the rutile phase in Degussa P25). These issues could lead to differences in the interaction of O₂ and other e− scavengers with the photocatalyst surface. In the case of TiO₂, Wackherr, it appears that O₂ bubbling already brought the reaction to its optimum and that any further enhancement was difficult. The situation was very different for Degussa P25. As far as the role of O₂ as electron acceptor is concerned, photoelectrons can be captured by O₂ to produce O₂•−, H₂O₂ (reactions 4, 7, and 8) and then eventually hydroxyl radicals (reactions 9-11):8,10,38

\[
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\[
H_2O_2 + O_2•− \rightarrow *OH + OH^- + O_2 \quad (11)
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When comparing the systems O₂ and O₂/H₂O₂ (oxygen bubbling in both cases, reported as purple stars and red circles, respectively, in Fig. 1), one can notice a small acceleration (by a factor of 1.2) caused by H₂O₂ addition in the case of TiO₂ Wackherr, and a more marked H₂O₂ effect (2.2 times) with Degussa P25. Despite the more important role of H₂O₂ in the MET degradation with Degussa P25 and O₂/H₂O₂ was still a bit slower compared to TiO₂ Wackherr with otherwise identical conditions. The fact that a photocatalyst with lower surface area (TiO₂ Wackherr) could induce faster MET degradation compared with Degussa P25 is most likely accounted for by lower radiation scattering, which allows a better use of the incoming photons.13

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\[
BrO_3^- + 2 H^+ + 2 e^- \rightarrow BrO_5^{2-} + H_2O \quad (12)
\]
strong oxidant $\text{SO}_4^{2-}$, but $\text{SO}_4^{2-}$ is also formed and it can act as a hole scavenger (reaction (14)). The trade-off between $h^+$ and $\text{SO}_4^{2-}$ could result into a limited enhancement effect, or even into no effect.\textsuperscript{10}

$$S_4\text{O}_6^{2-} + e^- \rightarrow \text{SO}_4^{2-} + \text{SO}_4^{2-} \quad (13)$$

$$\text{SO}_4^{2-} + h^+ \rightarrow \text{SO}_4^{2-} \quad (14)$$

Another issue is that sulfate, formed in reaction (13), can be adsorbed on the TiO$_2$ surface and decrease the photocatalytic activity of the oxide.\textsuperscript{10} Since $S_4\text{O}_6^{2-}$ turned out to be quite ineffective as electron acceptor in the removal of MET, it was not subjected to further investigation. The very low interaction between $\text{SO}_4^{2-}$ and MET, compared to other systems, was confirmed through theoretical analysis as well (vide infra).

The results reported, and in particular the much faster transformation of MET with O$_2$ compared to N$_2$ bubbling, highlight the importance of electron acceptors in the degradation process. The addition of further electron acceptors may enhance degradation, but the reaction pathways are probably modified as well. Fig. 2 reports chromatograms obtained using TiO$_2$ Wackherr and Degussa P25 in the presence of the studied electron acceptors, showing that the occurrence of certain intermediates (represented by unassigned peaks) significantly depended on the applied electron acceptor and catalyst. Moreover, according to literature data,\textsuperscript{10,38,40,41} it is suggested that the application of an optimal concentration of electron acceptors is of great importance to achieve the maximum removal of organic compounds from the system. For this reason, the effects of the acceptor concentrations were studied in this case as well.

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**Fig. 2 Chromatograms obtained after 10 min of MET exposure to UV irradiation in the presence of TiO$_2$ Wackherr (a) and Degussa P25 (b), using different electron acceptors (1: O$_2$; 2: H$_2$O$_2$; 3: S$_2$O$_8^{2-}$; 4: BrO$_3^-$). $\lambda_{\text{ex}} = 225$ nm**
3.2. Effect of the initial concentration of hydrogen peroxide

The influence of the concentration of H$_2$O$_2$ on the efficiency of MET removal was investigated in the range of 1.0 to 5.0 mM (Fig. 3). For both Degussa P25 and TiO$_2$ Wackherr, the optimal concentration of H$_2$O$_2$ was 3 mM. Under such conditions, after 10 min irradiation of the O$_2$/H$_2$O$_2$ system, the degradation of MET reached 89% with TiO$_2$ Wackherr and 86% with Degussa P25 (Fig. 3).

The presence of H$_2$O$_2$ at concentration values above 3 mM resulted in lower MET degradation compared to the optimal conditions. The most likely reason is that H$_2$O$_2$ acts as an OH scavenger, generating the much less reactive hydroperoxyl/superoxide radicals (HO$_2^*$/O$_2^*$, reaction 15). Moreover, HO$_2^*$ can further react with •OH to form oxygen and water, which are not directly involved into MET degradation (reaction 16).

$$\text{HO}_2^* + \text{•OH} \rightarrow \text{O}_2 + \text{H}_2\text{O}$$

Additionally, H$_2$O$_2$ at elevated concentration could react with TiO$_2$ to form peroxo compounds, which are detrimental to the photocatalytic action. $^{42}$

