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Review

Reactions of chlorine with inorganic and organic compounds during water treatment—Kinetics and mechanisms: A critical review

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ABSTRACT

Numerous inorganic and organic micropollutants can undergo reactions with chlorine. However, for certain compounds, the expected chlorine reactivity is low and only small modifications in the parent compound's structure are expected under typical water treatment conditions. To better understand/predict chlorine reactions with micropollutants, the kinetic and mechanistic information on chlorine reactivity available in literature was critically reviewed. For most micropollutants, HOCl is the major reactive chlorine species during chlorination processes. In the case of inorganic compounds, a fast reaction of ammonia, halides (Br^- and I^-), SO_3^{2-}, CN^-, NO_2^-, As(III) and Fe(II) with HOCl is reported (10^3–$10^9\,M^{-1}\,s^{-1}$) whereas low chlorine reaction rates with Mn(II) were shown in homogeneous systems. Chlorine reactivity usually results from an initial electrophilic attack of HOCl on inorganic compounds. In the case of organic compounds, second-order rate constants for chlorination vary over 10 orders of magnitude (i.e. <0.1–$10^9\,M^{-1}\,s^{-1}$). Oxidation, addition and electrophilic substitution reactions with organic compounds are possible pathways. However, from a kinetic point of view, usually only electrophilic attack is significant. Chlorine reactivity limited to particular sites (mainly amines, reduced sulfur moieties or activated aromatic systems) is commonly observed during chlorination processes and small modifications in the parent compound's structure are expected for the primary attack. Linear structure–activity relationships can be used to make predictions/estimates of the reactivity of functional groups based on structural analogy. Furthermore, comparison of chlorine to ozone reactivity towards aromatic compounds (electrophilic attack) shows a good correlation, with chlorine rate constants being about four orders of magnitude smaller than those for ozone.

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Contents

1. Introduction

Due to their capability for disinfection (microorganisms) and oxidation (e.g. taste and odor control, elimination of micropollutants, etc.), chemical oxidants (i.e. ozone, chlorine, chlorine dioxide, chloramines, etc.) are commonly used in water treatment processes (Hoff and Geldreich, 1981; Wolfe et al., 1984; Morris, 1986; Burlingame et al., 1992; Hoigné, 1998; Gottschalk et al., 2000; von Gunten, 2003; Legube, 2003; Bruchet and Duguet, 2004). However, under certain circumstances, oxidants can induce formation of potentially harmful by-products or transformation products due to their reactivity with water matrix components or micropollutants (Cancho et al., 2000; Bichsel and von Gunten., 2000; Simmons et al., 2002; Richardson et al., 2003; Plewa et al., 2004; Richardson, 2005; Krasner et al., 2006).

Owing to its low cost, chlorine is globally the most used chemical oxidant for drinking water disinfection. Drinking water disinfection commonly involves the use of chlorine at one or two point(s) in the treatment process, i.e., for pretreatment (to induce a primary disinfection at the beginning of the treatment process) and/or for post-treatment (to maintain a disinfectant residual in the distribution system). Despite its low activity on microorganisms in biofilms, chlorine can lead to a significant removal of the majority of planktonic bacteria (Le Chevallier et al., 1988; Bois et al., 1997). Added near the end of the treatment process, i.e., before water release in the distribution system (post chlorination), chlorine thus plays an important role to limit the growth of heterotrophic microorganisms. As a chemical oxidant, though less reactive than ozone, chlorine can transform numerous inorganic and organic micropollutants found in water (e.g. Fe(II), As(III), NO_2^-, phenols, pesticides, pharmaceuticals, etc.) (Johnson and Margerum, 1991; Magara et al., 1994; Folkes et al., 1995; Gallard and von Gunten, 2002; Lahoutifard et al., 2003; Diurk and Colette, 2006; Dodd et al., 2006; von Gunten et al., 2006). Chlorination usually represents an efficient process to remove/transform inorganic micropollutants. However, due to the potentially harmful chlorinated transformation products, chlorination is usually not applied for oxidation of organic micropollutants.

Similar to other disinfection processes, chlorination presents certain disadvantages in spite of its broad use and its benefits for the improvement of microbial water quality: (i) Due to its pH-dependent aqueous chemistry, various species of chlorine (HOCl, ClO^-, Cl_2, etc.) may be present in solution (Doré, 1989). These forms of chlorine show significant differences in their reactivity with microorganisms and micropollutants. Therefore, variability in oxidation or disinfection efficiency can be observed depending on the pH of the water. (ii) Chlorine interacts with dissolved natural organic matter (DNOM). Numerous so-called disinfection by-products (DBPs) can result from the reaction of chlorine with DNOM. Among these DBPs, trihalomethanes (THMs) and haloacetic acids (HAAs) were the first chlorine DBPs reported and are currently regulated in the EU (THMs) and the USA (THMs, HAAs) (Richardson, 2005). Currently, about 600 DBPs are identified, among them some highly toxic compounds such as iodo and bromo compounds (Bichsel and von Gunten, 2000; Richardson et al., 2003; Plewa et al., 2004; Krasner et al., 2006), MX (Onstad and Weinberg, 2005; Krasner et al., 2006), halonitromethanes (Krasner et al., 2006) and *N*-nitrosodimethylamine (Mitch et al., 2003). These individual DBPs or mixtures of DBPs could represent a potential human health risk (Cancho et al., 2000; Simmons et al., 2002; Richardson et al., 2003; Plewa et al., 2004; Richardson, 2005; Krasner et al., 2006). (iii) Because organic micropollutants are typically not mineralized, numerous transformation products can be formed as a result of the oxidation of organic compounds during water chlorination processes (Magara et al., 1994; Gallard and von Gunten, 2002; Hu et al., 2002a,b, 2003; Moriyama et al., 2004; Dodd and Huang, 2004; Dodd et al., 2005; Rule et al., 2005; Diurk and Colette, 2006; von Gunten et al., 2006). Little is known on the stability and the biological effects of these compounds. However, in some cases, certain transformation products are fairly stable against further transformation and could persist for hours to days even in presence of residual chlorine. Moreover, in the case of some

endocrine disruptors (i.e. nonylphenol, bisphenol A and hormones), some pesticides (i.e. chlorpyrifos), some pharmaceuticals (i.e. acetaminophen) and some azo-dyes, potentially toxic or biologically active chlorination products were reported (Hu et al., 2002a,b, 2003; Wu and Laird, 2003; Bedner and MacCrehan, 2006; Moriyama et al., 2004; Oliveira et al., 2006). (iv) In bromide-containing waters, chlorination leads to bromine formation. Bromine is usually more reactive than chlorine, especially with phenolic compounds (Gallard et al., 2003; Acero et al., 2005b). Under these conditions, bromination can be highly significant and brominated products can be formed (Gallard et al., 2003; Acero et al., 2005b; Hu et al., 2006).

This study presents an overview on chlorination of drinking water with an emphasis on kinetics and mechanisms of chlorine reactions. Based on literature data, an overview over chlorine reactivity with inorganic and organic compounds is presented. For typical functional groups, chlorination kinetics and mechanisms are described. By structural analogy, linear structure–activity relationships are proposed. Finally, for some organic micropollutants relevant for urban water management, a discussion on expected and observed chlorine reactivities is provided.

2. Aqueous chlorine chemistry

In water treatment, gaseous chlorine Cl_2 or hypochlorite are commonly used for chlorination processes. Chlorine gas (Cl_2) hydrolyzes in water according to the following reaction:

$$Cl_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HOCl + Cl^- + H^+, \quad K_{Cl_2} = k_1/k_{-1}, \tag{1}$$

where k_1 and k_{-1} values, calculated at $\mu = 0\,M$ and 25 °C from Wang and Margerum, are $22.3\,s^{-1}$ and $4.3 \times 10^4\,M^{-2}\,s^{-1}$, respectively. For temperatures between 0 and 25 °C, K_{Cl_2} ranges from 1.3×10^{-4} to $5.1 \times 10^{-4}\,M^2$ (Wang and Margerum, 1994). Hypochlorous acid resulting from reaction (1), is a weak acid which dissociates in aqueous solution:

$$HOCl \rightleftharpoons ClO^- + H^+, \quad K_{HOCl} \tag{2}$$

with K_{HOCl} reported in literature between 1.5×10^{-8} ($pK_{HOCl,\,0\,°C} = 7.82$) and 2.9×10^{-8} ($pK_{HOCl,\,25\,°C} = 7.54$) for temperatures between 0 and 25 °C (Morris, 1966). Under typical water treatment conditions in the pH range 6–9, hypochlorous acid and hypochlorite are the main chlorine species. Depending on the temperature and pH level, different distributions of aqueous chlorine species are observed. Fig. 1 shows the distribution of Cl_2, HOCl and ClO^- as a function of the pH at 25 °C and for a chloride concentration of $5 \times 10^{-3}\,M$ ($177.5\,mg\,L^{-1}$). For these high chloride concentrations, Fig. 1 shows that Cl_2 hydrolysis is almost complete at pH >4. Therefore, Cl_2 can usually be neglected under typical drinking water treatment conditions.

In addition to these major chlorine species, other chlorine intermediates, including trichloride (Cl_3^-) and chlorine hemioxide (Cl_2O) (or H_2OCl^+ species, mainly induced at pH <4 (Arotsky and Symons, 1962) and recently discussed; Cherney et al., 2006), can also be formed (Fig. 2). In solution, ratios of these compounds are a function of temperature, pH and chloride concentration. Under typical water treatment conditions, their concentrations are very low (Zimmermann and Strong, 1957; Reinhard and Stumm, 1980).

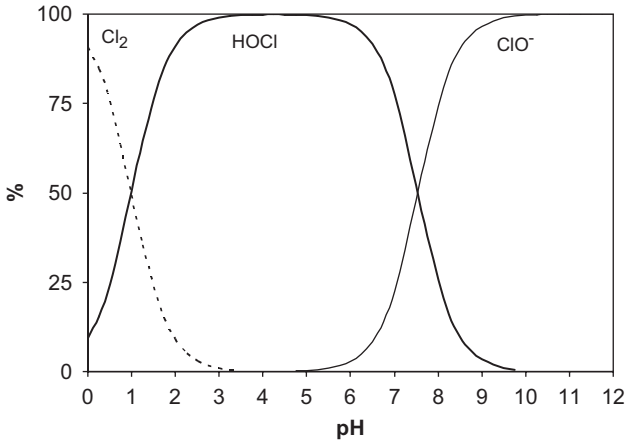


Fig. 1 – Relative distribution of main aqueous chlorine species as a function of pH at 25 °C and for a chloride concentration of $5 \times 10^{-3}\,M$ ($177.5\,mg\,L^{-1}$).

3. Oxidation of inorganic and organic compounds by chlorine

The reactivity of chlorine depends on chlorine speciation as a function of pH. Among the different aqueous chlorine species, hypochlorous acid is the major reactive form during water treatment. The other species are typically present in concentrations that are too low or show insufficient reactivity to be significant (Morris, 1978). For most of the chlorination reactions, the elementary reaction can be formulated as

$$HOCl + B \rightarrow \text{products}, \tag{3}$$

where B is an organic or inorganic compound.

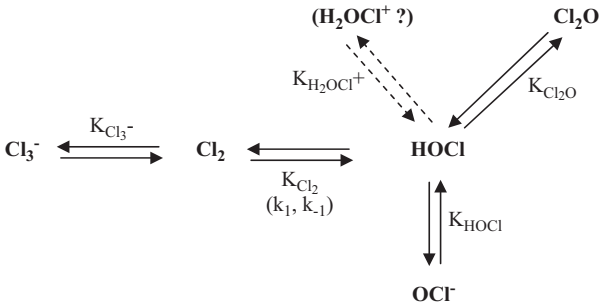
Other elementary reactions have been proposed under acidic conditions. They are acid-catalyzed reactions of hypochlorous acid or Cl_2 reactions with B (Thomm and Wayman, 1969; Margerum et al., 1978; Kumar et al., 1986; Kumar and Margerum, 1987; Nagy et al., 1988; Rebenne et al., 1996; Gallard and von Gunten, 2002; Gallard et al., 2004; Deborde et al., 2004; Pinkston and Sedlak, 2004; Acero et al., 2005a; Dodd and Huang, 2007):

$$H^+ + HOCl + B \rightarrow \text{products}, \tag{4}$$

$$Cl_2 + B \rightarrow \text{products}. \tag{5}$$

The acid-catalyzed reaction was sometimes associated to a H_2OCl^+ species (Rebenne et al., 1996; Gallard and von Gunten, 2002; Gallard et al., 2004; Deborde et al., 2004). Recently however, the existence of H_2OCl^+ and its reactivity has been strongly questioned. In their publication on aqueous free chlorine speciation and reactivity in the pH range 1–12, Cherney et al. (2006) argued that Cl_2(aq) is the most probable reactive chlorine species at low pH.

For most of the chlorine reactions with inorganic and organic compounds, the kinetics of the oxidation is second



Equations	equilibrium constants (25°C)	references
$HOCl \rightleftarrows ClO^- + H^+$	$K_{HOCl} = 2.9 \times 10^{-8}$	(Morris, 1966)
$Cl_2 + H_2O \rightleftarrows HOCl + H^+ + Cl^-$	$K_{Cl_2} = 5.1 \times 10^{-4}\ M^2$ ($k_1 = 22.3\ s^{-1}$, $k_{-1} = 4.3 \times 10^4\ M^{-2}\ s^{-1}$)	(Wang and Margerum, 1994)
$H_2OCl^+ \rightleftarrows HOCl + H^+$	$K_{H_2OCl^+} = 10^{-3}$-10^{-4}	(Arotsky and Symons, 1962)
$2\ HOCl \rightleftarrows Cl_2O + H_2O$	$K_{Cl_2O} = 8.7 \times 10^{-3}$	(Reinhard and Stumm, 1980)
$Cl_2 + Cl^- \rightleftarrows Cl_3^-$	$K_{Cl_3^-} = 0.191$	(Zimmermann and Strong, 1957)

Fig. 2 – Chlorine equilibria in solution at 25 °C. Adapted from Doré (1989).

order, i.e., first order in the free active chlorine concentration ($[HOCl]_T$) and first order in the total compound concentration ($[B]_T$):

$$-\frac{d[B]_T}{dt} = k_{app}[HOCl]_T[B]_T, \quad (6)$$

where k_{app} is the apparent second-order rate constant, $[HOCl]_T = [HOCl]+[ClO^-]$ and $[B]_T$, the total concentration of B in solution (i.e. sum of concentrations of various species of B).

For a given compound, HOCl and ClO^- reactivities are usually significantly varied. In addition, different species of B can be present in solution. Therefore, a pH dependence of the apparent second-order rate constant is typically observed for chlorination reactions (Armesto et al., 1994a; Rebenne et al., 1996; Abia et al., 1998; Gallard and von Gunten, 2002; Gallard et al., 2004; Deborde et al., 2004; Dodd et al., 2005; Acero et al., 2005a, b). In the case of a compound B with two species in solution (HB/B^-), the kinetics of chlorination represented by Eq. (6) can be written as follows by considering HOCl reactivity with each of these two forms (Eq. (3)):

$$-\frac{d[B]_T}{dt} = k_{3,1}[HOCl][HB] + k_{3,2}[HOCl][B^-], \quad (7)$$

where $k_{3,1}$ and $k_{3,2}$ are second-order rate constants for the reaction of HOCl with each species of B according to Eq. (3). By combining Eqs. (6) and (7) and by considering the acidity constant of both chlorine (K_{HOCl}) and B (K_B), the pH dependence of the apparent second-order rate constant can be formulated by

$$k_{app} = \frac{k_{3,1}[H^+]^2 + k_{3,2}[H^+]K_B}{[H^+]^2 + K_{HOCl}[H^+] + [H^+]K_B + K_{HOCl}K_B}. \quad (8)$$

Under these conditions, the maximum of k_{app} is obtained for

$$\frac{dk_{app}}{d[H^+]} = 0, \quad (9)$$

which results in

$$[H^+]^2 \approx K_{HOCl}K_B \quad \text{or} \quad pH \approx \tfrac{1}{2}(pK_{HOCl} + pK_B) \quad (\text{when } k_{3,1} \ll k_{3,2}).$$

Fig. 3 shows this pH dependence of k_{app} in the case of the ammonia–chlorine reaction at 25 °C.

3.1. *Oxidation of inorganic compounds*

3.1.1. *Ammonia*

Due to its acid–base character, two species of ammonia (NH_3 and NH_4^+) are present in aqueous solutions. Chlorine reactivity with NH_4^+ species was reported to be negligible (Qiang and Adams, 2004). During aqueous chlorination, hypochlorous acid reacts with NH_3 to generate NO_3^- and N_2 for $[HOCl] \gg [NH_3]$. This oxidation results from successive reactions which firstly induce chloramine (mono-, di- and trichloramines) formation (Eqs. (10)–(12)) (Weil and Morris, 1949; Morris and Isaac, 1983; Jafvert and Valentine, 1992; Qiang and Adams, 2004)

$$NH_3 + HOCl \rightarrow NH_2Cl + H_2O, \quad (10)$$

$$NH_2Cl + HOCl \rightarrow NHCl_2 + H_2O, \quad (11)$$

$$NHCl_2 + HOCl \rightarrow NCl_3 + H_2O. \quad (12)$$

Table 1 reports rate constants for Eqs. (10)–(11) at 25 °C and illustrates the temperature dependence of these rate constants. These results show that the chlorine reactivity decreases as the number of chlorine atoms on the nitrogen increases. This is a confirmation of the presumed initial mechanism of an electrophilic attack of HOCl on the chloramine nitrogen (Morris, 1978; Jafvert and Valentine, 1992). Concerning Eq. (12), a general-base-catalyzed mechanism was proposed with more complex reaction kinetics (Hand and Margerum, 1983). Therefore, no rate constant for chlorine reaction with $NHCl_2$ was reported in Table 1. As previously

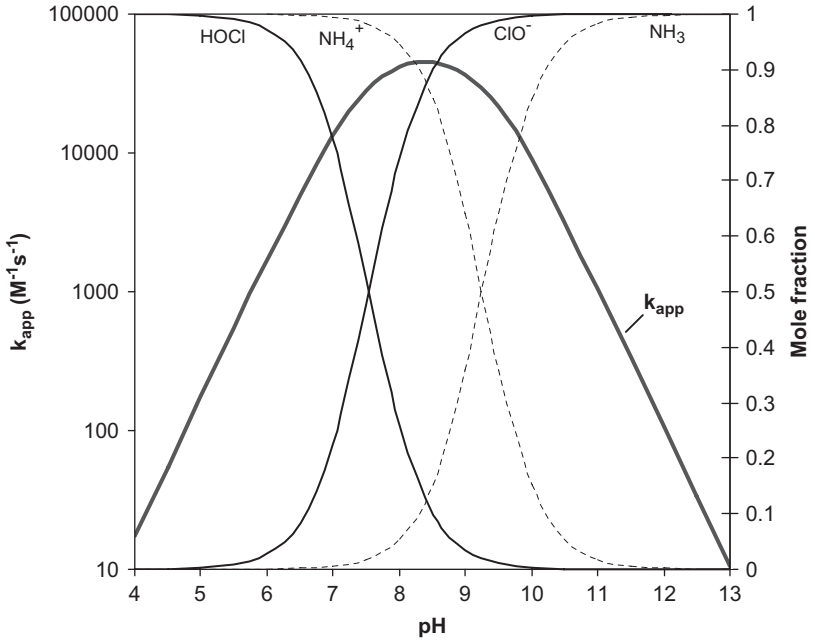


Fig. 3 – pH dependence of the apparent second-order rate constants of ammonia chlorination at 25 °C (obtained from rate constants given by Qiang and Adams (2004)).

suggested for Eqs. (10) and (11), an electrophilic attack of hypochlorous acid on the dichloramine nitrogen was hypothesized for trichloramine formation. In the latter case, this electrophilic attack would be accompanied by a simultaneous general-base-assisted removal of a proton from dichloramine (Hand and Margerum, 1983).

