



## Photocatalytic degradation of metoprolol tartrate in suspensions of two TiO<sub>2</sub>-based photocatalysts with different surface area. Identification of intermediates and proposal of degradation pathways

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### ABSTRACT

This study investigates the efficiency of the photocatalytic degradation of metoprolol tartrate (MET), a widely used β<sub>1</sub>-blocker, in TiO<sub>2</sub> suspensions of Wackherr's "Oxyde de titane standard" and Degussa P25. The study encompasses transformation kinetics and efficiency, identification of intermediates and reaction pathways. In the investigated range of initial concentrations (0.01–0.1 mM), the photocatalytic degradation of MET in the first stage of the reaction followed approximately a pseudo-first order kinetics. The TiO<sub>2</sub> Wackherr induced a significantly faster MET degradation compared to TiO<sub>2</sub> Degussa P25 when relatively high substrate concentrations were used. By examining the effect of ethanol as a scavenger of hydroxyl radicals (<sup>•</sup>OH), it was shown that the reaction with <sup>•</sup>OH played the main role in the photocatalytic degradation of MET. After 240 min of irradiation the reaction intermediates were almost completely mineralized to CO<sub>2</sub> and H<sub>2</sub>O, while the nitrogen was predominantly present as NH<sub>4</sub><sup>+</sup>. Reaction intermediates were studied in detail and a number of them were identified using LC-MS/MS (ESI<sup>+</sup>), which allowed the proposal of a tentative pathway for the photocatalytic transformation of MET as a function of the TiO<sub>2</sub> specimen.

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### 1. Introduction

When speaking of pollutants in the environment one usually thinks of chemicals that are used to treat plants and soil, of radioactive wastes and of exhaust gases. Active components of drugs have slowly – one might say, 'by the back door', entered the environment, primarily aimed at helping people. The notion of active pharmaceutical ingredients (APIs) includes highly bioactive compounds that are used in the treatment or prevention of diseases, thanks to their reaction with specific targets in the animal or human body such as receptors or enzymes. Due to their increasing consumption, growing emissions of APIs affect the natural environment from hospitals, pharmaceutical industries or domestic waters. In the latter case, incorrect disposal of non-used or expired drugs and human excretions after partial metabolism of the drugs by the body are the main

pathways involved [1]. The use of antibiotics in cattle breeding is a further important route of pharmaceuticals to the environment [2].

APIs have been detected in ground and surface water [3–5], drinking water [6,7], ocean water, sediment and soil [8]. In the latest years there has been a tendency to synthesize drugs that are resistant to common biotransformation processes, with the purpose of protracting their persistence in the organism. However, very stable molecules are obtained as a result [9,10], the environmental occurrence of which, at either low or high concentrations, can bring harmful toxicological effects [11,12].

The metoprolol tartrate salt {MET, 1-[4-(2-methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol tartrate (2: 1)} is a selective β-blocker that is used to treat a variety of cardiovascular diseases, such as hypertension, coronary artery disease and arrhythmias [13]. MET is characterized by an increasing use in recent years and, as a consequence, its occurrence in aqueous effluents is expected to increase as well [14,15]. MET shows slow direct phototransformation and/or hydrolysis [16,17]. An efficient way to deal with this problem is the degradation of the drug by advanced oxidation processes (AOPs) based on the formation of hydroxy (<sup>•</sup>OH) and other radicals [18]. MET contains a secondary amine group and a weakly/moderately activated aromatic ring that are

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likely targets of molecular ozone and of  $\bullet\text{OH}$  [13]. Yang et al. investigated the degradation of selected  $\beta$ -blockers (atenolol, metoprolol and propranolol) in aqueous suspensions of  $\text{TiO}_2$  Degussa P25 and proposed a preliminary mechanism of degradation of these compounds [19]. Romero et al. have also investigated and compared the intermediates of the degradation of metoprolol and propranolol by AOPs [20].

The aim of this work was to make a detailed comparison of the kinetics and mechanism of photodegradation of MET, sensitized by  $\text{TiO}_2$  Wackherr and Degussa P25 in aqueous solutions under a variety of experimental conditions. The effects of the initial concentration of MET and of catalyst loading were studied, along with the presence of  $\bullet\text{OH}$  scavengers. An attempt has also been made to identify the intermediates formed during the photooxidation process and to propose possible reaction pathways for the photocatalytic degradation of MET in UV-irradiated aqueous suspensions of  $\text{TiO}_2$ .

## 2. Materials and methods

### 2.1. Chemicals and solutions

All chemicals were of reagent grade and were used without further purification. The drug ( $\pm$ )-Metoprolol(+)-tartrate salt,  $\geq 99\%$ , was purchased from Sigma–Aldrich; 85%  $\text{H}_3\text{PO}_4$  was purchased from Lachema, Neratovice; 96% ethanol was obtained from Centrohem, Stara Pazova; 99.8% acetonitrile (ACN) was a product of J.T. Baker. All solutions were made using doubly distilled water. The  $\text{TiO}_2$  Degussa P25 (75% anatase and 25% rutile, surface area  $50 \pm 1.0 \text{ m}^2 \text{ g}^{-1}$ , crystallite size about 20 nm, non-porous) and Wackherr's "Oxyde de titane standard" (100% anatase, surface area  $8.5 \pm 1.0 \text{ m}^2 \text{ g}^{-1}$ , crystallite size 300 nm, hereafter " $\text{TiO}_2$  Wackherr"), produced by the sulfate process were used as photocatalysts [21].

### 2.2. Photodegradation procedures

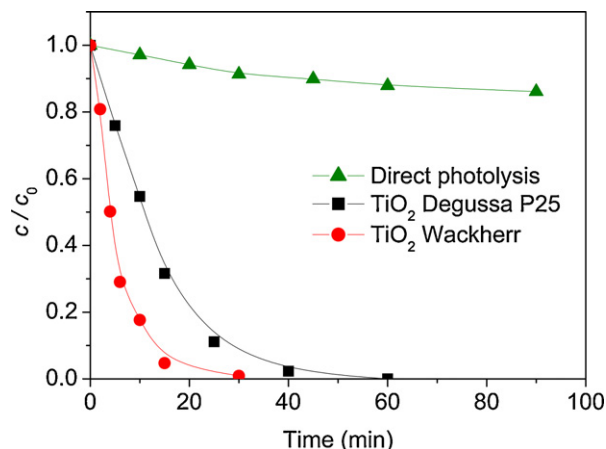
Photocatalytic degradation was carried out as described previously [22]. In a typical experiment, and unless otherwise stated, the initial MET concentration was 0.05 mM and the  $\text{TiO}_2$  loading (Degussa P25 or Wackherr) was  $1.0 \text{ mg mL}^{-1}$ . All experiments were performed at the natural pH (ca. 7).