3.3. Effect of the initial concentration of potassium bromate

Fig. 4 reports the MET degradation efficiency in the presence of different initial concentrations of BrO$_3^-$. In the case of TiO$_2$ Wackherr, as already discussed, the bromate effect was very limited. In contrast, Degussa P25 showed a degradation increase that quickly tended to a plateau. In the latter case the most effective MET degradation was observed for 3 mM bromate, but very little difference could be detected in the 3-5 mM BrO$_3^-$ concentration range. While e$^-$ scavenging and a potential involvement of BrO$_3^-$ (formed in reaction 12) could possibly enhance degradation, at elevated BrO$_3^-$ levels the system reactivity could be limited by the formation of bromide (reaction 17). The latter could both adsorb on the photocatalyst surface and be involved in h$^+$ and •OH scavenging.$^{4,10,43,44}$

$$\text{BrO}_3^- + 6\text{H}^+ + 6\text{e}^- \rightarrow [\text{BrO}_2^-, \text{HOBr}] \rightarrow \text{Br}^- + 3\text{H}_2\text{O}$$

In the studied systems the electron acceptors are expected to inhibit the e$^-$/h$^+$ recombination processes, but they could have additional effects (e.g., production of reactive species by photolysis, such as •OH from H$_2$O$_2$, see reaction (9)). These effects can be highlighted in the absence of TiO$_2$. For this reason, MET was irradiated alone and in the presence of O$_2$/H$_2$O$_2$ and O$_2$/BrO$_3^-$, without TiO$_2$ (Fig. 5). The degradation of MET was considerably slower compared to photocatalytic conditions, but in the presence of H$_2$O$_2$ around 50% of MET was removed from the system after 60 minutes irradiation. In this case, acceleration of degradation compared to MET direct photolysis would probably be accounted for by •OH, generated by H$_2$O$_2$ irradiation. Indeed, the hydroxyl radical reacts rapidly and non-selectively with most organic compounds, either by H-abstraction or by addition to C=C unsaturated bonds. $^{45}$ Although slower compared to MET photocatalytic degradation, the use of H$_2$O$_2$ under irradiation could be attractive due to its simplicity. Some enhancement of MET degradation was also observed in the presence of irradiated bromate, in particular at longer irradiation times (> 30 min), in agreement with literature reports. $^{46}$

![Fig. 3 Effect of the initial concentration of H$_2$O$_2$ on MET removal using O$_2$/UV/TiO$_2$ for the first 10 min irradiation.](image)

![Fig. 4 Effect of the initial concentration of BrO$_3^-$ on MET removal using O$_2$/UV/TiO$_2$ for the first 10 min of irradiation.](image)

![Fig. 5 Kinetics of the direct and indirect photolysis of MET under UV irradiation in the presence of O$_2$ or BrO$_3^-$ or O$_2$/H$_2$O$_2$.](image)
3.4. Evaluation of the degree of mineralization

3.4.1 Systems with hydrogen peroxide

H₂O₂ was poorly retained by the analytical column, but its considerable absorption at 225 nm allowed a rough estimation of its concentration to be derived from the chromatograms. By so doing, a considerable decrease of H₂O₂ concentration under photocatalytic conditions could be highlighted with both TiO₂ Wackherr and Degussa P25. Note that such an approach could overestimate H₂O₂ in the degraded systems, because of the possible interference by other poorly retained compounds. Therefore, the extent of H₂O₂ degradation could be underestimated. The chromatograms reported in Fig. 6 also show that the variety and the amount of intermediates depended on the type of photocatalyst. We made similar conclusions also in our previous works, where degradation mechanism and toxicity of investigated systems were studied in details. Interestingly, most intermediates formed with both photocatalysts had lower retention times compared to MET: they mainly consisted of ring-hydroxylated compounds and of derivatives arising from oxidative cleavage of the shorter lateral chain of MET (that containing the methoxy group). The mixture of intermediates with Degussa P25 was considerably more toxic than that obtained with TiO₂ Wackherr.⁷⁷

\[
\text{Fig. 6. Chromatograms obtained after 10 min of MET irradiation in the presence of TiO}_2 \text{ Wackherr (a) and Degussa P25 (b): O}_2/\text{H}_2\text{O}_2 \text{ system in both cases (O}_2 \text{ bubbling, 3 mM H}_2\text{O}_2, \lambda_{\text{max}} = 225 \text{ nm}}
\]

Therefore, the ability of the systems to achieve MET mineralization is particularly important in the case of the Degussa P25 photocatalyst. Further experimental results obtained in the present work indicate that the adsorption of MET on the catalysts doesn’t differ more than 10%, which leads to conclusion that the adsorption of the investigated compound doesn’t have significant influence on the efficiency of photocatalytic degradation. As far as mineralization is concerned, soon after complete removal of MET from the system, 88% of organic compounds (measured as organic carbon) were still present with TiO₂ Wackherr in the absence of H₂O₂, and even 94% (that is, only 6% mineralization) with 3 mM H₂O₂ (Fig. 7a). The degree of mineralization after MET disappearance was significantly higher using Degussa P25, which gave 33% residual organic carbon without H₂O₂ and 72% with H₂O₂ (Fig. 7b). Photonic efficiencies calculated from data obtained for 60 min of mineralization of MET in the presence of TiO₂ Wackherr and Degussa P25 without H₂O₂ were 0.068% and 0.223%, respectively. Also, for the systems TiO₂ Wackherr and Degussa P25 in the presence of H₂O₂, the photonic efficiency was 0.012% and 0.066%, respectively. The better performance of Degussa P25 toward mineralization, compared to TiO₂ Wackherr, could be accounted for by its higher surface area. Indeed, a photocatalyst with low surface area, such as TiO₂ Wackherr, could undergo surface poisoning by the degradation intermediates.¹³ As an alternative or in addition, the mineralization of MET could be connected with reactions involving h⁺. The latter are favoured in the presence of Degussa P25 compared with TiO₂ Wackherr, which induces ·OH reactions to a higher extent.¹³ This issue would be consistent with the previously discussed finding (Fig. 2) that different chromatographic peaks, corresponding to different intermediates, could be detected with the two photocatalysts.