In contrast to free chlorine (i.e. HOCl, ClO^- and Cl_2), chloramines (NH_2Cl, $NHCl_2$ and NCl_3) and organic chloramines represent combined chlorine. Similar to free chlorine, combined chlorine has oxidative properties. Therefore, in presence of NH_3 during chlorination, the prediction of chloramine formation and decomposition is important to optimize disinfection and minimize undesirable by-product formation. The chemistry of chloramines, breakpoint chlorination and THM formation were reviewed in detail in the Jolley et al. symposium series in the 1980s (Jolley, 1978; Jolley et al., 1978, 1980, 1983, 1985). The dynamics of chloramine systems have been described in several models (Weil and Morris, 1949; Jafvert and Valentine, 1992; Ozekin et al., 1996; Vikesland et al., 2001).

3.1.2. *Halides and other anionic inorganic compounds (SO_3^{2-}, CN^-, NO_2^- or sulfide)*

During chlorination, due to chlorine and halide standard redox potentials, hypochlorous acid and hypochlorite can oxidize bromide and iodide. Rate constants for these reactions are summarized in Table 1. Due to its high oxidizing capability, hypochlorous acid is the dominant reactive species for the reaction with halides ($k_{HOCl} \geqslant 10^6\ k_{ClO^-}$).

A mechanism via Cl^+ transfer from hypochlorous acid to the halide (X^-) was proposed for these compounds. This mechanism results in an XCl-type intermediate which then mainly leads to OX^- due to hydrolysis (Kumar et al., 1986; Kumar and Margerum, 1987; Johnson and Margerum, 1991):

$$HOCl + X^- \rightarrow XCl + OH^-, \quad (13)$$

$$XCl + 2OH^- \rightarrow OX^- + Cl^- + H_2O. \quad (14)$$

As shown earlier in the case of chloride in acidic solution, a HOCl acid-catalyzed reaction was also described in the case of bromide and iodide (Eq. (15)) (Kumar and Margerum, 1987; Nagy et al., 1988)

$$HOCl + H^+ + X^- \rightleftharpoons H_2O + XCl. \quad (15)$$

As shown in the case of non-acid-catalyzed reactions, rate constants of HOCl acid-catalyzed reactions with halides increase in the order $Cl^- < Br^- \ll I^-$ (Table 1). This order of reaction rates is in agreement with the nucleophilic character (represented by N and reported in Table 1) of each of these ions (Hine, 1962). It confirms the initial electrophilic mechanism suggested for these anions. As a result of oxidation of bromide- and iodide-containing waters, bromine and iodine can be formed during chlorination. Similar to chlorine, these entities have electrophilic properties which can lead to brominated and iodinated products (Bichsel and von Gunten, 2000; Richardson et al., 2003; Plewa et al., 2004; Richardson, 2005).

Similar to halides, the oxidation of SO_3^{2-}, CN^- and NO_2^-, mainly occurs via the HOCl species. HOCl reacts with an initial electrophilic attack via Cl^+ which leads to $ClSO_3^-$, ClCN and $ClNO_2$ (Fogelman et al., 1989; Gerritsen and Margerum, 1990; Johnson and Margerum, 1991). After hydrolysis, $ClSO_3^-$ and ClCN yield SO_4^{2-} and OCN^-, respectively, whereas $ClNO_2$ results in NO_3^- formation (Fogelman et al., 1989; Gerritsen and Margerum, 1990; Johnson and Margerum, 1991). Two reaction pathways for $ClNO_2$ decomposition to NO_3^- can occur: Either loss of Cl^- to yield NO_2^+, then NO_3^- (Eqs. (16), (17)), or reaction

Table 1 – Kinetics of oxidation of selected inorganic compounds with chlorine

Compounds	N[a]	pK_a	Elementary reaction rate constants (25 °C)			Apparent rate constants at given pH or pH 7[b] (25 °C)	Arrhenius equation (with K_{HOCl} in $M^{-1}s^{-1}$ and T, temperature in Kelvin)	References
			k_{HOCl+H^+} ($M^{-2}s^{-1}$)	k_{HOCl} ($M^{-1}s^{-1}$)	k_{ClO^-} ($M^{-1}s^{-1}$)	k_{app} ($M^{-1}s^{-1}$)		
Ammonia (NH_3)		9.25		3.07×10^6		1.3×10^{4b}	$k_{HOCl} = 5.4 \times 10^9 \exp(-2237/T)$	Qiang and Adams (2004)
				4.2×10^6		1.8×10^{4b}	$k_{HOCl} = 6.6 \times 10^8 \exp(-1510/T)$	Morris and Isaac (1983)
				2.9×10^6		1.3×10^{4b}		Margerum et al. (1978)
Monochloramine (NH_2Cl)				1.5×10^2		1.2×10^{2b}		Margerum et al. (1978)
				3.5×10^2		2.7×10^{2b}	$k_{HOCl} = 3 \times 10^5 \exp(-2010/T)$	Morris and Isaac (1983)
Chloride (Cl^-)	3.04		2.8×10^4	$\leqslant 0.16$		$\leqslant 0.13^b$		Nagy et al. (1988) Gerritsen and Margerum (1990)
Bromide (Br^-)	3.89			6.84×10^3		5.3×10^{3b}	$k_{HOCl} = 1.57 \times 10^6 \exp(-1620/T)$	Bousher et al. (1986)
				2.95×10^3		2.3×10^{3b}		Farkas et al. (1949)
			1.32×10^6	1.55×10^3	9×10^{-4}	1.2×10^{3b}		Kumar and Margerum (1987)
Iodide (I^-)	5.04		3.5×10^{11}	1.4×10^8	< 30	1.1×10^{8b}		Nagy et al. (1988) Gerritsen and Margerum (1990)
Sulfite (SO_3^{2-})	5.1	7.2		$7.6\ (\pm 0.4) \times 10^8$	$2.3\ (\pm 0.2) \times 10^4$	2.3×10^{8b}		Fogelman et al. (1989)
Cyanide (CN^-)	5.1	9.2		$1.22\ (\pm 0.03) \times 10^9$	$310\ (\pm 20)$	6×10^{6b}		Gerritsen and Margerum (1990)
Arsenous acid (As(III)):						2.9×10^{5b}		
$As(OH)_3$		9.2		$4.3\ (\pm 0.8) \times 10^3$				Dodd et al. (2006)
$As(OH)_2O^-$		12.1		$5.8\ (\pm 0.1) \times 10^7$				Dodd et al. (2006)
$As(OH)O_2^{2-}$		12.7		$1.4\ (\pm 0.1) \times 10^9$				Dodd et al. (2006)
Iron (Fe(II))						$1.7\ (\pm 0.1) \times 10^4$ (pH ≈ 4)		Folkes et al. (1995)
Manganese (Mn(II))						$\approx 6.4 \times 10^{-4c}$ (pH 8)		Hao et al. (1991)

[a] Nucleophilicity, obtained from Hine (1962).
[b] Calculated from literature data for pH 7 (by considering $pK_{aHOCl} = 7.54$ and pK_a compound values reported in the table).
[c] Obtained at 22 °C.

with NO_2^- to firstly induce N_2O_4 and then NO_3^- (Eqs. (18) and (19)) (Johnson and Margerum, 1991):

$$NO_2Cl \rightleftharpoons NO_2^+ + Cl^-, \quad (16)$$

$$NO_2^+ + OH^- \rightarrow NO_3^- + H^+ \quad (17)$$

and/or

$$NO_2Cl + NO_2^- \rightleftharpoons N_2O_4 + Cl^-, \quad (18)$$

$$N_2O_4 + OH^- \rightarrow NO_3^- + NO_2^- + H^+. \quad (19)$$

Because in the case of NO_2^- the initial step is reversible (Eq. (13)) and followed by two parallel reaction pathways (Eqs. (16)–(19)), complex chlorination kinetics are observed during NO_2^- oxidation by HOCl (Johnson and Margerum, 1991; Lahoutifard et al., 2003). For the other compounds (i.e. halides, SO_3^{2-} and CN^-), as shown by Gerritsen and Margerum (1990), a correlation between the rate constants and the nucleophilic character can be expected by considering the initial Cl^+ transfer from HOCl to the anion. Fig. 4 represents the Swain–Scott relationship (Eq. (20)) for these inorganic compounds according to Gerritsen and Margerum (1990). This relationship correlates rate constants with the nucleophilicity (N) of anions and the sensitivity of the reaction site (Swain and Scott, 1953; Hine, 1962; Gerritsen and Margerum, 1990):

$$\log(k/k_0) = sN. \quad (20)$$

For SO_3^{2-}, I^-, Br^-, Cl^- and CN^-, nucleophilicity values given in literature are reported in Table 1 (Hine, 1962). A good correlation confirming the initial electrophilic attack of chlorine is shown in Fig. 4. For all these inorganic compounds, weak variations of nucleophilicity induce strong changes in HOCl reactivity. Therefore, a high sensitivity of chlorine reactivity with regard to the nucleophilic character can be expected.

No literature data on kinetics and intermediates for chlorination were found concerning sulfides. However, according to certain authors, chlorine reaction with sulfides proceeds rapidly (White, 1986; Doré, 1989). Based on the known nucleophilic character of HS^- ($N = 5.1$) (Hine, 1962) and hypothesing a similar initial chlorine electrophilic attack to those previously described for halides or other anionic inorganic compounds, a rate constant in order of 10^8–$10^9\,M^{-1}\,s^{-1}$ can be expected for HS^-. Generally, sulfate and sulfur are postulated as the primary products during chlorination of sulfide. Depending on the pH, the temperature and the chlorine concentration, different ratios of these transformation products were observed. Under basic conditions, other reaction products such as sulfite, thiosulfate or polysulfides may be formed (Choppin and Faulkenberry, 1937).

For the majority of anionic inorganic compounds, a fast reaction with chlorine can be expected under water treatment conditions. From a mechanistic point of view, an initial electrophilic attack of HOCl on the inorganic compounds was commonly described. A 2-electron transfer was usually observed to form first stable oxidation products. A 1-electron transfers does not seem to be relevant for water treatment conditions.

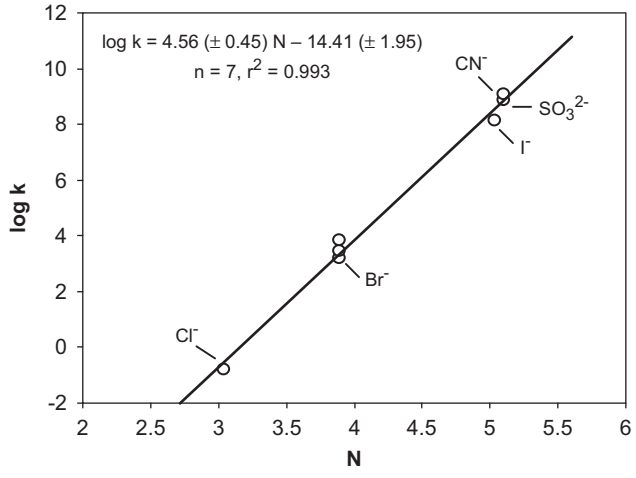


Fig. 4 – Swain–Scott plot of log *k* for the reaction of HOCl with Cl^-, Br^-, I^-, SO_3^{2-} and CN^- versus the nucleophilicity (N) of the anions at 25 °C. Adapted from Gerritsen and Margerum (1990). Rate constants are from Table 1.

3.1.3. *As(III), Fe(II) and Mn(II)*

Soluble inorganic arsenic occurs in surface waters and groundwaters mainly as a combination of As(III) and As(V) (Cullen and Reimer, 1989). Many conventional drinking water treatment processes remove As(III) substantially less efficiently than As(V) (United States Environmental Protection Agency, 2000). If total arsenic is mostly As(III), arsenic removal can be improved by preoxidation of As(III) to As(V) (United States Environmental Protection Agency, 2000; Ghurye and Clifford, 2004; Leupin et al., 2005). Depending on the pH level, one main species ($As(OH)_3$) and two minor species ($As(OH)_2O^-$ and $As(OH)O_2^{2-}$) of As(III) (Table 1) are commonly present in solution. For each of these species, ClO^- reactivity was shown to be negligible. HOCl rate constants are reported in Table 1 (Dodd et al., 2006). Similar to halides, SO_3^{2-}, CN^- and NO_2^-, an initial mechanism via Cl^+ transfer from HOCl to the As atom with concomitant loss of OH^- inducing an $As(III)Cl^+$ intermediate was proposed for all three main As(III) species. After hydrolysis, Cl^- and As(V) formation was proposed (Dodd et al., 2006). For the As(III) species, the nucleophilic characters increase in the order $As(OH)_3 < As(OH)_2O^- < As(OH)O_2^{2-}$. The suggested mechanism is thus in agreement with increasing HOCl reactivity in the order $As(OH)_3 < As(OH)_2O^- < As(OH)O_2^{2-}$ (Table 1).

In natural waters, soluble iron and manganese usually exist in their divalent ferrous and manganous form, respectively (Stumm and Morgan, 1970; Sawyer and McCartly, 1978; Pouvreau, 1984). These species of iron and manganese lead to several disadvantageous results during drinking water treatment processes (i.e. metallic, astringent or medicinal taste problems, coloring of water, growths of certain microorganisms and pipe corrosion phenomena, etc.) (Wong, 1984). Fe(II) and Mn(II) oxidation to insoluble Fe(III) and Mn(III, IV) species followed by filtration processes represents the main iron and manganese removal method used during water treatment. Table 1 reports the apparent chlorination rate constants at pH 4 for Fe(II) and pH 8 for Mn(II). These results demonstrate a nearly instantaneous iron oxidation during chlorination at pH 4. At higher pH, a higher apparent rate

constant can be expected for its reaction with chlorine due to the iron speciation in solution. Mainly Fe(II) hydroxy complexes which increase with increasing pH are quickly oxidized. For Mn(II), a slow direct oxidation by chlorine has been described (Mathews, 1947; White, 1986; Knocke et al., 1987; Hao et al., 1991). However, an autocatalytic model in which the major mechanism for Mn(II) removal is its adsorption to precipitated MnO_2 was described during Mn(II) chlorination (Hao et al., 1991):

$$HOCl + Mn^{2+} + H_2O \rightarrow MnO_2 + Cl^- + 3H^+ \quad \text{(slow)}, \tag{21}$$

$$MnO_2 + Mn^{2+} \rightarrow (Mn - MnO_2)^{2+} \quad \text{(fast)}, \tag{22}$$

$$(Mn - MnO_2)^{2+} + HOCl + H_2O \rightarrow 2MnO_2 + Cl^- + 3H^+ \quad \text{(moderate)}. \tag{23}$$

At pH 8 and 22 °C, the apparent rate constants for Eqs. (21) (homogenous oxidation) and (22)/(23) (heterogenous catalytic effect) are approximately 6.4×10^{-4} and $4 \times 10^6\,M^{-2}\,s^{-1}$, respectively (Hao et al., 1991). Under water treatment conditions, the use of chlorine in a heterogenous MnO_2 filter is an efficient process for a fast Mn(II) removal.

3.2. *Oxidation of organic compounds*

As previously shown in the case of inorganic compounds, hypochlorous acid is also the dominant reactive species for the reaction with the majority of organic compounds. Due to its oxidizing power and its chemical structure characterized by the Cl–O bond polarization ($Cl^{\delta+} \rightarrow OH^{\delta-}$), three kinds of reactions of hypochlorous acid with organic compounds can be described: (i) oxidation reactions, (ii) addition reactions to unsaturated bonds, (iii) electrophilic substitution reactions at nucleophilic sites. Hypochlorous acid thus presents high selectivity towards organic micropollutants and its reactivity is usually restricted to limited sites (reducing, nucleophilic and unsaturated sites). Hypochlorous acid generally induces small modifications in the parent compound's structures leading to more oxidized or chlorinated molecules (Doré, 1989).

3.2.1. *Aliphatic organic compounds*

3.2.1.1. Reaction with unsaturated bonds (olefins). Hypochlorous acid reactions with unsaturated bonds are generally slow or negligible. A low chlorine reactivity with the conjugated double bond of sorbic acid (with an apparent rate constant of $2.3\,M^{-1}\,s^{-1}$ at pH 7.2; Prütz, 1998a) was reported, whereas no chlorine reactivity with the progesterone double bond was observed (Deborde et al., 2004). From a mechanistic point of view, HOCl addition reactions are expected during chlorination of olefins. A mechanism via an initial Cl^+ transfer to the double bonds to give a chloronium ion followed by addition of OH^- was proposed (Fig. 5) (Morris, 1978; Ghanbari et al., 1983). During chlorination of some unsaturated fatty acids and some terpenes, chlorohydrin formation has been shown (Kopperman et al., 1976; Carlson and Caple, 1978; Ghanbari et al., 1983; Gibson et al., 1986). These compounds could lead to epoxide formation after HCl elimination under alkaline conditions (Kopperman et al., 1976; Carlson and Caple, 1978).

Due to low chlorination rate constants, hypochlorous acid addition reactions on unsaturated bonds are generally too slow to be observed under water treatment conditions. However, when double bonds are activated by electron-donor groups, chlorine reactions on unsaturated moieties of matrix components could be expected for high chlorine exposures.

3.2.1.2. Reaction with oxygenated moieties: alcohols, aldehydes, ketones and acids. Chlorine reactivity towards oxygenated moieties is usually limited, especially in the case of acid moieties which have a high stability in the presence of chlorine. However, in some cases (such as compounds including a methylene group between two carbonyl functions), a high chlorine reactivity was shown (de Laat et al., 1982; Folkes et al., 1995; Pattison and Davies, 2001; Tachikawa et al., 2002).

Reaction with carbonyl functional groups. Aldehyde or ketone chlorination generally results from initial substitution reactions on the α-carbon to the carbonyl group (Roberts and Caserio, 1968). It firstly induces the successive replacement of hydrogen by chlorine and subsequently produces acetate and chloroform via the haloform reaction. Two forms of the reaction are known for halogenation steps: acid-catalyzed and base-catalyzed. The base-catalyzed reaction pattern is the one that is predominant for reaction in dilute aqueous solution at pH > 5. It results in keto-enolization which kinetically controls the substitution steps at neutral pH (Fig. 6) (Morris, 1978; Doré, 1989; Larson and Weber, 1994).

Due to its electron-donor or withdrawing effect, the nature of the R group (bound to the carbonyl of acetyl function) influences the reaction rate. Electron-withdrawing groups make the hydrogen atoms of the methyl group more acidic, thus increasing chlorine substitution, whereas electron-donor groups decrease methyl acidity and therefore chlorine substitution (de Laat, 1981). Similarly, presence of a substituent on the α-carbon group can influence the chlorine reactivity. In the case of β-diketones, such as acetylacetone or monochlorodimedon, the methyl group lies between two carbonyl functions. The hydrogen atoms of the methyl group are then very easily dissociated and the chlorine substitution is thus much faster (Table 2). In the case of acetylacetone

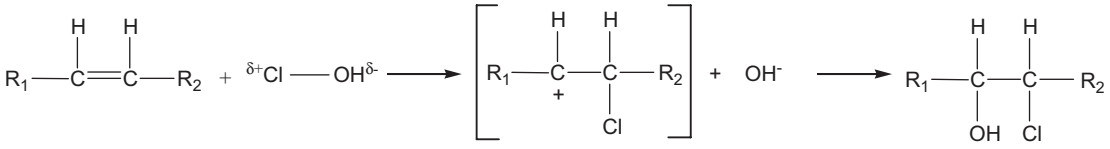


Fig. 5 – Mechanism for chlorination of unsaturated bonds (if R_2 is a better electon-donor than R_1). Adapted from Morris (1978) and Ghanbari et al. (1983).