### 2.3. Analytical procedures

For the LC–DAD kinetic studies of MET photodegradation, aliquots of 0.50 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,  $0.22 \mu\text{m}$ ) membranes. Lack of adsorption of MET on the filters was preliminarily checked. After that, a 20- $\mu\text{L}$  sample was injected and analyzed on an Agilent Technologies 1100 Series liquid chromatograph, equipped with an Eclipse XDB-C18 column ( $150 \text{ mm} \times 4.6 \text{ mm}$  i.d., particle size  $5 \mu\text{m}$ ,  $25^\circ\text{C}$ ). The UV/vis DAD detector was set at 225 nm (wavelength of MET maximum absorption). The mobile phase (flow rate  $0.8 \text{ mL min}^{-1}$ ) was a mixture of ACN and water, the latter acidified with 0.1%  $\text{H}_3\text{PO}_4$ , with the following gradient: 0 min 15% ACN which increased to 30% ACN in 5 min, after which 30% ACN was constant for 5 min; post time was 3 min. Reproducibility of repeated runs was around 3–10%.

Kinetics of the aromatic ring degradation was monitored spectrophotometrically at 225 nm [23].

For ion chromatographic determinations, aliquots of 3 mL of the reaction mixture were taken at regular time intervals, filtered through membrane filters and analyzed on an ion chromatograph



**Fig. 1.** Kinetics of the photolytic (no  $\text{TiO}_2$ ) and photocatalytic degradation of MET (initial concentration  $c_0 = 0.05 \text{ mM}$ ). When present, the  $\text{TiO}_2$  loading was  $1.0 \text{ mg mL}^{-1}$ .

Dionex ICS 3000 Reagent Free IC system with conductometric detector [22].

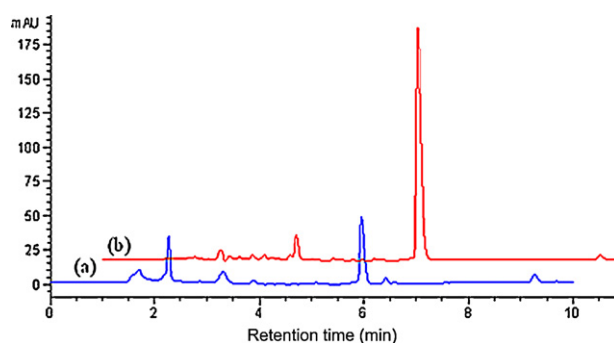
For the LC–MS/MS (ESI+) evaluation of intermediates, the initial MET concentration was 3 mM. The selected reaction monitoring (SRM) mode (parameters are given in Table 1) was used for obtaining peak areas of the analytes, in order to track the reaction kinetics. Detailed information on experimental conditions can be found in the Supplementary Material.

For total organic carbon (TOC) analysis, aliquots of 10 mL 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.

## 3. Results and discussion

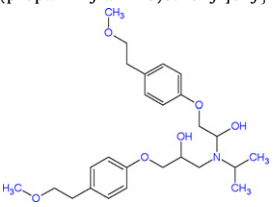
### 3.1. Effect of the kind of $\text{TiO}_2$

The photocatalytic activity of  $\text{TiO}_2$  Wackherr was compared to that of the most often used  $\text{TiO}_2$  Degussa P25 under UV irradiation (Fig. 1). Significant MET degradation could be observed under UV, and the process involving  $\text{TiO}_2$  Wackherr was significantly faster than direct photolysis or transformation with Degussa P25. Furthermore, the variety and amount of intermediates depended on the type of catalyst (Fig. 2). The faster degradation of MET with  $\text{TiO}_2$  Wackherr compared to Degussa P25 is an interesting result, although it is hardly unexpected [21,22,24]. Note that  $\text{TiO}_2$  Wackherr has much larger particles than Degussa P25 (3–4 times larger average radii in solution), which produces a surface area that is



**Fig. 2.** Chromatograms obtained after 10 min of MET ( $c_0 = 0.05 \text{ mM}$ ) degradation under UV irradiation in the presence of  $\text{TiO}_2$  Wackherr (a) and Degussa P25 (b).  $\lambda_{\text{det}} = 225 \text{ nm}$ ,  $t_{\text{R}}(\text{MET}) = 5.8 \text{ min}$ .