\[
\text{Fig. 7. Kinetics of photocatalytic degradation of MET under UV irradiation and O}_2 \text{ bubbling, in the presence of TiO}_2 \text{ Wackherr (a) and Degussa P25 (b): (1) MET trend, no H}_2\text{O}_2; (2) MET trend, 3 mM H}_2\text{O}_2; (3) TOC trend, no H}_2\text{O}_2; (4) TOC trend, 3 mM H}_2\text{O}_2.}
\]

With both TiO₂ types, mineralization further increased up to the longest irradiation time (4 h). However, while H₂O₂ enhanced MET degradation (at least with Degussa P25), it slowed down mineralization with both photocatalysts. If the above hypothesis concerning h⁺ vs. ·OH is correct, the addition of H₂O₂ would shift the system reactivity towards the hydroxyl radical and the inhibition of mineralization would be automatically explained.

3.4.2 Systems with potassium bromate

In a similar way as H₂O₂, bromate was poorly retained by the analytical column but it could be detected due to significant radiation absorption at 225 nm. An approximate assessment of BrO₃⁻ concentration could thus be obtained from the chromatograms, similarly to H₂O₂ and with the same limitations. Contrary to H₂O₂, for which clear evidence of a
concentration decrease under photocatalytic conditions was obtained, no evidence was available from the chromatograms of a change in bromate concentration. Fig. 8 shows the chromatograms obtained after 10 minutes of MET degradation in the system O$_2$/BrO$_3^-$. In addition to the constant area of the peak to which bromate contributes, chromatograms obtained in the presence of TiO$_2$ Wackherr and Degussa P25 show significant differences in the amount and presence of peaks related to the degradation intermediates. This finding is in general agreement with earlier suggestions that different photocatalysts induce not only different transformation kinetics, but also different degradation mechanisms.\textsuperscript{13}

TOC measurements (Fig. 9) show that bromate slightly increased mineralization with TiO$_2$ Wackherr and slightly decreased it with Degussa P25. After 240 minutes of irradiation without BrO$_3^-$, the percentage of the residual organic compounds was reduced to 17% for TiO$_2$ Wackherr and to 4% for Degussa P25. In the presence of BrO$_3^-$, the corresponding values were 5% for TiO$_2$ Wackherr and 13% for Degussa P25. Photonic efficiencies of mineralization of MET after 60 min in the presence of TiO$_2$ Wackherr and Degussa P25 with KBrO$_3$ were 0.096%, and 0.194%, respectively.

3.5. Influence of radicals on MET – DFT insight

3.5.1. Structural and reactivity properties - Fukui functions and indices

To better understand the interaction between MET and the radicals produced by reaction between e$^-$ and electron acceptors, we conducted a DFT computational analysis of the following systems: MET/O$_2^-$, MET/O$_2^-$/OH, MET/O$_2^-$/BrO$_2^-$, and MET/O$_2^-$/SO$_4^2^-$. The optimized molecular geometries of the investigated systems, together with the specific dihedral angles, are given in Fig. 10. The presence of O$_2^-$ (Fig. 10b) modifies dihedral angles, which reduces MET stability. Moreover, the interaction between O$_2^-$ and MET is modified by other electron acceptors (Fig. 10c-d).

The interaction distance between O$_2^-$ and MET was the shortest (1.612 Å) when OH was also present, while it was the longest (3.904 Å) in the presence of SO$_4^2^-$. Concerning other radicals, the interaction distance with MET was ca. 3.4 and 6.4 Å for BrO$_2^-$ and SO$_4^2-$, respectively. The most interesting situation for the interaction of radicals with MET was found in the case of OH, where a new bond was formed. In various experimental studies carried out with molecules similar to MET, it was concluded that OH binds to the aromatic ring.\textsuperscript{13,49}

However, it was still unclear which carbon atom formed a bond with OH. According to our study, a bond is formed with the carbon atom number 4 (Fig. 10).

Structural properties indicate that the highest interaction between MET and radicals takes place in the MET/O$_2^-$/OH system. These data are in overall agreement with the experimental results reported before, which emphasized the important role of O$_2$ vs. deoxygenated systems and the effect of electron acceptors in the enhancement of "OH (and h$^+$) occurrence, through inhibition of e$^-$–h$^+$ recombination. This fact is also confirmed by the NBO analysis provided in section 3.5.3 (vide infra).