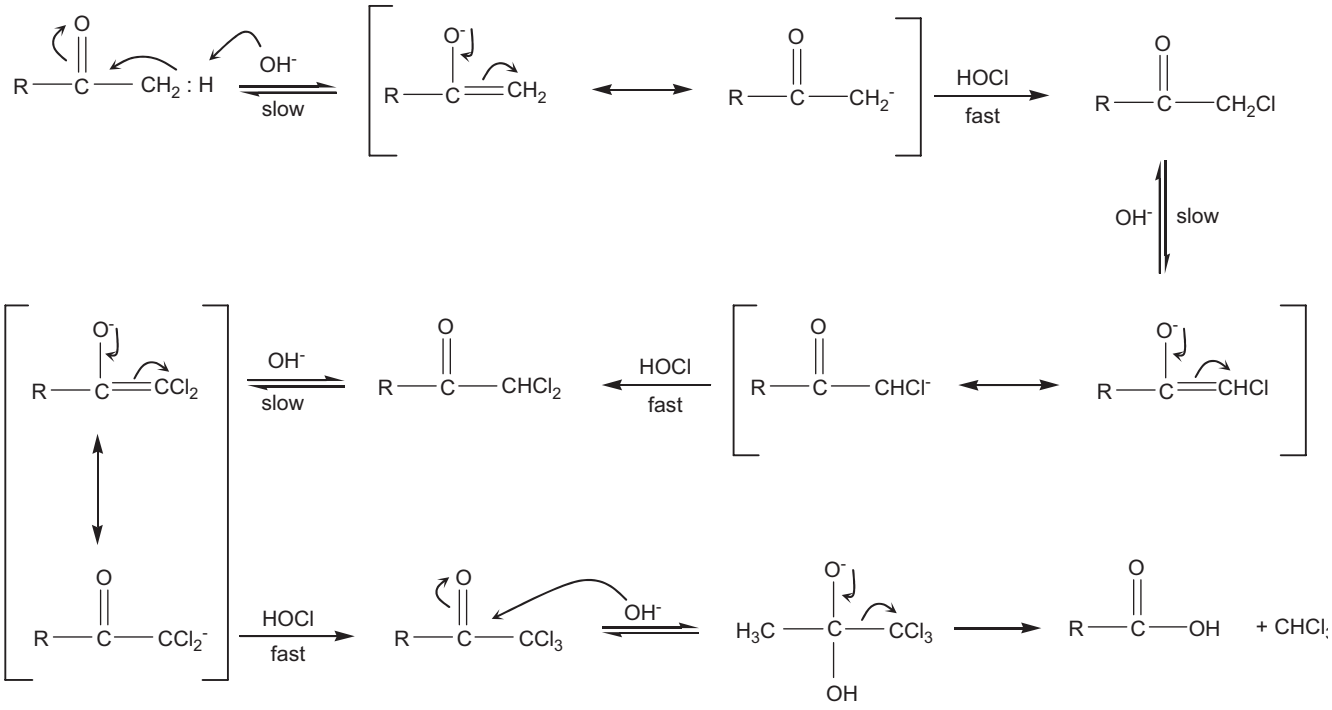


Fig. 6 – Base-catalyzed reaction pattern proposed for the reaction of chlorine with aldehydes and ketones. Adapted from Morris (1978), Doré (1989) and Larson and Weber (1994).

chlorination, 1,1-dichloroacetone, 1,1,1-trichloroacetone, acetate and chloroform were previously identified as transformation products. The chlorination mechanism proposed is shown in Fig. 7 (de Laat et al., 1982).

Finally, during chlorination of acetone, hydrolysis reactions of mono- and di-chlorinated transformation products have also been reported parallel to this halogenation mechanism. These reactions could result in mono- and di-hydroxy acetone which then ultimately would lead to lactate formation after a rearrangement mechanism (Guthrie et al., 1984; Guthrie and Cossar, 1986).

Reaction with alcohol functional groups. Generally, primary and secondary alcohols can be oxidized to carbonyl compounds after dehydrogenation. Primary alcohols thus give aldehyde induction and then acid production, whereas secondary alcohols induce ketones formation (Roberts and Caserio, 1968). Concerning chlorination, only few studies on chlorine reactivity with alcohol functions were reported in literature because these reactions are very slow. However, in the case of some organic compounds, such oxidation mechanisms and transformation products were proposed. In a study on 17β-estradiol chlorination at 25 °C, pH 7.5 and in the presence of an excess of oxidant (1.46 mg L^{-1} of chlorine versus 50 μg L^{-1} of estradiol), Hu et al. (2003) reported several transformation products resulting from alcohol moiety oxidation to ketone.

3.2.1.3. Reaction with sulfur-containing moieties. Reduced sulfur moieties can easily be oxidized in presence of chlorine. In the case of thiol-containing compounds, as previously shown for cysteine and glutathione, thiols oxidation mainly leads to disulfide and sulfonic acid (Pereira et al., 1973; Winterbourn and Brennan, 1997; Armesto et al., 2000). In the case of methionine or S-triazines (including RSR′ structure), an initial production of sulfoxides was observed (Drozdz et al., 1988; Lopez et al., 1994; Armesto et al., 2000).

From a mechanistic point of view, chlorine reaction with thiol-containing compounds results from an initial chlorination of the sulfur group to yield a sulfenyl chloride intermediate (Silverstein and Hager, 1974; Folkes et al., 1995; Prütz, 1996; Winterbourn and Brennan, 1997; Armesto et al., 2000; Fu et al., 2002). Depending on the chlorination conditions, three main competing reaction pathways were then described from this intermediate (Fig. 8): (i) complex hydrolysis mechanism via sulfenic (RSOH) and sulfinic (RSO_2H) acids, to form sulfonic acid (RSO_3H) (Doré, 1989; Folkes et al., 1995; Armesto et al., 2000; Fu et al., 2002; Hawkins et al., 2003); (ii) reaction with a second thiol-containing molecule to lead to disulfide compound (RSSR) (Winterbourn and Brennan, 1997; Armesto et al., 2000; Fu et al., 2002), then ultimately sulfonic acid, via a probable oxygenated disulfide derivative formation (e.g. RSOSR) (Pereira et al., 1973; Savige and Maclaren, 1966; Doré, 1989; Hawkins et al., 2003); (iii) reaction in excess of chlorine to give sulfonyl chloride (RSO_2Cl) which in turn would lead to sulfonic acid or thiosulfonate (Prütz, 1996; Winterbourn and Brennan, 1997; Fu et al., 2002; Davies and Hawkins, 2000). Added to these different pathways, in presence of amino compounds ($R'NH_2$), reaction of sulfenyl and sulfonyl chloride intermediates with the amino group to form sulfenamide (RSNR′), sulfinamide (RSONR′) and sulfonamides (RSO_2NR') was also described (Winterbourn and Brennan, 1997; Fu et al., 2002). Moreover, under certain conditions (e.g. at high temperature, in the presence of metal ions or under UV irradiation), a decomposition mechanism of the sulfenyl

Table 2 – Kinetics of chlorination of selected organic compounds including double bonds, oxygenated and/or sulfur moieties

Compounds	pKa[a]	Second-order rate constants				Apparent rate constants at given pH or pH 7[b] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
		k_{HOCl} ($M^{-1}s^{-1}$)			k_{ClO^-} ($M^{-1}s^{-1}$)			
		HB	B^-	B^{2-}				
Double bonds and oxygenated functions								
Double bonds+acid								
Sorbic acid						2.3 (pH 7.2)		Prütz (1998a)
Steroids								
Progesterone		Negligible				Negligible	20	Deborde et al. (2004)
Alcohol								
Ribose						Negligible (pH ≈ 7)		Prütz (1996)
Ketone								
Monochlorodimedon						$6.9 (\pm 0.1) \times 10^6$ (pH 5)	25	Folkes et al. (1995)
						$3.6 (\pm 0.7) \times 10^6$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
						$> 7.6 (\pm 0.67) \times 10^6$ (estimated) (pH 7)	22–25	Tachikawa et al. (2002)
Sulfur compounds								
Sulfur-containing amino acids								
Cysteine	8.15 and 10.29			1.2×10^{9c}	$1.9 \times 10^{5c,d}$	$\approx 6.2 \times 10^{7b,e}$	25	Armesto et al. (2000)
				3.3×10^{8c}	$5.5 \times 10^{5c,d}$	$\approx 1.7 \times 10^{7b,e}$	22	Pattison and Davies (2001)
Methionine	9.05		$8.70 (\pm 0.20) \times 10^{8c}$			$6.8 \times 10^{8b,f}$	25	Armesto et al. (2000)
Sulfur-containing protein								
Glutathione (GSH)						$\geqslant 1 \times 10^7$ (pH 5; 7.4 and 9)	25	Folkes et al. (1995)
Disulfide compound								
3,3′-dithiobis-propionic acid (DTPA)						$> 1 \times 10^5$ (pH ≈ 7)		Prütz (1996)
						$1.6 (\pm 0.6) \times 10^5$ (pH 7.2–7.4)	22	Pattison and Davies (2001)

[a] pKa values for amines and sulfur functions.
[b] Calculated from literature data for pH 7 (by considering $pK_{HOCl} = 7.54$ and pKa compound values reported in the Table).
[c] Measured at high pH values.
[d] Rate constant for the reaction of ClO^- with sulfur ionized form.
[e] Calculated by considering chlorine reaction with ionized sulfur group (S^-) as the major reaction.
[f] Calculated by considering sulfur group as the main chlorine reactive site (i.e. similar second-order rate constants (k_{HOCl}) for all methionine species).

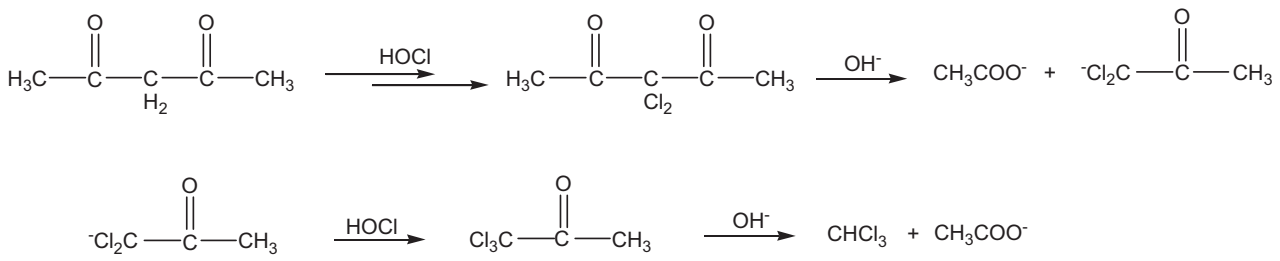


Fig. 7 – Reaction pathway proposed for acetylacetone chlorination. Adapted from de Laat et al. (1982).

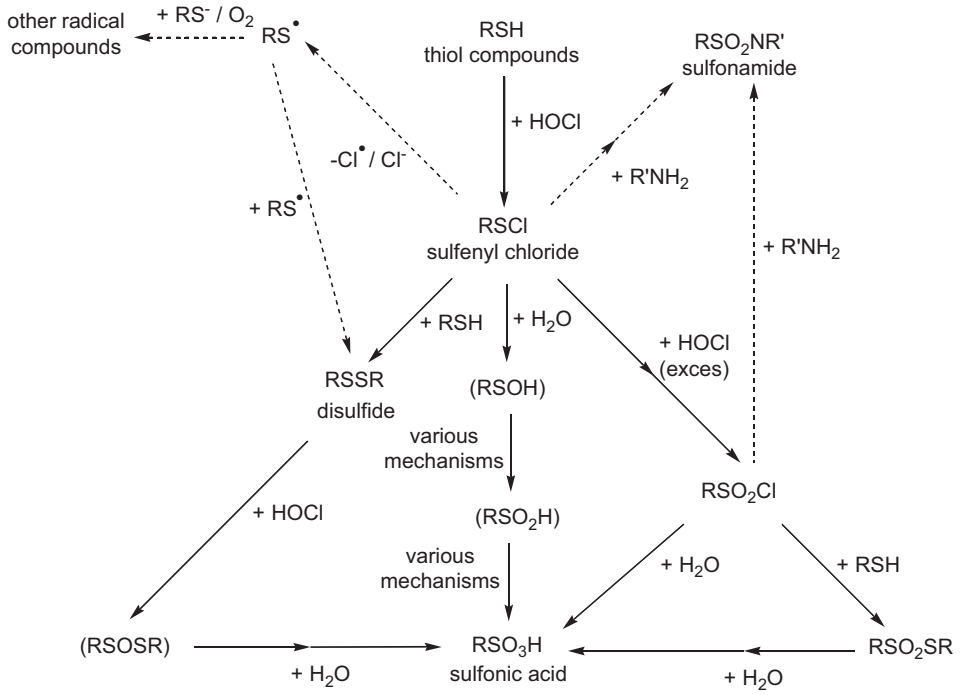


Fig. 8 – Summary of different competiting reaction pathways proposed for the reaction of HOCl with thiol-containing compounds. Adapted from Folkes et al. (1995), Winterbourn and Brennan (1997), Davies and Hawkins (2000), Fu et al. (2002) and Hawkins et al. (2003).

chloride intermediate via thiyl radicals was observed (Davies and Hawkins, 2000). In the case of thioether (RSR′) chlorination, a less complex mechanism was reported because only one main transformation product (sulfoxide) was usually observed (Fig. 9) (Drozdz et al., 1988; Armesto et al., 2000; Hawkins et al., 2003). Similar to thiol-containing compounds, the chlorine attack on RSR′ molecule will initially take place through chlorine transfer to yield a chlorosulfonium cation intermediate. After hydrolysis, sulfoxide compounds are formed (Armesto et al., 2000). This latter compound is usually more stable to chlorination (Drozdz et al., 1988; Armesto et al., 2000). However, in the case of S-triazines, further slow transformation of sulfoxide to sulfone was described (Lopez et al., 1994).

Table 2 reports second-order rate constants for methionine, cysteine and glutathione. Table 2 also gives rate constants obtained for the disulfide compound, 3,3′-dithiobis-propionic acid (DTPA). In the case of cysteine, in addition to the expected high HOCl reactivity, the ClO^- reactivity is also quite high ($k_{ClO^-} \approx 2–5 \times 10^5\,M^{-1}\,s^{-1}$) (Armesto et al., 2000; Pattison and Davies, 2001). Generally, a high reactivity of chlorine with reduced sulfur functions (i.e. thiols, disulfides and thioethers) is demonstrated by these results. In the case of sulfur-containing amino acids (methionine and cysteine), rate constants for the reaction with sulfur moieties are typically 1–2 orders of magnitude higher than those with amines. The primary chlorine attack is thus expected on the sulfur functional group (Armesto et al., 2000; Pattison and Davies, 2001). Similarly, in the case of DTPA, a high chlorine reactivity with the disulfide functional group can be expected by considering the high stability of the acidic function in the presence of chlorine.

3.2.1.4. Reaction with nitrogen-containing moieties. Aliphatic amines. The reactivity of HOCl with aliphatic amines (primary, secondary and tertiary) is high and results in rapid chloramine formation. Due to their acid–base character, two species of amines (neutral and protonated) are usually

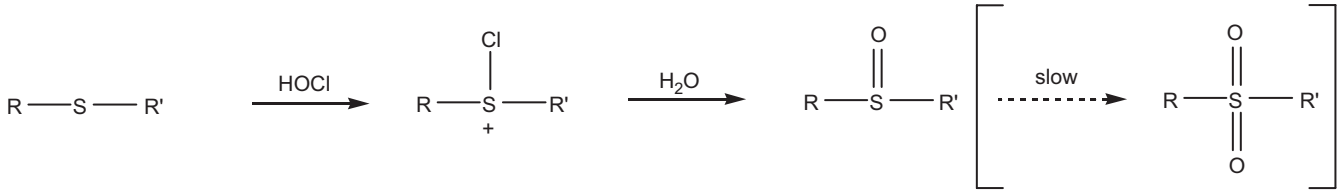


Fig. 9 – Reaction pathway proposed for the chlorination of an RSR′ sulfur-containing compounds. Adapted from Drozdz et al. (1988), Lopez et al. (1994) and Armesto et al. (2000).

present in solution, depending on the pH. However, during chlorination, only the HOCl reactivity with the neutral form of amines was shown to be significant (Antelo et al., 1995; Abia et al., 1998).

Table 3 reports second-order rate constants for the reaction of HOCl with the neutral species of amines (primary, secondary and tertiary): For primary and secondary amines, rate constants are in the range 10^7–$10^8\,M^{-1}\,s^{-1}$; for tertiary amines, a lower chlorine reactivity with rate constants of about 10^3–$10^4\,M^{-1}\,s^{-1}$ is reported. Fig. 10 represents the Taft's plot for chlorination of basic aliphatic amines obtained from rate constants used by Abia et al. (1998). This relationship correlates the logarithm of the rate constants with the Taft's constants (σ^*) of the aliphatic amines. For comparison, other rate constants from literature are also included in Fig. 10 (Weil and Morris, 1949; Morris, 1967; Antelo et al., 1992). The Taft's constant was calculated from

$$\sigma^* = \sum \sigma^*_{R1,R2,R3} \quad (24)$$

with $\sigma^*_{R1,R2,R3}$, the Taft'constant of each nitrogen substituent obtained from Perrin et al. (1981). Generally, rate constants of amines decrease in the order primary amines > secondary amines ≫ tertiary amines, with tertiary amine rate constants at least two orders of magnitude lower than those of primary or secondary amines. As previously shown by Abia et al. (1998), primary and secondary amines can be represented in the same plot in the Taft correlation, suggesting a similar chlorination mechanism for these compounds. The slope of the straight line for these compounds is low ($\rho = 1.14 \pm 0.26$). A low sensitivity of chlorination reaction to nitrogen substituents is therefore expected for chlorine reactions with primary and secondary amines. This low sensitivity inducing a small slope in the Taft correlation could explain the smaller correlation coefficient obtained by considering rate constants obtained from several references. For all basic amines, a Cl^+ transfer from HOCl to the nitrogen atom was proposed (Abia et al., 1998). However, due to the different sign of the ρ parameter between amines, and also due to the higher chlorine reactivity with primary and secondary amines, different initial chlorination steps are expected. In the case of primary and secondary amines, the higher chlorine reactivity can be explained by a water-assisted mechanism if we consider the analysis of the free energy profiles. For these amines, a positive sign of the ρ parameter is observed. A negative charge development at the transition state is hypothesized. An asynchronous process in which proton transfer from the nitrogen to water precedes chlorine transfer from the HOCl molecule to the amine was suggested. Fig. 11a represents the chlorination scheme proposed for primary and secondary amines. According to this mechanism, water molecules are first hydrogen-bonded to both HOCl and nitrogen followed by proton and chlorine transfer. In the case of tertiary amines, such a water-assisted mechanisms cannot be observed due to the absence of a hydrogen bond to the nitrogen atom. Due to the negative sign of the ρ parameter, another chlorination process was proposed for tertiary amines. This mechanism, presented in Fig. 11b, includes an elementary step in which a positive charge is developed on the nitrogen atom (Abia et al., 1998). For tertiary amines, a chlorammonium intermediate is observed first (Ellis and Soper, 1954). This very reactive intermediate could catalytically halogenate numerous substrates present in solution (Prütz, 1998a; Masuda et al., 2001; Dodd et al., 2005).