**Table 1**  
Intermediates proposed structures for the photocatalytic degradation of MET.

Compound	Precursor ion [M+H] <sup>+</sup>	Molecular formula	Name of compound	Collision energy (%)	MS <sup>2</sup> product ion (m/z, % rel. abundance)	Collision energy for MS <sup>2</sup> product ion	MS <sup>3</sup> product ion <sup>§</sup> (m/z, % rel. abundance)
1	268	C <sub>15</sub> H <sub>25</sub> NO <sub>3</sub>	1-[4-(2 methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol	35	116(51), 159(25), 176(26), <b>191(100)</b> , 218(66), 226(29), 250(26)	30	159(100)
2	134	C <sub>6</sub> H <sub>15</sub> NO <sub>2</sub>	3-(propan-2-ylamino)propane-1,2-diol	30	74(21), 92(64), <b>116(100)</b>	28	72(100)
3	282	C <sub>15</sub> H <sub>23</sub> NO <sub>4</sub>	4-(2-methoxyethyl)phenyl	33	116(23), <b>159(100)</b> , 176(24), 205(48), 240(59), 264(34)	33	131(100), 141(31)
4	298	C <sub>15</sub> H <sub>23</sub> NO <sub>5</sub>	2-hydroxy-3-(propan-2-ylamino)propanoate Hydroxy derivative 4-(2-methoxyethyl)phenyl 2-hydroxy-3-(propan-2-ylamino)propanoate	33	116(42), 175(21), 252(38) 256(33), 266(51), <b>280(100)</b>	32	120(22), 147(24), 175(91), 176(65), 192(100), 221(23), 252(22)
5	314	C <sub>15</sub> H <sub>23</sub> NO <sub>6</sub>	Dihydroxy derivative 4-(2-methoxyethyl)phenyl 2-hydroxy-3-(propan-2-ylamino)propanoate	32	264(20), <b>282(100)</b> , 286(35) 296(99)	33	176(25), 210(62), 236(44), 238(75), 252(100), 264(38)
6*	330	C <sub>15</sub> H <sub>23</sub> NO <sub>7</sub>	Trihydroxy derivat 4-(2-methoxyethyl)phenyl 3-[(1-methylethyl)amino]propanoate	32	134(45), 215(21), 284(27), 286(40), 298(29), 302(56), <b>312(100)</b> , 330(34)		
7	284	C <sub>15</sub> H <sub>25</sub> NO <sub>4</sub>	Hydroxy derivative 1-[4-(2 methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol	33	116(94), 175(48), 191(43), 207(52), 234(39), 242(19), <b>266(100)</b>	31	191(23), 192(36), 207(23), 234(100)
8	300	C <sub>15</sub> H <sub>25</sub> NO <sub>5</sub>	Dihydroxy derivative 1-[4-(2 methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol	35	250(26), 258(84), 268(55), <b>282(100)</b> , 300(22)	33	240(28), 250(100), 264(20)
9	316	C <sub>15</sub> H <sub>25</sub> NO <sub>6</sub>	Trihydroxy derivat 1-[4-(2 methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol	33	116(27), 274(85), <b>298(100)</b>	30	98(100), 256(23), 266(55), 280(69), 298(28)
10	332	C <sub>15</sub> H <sub>25</sub> NO <sub>7</sub>	Tetrahydroxy derivat 1-[4-(2 methoxyethyl)phenoxy]-3-(propan-2-ylamino)propan-2-ol	30	282(46), 300(44), <b>314(100)</b>	28	282(100), 296(47)
11	252	C <sub>14</sub> H <sub>21</sub> NO <sub>3</sub>	1-(4-ethenylphenoxy)-3-(propan-2-ylamino)propane-1,2-diol	33	133(24), <b>175(100)</b> , 210(59), 220(21), 234(32)	28	147(100)
12	238	C <sub>13</sub> H <sub>19</sub> NO <sub>3</sub>	4-[2-hydroxy-3-(propan-2-ylamino)propoxy]benzaldehyde	33	161(64), <b>196(100)</b> , 220(32)	28	74(34), 161(100), 178(49)
13	254	C <sub>13</sub> H <sub>19</sub> NO <sub>4</sub>	Hydroxy derivative 4-[2-hydroxy-3-(propan-2-ylamino)propoxy]benzaldehyde	34	116(22), <b>177(100)</b> , 212(45), 236(22)	34	159(100)
14**	337	C <sub>18</sub> H <sub>28</sub> N <sub>2</sub> O <sub>4</sub>	Hydroxy derivative (4-[(1E)-3-(propan-2-ylamino)prop-1-en-1-yl]oxy)phenyl){[(E)-2-(propan-2-ylamino)ethenyl]oxy}methanol	35	260(24), 278(20), 295(45), 300(20), <b>319(100)</b>	29	234(86), 259(62), 291(22), 301(100), 319(22)
15**	462	C <sub>26</sub> H <sub>39</sub> NO <sub>6</sub>		30	388(24), 430(70), <b>444(100)</b> , 461(23)	30	270(46), 308(31), 322(30), 360(44), 382(33), 398(44), 412(100), 426(62)

\* Intermediates in case of TiO<sub>2</sub> Wackherr.

\*\* Intermediates in case of Degussa P25.

§ Precursor ion is marked with bold.

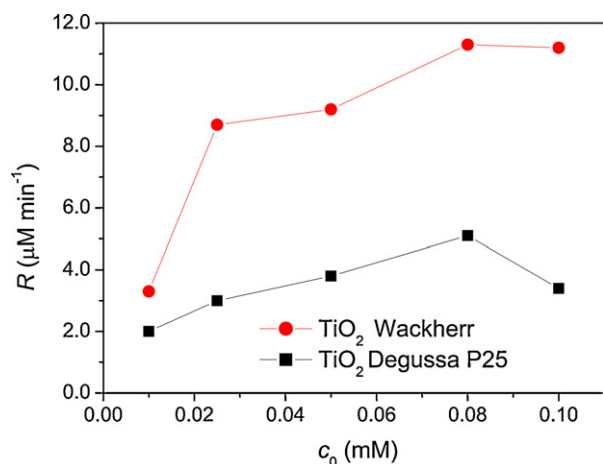


Fig. 3. Effect of the initial MET concentration ( $c_0$ ) on the initial rate of its decomposition ( $R$ ) determined for the first 10 and 20 min of irradiation in the case of  $\text{TiO}_2$  Wackherr and Degussa P25, respectively.  $\text{TiO}_2$  loading was  $1.0 \text{ mg mL}^{-1}$ .

almost six times lower [21]. However, the higher radiation scattering by Degussa P25 compared to  $\text{TiO}_2$  Wackherr ensures that the former photocatalyst is less efficient in using radiation [21,24]. Furthermore, the photocatalytic degradation rates are often decreased by the so-called back reactions, which operate the reduction of partially oxidized transients to give back the initial substrate [21,24]. There is evidence that the back reactions are more important in the case of Degussa P25 than for  $\text{TiO}_2$  Wackherr [21,22, and *vide infra*]. The combination of more efficient use of radiation and slower back reactions could compensate for the lower surface area of  $\text{TiO}_2$  Wackherr, and account for the higher initial reaction rates.

Fig. 1 shows that MET can be degraded by direct photolysis, which was however significantly slower than the photocatalytic processes. It should also be considered that radiation absorption and scattering by  $\text{TiO}_2$  can substantially inhibit direct photolysis under photocatalytic conditions [25]. In the presence of a  $\text{TiO}_2$  loading of  $1.0 \text{ mg mL}^{-1}$ , UV absorption by diluted species in solution can safely be neglected [21,22]. Therefore, one expects a negligible rate of MET direct photolysis under the adopted photocatalytic conditions.

The curves shown in Fig. 1 were the basis to calculate the initial rate ( $R$ ) of MET degradation, in the context of a pseudo-first order kinetics. In the presence of  $\text{TiO}_2$  Wackherr,  $R$  was approximately 2.5 times higher than with Degussa P25 ( $R(\text{Wackherr}) = 9.2 \text{ } \mu\text{M min}^{-1}$ , irradiation time up to 10 min, vs.  $R(\text{Degussa P25}) = 3.8 \text{ } \mu\text{M min}^{-1}$ , irradiation time up to 20 min). The direct photolysis rate ( $R = 0.1 \text{ } \mu\text{M min}^{-1}$ , irradiation time up to 20 min) was about two orders of magnitude lower than  $R(\text{Wackherr})$ . Details of the kinetic treatment are given in the Supplementary Material.