In order to understand the reactive properties of MET, we will refer to Fukui functions and Fukui indices. Fukui functions are presented in Fig. 11, while Fukui indices (f$_{SN}$ HOMO and f$_{SN}$ LUMO) are given in Table 2. Fukui indices are commonly used since they describe the electron density when the molecule is...
subjected to a reaction that modifies the electron density itself.\textsuperscript{50–52} Concerning the Fukui functions ($f^-$ and $f^+$), the red colour corresponds to the negative values while the blue colour corresponds to the positive ones. Negative values of $f^-$ correspond to regions that lose electron density when the molecule is subjected to electrophilic attack, or when the molecule itself acts as a nucleophile. Positive values of $f^+$ correspond to areas that gain electron density when the an molecule is subjected to nucleophilic attack, or when it acts as electrophile.

The $f_{\text{NN}}$ HOMO indices are related to the $f^-$ Fukui function, while the $f_{\text{NN}}$ LUMO ones are related to $f^+$. In other words, a high positive value of $f_{\text{NN}}$ HOMO indicates that the relevant atom can donate electrons, thereby acting as a nucleophile, while an elevated $f_{\text{NN}}$ LUMO indicates that the atom can receive electrons, thus acting as an electrophile. Having in mind the fact that a new bond was formed between MET and $^4$OH, special attention was paid to the C4 atom of the MET aromatic ring, namely the atom involved in bond formation. According to positive surface of Fukui $f^-$ function, the MET molecule has an electrophilic nature on both tail parts. On the other hand, the negative value of $f^-$ located at the aromatic ring, and automatically at the C4 atom, suggests that this atom could act as a nucleophile as well. Significant values of both Fukui functions are located at the oxygen atom O7 (Fig. 11), while its Fukui indices emphasize nucleophilic nature (Table 2).

Fig. 10 Optimized geometries of the investigated structures with specific angles (degrees) and distances (Å) for: a) MET; b) MET/\(\cdot\)2O\(_2\); c) MET/\(\cdot\)2O\(_2\)/\(\cdot\)OH; d) MET/\(\cdot\)2O\(_2\)/Br\(_{2}\)O\(_2\); and e) MET/\(\cdot\)2O\(_2\)/SO\(_4\)\(_2\)
Concerning Fukui indices, the value of $f_{\text{NN}}$ HOMO for the atom C4 again emphasizes its nucleophilic nature, while the highest value of this index is recorded for the C2 atom. The highest value of $f_{\text{NN}}$ LUMO is obtained for the atom C6. Overall, Fukui indices have significantly high values for atoms belonging to the aromatic ring.

One should be careful when interpreting the results of Fukui functions and indices, since they are not reliable to absolutely identify the most reactive electrophilic or nucleophilic sites within a particular molecule. In such a case, they can serve only as qualitative indicators of reactivity. However, according to both Fukui functions and indices, the C4 atom of the MET aromatic ring is a potential reaction site, which is confirmed in the case of the MET/O$_2^-$/OH system.

3.5.2. Molecular Electrostatic Potential (MEP) surfaces

Representative MEP surfaces of the investigated structures are given in Fig. 12. The blue colour corresponds to the areas with the highest electrostatic potential, the red colour corresponds to the lowest electrostatic potential, while the green colour indicates intermediate values. MEP surfaces clearly indicate that significant changes of charge distribution would occur in MET in the presence of radicals. In particular, the introduction of radical species would change significantly the maximal and minimal MEP values, and the associated change would be the highest for SO$_4^2^-$. In the MEP surface of MET alone (Fig. 12) there are two specific sites containing a significant negative charge, located in the near vicinities of oxygen and nitrogen atoms. As expected, these sites would be the centres of reactivity with radicals. In the equilibrium state, O$_2^-$ was located above the hydroxyl group and the closest adjacent H atom. The hydroxyl radical was bound to the aromatic ring, and the H atom of *OH acquired a significantly positive MEP value.

The situations changed when BrO$_2^-$ and SO$_4^2-$ were present in the system. The location of the radical O$_2^-$ was similar to previous cases, but the MEP values around O$_2^-$ were much higher than before and also the values around oxygen atoms increased significantly. These different charge distributions indicate interesting chemical interactions between MET and the studied radicals, which will be further discussed in the following section.

3.5.3. Natural Bond Order (NBO) analysis

The nature of molecular interactions can be investigated employing the NBO analysis, specifically based on the observation of the electron delocalization energies between NBO orbitals. The significance of the chemical or physical interactions between MET and radical species can be assessed by using the total sum of the delocalization energies, $\Sigma E(2)$, obtained by summing the electron delocalization energies of all the significant interactions between the NBO orbitals of interacting molecules. The $\Sigma E(2)$ values are reported in Table 3. A larger $\Sigma E(2)$ means that the interactions, resulting from electron delocalization from donor to acceptor NBO between MET and radicals, are more important. As a consequence, $\Sigma E(2)$ values are a measure of the importance of chemical interaction between the investigated species. On the other side, lower $\Sigma E(2)$ might suggest electrostatic interaction between the studied species.
According to NBO results, the highest and the most important chemical interactions took place in the MET/O₂⁻/•OH system. This is consistent with above findings, which suggested that a new bond was formed in this system between the C4 atom of MET and •OH. The interactions resulting from electron delocalization from O₂⁻ to MET NBOs are significant, since ΣE(2) ≈ 28 kcal mol⁻¹. In contrast, chemical interactions resulting from electron delocalization from MET to O₂⁻ NBOs are insignificant. There is a significant electron delocalization from O₂⁻ to MET NBOs in the case of the MET/O₂⁻ system, as suggested by the quite elevated ΣE(2) ≈ 34 kcal mol⁻¹. This is the highest value of ΣE(2) among all the cases investigated in this work, and it clearly indicates a chemical interaction between O₂⁻ and MET. This means that dissolved oxygen, in addition to inhibiting e⁻–h⁺ recombination and enhancing, as a consequence, the occurrence and subsequent reactivity of •OH and h⁺, could further contribute to MET degradation through the formation of O₂⁻.