For more acidic amines including an electron-withdrawing substituent (such as glycinamide, N-chloromethylamine or 3,3′-iminodipropionitrile), correlations such as presented in Fig. 10 are not applicable. Due to a high electron-withdrawing character of one or several substituents, a different initial chlorination mechanism is expected for these compounds.

Amides. Table 4 reports some rate constants for chlorine reactions with amides. Similar to amines, amides chlorination could induce chloramination reaction via Cl^+ transfer from chlorine to the nitrogen atom. However, due to the electron-withdrawing character of the carbonyl function, amides are usually much less basic than amines. Therefore, a smaller chlorine reactivity with amide functions is commonly observed (Morris, 1967; Pattison and Davies, 2001).

Various mechanisms and elementary reactions were suggested in literature for amide chlorination: (i) It was suggested that ClO^- is the main reactive agent in an alkaline medium (Thomm and Wayman, 1969; Prütz, 1999). This reactivity was shown to fit well with the pH dependence of the kinetics of the reaction of chlorine with several cycloamides (Prütz, 1999). It could result from an initial hydrogen bond formation between the amido hydrogen and O^- group. Under these circumstances, an electron-withdrawing effect of the substituents leads to a weaker NH bond which in turn leads to a higher expected rate of the ClO^- reaction (Thomm and Wayman, 1969). (ii) Since the dissociation of amides occurs quite readily (pK_a's on the order of 16 for amides versus 20 for acetone (Serjeant and Dempsey, 1979; Robert and Caserio, 1968)), anionic structures resembling enolates could be formed. Therefore, another possible mechanism via a pattern similar to that of the haloform reaction could also be considered (Section 3.2.1.2). Such a mechanism was suggested by Morris (1978).

Amino acids and peptides. Chlorine reaction with amino acids and peptides (only terminal amines) is usually fast

Table 3 – Kinetics of chlorination of selected aliphatic organic amines

Compounds	pK_a	Elementary reaction rate constants k_{HOCl} ($M^{-1}s^{-1}$)	Apparent rate constants at given pH or pH 7[a] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
Primary amines					
$MeNH_2$	10.66	1.9×10^8	3.2×10^{4a}	25	Margerum et al. (1978) cited by Abia et al. (1998)
		3.6×10^8	6.1×10^{4a}	25	Morris (1967) calculated from Weil and Morris (1949)
			4.23×10^4 (pH 6.8)	22	Yoon and Jensen (1993) calculated from Gray et al. (1978)
$EtNH_2$	10.81	1.98×10^8	2.4×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
$PrNH_2$	10.56	1.83×10^8	3.9×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
$BuNH_2$	10.49	1.63×10^8	4.1×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
		1.03×10^8	2.6×10^{4a}	25	Antelo et al. (1992)
$iPrNH_2$	10.67	1.88×10^8	3.1×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
$iBuNH_2$	10.49	1.57×10^8	3.9×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
		8.68×10^7	2.2×10^{4a}	25	Antelo et al. (1992)
$sBuNH_2$	10.56	8.9×10^7	1.9×10^{4a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
		5.16×10^7	1.1×10^{4a}	25	Antelo et al. (1992)
$tBuNH_2$	10.69	5.44×10^7	8.6×10^{3a}	25	Abia et al. (1998) calculated from Antelo et al. (1995)
		3.2×10^7	5.1×10^{3a}	25	Antelo et al. (1992)
			$2.5 (\pm 0.2) \times 10^3$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Secondary amines					
Me_2NH	10.72	6.05×10^7	8.9×10^{3a}	25	Abia et al. (1998)
		3.3×10^8	4.9×10^{4a}	25	Morris (1967) calculated from Weil and Morris (1949)
		5×10^7	7.4×10^{3a}	25	Morris (1967) calculated from Edmond and Soper (1949)
MeEtNH	10.92	5.16×10^7	4.8×10^{3a}	20	Abia et al. (1998)
		6.45×10^7	6×10^{3a}	25	
		7×10^7		35	
Et_2NH	11.02	3.71×10^7	2.7×10^{3a}	20	Abia et al. (1998)
		4.14×10^7	3.1×10^{3a}	25	
		4.64×10^7		30	
		6.46×10^7		35	
		1.4×10^7	1×10^{3a}	25	Morris (1967) calculated from Edmond and Soper (1949)
		1.4×10^8	1×10^{4a}	25	Morris (1967) calculated from Friend (1954)
Pr_2NH	10.94	3.04×10^7	2.7×10^{3a}	20	Abia et al. (1998)
		3.81×10^7	3.4×10^{3a}	25	
		4.46×10^7		30	
		4.53×10^7		35	
		4.3×10^7	3.8×10^{3a}	25	Morris (1967) calculated from Edmond and Soper (1949)
iPr_2NH	11.48	1.36×10^7	3.5×10^{2a}	20	Abia et al. (1998)
		1.8×10^7	4.6×10^{2a}	25	
		1.94×10^7		30	
		2.7×10^7		35	
iBu_2NH	10.41[b]	2.2×10^7	6.6×10^{3a}	25	Abia et al. (1998)

Table 3 (*continued*)

Compounds	pK_a	Elementary reaction rate constants k_{HOCl} ($M^{-1}s^{-1}$)	Apparent rate constants at given pH or pH 7[a] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
Tertiary amines					
Trimethylamine	9.75	5×10^4	6.9×10^{1a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
(*N*-Me)-piperidine	10.08	8×10^4	5.2×10^{1a}	25	Canle (1994) cited by Abia et al. (1998)
Diethylethanolamine	9.82	1.4×10^5	1.6×10^{2a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
Dimethylethanolamine	9.26	3×10^4	1.3×10^{2a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
Methyldiethanolamine	8.52	6.4×10^3	1.5×10^{2a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
Ethyldiethanolamine	8.92	1.6×10^4	1.5×10^{2a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
Triethanolamine	7.98	1.2×10^3	8.8×10^{1a}	25	Abia et al. (1998) calculated from Antelo et al. (1985)
More acidic aliphatic amines					
Ethyl guanidine			19 (±2) (pH 7.2–7.4)	22	Pattison and Davies (2001)
Acetamidine			130 (±20) (pH 7.2–7.4)	22	Pattison and Davies (2001)
CH_3NHCl		3.52×10^2	2.7×10^{2a}	25	Margerum et al. (1978)
		$2.88\ (\pm 0.18) \times 10^2$	2.2×10^{2a}	20	Poncin et al. (1984)
Glycinamide	7.9	$4.3\ (\pm 0.3) \times 10^6$	3.7×10^{5a}	25	Armesto et al. (2001)
3,3′-iminodipropionitrile	5.3	2.6×10^5	2×10^{5a}	20	Abia et al. (1998)
		2.9×10^5	2.2×0^{5a}	25	
		3.5×10^5		30	
		3.7×10^5		35	

[a] Calculated from literature data for pH 7 (by considering $pK_{HOCl} = 7.54$ and pK_a compound values reported in the table).
[b] Estimated pK_a from SPARC on-line calculator Weber and Kenneke).

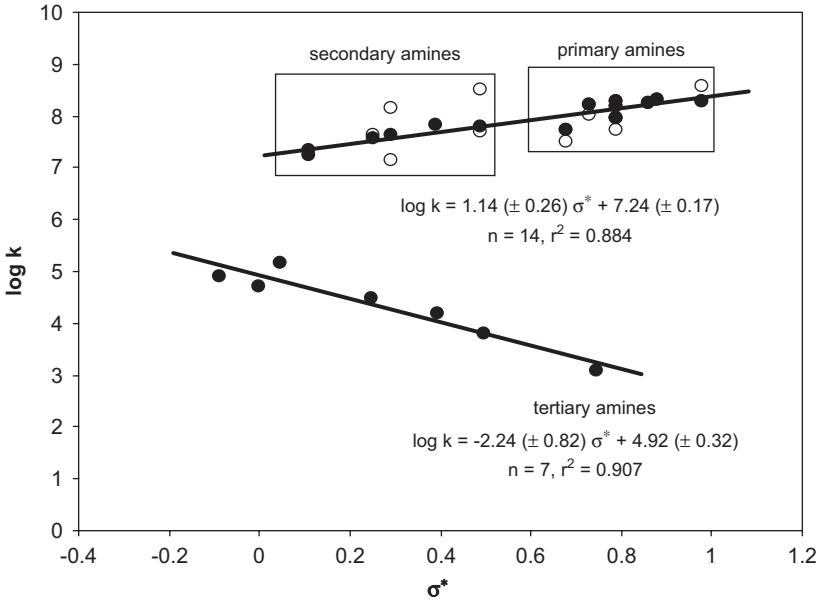


Fig. 10 – Taft's correlation for chlorination of basic aliphatic amines at 25 °C: Full symbols (●) represent rate constant values used by Abia et al. (1998) and were used for calculation of correlation coefficients and Taft's plot equations; open circles (○) represent other rate constants reported in literature.

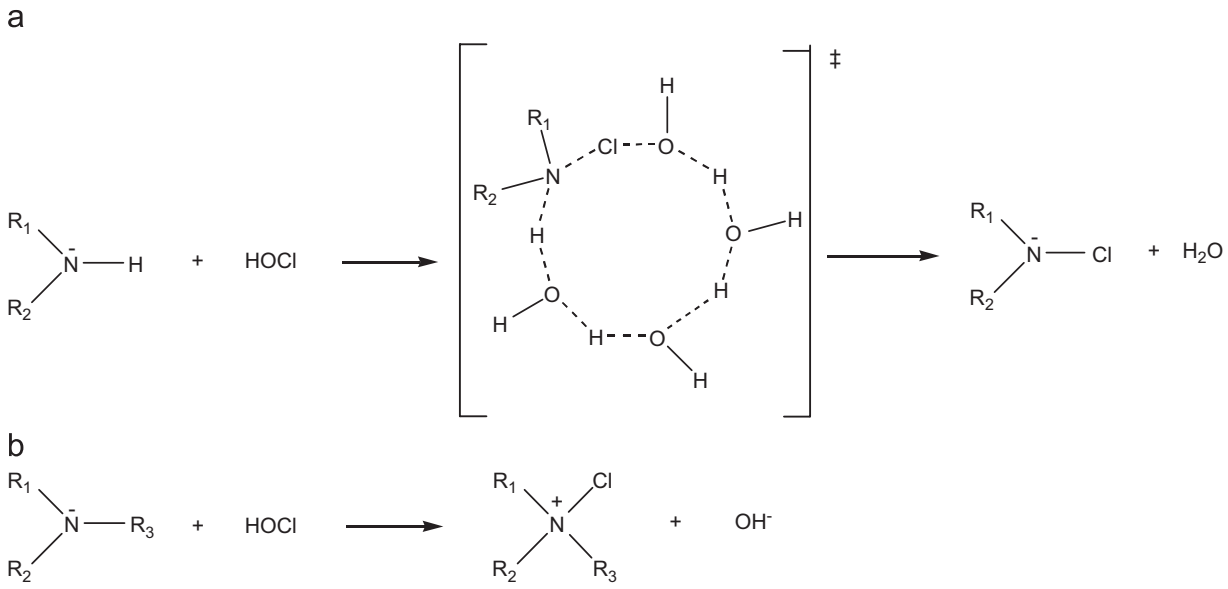


Fig. 11 – Reaction schemes proposed by Abia et al. (1998) for the chlorination of organic aliphatic amines: (a) primary and secondary amines; (b) tertiary amines.

(Table 5). For compounds containing no sulfur, it results in initial *N*-halo-(amino acids or peptides) formation (Armesto et al., 1994b). In the case of α-amino acids, a decarboxylation and a desamination follows this initial chloramination step which leads to a carbonyl compound, ammonia and a nitrile (Fig. 12) (Stanbro and Smith, 1979; le Cloirec and Martin, 1985; Doré, 1989; Nweke and Scully, 1989; Armesto et al., 1994c; Conyers and Scully, 1997; Hawkins et al., 2003). In the case of peptides, the initial N-chloramination would take place on the nitrogen atom at the amino-terminal function. No chlorine reactivity with the carboxy-terminal residue or the peptide bond was previously shown (Armesto et al., 1994a, 2001; Abia et al., 1998). Similar to α-amino acids, further decarboxylation and desamination mechanisms were shown for glycylphenylalanine and alanylphenylalanine (Keefe et al., 1997; Fox et al., 1997).

Table 5 reports rate constants for peptides and amino acids chlorination. Rate constants similar to those obtained for basic aliphatic amines were shown for amino acids containing no sulfur. Therefore, similar initial chloramination mechanisms to those previously described with primary, secondary and tertiary amines are expected for these compounds (Abia et al., 1998). For sulfur-containing compounds, chlorine reaction takes place mainly at the sulfur functionality (Pattison and Davies, 2001; Armesto et al., 2000). As previously shown in Section 3.2.1.3, disulfide compounds, sulfonic acids or sulfoxide derivative formation was reported as a result of cysteine and methionine chlorination (Pereira et al., 1973; Drozdz et al., 1988; Armesto et al., 2000).

3.2.2. *Aromatic compounds*

3.2.2.1. *Monocyclic aromatic hydrocarbons*. In addition to specific reactions on certain moieties bound to the aromatic ring, chlorine reacts with aromatic compounds mostly by electrophilic substitutions. Initially, these reactions occur mainly in *ortho* or *para* position to a substituent (Roberts and Caserio, 1968). Chlorination of phenols constitutes one of the best-studied mechanisms of electrophilic substitution (Burttschell et al., 1959; Lee and Morris, 1962; Gallard and von Gunten, 2002; Acero et al., 2005b). Due to the activating *ortho*/*para* directing hydroxyl group, the chlorination of phenol proceeds by a stepwise substitution of the 2, 4 and 6 positions (Fig. 13). For substituted phenols, an atom partial charge approach can be used to establish the chlorine reactive sites. This approach was previously applied by Hu et al. (2002a, 2003).

The substituents on the aromatic ring influence the substitution reaction rate. Electron-donor properties of the substituents increase the charge density of the aromatic ring and lead to a faster substitution reaction. In the case of phenols, dihydroxybenzenes and alkyloxybenzenes, several elementary reactions were proposed to explain and model the global chlorination reaction for a given pH: (i) HOCl reactions with ionized and neutral species of each of these compounds and (ii) acid-catalyzed reaction of HOCl with the neutral form (Eqs. (25)–(27) in the case of phenol (Gallard and von Gunten, 2002))

$$\mathrm{HOCl} + \mathrm{phenol} \rightarrow \mathrm{product}, \quad (25)$$

$$\mathrm{HOCl} + \mathrm{phenoxide\ ion} \rightarrow \mathrm{product}, \quad (26)$$

$$\mathrm{H^+} + \mathrm{HOCl} + \mathrm{phenol} \rightarrow \mathrm{product}. \quad (27)$$

Rate constants of these elementary reactions are reported in Table 6. From these results, the influence of the substituent on the rate of the reaction is clearly highlighted by comparing rate constants of phenol and phenoxide ion (Eqs. (26)–(27)). The phenoxide ion reacts 10^5 times faster than the neutral form of the phenol. This phenomenon seems to be confirmed for all monosubstituted aromatic compounds if the rate constants are compared to the electron-donor character of

Table 4 – Kinetics of chlorination of selected amides

Compounds	Elementary reaction rate constants			Apparent rate constants	T (°C)	References
	k_{Cl_2} ($M^{-1}s^{-1}$)	k_{HOCl} ($M^{-1}s^{-1}$)	k_{ClO^-} ($M^{-1}s^{-1}$)	k_{app} ($M^{-1}s^{-1}$)		
Amides						
N-methyl formamide	1.95	1.70×10^{-3}	0.21		25	Thomm and Wayman (1969)
N-methyl acetamide	83.3	1.70×10^{-3}	1.82×10^{-2}		25	Thomm and Wayman (1969)
		1.40×10^{-3}			25	Morris (1967) calculated from Mauger and Soper (1946)
N-methyl propanamide	1.47×10^{2}	1.70×10^{-2}	9.20×10^{-3}		25	Thomm and Wayman (1969)
Urea		0.075[a]		0.63 (pH 7.3)	25	Morris (1967) calculated from Samples (1959)
(*N*,*N*′)-di-methylurea	4.50×10^{5}	≈0.82	<0.0083		25	Thomm and Wayman (1969)
Propionamide				$4.1 (\pm 1) \times 10^{-2}$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Isobutyramide				$3.3 (\pm 1.6) \times 10^{-2}$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Trimethylacetamide				$8 (\pm 4) \times 10^{-3}$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Cycloamides						
Cyclo(Gly)$_2$				25 (±5)[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
			250			Prütz (1999)
Cyclo(Ala)$_2$				8.2 (±2.1)[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
Cyclo(Ser)$_2$				16 (±3)[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
			150			Prütz (1999)
Cyclo(Asp)$_2$				1.9 (±0.9)[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
			5.5			Prütz (1999)
Cyclo(Gly-Phe)			150			Prütz (1999)
Cyclo(Gly-Pro)			55.3			Prütz (1999)
Cyclo(Asp-Gly)			37			Prütz (1999)
Amide+acid						
N-acetyl-Ala				$1.2 (\pm 1) \times 10^{-3}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
N-acetyl-(Ala)$_2$				$8 (\pm 4) \times 10^{-3}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
N-acetyl-(Ala)$_3$				$2.3 (\pm 1.8) \times 10^{-2}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
N-acetylglycine		5×10^{-2}[b]			25	Morris (1967) calculated from Mauger and Soper (1946)
Amide+ester						
N-acetyl-Leu-OMe				$1.5 (\pm 0.7) \times 10^{-2}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
N-acetyl-(Ala)$_2$-OMe				$6 (\pm 1.5) \times 10^{-2}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)
N-acetyl-(Ala)$_3$-OMe				$1.1 (\pm 0.2) \times 10^{-1}$[a] (pH 7.2–7.4)	22	Pattison and Davies (2001)

[a] Rate constant of each amide group.
[b] Rate constant for HOCl reactivity with ionized species.

the substituted group (represented by σ_i, the Hammett constant of the first substituent). Fig. 14 represents the logarithm of HOCl rate constants as a function of σ_i for phenoxide ion, phenol, anisole and butylphenylether. Fig. 14 was made by considering $\sigma_i \approx \sigma_{ortho} \approx \sigma_{para}$ (Jonsson et al., 1993; Tratnyek and Hoigné, 1994) and using Hammett constant

Table 5 – Kinetics of chlorination of selected amino acids, peptides and ester derivatives