MET is remarkably stable in aqueous solution: no modification was observed in a MET solution kept in the dark for 550 days, which allows excluding e.g. hydrolysis as a significant transformation pathway.

### 3.2. Effect of the initial concentration of MET

The rate of photocatalytic degradation increased with increasing MET concentration from 0.01 to 0.08 mM (Fig. 3). In the case of  $\text{TiO}_2$  Wackherr the rate reached a plateau above 0.08 mM MET, while with  $\text{TiO}_2$  Degussa P25 the maximum rate was observed for 0.08 mM MET.

A saturative rate trend with increasing MET concentration could be accounted for by the scavenging of reactive species by the

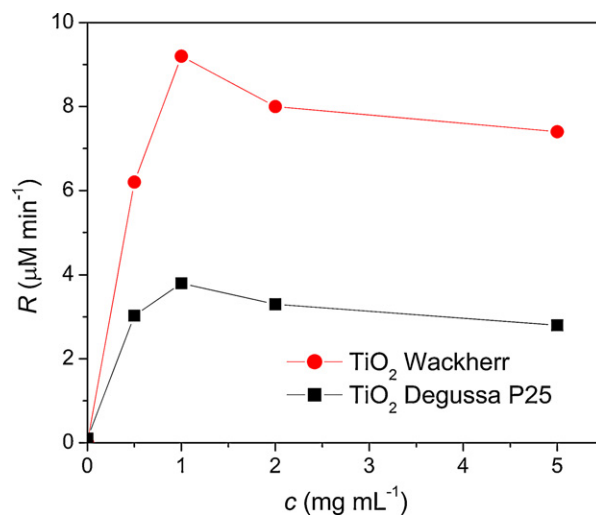


Fig. 4. Influence of  $\text{TiO}_2$  loading on MET ( $c_0 = 0.05 \text{ mM}$ ) degradation rate determined for the first 10 min irradiation (in the case of  $\text{TiO}_2$  Wackherr) and 20 min irradiation (in the case of  $\text{TiO}_2$  Degussa P25).

substrate. The reaction of MET with  $\bullet\text{OH}$  and  $\text{h}^+$  on the surface of  $\text{TiO}_2$  is in competition with the thermal recombination processes  $\bullet\text{OH}/\text{e}^-$  and  $\text{h}^+/\text{e}^-$ . An excess of the substrate would completely inhibit the recombination reactions, so that the rate of substrate degradation could at most be equal to the trapping rate of  $\bullet\text{OH}$  and  $\text{h}^+$  on the  $\text{TiO}_2$  surface [26–28]. However, this explanation could not account for the maximum that was observed in  $R$  vs.  $c_0$  with Degussa P25. The decrease of  $R$  with  $c_0$  after the maximum is usually accounted for by recombination reactions between partially oxidized transients and the conduction-band electrons [29]. Organic compounds usually require the loss of pairs of electrons to yield stable oxidation intermediates. Abstraction of one electron from the substrate would yield a radical transient, which could either undergo further oxidation to a non-radical intermediate, or react with an electron to give back the initial substrate. The second process, so-called back or recombination reaction, is favored by elevated substrate concentration and accounts for the decrease with increasing substrate of the initial transformation rates [24,29].

The trends observed in Fig. 3 suggest that the back reactions are more important in the case of Degussa P25 compared to Wackherr. Note that MET degradation rates do not differ much among the two photocatalysts for 0.01 mM substrate, while the difference becomes considerable at higher MET concentrations. Most of the transformation rate difference between Wackherr and Degussa P25 at, say, 0.05 mM MET or higher, would thus be accounted for by the back reactions. Similar results have been observed in the case of benzoic acid and of picloram [21,22].

### 3.3. Effect of catalyst loading

The trend of MET degradation rate with photocatalyst loading, in the range from 0.5 to  $5.0 \text{ mg mL}^{-1}$ , was similar for both  $\text{TiO}_2$  Wackherr and Degussa P25 (Fig. 4). In both cases the degradation rate was maximum for a  $\text{TiO}_2$  loading of  $1 \text{ mg mL}^{-1}$ , but it was significantly higher with  $\text{TiO}_2$  Wackherr. The most likely reason for the difference between the two photocatalysts is that the back reactions (at 0.05 mM MET) affect Degussa P25 more than  $\text{TiO}_2$  Wackherr.

One might think that an increase of the catalyst loading above an optimum has no effect on the photodegradation rate, because all the light available is already utilized. However, a higher  $\text{TiO}_2$  loading leads to an aggregation of the photocatalyst particles that decreases the contact surface area between reactant and photocatalyst. The

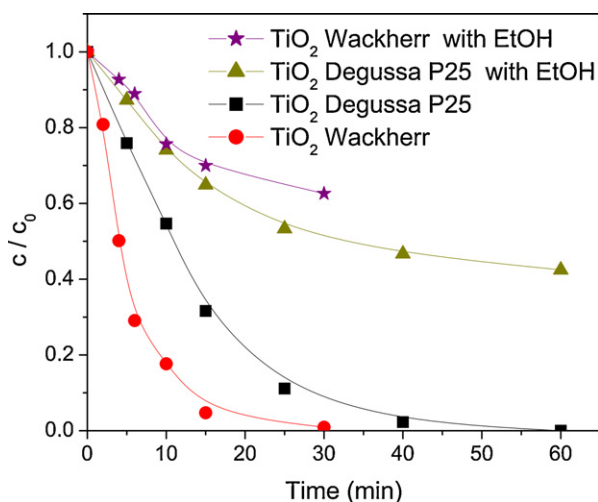


Fig. 5. Effect of 0.34 M ethanol on MET ( $c_0 = 0.05$  mM) degradation in the presence of TiO<sub>2</sub> (1 mg mL<sup>-1</sup>).

consequence is a decrease of the number of active sites and a lower rate of photodegradation. Moreover, the increase of the solution turbidity and of light dispersion by the particles may also produce a lower degradation rate [21,30,31].

#### 3.4. Effect of ethanol as hydroxyl radical scavenger

To check whether the photocatalytic degradation of MET takes place via  $\cdot\text{OH}$ , ethanol (400  $\mu\text{L}$ , *i.e.* 0.34 M in the final solution) was added to the reaction mixture containing MET and TiO<sub>2</sub>. The results presented in Fig. 5 show that ethanol considerably inhibits degradation. With Degussa P25, the reaction was about three times slower with ethanol ( $R = 1.2 \mu\text{M min}^{-1}$ ) than in the absence of the alcohol ( $R = 3.8 \mu\text{M min}^{-1}$ ). In the case of TiO<sub>2</sub> Wackherr the difference was even more marked: the rate with ethanol ( $R = 1.4 \mu\text{M min}^{-1}$ ) was seven times lower than without ethanol ( $R = 9.2 \mu\text{M min}^{-1}$ ).