Fig. 12 Representative MEP surfaces of the investigated systems: a) MET; b) MET/O₂⁻; c) MET/O₂⁻/•OH; d) MET/O₂⁻/BrO⁻; and e) MET/O₂⁻/SO⁴⁻.
In the case of MET/O$_2^-$/BrO$_2^-$, the $\Sigma E(2)$ of electron delocalization from BrO$_2^-$ to MET NBOs is ca. 6 kcal mol$^{-1}$, which suggests weak chemical interaction when compared with previous cases. The chemical interaction between O$_2^-$/MET in this system turned out to be insignificant, as indicated by a $\Sigma E(2)$ value from O$_2^-$ to MET of only 0.64 kcal mol$^{-1}$.

While important chemical reaction between MET and BrO$_2^-$ seems to be excluded, it should be reminded that bromate was able to significantly enhance MET photocatalytic degradation in the case of Degussa P25. In this case, the effect of bromate should probably be ascribed to its mere ability to scavenge $e^-$, which inhibits the $e^-\cdot h^+$ recombination and enhances the occurrence and subsequent reactivity of "OH and h$^+$. Moreover, the enhancement effect with Degussa P25 combined with no bromate effect on TiO$_2$ Wackherr suggests that an important role in MET degradation could be played by different properties of the photocatalyst, lifetime of h$^+$ and concentration of radical species.

In the case of MET/O$_2^-$/SO$_4^{2-}$, the interactions between MET and the corresponding radicals would just be of an electrostatic nature, as suggested by the very low values of the $\Sigma E(2)$ energies, all below the default threshold of 0.05 kcal mol$^{-1}$. This result excludes chemical reactivity between MET and SO$_4^{2-}$, and it helps explaining the very limited effect of S$_2$O$_5^-$ on the photocatalytic degradation of MET. Indeed, electron scavenging by persulfate would be offset by drawbacks connected with SO$_4^{2-}$ formation (adsorption on the photocatalyst surface, which reduces the photocatalytic activity), while SO$_4^{2-}$ would not be able to favour degradation by significantly reacting with MET.

### 3.6. LC–ESI–MS/MS identification of degradation intermediates

By using the LC–ESI–MS/MS technique, intermediates of MET degradation in the presence of different electron acceptors (O$_2$, O$_2$/H$_2$O and O$_2$/KBrO$_3$) with both catalysts were investigated (see ESL$^3$, Fig. S1-S22 and Table S1). Intermediates formed in the absence of electron acceptors (systems with N$_2$) were not investigated because the rate of MET degradation was very low. Therefore, the concentration of intermediates was low as well and they couldn’t be identified. Because the collision-induced dissociation patterns of MET degradation were defined previously,$^9$ it was possible to identify the detected peaks by using the product ion MS$^2$ spectra. The retention times of all identified degradation intermediates P1–P10 (1.18–3.98 min) were shorter than that of MET (4.43 min), due to the cleavage of the molecule and the formation of polar moieties.

During the degradation of MET with TiO$_2$, Wackherr/O$_2$, a total of seven peaks (labeled P1–P7) corresponding to degradation intermediates were detected (ESI$^3$, Table S1 and Fig. 13). Intermediate P1 represents a compound with $M_{\text{rel}}=133$, indicating the presence of a nitrogen atom in its structure. Based on its fragmentation pattern (ESI$^3$, Table S1) and literature data, it was concluded that this compound is 3-[(propan-2-ylamino)propane-1,2-diol, already identified.$^{13}$

Intermediates P2 and P3 both correspond to compounds with $M_{\text{rel}}=253$, but with different MS$^2$ spectra. Based on MS$^2$ spectra and literature data,$^{13,60}$ it could be stated that P2 is hydroxy derivative 4-[2-hydroxy-3-[(propan-2-ylamino)propoxy]benzaldehyde, that was previously identified as MET degradation product. Fragment 212 (C$_{13}$H$_{22}$NO$_3$) present in P2, is formed by loss of water and isopropyl moiety, which was further dehydrated to the m/z 177 (i.e., loss of water and ethylene group). Radjenović et al. also identified this compound and they stated that the characteristic fragment ion m/z 133 was detected in the spectrum of the parent compound and degradation products,$^{60}$ which is also in agreement with our results. The herewith provided MS$^2$ spectra of P2 (Table S1) are in very good agreement with those previously reported.$^{13,60}$

It was not possible to determine the positions of the hydroxyls, due to the small number of fragments formed in MS$^2$ experiments. However, based on the theoretical results (Table 3 and Figs. 10 and 12), we can assume that "OH might be bonded to the C4 atom of the aromatic ring. Fragment 116 (C$_7$H$_{12}$ON) common to many MET degradation products, and observed in the MS$^2$ spectrum of P3, corresponds to N-(1-methyllethyl)-2-oxopropan-1-aminium and indicates the intact O-bound moiety i.e. hydroxylation of either benzene ring or C$_2$-chain. Ion 177 fragments by consecutive loss of water (m/z = 18) and ethene (m/z = 28), indicating the presence of an hydroxethyl moiety.