Compounds	pKa[a]	Second-order rate constants			Apparent rate constants at given pH or pH 7[b] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
		k_{HOCl} ($M^{-1}s^{-1}$)		k_{ClO^-} ($M^{-1}s^{-1}$)			
		B^-	B^{2-}				
Amino acids/peptides and derivatives containing no sulfur							
Amino acids (primary amine)							
Glycine	9.78	1.13×10^8			1.5×10^{5b}	25	Armesto et al. (1993)
		5×10^7			6.4×10^{4b}	25	Armesto et al. (1994b)
		7.66×10^7			9.9×10^{4b}	20	Isaac (1981) cited by Isaac et al. (1985)
					$1\ (\pm 0.1) \times 10^5$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
					7.08×10^4 (pH 6.8)	22	Yoon and Jensen (1993) calculated from Gray et al. (1978)
		5×10^7			6.4×10^{4b}	25	Margerum et al. (1978)
Alanine	9.87	3.4×10^7			3.6×10^{4b}	25	Armesto et al. (1993)
		5.4×10^7			5.6×10^{4b}	25	Armesto et al. (1994b)
		5.4×10^7			5.6×10^{4b}	25	Margerum et al. (1978)
					$5.4\ (\pm 0.1) \times 10^4$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
β-alanine	10.06[c]	8.9×10^7			6×10^{4b}	25	Margerum et al. (1978)
Serine					$1.7\ (\pm 0.1) \times 10^5$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Valine					$7.4\ (\pm 0.3) \times 10^4$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
2-amino butyric acid	9.83	8×10^7			9.2×10^{4b}	25	Armesto et al. (1993)
		4.56×10^7			5.2×10^{4b}	25	Antelo et al. (1992)
3-aminobutyric acid	9.54[d]	3.89×10^7			8.7×10^{4b}	25	Antelo et al. (1992)
3-aminoisobutyric acid	9.54[d]	7.15×10^7			1.6×10^{5b}	25	Antelo et al. (1992)
4-aminobutyric acid	10.1[d]	7.56×10^7			4.7×10^{4b}	25	Antelo et al. (1992)
2-amino hexanoic acid	9.83	3.2×10^7			3.7×10^{4b}	25	Armesto et al. (1993)
ε-aminocaproic acid					$4.7\ (\pm 0.7) \times 10^3$ (pH 7.2–7.4)	22	Pattison and Davies (2001)
Amino acids (secondary amine)							
Sarcosine	10.2	1.08×10^8			5.3×10^{4b}	25	Armesto et al. (1993)
2-piperidine carboxylic acid	10.52	6.95×10^7			1.6×10^{4b}	25	Armesto et al. (1994b)
3-piperidine carboxylic acid	10.67	1.12×10^8			1.9×10^{4b}	25	Armesto et al. (1994b)
4-piperidine carboxylic acid	10.55	7.1×10^7			1.6×10^{4b}	25	Armesto et al. (1994b)
Proline	10.65	2×10^7			3.5×10^{3b}	25	Armesto et al. (1993)
Amino acids (tertiary amine)							
(*N*,*N*)-di-Me-glycine	9.94	5×10^4			4.5×10^{1b}	25	Canle (1994) cited by Abia et al. (1998)
Amino acids (quaternary amine)							
Betaine		Negligible[e]			Negligible[b]	25	Armesto et al. (1994b)
Peptides (primary amine)							
Glycyl-glycine	8.25	$9.1\ (\pm 0.3) \times 10^6$			3.8×10^{5b}	25	Armesto et al. (2001)
		5.3×10^6			2.2×10^{5b}	25	Margerum et al. (1978)
					1.97×10^5 (pH 6.8)	22	Yoon and Jensen (1993) calculated from Gray et al. (1978)

Table 5 (*continued*)

Compounds	pKa[a]	Second-order rate constants			Apparent rate constants at given pH or pH 7[b]	T (°C)	References
		k_{HOCl} ($M^{-1}s^{-1}$)		k_{ClO^-} ($M^{-1}s^{-1}$)	k_{app} ($M^{-1}s^{-1}$)		
		B^-	B^{2-}				
		7.91×10^6				15	Armesto et al. (1994a)
		8.13×10^6			3.4×10^{5b}	20	
		9.01×10^6			3.7×10^{5b}	25	
		8.25×10^6				30	
		9.01×10^6				35	
		6.54×10^6				40	
Gly-Sar	8.58	$1.26 (\pm 0.06) \times 10^7$			2.5×10^{5b}	25	Armesto et al. (2001)
Gly-Ala	8.31	$8.8 (\pm 0.9) \times 10^6$			3.2×10^{5b}	25	Armesto et al. (2001)
Gly-Val	8.3	$9.5 (\pm 0.7) \times 10^6$			3.5×10^{5b}	25	Armesto et al. (2001)
Gly-Ile	8.1	$6.4 (\pm 0.5) \times 10^6$			3.7×10^{5b}	25	Armesto et al. (2001)
Gly-Leu	8.13	$6.4 (\pm 0.4) \times 10^6$			3.4×10^{5b}	25	Armesto et al. (2001)
Gly-Pro	8.65	$1.5 (\pm 0.5) \times 10^7$			2.5×10^{5b}	25	Armesto et al. (2001)
Ala-Gly	8.27	$8.5 (\pm 0.8) \times 10^6$			3.4×10^{5b}	25	Armesto et al. (2001)
Val-Gly	7.94	$6 (\pm 0.4) \times 10^6$			4.8×10^{5b}	25	Armesto et al. (2001)
Leu-Ala	7.96	$8 (\pm 0.7) \times 10^6$			6.1×10^{5b}	25	Armesto et al. (2001)
Peptides (secondary amine)							
Pro-Gly	8.7	$1.8 (\pm 0.3) \times 10^7$			2.7×10^{5b}	25	Armesto et al. (2001)
Derivatives							
Glycine methyl ester	8.88	4.3×10^6			4.3×10^{4b}	25	Armesto et al. (1994b)
Glycine ethyl ester	8.88[f]	6.71×10^6			6.8×10^{4b}	20	Isaac (1981) cited by Isaac et al. (1985)
Glycyl-Glycine ethyl ester	8.07	$7.5 (\pm 0.2) \times 10^6$			4.6×10^{5b}	25	Armesto et al. (2001)
		7.66×10^6				15	Armesto et al. (1994a)
		7.65×10^6			4.7×10^{5b}	20	
		7.53×10^6			4.6×10^{5b}	25	
		7.23×10^6				30	
		6.8×10^6				35	
Sulfur-containing amino-acids and proteins							
Cysteine	8.15 and 10.29		1.2×10^{9g}	$1.9 \times 10^{5g,h}$	$\approx 6.2 \times 10^{7b,i}$	25	Armesto et al. (2000)
			3.3×10^{8g}	$5.5 \times 10^{5g,h}$	$\approx 1.7 \times 10^{7b,i}$	22	Pattison and Davies (2001)
Methionine	9.05	$8.7 (\pm 0.2) \times 10^{8g}$			$6.8 \times 10^{8b,j}$	25	Armesto et al. (2000)
Glutathione (GSH)					$\geqslant 1 \times 10^7$ (pH 5; 7.4 and 9)	25	Folkes et al. (1995)

[a] pKa values for amines and sulfur functions.
[b] Calculated from literature data for pH 7 (by considering $pK_{HOCl} = 7.54$ and pKa compound values reported in the table).
[c] From Armesto et al. (1994b).
[d] Estimated pKa from SPARC on-line calculator (Weber and Kenneke).
[e] Rate constant for the zwitterion species.
[f] Estimated pK_a value from structural analogy with glycine methyl ester.
[g] Measured at high pH values.
[h] Rate constant for the reaction of ClO^- with sulfur ionized form.
[i] Calculated by considering chlorine reaction with ionized sulfur group (S^-) as the major reaction.
[j] Calculated by considering sulfur group as the main chlorine reactive site (i.e. similar second-order rate constants (k_{HOCl}) for all methionine species).

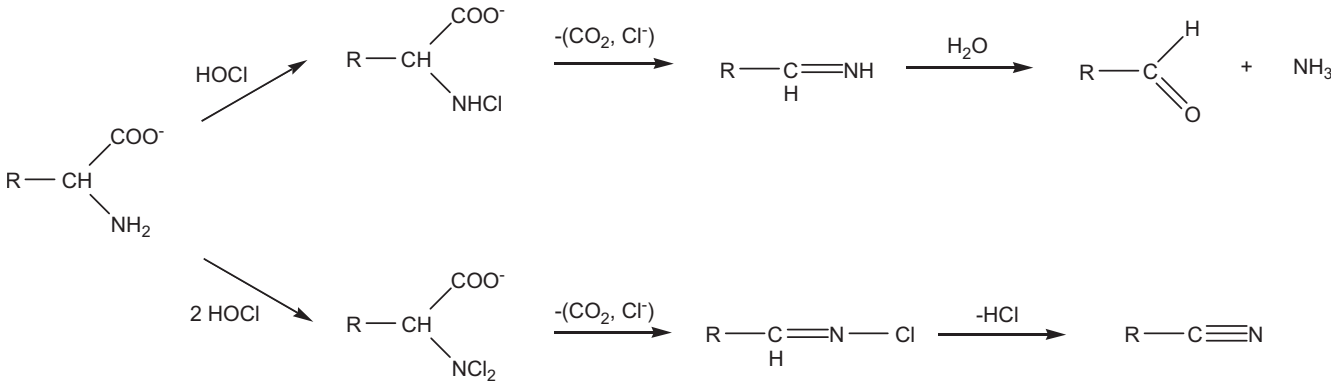


Fig. 12 – Proposed pathway for the reaction of HOCl with amino acids. Adapted from Stanbro and Smith (1979), le Cloirec and Martin (1985), Doré (1989), Nweke and Scully (1989), Armesto et al. (1994c), Conyers and Scully (1997) and Hawkins et al. (2003).

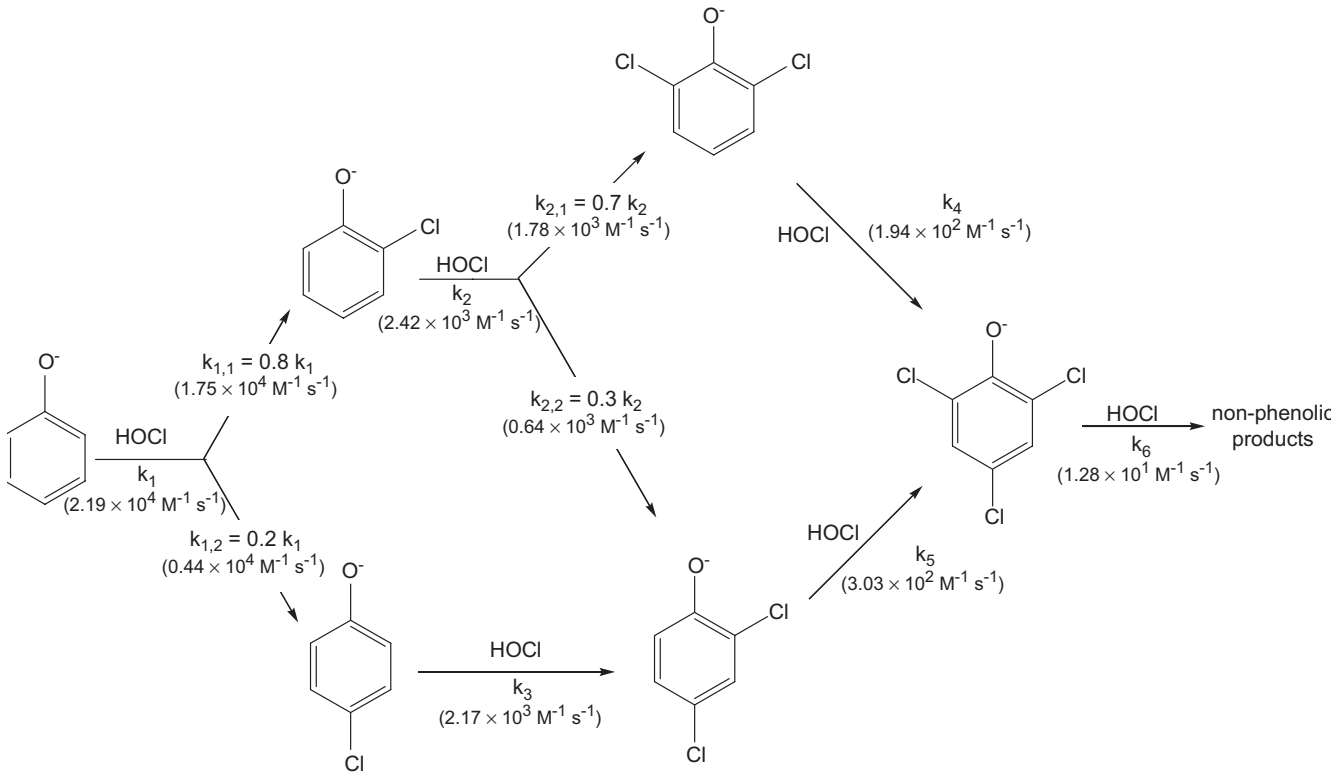


Fig. 13 – Reaction scheme for the chlorination of phenoxide ion (adapted from Lee and Morris (1962) and Burttschell et al. (1959)) with rate constants and ratios percentage obtained from Gallard and von Gunten (2002) and Acero et al. (2005b).

values from Perrin et al. (1981). For the considered compounds, Fig. 14 shows a good correlation between the electron-donor character of the substituent and second-order rate constants. From this graph, a weak chlorine reactivity via an electrophilic mechanism can be expected for most of the monosubstituted aromatic compounds (such as alkyl-, aryl-, alkyloxy-aromatics), usually including high σ_i ($\geqslant -0.45$) (Perrin et al., 1981). However, as the data set is limited and there are several low rate constants (obtained for phenol, anisole and butylphenylether), an estimation of other rate constants has to be done with caution.

Due to a similar initial electrophilic substitution mechanism, several quantitative structure activity relationships can also be obtained for polysubstituted aromatic compounds. Such relationships were frequently used to compare second-order rate constants of phenols or 1,3-dihydroxy-aromatic compounds (Rebenne et al., 1996; Gallard and von Gunten, 2002; Deborde et al., 2004; Acero et al., 2005b; Rule et al., 2005). Figs. 15 and 17 represent Hammett-type correlations for the rate constants of HOCl with substituted phenols and 1,3-dihydroxy-benzenes. These empirical relationships imply a linear correlation between the log of the reaction rate

Table 6 – Kinetics of chlorination of selected aromatic compounds

Compounds	pK_a	Elementary reaction rate constants					Apparent rate constants at given pH or pH 7[a] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
		$k_{HOCl+H+}$ ($M^{-2}s^{-1}$)	k_{HOCl} ($M^{-1}s^{-1}$)			k_{ClO^-} ($M^{-1}s^{-1}$)			
			HB	B^-	B^{2-}				
Phenolic compounds									
Phenol	9.99	249 (±98)	0.36 (±0.28)	$2.19\ (\pm0.08)\times10^4$			18[a]	22	Gallard and von Gunten (2002)
				$3.52\ (\pm0.19)\times10^4$			28[a]	25	Gallard and von Gunten (2002), calculated from Lee and Morris (1962)
4-methylphenol	10.26	$1.69\ (\pm0.49)\times10^3$	0.09 (±0.05)	$2.71\ (\pm0.49)\times10^4$			12[a]	22	Gallard and von Gunten (2002)
4-iodophenol	9.2	$6.39\ (\pm0.34)\times10^3$	0.52 (±0.28)	$2.01\ (\pm0.43)\times10^3$			10[a]	22	Gallard and von Gunten (2002)
4-chlorophenol	9.43	16 (±4)	0.02 (±0.005)	$2.17\ (\pm0.33)\times10^3$			6[a]	22	Gallard and von Gunten (2002)
				$3.16\ (\pm0.22)\times10^3$			9[a]	25	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
2-chlorophenol	8.56			$2.42\ (\pm0.08)\times10^3$			50[a]	25	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
2,4-dichlorophenol	7.85			303 (±9)			29[a]	25	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
2,6-dichlorophenol	6.97			$1.94\ (\pm0.11)\times10^2$			78[a]	25	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
2,4,6-trichlorophenol	6.15			12.84 (±0.69)			9[a]	25	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
2-bromophenol	8.45		0.5	2.6×10^3			70[a]		Acero et al. (2005b)
4-bromophenol	9.17		0.1	2.3×10^3			12[a]		Acero et al. (2005b)
2,4-dibromophenol	7.79		0.5	3×10^2			33[a]		Acero et al. (2005b
2.6-dibromophenol	6.67		2.1	1.5×10^2			80[a]		Acero et al. (2005b)
4-cyanophenol	7.86	0.37 (±0.12)	0.03 (±0.01)	84.6 (±3.8)			8[a]	22	Gallard and von Gunten (2002)
1,3-dihydroxy-benzenes									
Resorcinol	9.43 and 11.21	$8.5\ (\pm1.8)\times10^6$	<330	$1.36\ (\pm0.26)\times10^6$	$1.15\ (\pm0.1)\times10^8$		$\approx4\times10^3$[a]	22	Rebenne et al. (1996)
4-chlororesorcinol	8.09 and 10.75	$1.19\ (\pm0.15)\times10^6$	<65	$1.43\ (\pm0.16)\times10^5$	$6.73\ (\pm0.53)\times10^7$		$\approx9\times10^3$[a]	22	Rebenne et al. (1996)

4,6-dichlororesorcinol	7.53 and 10.35	$2.6 (\pm 1.2) \times 10^4$	47 ($\pm$17)	$3.21 (\pm 0.76) \times 10^4$	$5.91 (\pm 0.81) \times 10^7$		1×10^{4a}	22	Rebenne et al. (1996)
Orcinol	9.35 and 11.50	$9.8 (\pm 1.1) \times 10^6$	$1.25 (\pm 0.16) \times 10^3$	$5.18 (\pm 0.34) \times 10^6$	$4.2 (\pm 0.04) \times 10^8$		1.9×10^{4a}	22	Rebenne et al. (1996)
Alkyloxy-benzenes									
Anisole		1.9×10^4	0.019				0.02[a]	23	Pinkston and Sedlak (2004)
Butylphenylether		8.2×10^4	0.025				0.03[a]	23	Pinkston and Sedlak (2004)
3-methylanisole		1.2×10^6	0.33				0.35[a]	23	Pinkston and Sedlak (2004)
4-methylanisole		4.7×10^4	0.032				0.03[a]	23	Pinkston and Sedlak (2004)
1-phenoxy-2-propanol		2.5×10^4	0.014				0.01[a]	23	Pinkston and Sedlak (2004)
Benzoic acids									
Benzoic acid							Negligible		Larson and Rockwell (1979)
							Negligible (pH 4)		Rockwell and Larson (1978)
m-hydroxybenzoic acid							Negligible		Larson and Rockwell (1979)
Salicylic acid							$\approx$0.1 (pH 7.2)		Prütz (1998a)
Anthranilic acid							$>3 \times 10^4$(pH$\approx$7)		Prütz (1996)
Other substituted aromatic compounds									
3-phenylpropionic acid							Very slow (pH 7.2–7.4)	22	Pattison and Davies (2001)
Polycyclic aromatic compounds									
1-methoxynaphtalene		2.4×10^7	0.35				2[a]	23	Pinkston and Sedlak (2004)
Pyrene			0.28			0.059	0.23[a]	20	Hu et al. (2006)
Heterocyclic compounds									
Adenosine-5′-monophosphate (AMP)							6.4 (pH$\approx$7)		Prütz (1996)
Cytidine-5′-monophosphate (CMP)							66 (pH$\approx$7)		Prütz (1996)
			100				Negligible	83	(pH$\approx$6.9)
	Prütz (1998b)								
Uridine-5′-monophosphate (UMP)			200			3×10^4	5.5×10^3(pH$\approx$6.9)		Prütz (1998b)
Thymidine-5′-monophosphate (TMP)							4.3×10^3(pH$\approx$7)		Prütz (1996)
Guanosine-5′-monophosphate (GMP)							2.1×10^4(pH$\approx$7)		Prütz (1996)
3-methylthymidine							Negligible (pH$\approx$6.9)		Prütz (1998b)
Inosine							9.6×10^4(pH$\approx$7)		Prütz (1996)

[a] Calculated from literature data for pH 7 (by considering $pK_{HOCl} = 7.54$ and pK_a compound values reported in the table).