Photocatalytic processes can involve either reaction between the substrate and surface-adsorbed  $\cdot\text{OH}$ , or direct charge-transfer with valence-band holes [21]. Aromatic compounds are usually reactive with both  $\cdot\text{OH}$  and holes, while addition of alcohols or glycols is a good strategy to selectively block the  $\cdot\text{OH}$ -mediated processes. Indeed, alcohols are usually poorly reactive toward the holes [32,33].

The experimental data suggest that the photocatalytic degradation of MET mainly proceeds via  $\cdot\text{OH}$ , especially for TiO<sub>2</sub> Wackherr, while valence-band holes are expected in both cases to play a secondary role. However, the more marked ethanol effect on TiO<sub>2</sub> Wackherr compared to Degussa P25 suggests that holes might be somewhat more important for P25. A similar issue has already been observed with picloram [22]. A possible reason for this behavior may derive from the different composition of the two photocatalysts, because TiO<sub>2</sub> Wackherr is 100% anatase while Degussa P25 contains some 25% rutile [21]. However, the possible connection between crystalline phase and degradation pathways is still very unclear and needs additional studies.

The importance of the holes in the degradation over both photocatalysts is expected to be higher for MET than for picloram, for which the addition of ethanol had caused a definitely more marked inhibition of transformation [22]. Usually, reaction with holes is more important for hydrophobic compounds that are repelled from the aqueous solution and are thus more likely to undergo adsorption on the photocatalyst surface [34]. The longer lateral chain of MET compared to picloram could possibly account for a higher degree of surface adsorption and hole reaction.

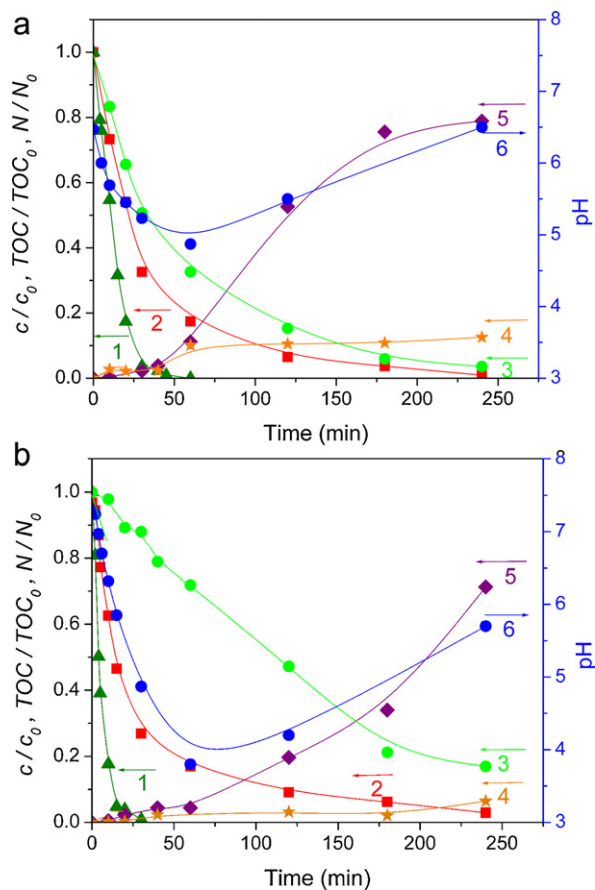


Fig. 6. Photocatalytic degradation of MET ( $c_0 = 0.05$  mM) in the presence of TiO<sub>2</sub> Degussa P25 (a) and TiO<sub>2</sub> Wackherr (b). (1) Disappearance of MET (LC-DAD,  $\lambda = 225$  nm); (2) disappearance of the aromatic ring (spectrophotometry,  $\lambda = 225$  nm); (3) TOC trend; (4) evolution of NO<sub>3</sub><sup>-</sup>; (5) evolution of NH<sub>4</sub><sup>+</sup>; (6) pH trend. TOC<sub>0</sub> and N<sub>0</sub> denote the overall initial amounts of organic carbon and of nitrogen in MET, respectively.

#### 3.5. Evaluation of the degree of mineralization

MET contains a secondary amino group, thus it could be expected that NH<sub>4</sub><sup>+</sup> and/or NO<sub>2</sub><sup>-</sup>/NO<sub>3</sub><sup>-</sup> ions might be formed in the photocatalytic degradation [35]. Both ammonium and nitrate were monitored, and the ammonium concentration was much higher (Fig. 6a and b, curves #5, compared to curves #4 for nitrate). After irradiation for 120 min, 63% of nitrogen was transformed in the presence of Degussa P25 and only 23% in the presence of TiO<sub>2</sub> Wackherr. The respective shares of ammonium were 53% and 20% of the total initial nitrogen.

Fig. 6a and b also reports the aromatic ring degradation (curves #2) that was determined spectrophotometrically on the basis of the ratio of peak heights at 225 nm, at a given time and before irradiation. It measures the proportion of MET and its intermediates with an aromatic ring to the initial amount of MET. The degradation of the aromatic ring was about 2.5 times slower than MET disappearance with Degussa P25, and even four times slower with TiO<sub>2</sub> Wackherr, which indicates the presence of different intermediates with an aromatic ring. Such intermediates were formed in higher amount with TiO<sub>2</sub> Wackherr than with Degussa P25, coherently with the chromatograms reported in Fig. 2a and b.

The pH monitoring during a photocatalytic process gives a valuable insight into the net changes occurring in the investigated system, although the change in pH directly corresponds to the degradation kinetics only in the case of much simpler molecules than MET [36]. As can be seen in Fig. 6a and b (curves #6), there was

an initial pH drop during the first hour of irradiation, possibly due to the formation of acidic intermediates. The pH value decreased down to 4 in the case of TiO<sub>2</sub> Wackherr and to 5 in the case of Degussa P25. Interestingly, the pH increase after the 1-h minimum had a parallel trend to the time evolution of ammonium, coherently with previous findings that the release of NH<sub>4</sub><sup>+</sup> under photocatalytic conditions consumes H<sup>+</sup> [37].