The presence of ion 159 fragments in MS$^2$ spectra of MET and

---

**Table 3. $\Sigma E(2)$ of interacting units between MET and radicals**

<table>
<thead>
<tr>
<th>System</th>
<th>Donor unit (NBOs of)</th>
<th>Acceptor unit (NBOs of)</th>
<th>$\Sigma E(2)$ [kcal mol$^{-1}$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET/O$_2^-$</td>
<td>MET</td>
<td>O$_2^-$</td>
<td>3.14</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
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<td>34.31</td>
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<td>0.23</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>OH</td>
<td>Bonded</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>MET</td>
<td>28.21</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>'OH</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>O$_2^-$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MET/O$_2^-$/BrO$_2^-$</td>
<td>MET</td>
<td>BrO$_2^-$</td>
<td>0.64</td>
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</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>BrO$_2^-$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>BrO$_2^-$</td>
<td>O$_2^-$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MET/O$_2^-$/SO$_4^{2-}$</td>
<td>MET</td>
<td>O$_2^-$</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>SO$_4^{2-}$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>SO$_4^{2-}$</td>
<td>MET</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>O$_2^-$</td>
<td>SO$_4^{2-}$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>SO$_4^{2-}$</td>
<td>O$_2^-$</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
P3 indicates preserved aromatic ring of MET. Detailed fragmentation of MET is described in the literature, where \( m/z \) 159 corresponds to the loss of 109 (18\(+42+17+32\)) mass units: water, propene, ammonia are lost from the right side and methanol from the left side of the chain.\(^\text{51}\) Thus, P3 represents either 

\[ 1-[4-(1-hydroxyethyl)phenoxyl]-3-(propan-2-ylamino)propan-2-ol or its 2-hydroxyethyl isomer. This compound was previously identified\(^\text{62,63}\) as the 1-hydroxyethyl isomer.

The three peaks, labelled P4, P5, and P6, corresponding to compounds with \( M_{m} = 281 \), were detected. Upon further evaluation of EICs for the observed fragment ions, it was determined that peak P4 contains two closely-eluting compounds labelled P4a and P4b. Due to close elution, it was impossible to obtain pure MS\(^2\) spectra of these compounds. Therefore, EIC traces for each ion had to be checked, to confirm the presence/absence of specific fragments in each chromatographic peak. To ease the comparison of spectra and interpretation, composite MS\(^2\) spectra were prepared by summing MS\(^2\) spectra obtained at different collision energies. Molecular mass, higher by 14 units than that of MET, implies the introduction of one oxygen and the abstraction of two \( \Delta m/z \) units. Early loss of isopropylamine and water (\( \Delta m/z = \) 42, yielding fragment 240) indicate the intact \( \text{P}^1\text{RNH}– \) moiety. There are five possible isomers of oxo-MET (excluding the one with oxygenated isopropyl), hereby designated A–E. Isomer A: 2-[4-[2-hydroxy-3-(propan-2-ylamino)propanoylethynyl]ethyl formate, isomer B: methyl [4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]acetate, isomer C: 1-[4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]-2-methoxyethanone, isomer D: 4-[2-methoxyethyl]phenyl-2-hydroxy-3-(propan-2-ylamino)propanoate, and isomer E: 2-hydroxy-3-[4-(2-methoxyethyl)phenoxyl]-N-(propan-2-yl)propanamide. Based on differences in observed spectra, we tentatively assigned structures to detected peaks. The loss of \( \text{H}_2\text{O} (\Delta m/z = 18, \) yielding fragment 264), was observable only in peak P6, and was followed by subsequent loss of propylamine (\( \Delta m/z = 59, \) yielding fragment 205). In all the other peaks the latter loss is immediate, and thus only ion 205 is observable, leading to the conclusion that ion 204 is stabilized in P6. Thus, we propose that P6 represents either isomer D or E, that would – after water loss – form an \( \alpha,\beta \)-unsaturated carboxyl compound, stabilized through electron delocalization. Peak P5 was characterized by the absence of two otherwise common ions for MET and derivatives: 135 (corresponding to ion produced by loss of \( \text{H}_2\text{O}, \) \( \text{iPrNH}_2 \), and phenyl-bound chain) and 116 (corresponding to loss of \( p \)-substituted phenoxy moiety). Fragment 177, produced by loss of 28 mass units (\( \text{CO},\text{C}_2\text{H}_4 \)) from ion 205, was also characteristic for this compound only. We concluded that CO loss is to be expected if ion 205 has 1-formyl-2-[4-(2-methoxyethyl)phenoxyl]ethenylum structure, i.e. if P5 could represent the isomer E (in that case, P6 would be the isomer D). The spectra of P4a and P4b differ from general pattern observed for P5 and P6 by much more pronounced fragments corresponding to loss of propene (\( \Delta m/z = 42 \)) or water and propylamine (\( \Delta m/z = 77 \)), and absence of otherwise common fragment 98 (either due to preferred loss of N-containing part as a neutral molecule, or due to low general abundance). Another common fragment, \( m/z \) 121, corresponding to protonated \( p \)-vinylphenol, was also absent in both peaks, which lead us to the conclusion that the oxidation possibly occurred at \( \alpha \)- and \( \beta \)-position of 2-methoxyethyl moiety, i.e. that peaks P4a and P4b possibly represent isomers B and C. The presence of abundant fragment 116 (corresponding to intact N-(1-methylethyl)-2-oxopropan-1-aminium, formed by cleavage of phenoxy bond) seems to support the assumption. However, at the moment, it was not possible to determine the exact oxygenation site for these two compounds.