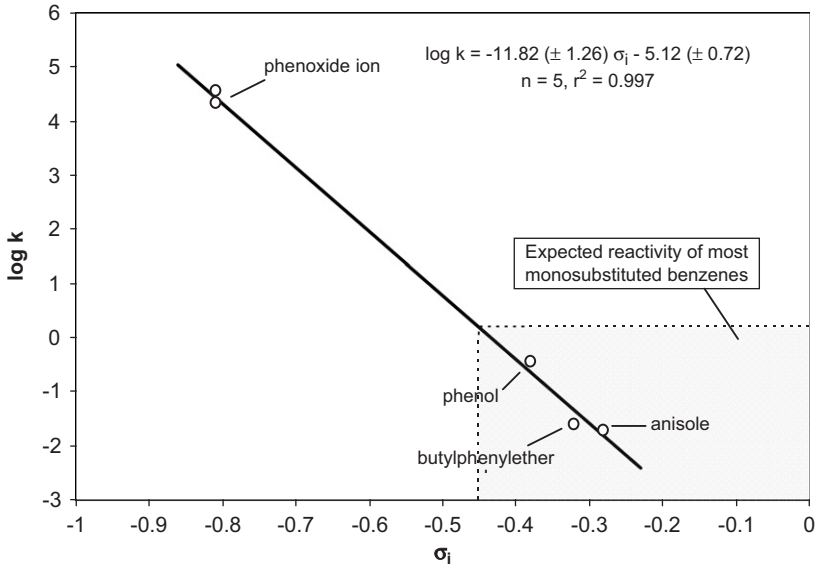


Fig. 14 – Linear correlation between the logarithm of the second-order rate constants for the reaction of phenoxide ion, phenol, anisole and butylphenylether with HOCl versus the estimated Hammett constants of the substituents on benzene (O^-, OH, OCH_3 and OC_4H_9) (*T* 22–25 °C). Rate constants are from Table 6.

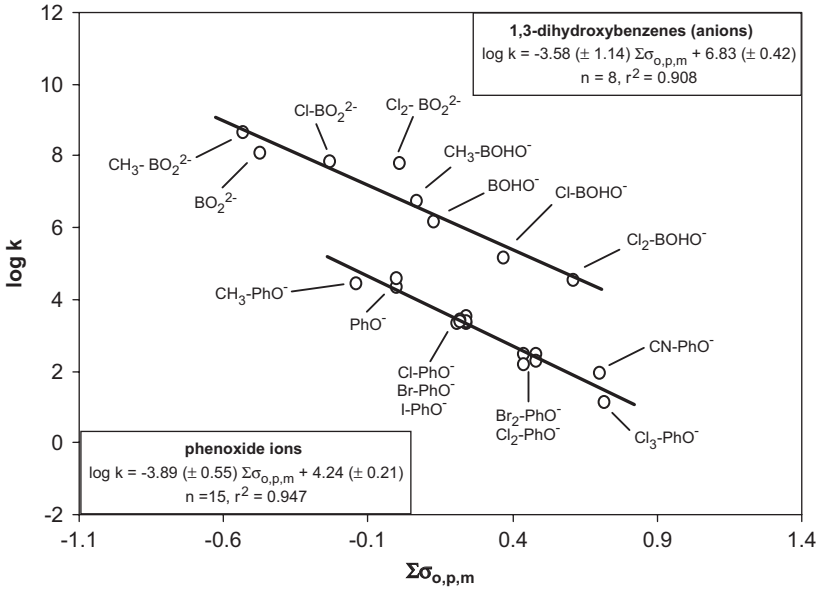


Fig. 15 – Cross-linear correlation between the second-order rate constants for the reactions of substituted phenoxide ions (PhO^-) and 1,3-dihydroxybenzene anions ($BOHO^-$ and BO_2^{2-}) with HOCl and the Hammett constants (T 22–25 °C). Rate constants are from Table 6.

constant for substituted compounds and their Hammett substituent constants ($\sum\sigma_{o,p,m}$) reflecting the effects of substituents on electron density of the aromatic ring by inductive and resonance effects:

$$\log k_{HOCl} = \log k^0_{HOCl} + \rho_{HOCl} \sum \sigma_{o,p,m}, \quad (28)$$

where k^0_{HOCl} is the rate constant for the reaction of HOCl with the reference compound and ρ_{HOCl} is the slope of the resulting line reflecting the sensitivity of the reaction rate to substituent effects.

Fig. 15 represents the most commonly used Hammett-type correlation for oxidation reactions of substituted phenoxide ions and 1,3-dihydroxy-benzene anions. In this figure, the unsubstituted phenoxide ion was used as a reference compound (i.e. $\sum\sigma_{o,p,m} = 0$) to calculate $\sum\sigma_{o,p,m}$ for each molecule. For *ortho*-substituted compounds, σ_{ortho} was taken to be equal to σ_{para} (Tratnyek and Hoigné, 1994). Under these conditions, good linear correlations were obtained for both phenoxide ions and dihydroxybenzene anions (with a slight shift in the case of 4,6-dichloro-1,3-dihydroxybenzene

dianion (Cl_2–BO_2^{2-})). For each of these compounds, a negative Hammett slope was noted, confirming the electrophilic substitution mechanism. However, phenols and dihydroxybenzenes follow two different Hammett relationships. For the same values of $\sum\sigma_{o,p,m}$, rate constants of 1,3-dihydroxybenzenes are more than one order of magnitude higher than those of phenols. It has been discussed previously that a higher sensitivity of dihydroxybenzenes towards HOCl substitution can thus be expected (Gallard and von Gunten, 2002). This is in contrast to ClO_2, where both mono- and dihydroxybenzenes gave the same linear regression (Tratnyek and Hoigné, 1994). These differences of behavior could be explained by different initial reaction mechanisms of HOCl and ClO_2. In the case of phenol, an electron abstraction to form a phenoxyl radical was reported to be the rate-limiting step during ClO_2 oxidation (Wajon et al., 1982), whereas an initial electrophilic attack at specific sites (*ortho* and *para* to the phenolic function) on the aromatic ring was described during chlorination (Lee and Morris, 1962; Burttschell et al., 1959). For both mechanisms, the nature of the substituents on the aromatic ring affects the reaction rate due to its electron-donating or -withdrawing effect. However, during chlorination (contrary to ClO_2 oxidation), each substituent will increase/decrease the chlorine attack at specific sites on the aromatic ring according to its electron-donor or withdrawing character. For example, similar to the phenolic group, a *meta* electron-donor substituent will mainly lead to chlorine substitution in *ortho* and/or *para* to the phenolic function, whereas a *para*/*ortho* electron-donor substituent will make an easier substitution in *meta* position to the phenolic function. Such a directing effect of the substituents could explain the higher sensitivity of 1,3-dihydroxybenzenes to HOCl substitution observed in Fig. 15. By considering the most probable site(s) of chlorine attack (unsubstituted *ortho* or/and *para* position(s) to the phenolic function (site(s) 1)) as shown in Fig. 16, a corrected Hammett-type correlation was proposed for phenol chlorination. In this new correlation, benzene was used as a reference compound (i.e. $\sum\sigma_{o,p,m} = 0$). As described in Fig. 16, $\sum\sigma_{o,p,m}$ were calculated for each compound according to attack on site 1. Under these conditions, by considering that $\sigma_{ortho} \approx \sigma_{para}$ (Tratnyek and Hoigné, 1994), similar $\sum\sigma_{o,p,m}$ values were obtained irrespective of the primary site of attack (Fig. 16). Fig. 17 represents this corrected Hammett-type correlation for the case of phenoxide ions and 1,3-dihydroxybenzene anions. For all these compounds, a good correlation between the log of the reaction rate constants and the $\sum\sigma_{o,p,m}$ was obtained ($r^2 > 0.88$). As previously observed in classical Hammett correlation for 1,3-dihydroxybenzenes (Fig. 15), 4,6-dichloro-1,3-dihydroxybenzene dianion (Cl_2–BO_2^{2-}) is slightly shifted towards the right compared to theoretical line, achieving better correlation ($r^2 > 0.94$) without considering this

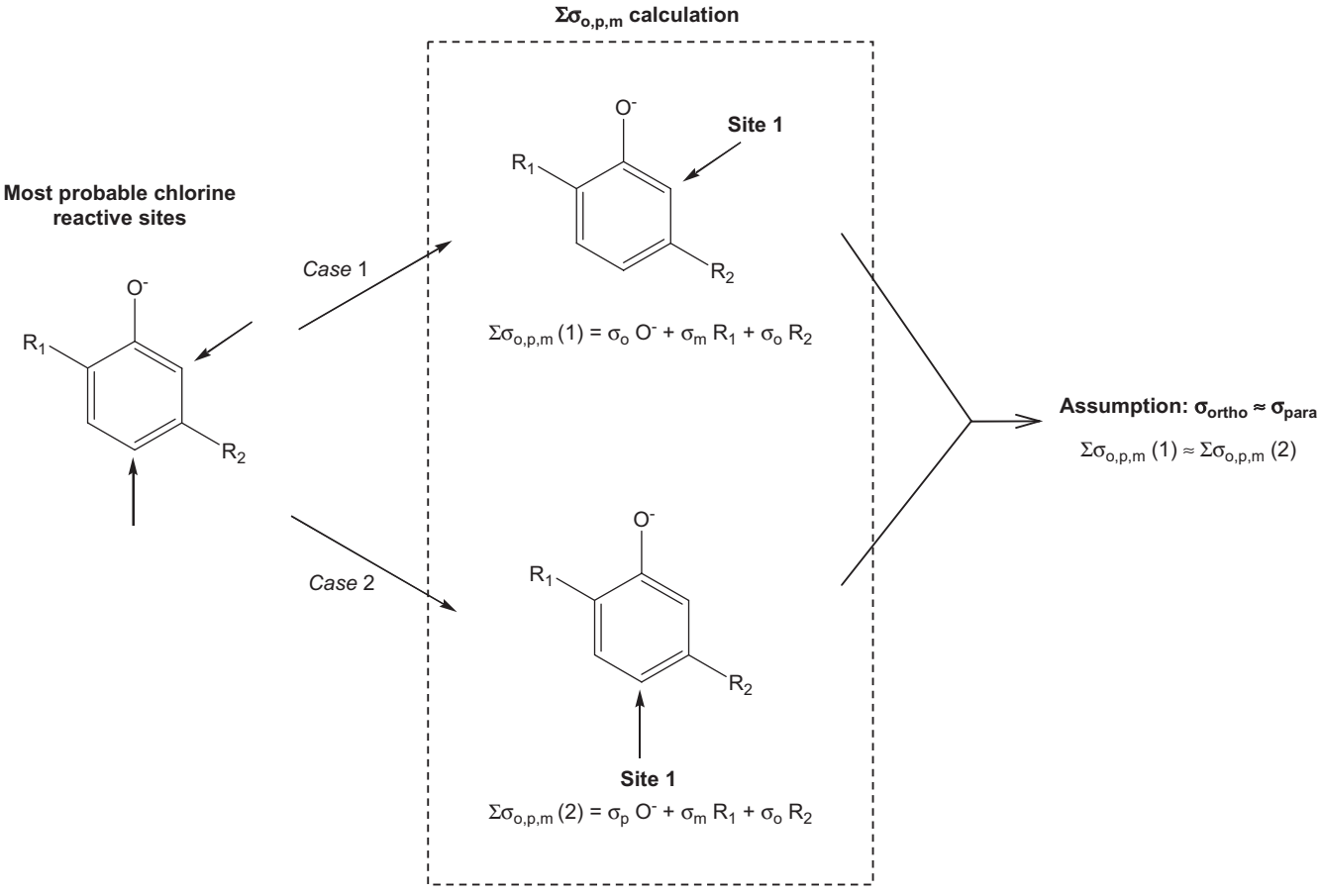


Fig. 16 – Example of $\sum\sigma_{o,p,m}$ calculation for the corrected Hammett-type correlation (Fig. 17).

compound. In contrast to Fig. 15, no difference in the correlations for phenoxide ions and 1,3-dihydroxybenzene ions was observed in Fig. 17.

For ozonation of hydroxybenzenes, an electrophilic attack on specific sites of the aromatic ring was also described in literature (Legube et al., 1980; Doré, 1989). Therefore, comparable to chlorination, a similar trend for the rate constants for aromatic compounds in ozone reactions can be expected. Fig. 18 represents a correlation between HOCl and O_3 rate constants for aromatic compounds for which electrophilic ozone and chlorine attack on the aromatic ring is expected (ozone rate constants are taken from Neta et al. (1988), Huber et al. (2003) or Deborde et al. (2005) in Table 7). For all of these compounds (ionized and neutral forms), a good correlation ($r^2 > 0.96$) is observed between $\log k_{HOCl}$ and $\log k_{O_3}$. For a given aromatic compound, rate constants for ozonation are about four orders of magnitude higher than for chlorination.

Electrophilic substitution reactions are thus the main chlorination mechanism for aromatic rings. In the case of benzoic acids, due to a deactivating *meta* directing COOH

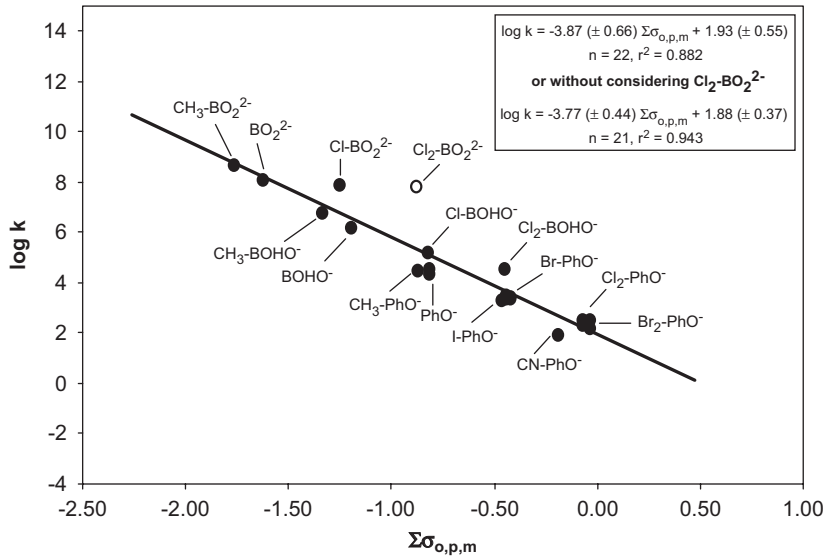


Fig. 17 – Corrected Hammett-type correlation of $\log k$ versus $\sum\sigma_{o,p,m}$ (determined from substituent position to the most probable chlorine reactive site) for the reaction of HOCl with phenoxide ions (PhO^-), 1,3-dihydroxybenzene anions ($BOHO^-$ and BO_2^{2-}) (Table 6) (*T* 22–25 °C).

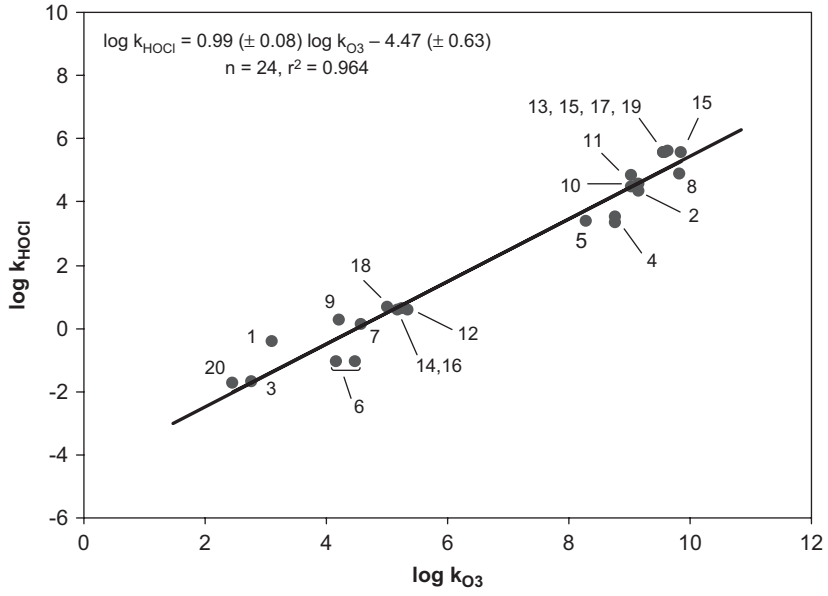


Fig. 18 – Linear correlation between the $\log k_{HOCl}$ and $\log k_{O_3}$ for selected aromatic compounds (mostly phenols) for which electrophilic chlorine and ozone attack is expected. Numbers of the compounds correspond to Table 7.

Table 7 – Rate constants for selected aromatic compounds for which electrophilic HOCl and O_3 attack is expected

No.	Compounds	k_{O_3} ($M^{-1}s^{-1}$)	References	k_{HOCl} ($M^{-1}s^{-1}$)	References
1	Phenol	1.3×10^3	Cited by Neta et al. (1988)	0.36	Gallard and von Gunten (2002)
2	Phenoxide ion	1.4×10^9	Cited by Neta et al. (1988)	2.19×10^4	Gallard and von Gunten (2002)
				3.52×10^4	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
3	4-chlorophenol	6×10^2	Cited by Neta et al. (1988)	0.02	Gallard and von Gunten (2002)
4	4-chlorophenoxide ion	6×10^8	Cited by Neta et al. (1988)	2.17×10^3	Gallard and von Gunten (2002)
				3.16×10^3	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
5	2-chlorophenoxide ion	2×10^8	Cited by Neta et al. (1988)	2.42×10^3	Gallard and von Gunten (2002) calculated from Lee and Morris (1962)
6	4-methylphenol	1.5×10^4	Cited by Neta et al. (1988)	0.09	Gallard and von Gunten (2002)
		3×10^4	Cited by Neta et al. (1988)		
7	4-*n*-nonylphenol	3.8×10^4	Deborde et al. (2005)	1.31	Deborde et al. (2004)
8	4-*n*-nonylphenol (ionized)	6.83×10^9	Deborde et al. (2005)	7.5×10^4	Deborde et al. (2004)
9	Bisphenol A	1.68×10^4	Deborde et al. (2005)	1.84	Gallard et al. (2004)
10	Bisphenol A (ionized 1)	1.06×10^9	Deborde et al. (2005)	3.1×10^4	Gallard et al. (2004)
11	Bisphenol A (ionized 2)	1.11×10^9	Deborde et al. (2005)	6.62×10^4	Gallard et al. (2004)
12	Estradiol	2.21×10^5	Deborde et al. (2005)	3.78	Deborde et al. (2004)
13	Estradiol (ionized)	3.69×10^9	Deborde et al. (2005)	3.64×10^5	Deborde et al. (2004)
14	17α-ethinylestradiol	1.83×10^5	Deborde et al. (2005)	4.33	Deborde et al. (2004)
15	17α-ethinylestradiol (ionized)	3.65×10^9	Deborde et al. (2005)	3.52×10^5	Deborde et al. (2004)
		7×10^9	Huber et al. (2003)		
16	Estrone	1.53×10^5	Deborde et al. (2005)	3.74	Deborde et al. (2004)
17	Estrone (ionized)	4.24×10^9	Deborde et al. (2005)	4.15×10^5	Deborde et al. (2004)
18	Estriol	1.01×10^5	Deborde et al. (2005)	4.82	Deborde et al. (2004)
19	Estriol (ionized)	3.89×10^9	Deborde et al. (2005)	3.56×10^5	Deborde et al. (2004)
20	Anisole	2.9×10^2	Cited by Neta et al. (1988)	0.019	Pinkston and Sedlak (2004)

The rate constants presented in this table are those used for the correlation shown in Fig. 18.

group, only a low chlorine reactivity was usually shown (Table 6). In addition to the electrophilic substitution mechanism, a decarboxylation mechanism was described for these compounds (Larson and Rockwell, 1979; Boyce and Hornig, 1983). In the case of aniline compounds, in addition to the electrophilic attack of HOCl on the aromatic ring, a chlorine attack on the amine function was considered. This is the major reaction and results in an initial chloramine formation which could lead to chloroaniline after rearrangement (Haberfield and Paul, 1965; Gassman et al., 1972; Dodd and Huang, 2004). Higher rate constants are usually observed for these compounds. For anthranilic acid (2-aminobenzoic acid), a rate constant higher than $3 \times 10^4\ M^{-1}s^{-1}$ was shown at pH 7 whereas only very low chlorine reactivity towards other substituted benzoic acids was noted (Table 6) (Larson and Rockwell, 1979; Prütz, 1996, 1998a).