TOC measurements showed that, after complete MET removal, about 33% of organic compounds (measured as organic carbon) still remained in the system with Degussa P25, and 89% with TiO<sub>2</sub> Wackherr. After 240 min irradiation, the percentage of remaining organic compounds decreased to 4% for Degussa P25 and 17% for TiO<sub>2</sub> Wackherr.

Based on all the above, it can be concluded that TiO<sub>2</sub> Wackherr is more efficient as catalyst in the degradation of MET itself, whereas the complete mineralization is faster in the presence of Degussa P25. Note that substrate degradation and complete mineralization are rather different phenomena that are influenced by different photocatalyst features. The initial degradation rate of a substrate is driven by its reactivity with the active sites present on the catalyst surface and also depends on the number of these sites. The resulting degradation rate can be decreased to a variable extent by the back reactions, which lead to the recombination of the partially oxidized radicals with conduction-band electrons [24,30]. The less important role of back reactions would largely account for the faster MET disappearance with TiO<sub>2</sub> Wackherr. In contrast, mineralization is a target that requires quite a long time to be reached and that can be influenced by additional processes, which could not be operational in the early stages of the reaction. One of these processes could be the poisoning of the catalyst surface upon adsorption of certain reaction intermediates/products, which could inhibit further degradation reactions [38]. Poisoning is expectedly more problematic for photocatalysts with lower surface area (such as TiO<sub>2</sub> Wackherr), which have a lower number of active sites that could more easily be blocked. A reasonable consequence could thus be the slower MET mineralization with TiO<sub>2</sub> Wackherr compared to Degussa P25.