In the presence of \( \text{H}_2\text{O}_2 \) three new intermediates were observed (P8, P9 and P10), while in the presence of \( \text{KBrO}_3 \) only P9 and P10 were detected. Intermediates P7 and P8 both have \( M_{m} = \) 299, which is by 32 mass units greater than for MET. This implies that they are dihydroxy MET derivatives.\(^\text{13,49}\) Significant differences in fragmentation patterns of the two compounds allow the determination of the positions of the hydroxyl groups.

Intermediate P7 was identified as 1-[4-[2-hydroxy-3-(propan-2-ylamino)propoxy]phenyl]-2-methoxyethan-1,2-diol. Initial loss of 62 mass units can be attributed to cleavage of the C-C bond between \( \text{CHOH} \) and \( \text{CH(OH)OCH}_3 \) units, leading to loss of methoxymethanol and formation of formyl group on benzene ring. Subsequent loss of propene (\( \Delta m/z = 42 \)) leads to formation of ion 196. This ion further fragments by cleavage of the Ph-O bond, to yield two complementary ions at \( m/z \) 74 and 105. Spectra of P8 are dominated by a series of fragments characteristic for MET – 159, 133, 116, 74, 72 and 56. Since these ions correspond to preserved \( \text{C}_2\text{H}_6\text{O}-\text{C}_2\text{H}_5\text{O}-\text{N} \) moiety (without any additional substitution, compared to MET), we assume that the two hydroxyls are located at peripheral groups – methoxy and/or propyl. The value of \( m/z = 282 \) corresponds to the parent compound after loss of water. However, it was not possible to determine where one or both hydroxyls are bound, due to the lack of any other diagnostic fragments. Intermediate P9 has \( M_{m} = 273 \), namely six mass units higher than MET. This is a consequence of \( \text{C}_6\text{H}_5 \) loss and the attachment of three hydroxyl groups. However, at lower \( m/z \) range, a series of fragments was observed – 116 (\( \text{C}_6\text{H}_4\text{NO} \)), 98 (\( \text{C}_6\text{H}_5\text{N} \)), 74 (\( \text{C}_6\text{H}_5\text{NO} \)), 56 (\( \text{C}_6\text{H}_5\text{N} \)) – corresponding to \( N-(1\text{-methylethyl})-2\text{-oxopropan-1-aminion} \) and its fragment, indicating a preserved 2-hydroxy-3-[1-methylethylaminio]propoxy group. Further fragmentation of ion 116 into 98 by the loss of water (\( \Delta m/z = 18 \)) supports the presumption that the three hydroxyls are bonded to the methoxyethylbenzene moiety. The absence of common ions 159, 133 and 121 supports the oxidative cleavage of benzene ring, with the loss of a \( \text{C}_2 \) unit. While this reaction was previously described,\(^\text{43}\) the hereby detected compound P9 exhibit MS\(^2\) spectra different from the published ones, indicating differences in the structure and suggesting that there are three OH groups bound to a benzene ring. This leads to the conclusion that the compound is a trihydroxy derivative of 1-amino-3-[4-(2-methoxyethyl)phenoxyl]propan-2-ol.

Intermediate P10, eluting at 1.57 min, corresponds to a compound with \( M_{m} = 315 \). The short retention time suggests that it is very polar, which would be accounted for by the three hydroxyl groups present in its structure, since its molecular mass is 48 mass units higher than that of MET.\(^\text{13}\) The fragments 116, 98, 74, and 56 in its MS\(^2\) spectra indicate that the propylaminopropene moiety stays intact, while the three hydroxyls are bonded to the methoxyethylbenzene part of the molecule. This compound has been previously identified as a trihydroxy derivative of 1-[4-(2-methoxyethyl)phenoxyl]-3-(propan-2-ylamino)propan-2-ol.\(^\text{13,49}\)
The occurrence of different intermediates under different conditions could be due to their different stabilities, and/or to differences in the degradation mechanism of MET. One issue could be the interaction of $\cdot\text{O}_2^-$ with MET (Table 3). Compared to the case of $\text{O}_2$ alone, the addition of $\text{H}_2\text{O}_2$ lowered such interaction by 1.2 times and that of $\text{KBrO}_3$ by 54 times. However, NBO analysis already suggested that in the case of MET degradation with Degussa P25, besides the reactive radicals, the properties of the catalyst and the lifetime of $\text{h}^+$ would play an important role. This issue was confirmed by the analysis of the mechanism. Namely, in the presence of Degussa P25/O$_2$, the intermediates P1, P3–P7, P9, and P10 were identified. Moreover, they were also identified in the presence of $\text{H}_2\text{O}_2$. This issue suggests that $\text{H}_2\text{O}_2$ in this case just increased the degradation rate of the parent compound (Fig. 1), which resulted in the faster formation of the intermediates because of an increased occurrence of $\cdot\text{OH}$. The intermediate P10 was not detected in the presence of $\text{KBrO}_3$, which might be due to the lower $\cdot\text{OH}$ concentration in the system.