3.2.2.2. *Polycyclic aromatic hydrocarbons*. In contrast to benzene, not all carbon–carbon bonds of polycyclic aromatic compounds are identical with regard to electron density (Roberts and Caserio, 1968). Therefore, a higher reactivity via substitution or addition mechanisms is usually shown in the case of polycyclic aromatic compounds (Table 6). Chlorine reactivity with these compounds mainly results in induction of C–OH, C = O and C–Cl bonds (Carlson et al., 1978; Liukkonen et al., 1983; Oyler et al., 1983; Hu et al., 2006).

3.2.2.3. *Heterocyclic structures, nucleobases and nucleotides*. In the case of heterocyclic structures, due to more complex intramolecular electronic and/or resonance structures, chlorine reactivity and main probable reaction sites are commonly more difficult to estimate. For such chemical structures, substitution, addition and oxidation reactions have been proposed (Doré, 1989; Gould et al., 1984a,b; Lin and Carlson, 1984).

In the case of pyrimidine nucleobases, an electrophilic reaction of chlorine with the heterocyclic NH groups (N1 and N3) and the carbon C5 on the aromatic ring have been reported (Hoyano et al., 1973; Gould et al., 1984a; Reynolds et al., 1988; Young and Uden, 1994). Moreover, for cytosine, a chlorine reaction on the exocyclic NH_2 group was described (Patton et al., 1972; Gould et al., 1984b). However, for all these compounds, the site of initial chlorine attack is still unclear. According to the considered study, unsubstituted carbon C5 (Gould et al., 1984a,b; Young and Uden, 1994) or nitrogen functions (Patton et al., 1972; Prütz, 1996, 1998b) have been reported to be the primary site of attack.

Table 6 reports chlorine reaction rate constants for selected nucleobases and nucleotides obtained from Prütz (1996, 1998b). According to these studies, chlorine reacts slowly with the exocyclic NH_2 groups of adenosine-5′-monophosphate (AMP), cytidine-5′-monophosphate (CMP) and guanosine-5′-monophosphate (GMP) but very fast with the

heterocyclic NH groups of GMP, inosine, thymidine-5′-monophosphate (TMP) and uridine-5′-monophosphate (UMP). In the case of 3-*N*-methylthymidine, no chlorine reactivity was reported. This confirms the proposed chlorine interaction at the heterocyclic NH group of thymidine. For TMP and UMP, with a heterocyclic NH group as acceptor, chlorine reactivity was shown to increase with pH. Therefore, a chlorine reaction which mainly involves ClO^- species was proposed (Prütz, 1996, 1998b). For all these nucleobases and nucleotides, a first chloramines formation was reported. In the case of TMP and UMP, the chlorinated products (including the heterocyclic chloramino group) were shown to be very reactive, for instance with gluthatione, disulfide or aliphatic amines (Prütz, 1998b).

4. Chlorine reactivity towards organic micropollutants relevant to water treatment

An overview over the chlorine reactivity (kinetic and mechanism) towards the main classes of organic and inorganic compounds has been provided in this study. For organic compounds with complex chemical structures, the main reactive sites can be derived by considering the known chlorine reactivity with the various functional groups. Because numerous kinetic and mechanistic studies on chlorination of pharmaceuticals, endocrine disruptors and cyanotoxins are available, a comparison between expected and observed chlorine reactivity with some of these compounds of concern for urban water management is performed in this chapter (Table 8). Based on the known chlorine reactivity with the main functional groups (i.e. by taking into account that the chlorine reactivity usually decreases in the order: reduced sulfur moieties > primary and secondary amines > phenols, tertiary amines ≫ double bonds, other aromatics, carbonyls, amides), the main chlorine reactive site was established. Based on this main reactive site and considering the entire chemical structure (e.g. substituent effects), the expected chlorine reactivity was derived. In this part, chlorine reactivity and primary products (mechanisms) are discussed. During chlorination, primary products can be considered as precursors of DBPs (Rule et al., 2005). However, due to usually low initial micropollutant concentrations, low DBP formation from these micropollutants (compared to DNOM) is expected.

4.1. *Endocrine disruptors and pharmaceuticals*

In recent years, there has been growing concern about the presence of endocrine disruptors and pharmaceuticals in the aquatic environment. Although usually present in low concentrations ($ng\,L^{-1}$-$\mu g\,L^{-1}$), numerous of these compounds have been reported in groundwaters and surface waters (Blackburn and Waldock, 1995; Ternes, 1998; Hirsch et al., 1999; Kolpin et al., 2002; Ying et al., 2002). Some of them could be responsible for feminization of fish (Jobling et al., 1998; Larsson et al., 1999). Therefore, information is needed primarily on possible benefits of chlorination of wastewater as a means for source control and protection of ecosystems. In addition, it has to be investigated whether drinking water chlorination is beneficial to minimize human exposure to these compounds.

Table 9 reports rate constants of chlorine reactions with selected endocrine disruptors and pharmaceuticals. From these data, pH dependence of apparent rate constants and half-life times for a chlorine concentration of $1\,mg\,L^{-1}$ were calculated (Fig. 19). For selected compounds, pH-dependent profiles and chlorine reactivities were observed according to their chemical structure (chemical functional group and speciation in solution).

For nonylphenol, bisphenol A, triclosan (and chlorinated derivatives), estrogenic steroid hormones and acetaminophen, the main chlorine reactivity is expected on the phenolic ring, if the weak chlorine reactivity with the other functional groups (alkyl, alcohol, amide, acid, etc.) is considered. For all these compounds, an initial electrophilic attack of chlorine in *ortho* and/or *para* position to the phenol moiety is expected. Such a reactivity was previously demonstrated by the identification of mono-, di- and tri-chlorinated transformation products of nonylphenol, bisphenol A, triclosan, acetaminophen and certain steroid hormones (Hu et al., 2002a, b, 2003; Yamamoto and Yasuhara, 2002; Moriyama et al., 2004; Rule et al., 2005; Bedner and MacCrehan, 2006). By considering the electron-donor character of the substituents (i.e. $Cl \ll NHCOR < R < OR$), the following order of reactivity, acetaminophen ≈ triclosan < bisphenol A ≈ nonylphenol < estrogens can be expected. This is in agreement with HOCl rate constants reported in literature for the ionized forms of these compounds (Table 9). However, due to the speciation of various phenolic compounds (pK_a values), different apparent rate constants can be observed for a given pH. In the case of triclosan (compared to the other selected phenolic micropollutants), the lower HOCl reactivity of the ionized form is compensated by its higher concentration at pH 7–8 which is a consequence of the lower pK_a. A higher apparent chlorine reactivity with triclosan is observed in this pH range (Fig. 19 and Table 9). Assuming $\sigma_p\ C_9H_{19} \approx \sigma_p\ C_5H_{11}$, $\sigma_p\ (CH_3)_2C_6H_4O\text{-}H \approx \sigma_p\ CH_2C_6H_5$ and $\sigma_p\ OC_6H_3Cl_2 \approx \sigma_p\ OC_6H_5$, the estimated rate constants of the reaction of chlorine with the ionized form(s) of nonylphenol, bisphenol A, acetaminophen and triclosan can be calculated from Hammett-type correlations described in Section 3.2.2.1 (Table 10). For all these molecules, a reasonable agreement between experimental and theoretical values is obtained if we take into account the uncertainty of Hammett values and the experimentally determined rate constants. From these results, none of the two Hammett-type models consistently estimates chlorine reactivity better. For acetaminophen, both models slightly overestimate the chlorine rate constant. In the case of phenolic estrogens, such estimations are more difficult to obtain due to the complexity of the chemical structures. However, because of two electron-donor alkyl-type substituents in *meta* and *para* to the phenolic function, it is not surprising that the chlorine reactivity with these compounds is higher than for nonylphenol and bisphenol A and lower than for 1,3-dihydroxybenzenes. For these compounds, assuming substituents of the phenolic ring similar to two C_5H_{11} groups in *meta* and *para* position to the phenolic function, theoretical rate constants obtained are reported in Table 10.

Table 8 – Selected organic micropollutants (arrows show the sites of the molecules where chlorine attack can be expected)

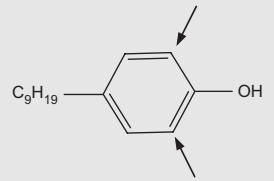
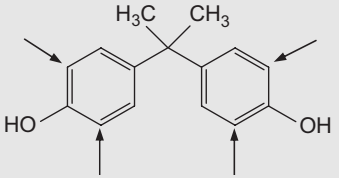
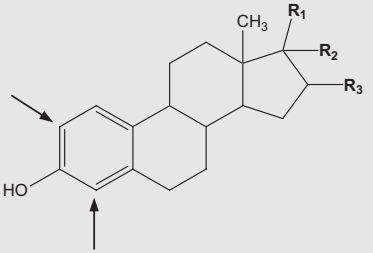
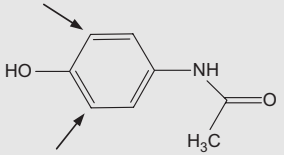
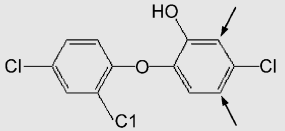
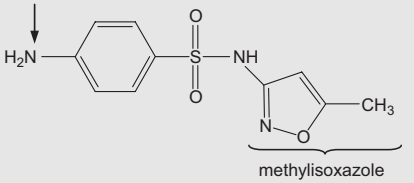
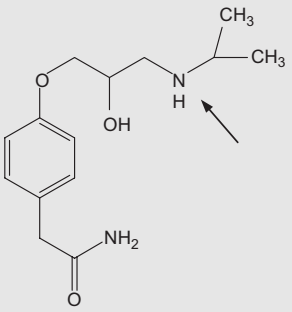
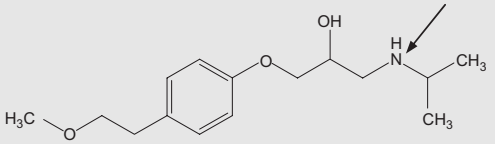
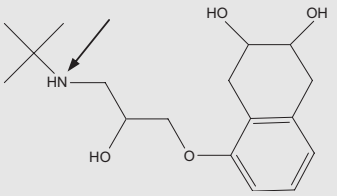
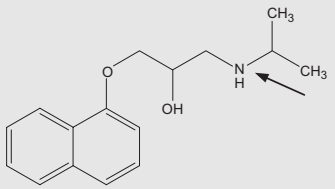
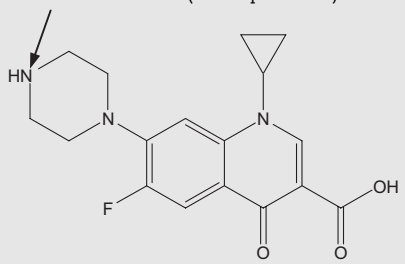
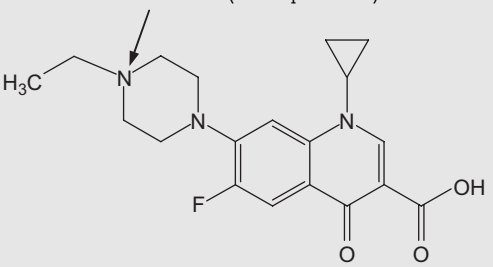
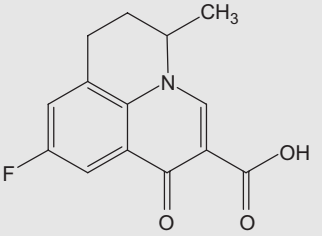
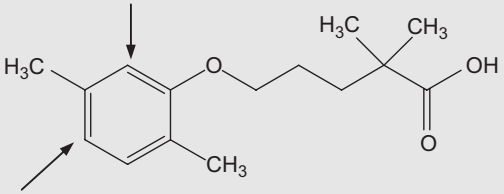
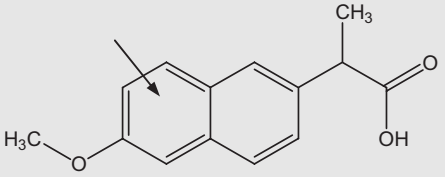
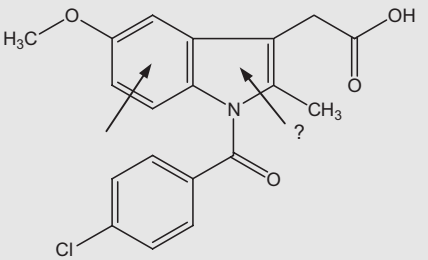
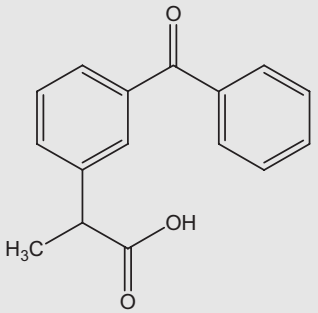
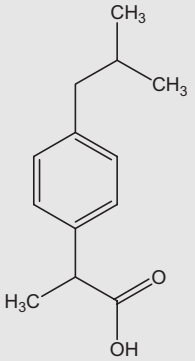
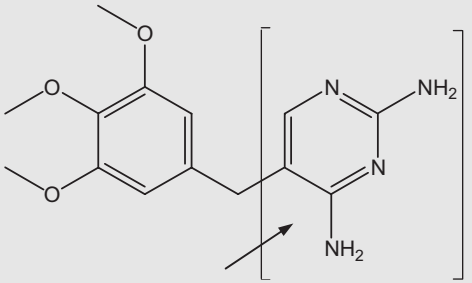
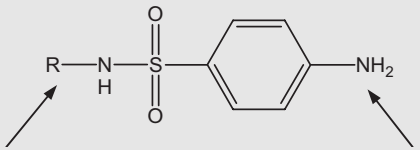
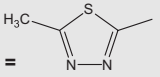
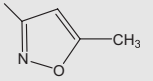
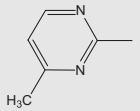
Endocrine disruptors and pharmaceuticals			
Compound	Nonylphenol	Bisphenol A	Steroids: estradiol, estriol, etrone, ethinylestradiol
Use	Non-ionic detergent metabolite	Plasticizer	Reproductive hormones
Structure			
			Estradiol: R_1 = OH, R_2 = H, R_3 = H Estrone: R_1 = ketone, R_2 = H, R_3 = H Estriol : R_1 = OH, R_2 = H, R_3 = OH Ethinylestradiol: R_1 = OH, R_2 = C≡H, R_3 = H
Compound	Acetaminophen	Triclosan	Sulfamethoxazole
Use	Analgesic	Antimicrobial agent	Antibacterial (sulfonamide)
Structure			
Compound	Atenolol	Metoprolol	Nadolol	Propranolol
Use	β-blocker	β-blocker	β-blocker	β-blocker
Structure				

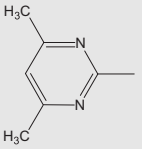
Table 8 (*continued*)

Endocrine disruptors and pharmaceuticals		
Compound Use Structure	Ciprofloxacin Antibacterial (fluoroquinolone) 	Enrofloxacin Antibacterial (fluoroquinolone) 	Flumequine Antibacterial (fluoroquinolone) 
Compound Use Structure	Gemfibrozil Lipid regulator 	Naproxen Analgesic 	Indometacine Analgesic 
Compound Use Structure	Ketoprofen Analgesic 	Ibuprofen Analgesic 	Trimethoprim Antibacterial (pyrimidine) 
Compound Use Structure		Sulfamethizole, sulfamerazine, sulfamethazine, sulfathiazole, sulfadimethoxine Antibacterial (sulfonamide) **Sulfamethizole R =** 	**Sulfamethoxazole R =** 

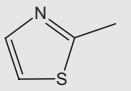
Sulfamerazine R=



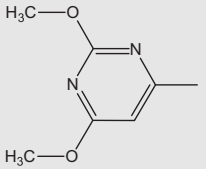
Sulfamethazine R =



Sulfathiazole R =



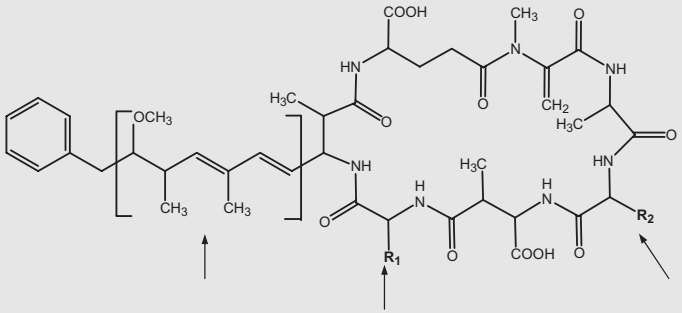
Sulfadimethoxine R =



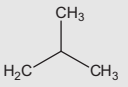
Compound Structure

Cyanotoxins

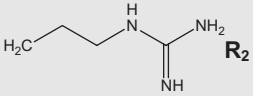
Microcystins LA, LR, RR, YR



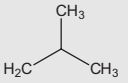
LA: $R_1 = CH_3$ $R_2 =$



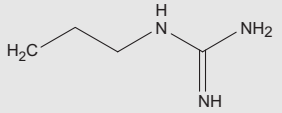
LR: $R_1 =$



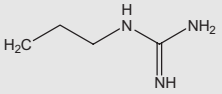
$R_2 =$



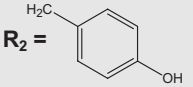
RR : $R_1 = R_2 =$



YR : $R_1 =$

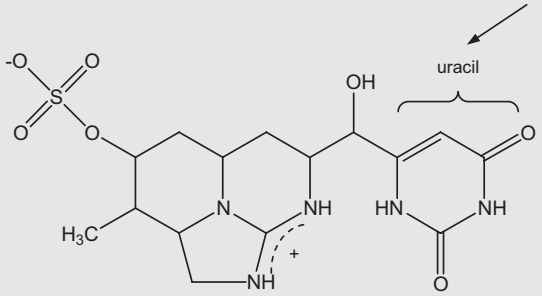


$R_2 =$



Compound Structure

Cylindrospermopsin



Anatoxin-a

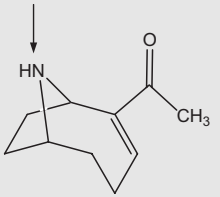


Table 9 – Kinetics of chlorine reaction with selected organic micropollutants relevant for water treatment