### 3.6. Intermediates and mechanism of photodegradation

The degradation of organic pollutants is often accompanied by the formation of intermediates that can potentially be harmful to the environment [39,40]. To detect and identify potential intermediates, use was made of the LC–DAD and LC–MS/MS techniques. On the basis of the chromatograms shown in Figs. 2a and b and 7 it can be concluded that a number of compounds were formed. The identified intermediates (Fig. 7 and Table 1) and the kinetic results (Fig. 8) allowed for the proposal of a possible mechanism for MET photocatalytic degradation (Fig. 9).

Fig. 7 gives the LC–MS chromatograms of MET and its intermediates registered after 240 min of photocatalytic degradation in the presence of Degussa P25 and/or TiO<sub>2</sub> Wackherr (some of the detected intermediates were specific of a particular photocatalyst). Fig. 8 shows the kinetics of formation/disappearance of the intermediates upon irradiation. The figure shows that intermediates **2**, **5**, **8**, **9** and **10** formed in larger amounts in the case of Degussa P25, whereas compounds **3**, **7**, **11**, **12** and **13** were more concentrated in the presence of TiO<sub>2</sub> Wackherr. Compound **4** was present at approximately equal concentration in both cases. Compound **6** was peculiarly identified only with TiO<sub>2</sub> Wackherr and only after 240 min irradiation. In contrast, compounds **14** and **15** were detected only with Degussa P25.

The different kinetics and the detection of peculiar intermediates with the two photocatalysts suggest that the degradation pathways with TiO<sub>2</sub> Wackherr and Degussa P25 might not be

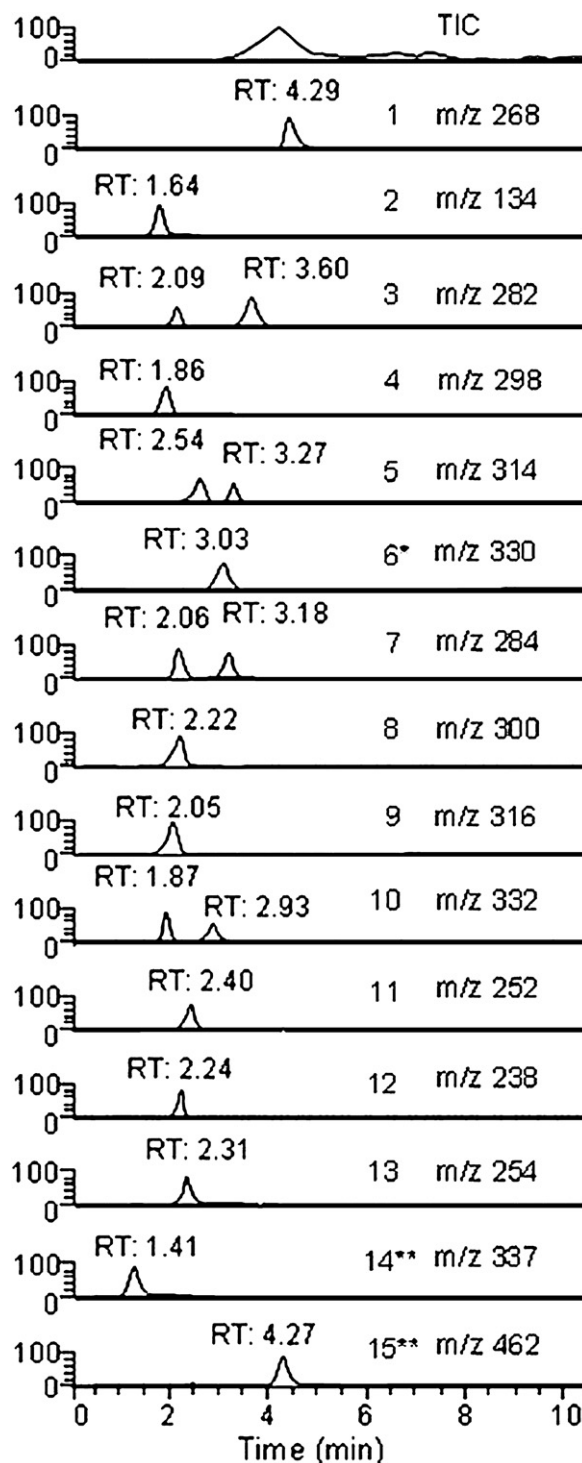
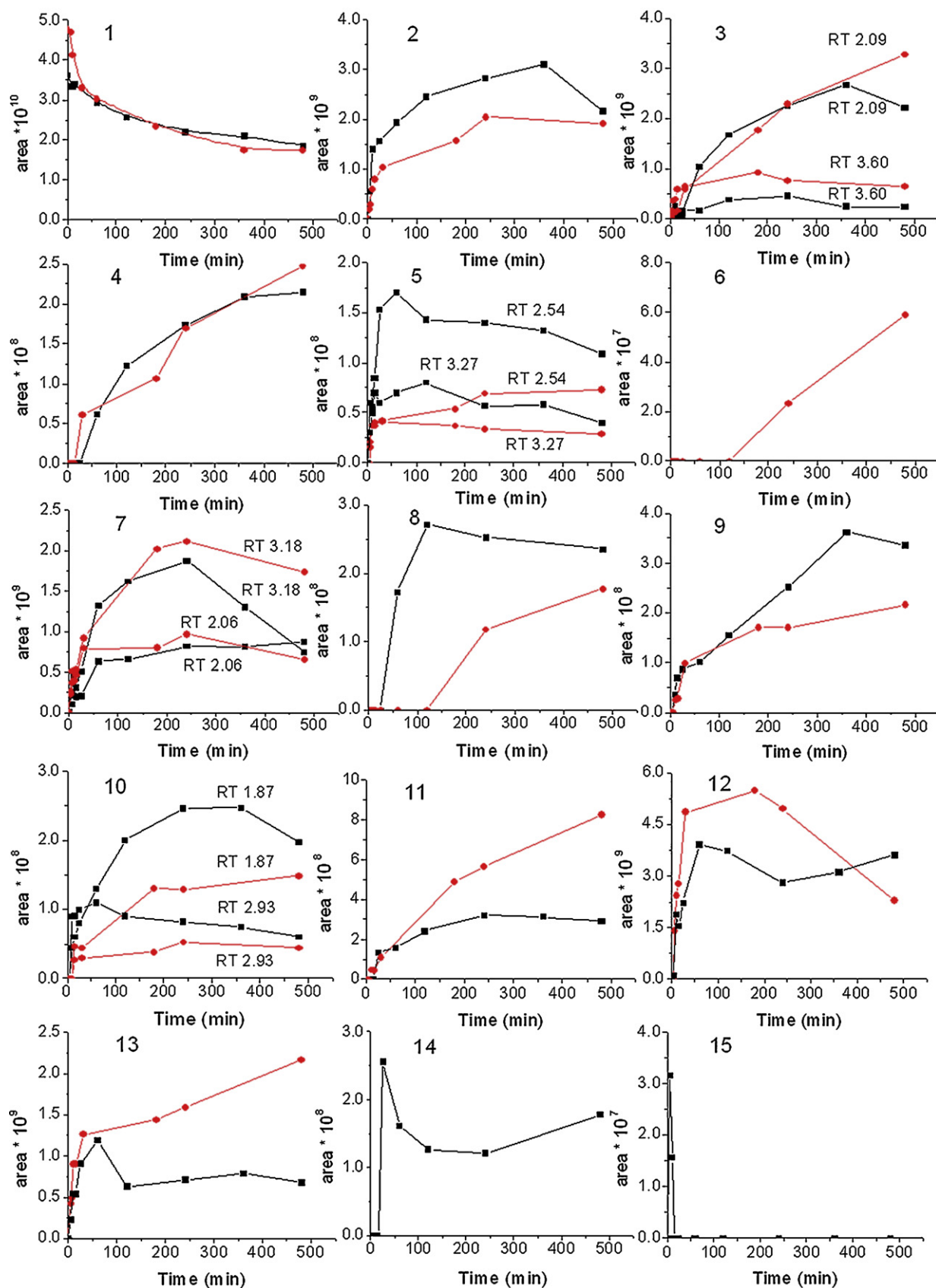