Similarly to our previous work, here it was confirmed that different sets of MET intermediates are formed with different photocatalysts. Indeed, P2 and P8 were not detected in the presence of Degussa P25/O$_2$, while P8, P9 and P10 were not found with TiO$_2$ Wackherr/O$_2$. By comparing the O$_2$/H$_2$O$_2$ systems with Degussa P25, P2 and P8 were again not identified, while in the case of TiO$_2$ Wackherr all intermediates were identified. In the presence of O$_2$/KBrO$_3$ with Degussa P25 the intermediate P10 was absent, while in the presence of TiO$_2$ Wackherr P10 was present, but P8 was absent.

In the present work, a lower number of intermediates was detected in comparison with previous work. That is probably a consequence of the significantly lower concentration of MET (by 60 times) used in the present work, which prevented the formation of dimeric species. Moreover, the concentrations (peak areas) of some intermediates in this work were very low and thus their identification was not possible.

4. Conclusions

This study shows that TiO$_2$ is a very effective photocatalyst for MET degradation, in the presence of electron acceptors such as $\text{O}_2$, $\text{H}_2\text{O}_2$, and $\text{BrO}_3^-$. The effect of the investigated electron acceptors depends on their initial concentration and on the nature of the photocatalyst. Moreover, while enhancing the transformation of MET (at least with Degussa P25), $\text{H}_2\text{O}_2$ decreased the rate of MET mineralization with both TiO$_2$ types. This contrasting effect might be accounted for by differences in reaction pathways ($\text{h}^+$ vs. $\cdot\text{OH}$) induced by the photocatalysts with and without $\text{H}_2\text{O}_2$, as the $\cdot\text{OH}$ pathway (enhanced by $\text{H}_2\text{O}_2$) possibly did not favour the mineralization of the substrate. The same phenomenon could also account for the higher degree of mineralization achieved, without $\text{H}_2\text{O}_2$, as the $\cdot\text{OH}$ pathway (enhanced by $\text{H}_2\text{O}_2$) possibly did not favour the mineralization of the substrate. The same phenomenon could also account for the higher degree of mineralization achieved, without $\text{H}_2\text{O}_2$, as the $\cdot\text{OH}$ pathway (enhanced by $\text{H}_2\text{O}_2$) possibly did not favour the mineralization of the substrate. The same phenomenon could also account for the higher degree of mineralization achieved, without $\text{H}_2\text{O}_2$, as the $\cdot\text{OH}$ pathway (enhanced by $\text{H}_2\text{O}_2$) possibly did not favour the mineralization of the substrate.

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DFT calculations and NBO analysis suggested that \(^{\cdot}\text{OH}\) and possibly \(^{\cdot}\text{O}_2\) could undergo chemical reaction with MET. It is, therefore, suggested that dissolved oxygen would not only enhance \(^{\cdot}\text{OH}/h^+\) reactivity by scavenging \(^{\cdot}\text{e}^-\) and, therefore, inhibiting \(^{\cdot}\text{e}^-\text{h}^+\) recombination; oxygen could additionally favour MET degradation through the formation of \(^{\cdot}\text{O}_2\). In contrast, reaction between MET and \(\text{BrO}_2\) or \(\text{SO}_4^{2-}\) would be excluded. In the case of \(\text{SO}_4^{2-}\), the finding helps explaining the limited effect of addition to MET degradation: \(^{\cdot}\text{e}^-\) scavenging by \(\text{SO}_4^{2-}\) would be largely offset by the formation of sulfate in addition to \(\text{SO}_4^{2-}\). While sulfate decreases the photocatalytic activity by adsorbing on the surface of \(\text{TiO}_2\), \(\text{SO}_4^{2-}\) would not be able to take part in MET transformation. Interestingly, both DFT calculations and the approach based on Fukui functions and Fukui indices consistently suggested that \(^{\cdot}\text{OH}\) would react with the MET aromatic ring, and particularly with its C4 atom.

Experimental study by LC–ESI–MS/MS indicated binding of OH groups to different parts of MET, while results of theoretical analysis obtained in this investigation indicated binding of OH group to the aromatic ring. According to the theoretical results, bonding of OH group to the C4 atom of benzene ring of P2 was suggested. It was shown experimentally that the binding of OH groups does not occur on the propylaminopropene group chain (P8, P9, and P10) and that ring opening doesn’t occur as well, which is also in agreement with theoretical analysis. Besides, intermediates that are peculiar for the systems containing \(\text{H}_2\text{O}\) and KBrO3 were identified as well. Namely, P8, P9, and P10 were detected with \(\text{TiO}_2\) Wackheri/\(\text{O}_2\text{H}_2\text{O}\) and P9 and P10 with \(\text{TiO}_2\) Wackheri/\(\text{KBrO}_3\). While the same intermediates were identified with Degussa P25/O2 and Degussa P25/O2/H2O2, the intermediate P10 was not identified with Degussa P25/O2/KBrO3.

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