Fig. 7. LC–MS total ion chromatogram (TIC) and extracted ions chromatograms of MET and its intermediates, obtained after 240 min of MET photocatalytic degradation (3 mM). The numbers (1–15) correspond to compounds in Table 1. \* only found with TiO<sub>2</sub> Wackherr, \*\* only found with TiO<sub>2</sub> Degussa P25.

identical. On the basis of the identified intermediates and kinetic data, we propose a tentative scheme of MET photocatalytic degradation (Fig. 9).

In a first stage, after the breaking of a C–C bond in the aliphatic part of the MET molecule (**1**), amino-diol **2** was identified as one of the dominant intermediates. Intermediate **2** was also identified by Yang et al. and Romero et al. [19,20]. The attack of •OH on the C atom next to the ether oxygen and the oxidation of the



**Fig. 8.** Kinetics of the photocatalytic degradation of MET (1) and of the appearance/disappearance of the intermediates (2–15), detected by LC-MS/MS (ESI+). ● TiO<sub>2</sub> Wackherr, ■ Degussa P25.

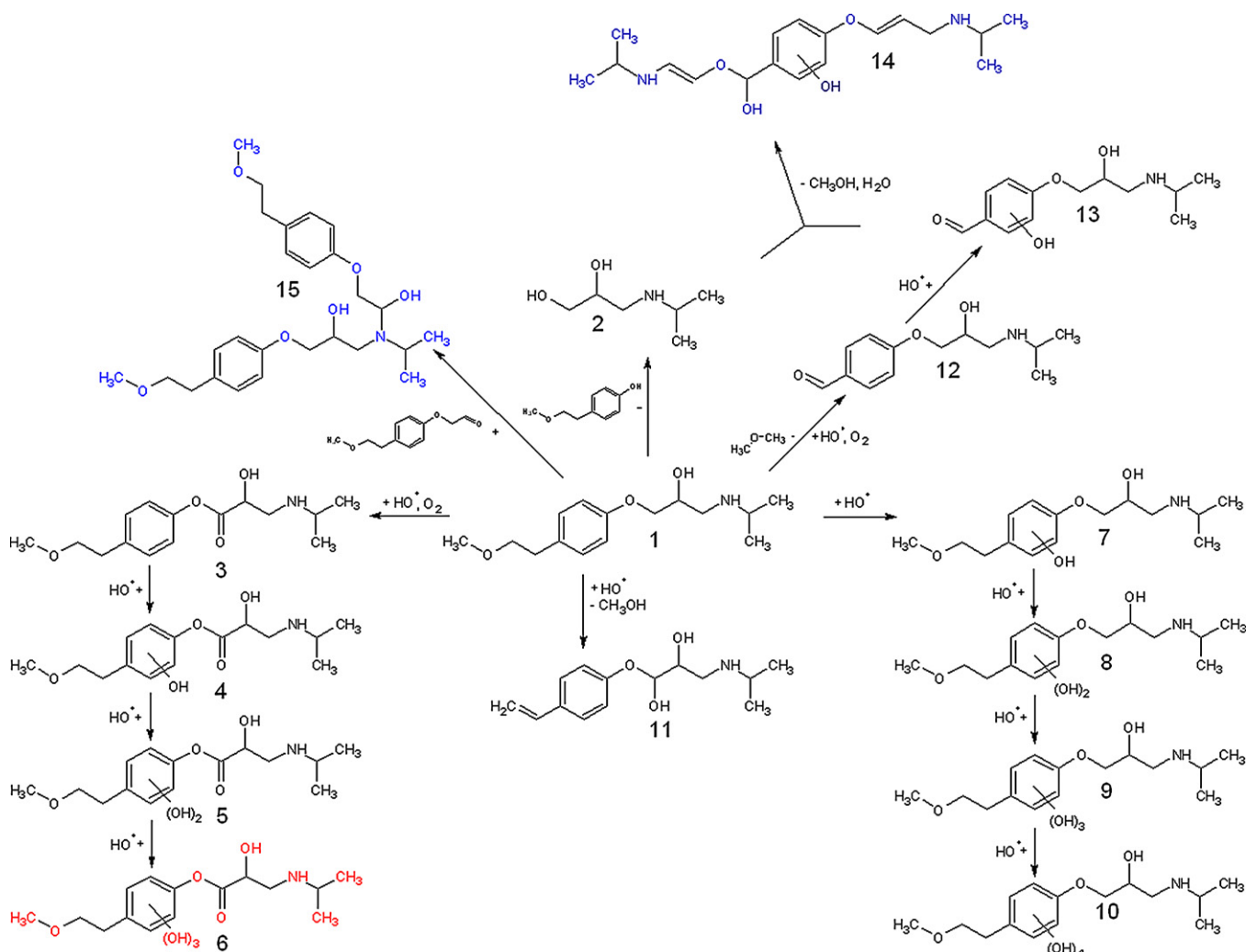


Fig. 9. Tentative pathways for the photocatalytic degradation of MET. Note that **6** was only identified with TiO<sub>2</sub> Wackherr, **14** and **15** only with Degussa P25.

hydroxyl group yields the keto-tautomer **3**, which forms two peaks at retention times 2.09 and 3.60 min (Fig. 7). Such a reaction mechanism via keto-enol tautomers has been previously reported for the photo-Fenton degradation of diclofenac [5]. In the case of TiO<sub>2</sub> photocatalytic degradation the enol tautomer was more abundant than the keto derivative, whereas in photo-Fenton experiments they have been detected in comparable amounts [41].

The •OH attack on the C atoms of the aromatic ring of **3** yielded the hydroxy (**4**) and dihydroxy (**5**) intermediates with both catalysts, and the trihydroxy intermediate (**6**) only in the case of TiO<sub>2</sub> Wackherr. Similarly, the binding of •OH to the benzene ring of the MET molecule resulted in the mono- (**7**), di- (**8**), tri- (**9**) and tetrahydroxy (**10**) intermediates. Based on the LC-MS/MS chromatograms (Fig. 7), the peaks of intermediate **7** appear at two retention times, viz. 2.06 and 3.18 min, probably because a hydroxyl group can be bound to both the *ortho* and *meta* positions of the aromatic ring with respect to the methoxyethyl group. Intermediates **7**–**10** were also identified by Yang et al. [19]. On the other hand, Romero et al. identified an intermediate with *m/z* (+) 300 that would correspond to our intermediate **8**, but they proposed a different structure that involved the opening of the aromatic ring [20].

The intermediate **11** could be formed by the loss of methanol combined with the attack of •OH on the C atom next to the ether oxygen in the aliphatic part of MET.

The intermediate **12** could be formed by loss of the ether group, H-abstraction, possibly upon •OH radical attack on the alkyl group, and O-atom addition. Attack of •OH on the aromatic ring of **12** could yield the hydroxylated intermediate **13**. There are two possible positions where the •OH attack could take place, thus one might expect to find two chromatographic **13** peaks as in the case of **7**. The fact that only one peak was found for **13** is probably a consequence of the fact that the –CHO substituent on the **12** aromatic ring has an electron-withdrawing and *meta*-orientating character, while the other substituent is an alkoxy group with an electron-donating and *ortho/para* orientating character [41]. The effects of both substituents would favor the •OH attack on the *meta* position to the –CHO group.

During degradation with Degussa P25, it is likely that compound **2** reacts with intermediate **13** and, upon release of methanol and water, produces intermediate **14**. Another intermediate identified with Degussa P25 alone is the dimeric species **15**, in agreement with the work of Kumar et al. [42]. However, this intermediate appeared only at the beginning of the degradation, when MET concentration was high.

Compounds **14** and **15** were identified in the presence of Degussa P25 but not with TiO<sub>2</sub> Wackherr. It has been shown previously that the reaction with h<sup>+</sup> was definitely more important for TiO<sub>2</sub> Degussa P25 than for Wackherr, and it is thus possible



that the formation of **14** and **15** involves reaction with  $h^+$ . Reaction with  $\bullet\text{OH}$  is expected to be slightly more important for  $\text{TiO}_2$  Wackherr than for Degussa P25. Coherently, the intermediate (**6**) that was only observed with  $\text{TiO}_2$  Wackherr is a polyhydroxylated compound that would likely be produced by the  $\bullet\text{OH}$  reaction.

All the intermediates underwent final degradation to  $\text{CO}_2$ ,  $\text{H}_2\text{O}$ ,  $\text{NH}_4^+$  and  $\text{NO}_3^-$ . The formation of  $\text{CO}_2$  and  $\text{H}_2\text{O}$  was postulated on the basis of TOC measurements (Fig. 6a and b, curves #3), and the complete mineralization was attained after over 4 h irradiation.

#### 4. Conclusions

The efficiency of the photocatalytic degradation of MET was studied in  $\text{TiO}_2$  suspensions of Degussa P25 and Wackherr. The degradation over both photocatalysts was considerably faster than the direct UV photolysis, and faster transformation was observed with  $\text{TiO}_2$  Wackherr compared to Degussa P25. In both cases MET was mineralized after about 4 h irradiation, and mineralization was faster with Degussa P25 despite the slower initial degradation rate. The mechanism of photocatalytic degradation was investigated in detail. Fourteen intermediates were identified by LC–MS/MS (ESI+). Hydroxylation of the aromatic ring, shortening of the methoxyl-containing lateral chain and cleavage of, or addition of  $\bullet\text{OH}$  to, the amine-containing one are the main pathways involved in the photocatalytic degradation process. In the case of Degussa P25, species arising from dimerization or combination of intermediates were also identified. The MET nitrogen atoms were converted predominantly into  $\text{NH}_4^+$ , and to a lesser extent into  $\text{NO}_3^-$ .

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#### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jhazmat.2011.10.017.

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