Compounds	pK_a	Elementary reaction rate constants						Apparent rate constants at given pH or pH 7[a] k_{app} ($M^{-1}s^{-1}$)	T (°C)	References
		k_{Cl_2} ($M^{-1}s^{-1}$)	k_{HOCl+H^+} ($M^{-2}s^{-1}$)	k_{HOCl} ($M^{-1}s^{-1}$)						
				H_2B^+	HB	B^-	B^{2-}			
4-*n*-nonylphenol	10.7		$3.02 (\pm 0.34) \times 10^4$		$1.31 (\pm 0.13)$	$7.5 (\pm 0.27) \times 10^4$		13[a]	20	Deborde et al. (2004)
Bisphenol A	9.6 and 10.2		3.78×10^4		1.84	3.1×10^4	6.62×10^4	62[a]	20	Gallard et al. (2004)
Triclosan 5 chloro-2-(2,4-dichlorophenoxy)phenol)	7.9				Negligible	$5.4 (\pm 1.82) \times 10^3$		4.7×10^{2a}		Rule et al. (2005)
5,6-dichloro-2-(2,4-dichlorophenoxy) phenol	6.44[b]				Negligible	600 (estimated)		3.6×10^{2a}		Rule et al. (2005)
4,5-dichloro-2-(2,4-dichlorophenoxy) phenol	6.44[b]				Negligible	300 (estimated)		1.8×10^{2a}		Rule et al. (2005)
4,5,6-trichloro-2-(2,4-dichlorophenoxy) phenol	5.81[b]				Negligible	40 (estimated)		29[a]		Rule et al. (2005)
17α-ethinylestradiol	10.4		$2.04 (\pm 0.16) \times 10^5$		$4.33 (\pm 0.53)$	$3.52 (\pm 0.1) \times 10^5$		1.1×10^{2a}	20	Deborde et al. (2004)
17β-estradiol	10.4		$2.24 (\pm 0.17) \times 10^5$		$3.78 (\pm 0.42)$	$3.64 (\pm 0.11) \times 10^5$		1.1×10^{2a}	20	Deborde et al. (2004)
Estrone	10.4		$2.62 (\pm 0.18) \times 10^5$		$3.74 (\pm 0.57)$	$4.15 (\pm 0.17) \times 10^5$		1.3×10^{2a}	20	Deborde et al. (2004)
Estriol	10.4		$1.82 (\pm 0.15) \times 10^5$		$4.82 (\pm 0.5)$	$3.56 (\pm 0.12) \times 10^5$		1.1×10^{2a}	20	Deborde et al. (2004)
Acetaminophen	9.7[c]				3.1	7×10^3		13[a]	23	Pinkston and Sedlak (2004)
Atenolol					Fast				23	Pinkston and Sedlak (2004)
Metoprolol					Fast				23	Pinkston and Sedlak (2004)
Nadolol					Fast				23	Pinkston and Sedlak (2004)
Propranolol					Fast				23	Pinkston and Sedlak (2004)
Sulfamethoxazole	1.7 and 5.6				1.1×10^3	2.4×10^3		1.8×10^{3a}	25	Dodd and Huang (2004)
					6.17×10^2	1.23×10^3		9.4×10^{2a}	25	Chamberlain and Adams (2006)
Ciprofloxacin	6.2 and 8.8			$4.3 (\pm 6.6) \times 10^3$	$3.8 (\pm 2.4) \times 10^{5d}$	$4.9 (\pm 1.9) \times 10^7$		7.6×10^{5a}	22	Dodd et al. (2005)
Enrofloxacin	6.1 and 7.7			29 ($\pm$5)	540 ($\pm$20)[d]	$1.6 (\pm 0.1) \times 10^3$		5.1×10^{2a}	25	Dodd et al. (2005)
Flumequine	6.5				Negligible	Negligible		Negligible[a]		Dodd et al. (2005)
Gemfibrozil			4.2×10^6		7.3×10^{-1}			0.9[a]	23	Pinkston and Sedlak (2004)
Naproxen			8.7×10^6		2.4			2.5[a]	23	Pinkston and Sedlak (2004)

Indometacine			6.9×10^7		67		57^a	23	Pinkston and Sedlak (2004)
Ibuprofen					Negligible		Negligible[a]	23	Pinkston and Sedlak (2004)
Ketoprofen					Negligible		Negligible[a]	23	Pinkston and Sedlak (2004)
Trimethoprim	3.2 and 7.1	$\approx 2 \times 10^5$ to 2×10^{6a}	$6.6\ (\pm 0.5) \times 10^{4e}$	6.2 ($\pm$1.2)	$1.6\ (\pm 0.1) \times 10^2$		58^a	25	Dodd and Huang (2007)
Sulfamethizole	1.86 and 5.29				3.64×10^2	7.28×10^2	5.6×10^{2a}	25	Chamberlain and Adams (2006)
Sulfamerazine	2.06 and 6.9				7.75×10^2	1.55×10^3	9.4×10^{2a}	25	Chamberlain and Adams (2006)
Sulfamethazine	2.07 and 7.49				1.44×10^3	2.89×10^3	1.4×10^{3a}	25	Chamberlain and Adams (2006)
Sulfathiazole	2.01 and 7.11				3.47×10^3	6.94×10^3	3.9×10^{3a}	25	Chamberlain and Adams (2006)
Sulfadimethoxine	2.13 and 6.08				1.04×10^4	2.07×10^4	1.5×10^{4a}	25	Chamberlain and Adams (2006)
Microcystin-LA							200 (pH 5.5) 110 (pH 7.9)	20	Ho et al. (2006)
Microcystin-LR[f]			2.07×10^7		116		127.8 (pH 6.1) 91.5 (pH 7) 33.1 (pH 8)	20	Acero et al. (2005a)
							200 (pH 5.5) 110 (pH 7.9)	20	Ho et al. (2006)
Microcystin-RR							130.3 (pH 6.1) 90.6 (pH 7) 33.8 (pH 8)	20	Acero et al. (2005a)
Microcystin-YR							98.8 (pH 7)	20	Acero et al. (2005a)
Cylindrospermopsin	6.5				38.1	1.96×10^3	1.2×10^{3a}	20	Rodriguez et al. (2007)
Anatoxin-a	9.4						0.71 (pH 7)	20	Rodriguez et al. (2007)

[a] Calculated from literature data for pH 7 (by considering $pK_{aHOCl} = 7.54$ and pK_a compound values reported in the table).
[b] Estimated pK_a from SPARC on-line calculator Weber and Kenneke).
[c] From Sorasuchart et al. (1999).
[d] Kinetic rate constants for reaction of HOCl with neutral/zwitterion species.
[e] Either acid-catalysis rate constant or Cl_2 rate constant have to be considered to model the apparent rate constant at acidic pH level.
[f] $k_{ClO^-} = 6.78\,M^{-1}s^{-1}$.

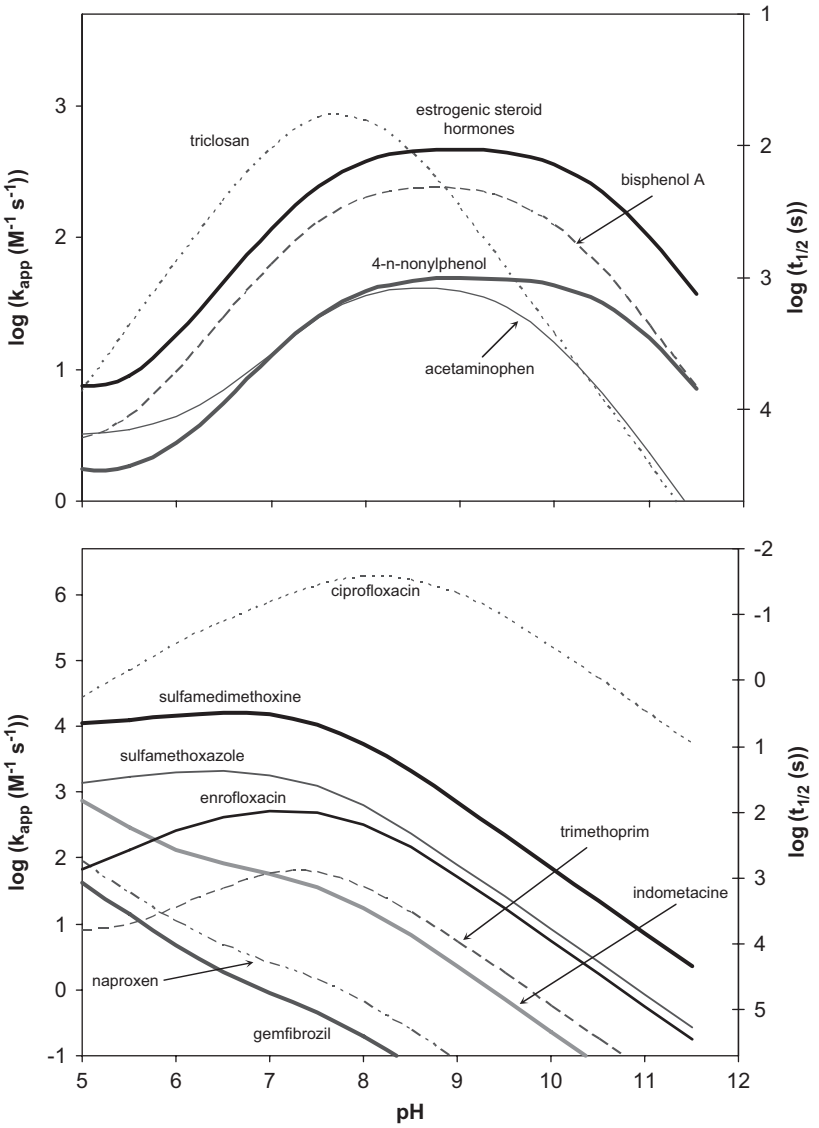


Fig. 19 – pH dependence of the apparent second-order rate constants and the half-life times for chlorine reaction with selected endocrine disruptors and pharmaceuticals at 20–25 °C. Half-lives are calculated for a chlorine concentration of 1 mg L^{-1} (14.1 μM).

In the case of atenolol, metoprolol, nadolol, propranolol, sulfamethoxazole, ciprofloxacin and enrofloxacin, the main chlorine attack can be expected on the more basic amine functional groups according to the non-reactivity of 3,5-dimethylisoxazole reported by Dodd and Huang (2004). Such reactivity was previously described in literature for all these compounds (Pinkston and Sedlak, 2004; Dodd and Huang, 2004; Dodd et al., 2005): (i) For compounds containing primary and secondary amines (i.e. β-blockers and ciprofloxacin), high rate constants (10^7–10^8 M^{-1} s^{-1}), similar to those shown with simple aliphatic amines (Table 3) were determined or suggested (in the case of β-blockers) (Pinkston and Sedlak, 2004; Dodd et al., 2005). (ii) Due to a high electron-withdrawing character of the SO_2R group, only the chlorine reaction with the aniline group was reported in the case of sulfamethoxazole. For this compound, a lower chlorination rate constant (10^3 M^{-1} s^{-1}) was observed (Dodd and Huang, 2004) because of the higher acidic character of the aniline group (pK_a 1.7). (iii) Finally, as previously shown for simple tertiary amines, a smaller chlorination rate constant was also reported for enrofloxacin. For this latter compound, as for other tertiary amines, formation of a very reactive chlorammonium intermediate was described (Dodd et al., 2005).

Similar to ciprofloxacin and enrofloxacin, flumequine is a fluoroquinolone antibacterial agent including a nitrogen atom, a double bond and an aromatic ring. The chlorine reactivity on the aromatic ring and the double bond was previously shown to be very low. Morever, a low chlorine reactivity with the nitrogen function of flumequine can be expected if we take into account the very acidic character of the nitrogen atom (estimated $pK_a \approx -10.08$ from SPARC online calculator (Weber and Kenneke)). Therefore, a more difficult chlorine attack on flumequine compared to ciprofloxacin and enrofloxacin is expected. This is in agreement

Table 10 – Estimated rate constants of the HOCl reaction with ionized form(s) of nonylphenol, bisphenol A, acetaminophen, triclosan and steroid hormones, calculated from the Hammett-type correlations described in Figs. 15 and 17

	Nonylphenol	Bisphenol A	Acetaminophen	Triclosan	Steroid hormones
Model substituents	$-C_5H_{11}$	$-CH_2C_6H_5$	$-NHCOCH_3$	$-OC_6H_5$ and Cl	$2\times-C_5H_{11}$
Theoretical values ($M^{-1}s^{-1}$)					
Obtained from Fig. 15	6.6×10^4	3.9×10^4	3.9×10^4	1.1×10^4	1.4×10^5
Obtained from Fig. 17	1.7×10^5	1.7×10^5	3×10^4	1.2×10^3	6.3×10^5
Experimental values ($M^{-1}s^{-1}$)	7.5×10^4	$3.1–6.6\times10^4$	7×10^3	5.4×10^3	$3.5–4.2\times10^5$

In the case of Fig. 17, correlation without considering Cl_2–BO_2^{2-} was used.

with the very low chlorine reactivity previously described for this compound (Dodd et al., 2005).

In the case of gemfibrozil and naproxen, the main chlorine reactivity in the *ortho* or *para* position to the alkyloxy functional group can be expected by considering the chemical structure of these molecules. The chlorine reactivity was shown to be very low in the case of anisole, methylanisole, butylphenylether and 1-phenoxy-2-propanol (10^{-1}–$10^{-2}\,M^{-1}s^{-1}$). For gemfibrozil, as previously shown (Pinkston and Sedlak, 2004), a similar reaction rate is expected if one considers both the methyl substituents on the aromatic ring and the presence of an acid functional group bound to the alkyloxy functional group. Probably due to the polyaromatic structure, a slightly higher chlorine reactivity with naproxen is observed. Similar to these compounds, the main chlorine reaction site on the alkyloxy-substituted aromatic ring could also be expected for indometacine. Due to pentaheterocycle in *meta*/*para* position to the alkyloxy functional group, a much higher reactivity of chlorine can be expected. However, in comparison to gemfibrozil and naproxen, the chemical structure of indometacine is more complex and includes a pentaheterocyle with a largely unknown chlorine reactivity. For this latter compound, other sites of chlorine attack can possibly be expected in addition to the alkyloxy-substituted aromatic ring.

Similar to gemfibrozil, indometacine and naproxen, electrophilic chlorine substitution on aromatic ring(s) could be expected in the case of ketoprofen and ibuprofen. However, due to electron-withdrawing and/or only weak electron-donor substituents (including alkyl and/or acidic functions), it is not surprising that no chlorine reaction with such compounds was observed (Pinkston and Sedlak, 2004). These findings are supported by the data shown in Fig. 14, and negligible or low rate constants reported for benzoic acids and 3-phenylpropionic acid.

In the case of trimethoprim, two main sites can be expected for chlorine attack: (i) heteroaromatic ring bound to amine functions (2,4-diaminopyrimidinyl moiety) and (ii) alkyloxy polysubstituted aromatic ring (3,4,5-trimethoxytolyl moiety). Despite of the presence of several electron-donor groups on the aromatic ring, chlorine reaction rates with alkyloxybenzenes were shown to be low (Table 6) compared to those with nitrogenous compounds. Thus, although the chlorine reactivity with the 2,4-diaminopyrimidynyl moiety is not known, a major chlorine reaction with this part of the molecule can be expected during trimethoprim chlorination. This hypothesis was recently confirmed in a study on chlorination kinetics and mechanism of trimethoprim. At pH >5, a chlorine reaction with the 2,4-diaminopyrimidinyl moiety was observed. This chlorine reactivity leads to halogenated and hydroxylated transformation products (Dodd and Huang, 2007). At more acidic pH, due to protonation of trimethoprim, the chlorine reactivity on the 2,4-diaminopyrimidinyl moiety becomes less important. A chlorine reactivity with the 3,4,5-trimethoxytolyl moiety inducing mono- and/or dichloro-substituted products was reported in this case. It was suggested that the latter reactivity results from Cl_2 or the acid-catalyzed HOCl reaction with trimethoprim (Dodd and Huang, 2007).

Finally, similar to sulfamethoxazole (previously described), other sulfonamide antibacterial agents such as sulfamethizole, sulfamerazine, sulfamethazine, sulfathiazole and sulfadimethoxine include an aniline group and a heterocyclic structure (for chemical structures see Table 8). For these compounds, the main chlorine reaction can be expected with the aniline group and/or the heterocyclic structure. Chlorination rate constants of sulfamethizole, sulfamerazine and sulfamethazine are in the same order of magnitude as those observed for sulfamethoxazole (Table 9, Chamberlain and Adams, 2006). Therefore, because the main chlorine reaction site on the aniline group is expected for sulfamethoxazole (Dodd and Huang, 2004), probably a similar reaction mechanism can be expected for these compounds. Due to higher chlorine rate constants observed in the case of sulfathiazole and sulfadimethoxine, the main reaction can be expected at the heterocyclic part of these molecules (Table 9, Chamberlain and Adams, 2006).

4.2. *Cyanotoxins*

Rate constants for chlorination of microcystins-LA, -LR, -RR and -YR at various pH values are reported in Table 10. By considering the entire chemical structures (Table 8), several reactive sites of chlorine attack can be expected depending on the considered microcystin: (i) phenolic ring, (ii) ethylguanidyl group, (iii) adda group, (iv) monosubstituted aromatic ring and (v) amide functions. The chlorine reactivity with the monosubstituted aromatic rings and amide functions should be very low and probably negligible considering the rate constants in Table 4 and the HOCl reactivity of most monosubstituted benzenes in Fig. 14. At pH 7.2–7.4, chlorination rate constants reported for sorbic acid (including a adda group) and ethylguanidine are 2.3 and $19\,M^{-1}s^{-1}$, respectively

(Pattison and Davies, 2001; Prütz, 1998a). For this pH, the calculated apparent rate constant obtained for phenol is about $30\,M^{-1}s^{-1}$ (Gallard and von Gunten, 2002). Therefore, according to literature data, the following order of chlorine reactivity is expected with microcystins: YR > RR > LR ≫ LA. In pure water experiments, no significant difference in microcystins (LR, RR and YR) transformation was reported by Acero et al. (2005a). Similarly, no difference of chlorine reactivity between microcystin-LA and -LR was observed by Ho et al. (2006). However, in natural waters, a higher microcystin-YR transformation rate was shown by Ho et al. (2006). Similarly, a faster reaction of chlorine with microcystin-LR than with microcystin-LA was observed. Under these conditions, the expected order of reactivity was observed (Ho et al., 2006).

Concerning cylindrospermopsin, the main chlorine reactivity can be expected on the uracil moiety by considering the probable high resistance of the rest of the molecule to chlorine attack. As previously reported for UMP, a fast chlorine reaction was reported ($\approx 10^3\,M^{-1}s^{-1}$ at pH 7) (Rodriguez et al., 2007). By structural analogy, the main initial chlorine reaction with the heterocyclic NH groups and/or carbon C5 of the uracil part can be expected. In agreement with this hypothesis, 5-chloro-cylindrospermopsin and a truncated carboxylic acid derivative of cylindrospermopsin (cylindrospermic acid) formation was reported during chlorination (Banker et al., 2001).

Finally, in the case of anatoxin-a, the main chlorine reactivity on the secondary amine function can be expected. Therefore, a high rate constant of HOCl with the neutral form of anatoxin-a is expected. However, contrary to this assumption, anatoxin-a was recently shown to be very stable during chlorination at pH 7 (Rodriguez et al., 2007).

5. Conclusion

It has been shown that numerous inorganic and organic micropollutants can be transformed by chlorine. However, for certain compounds, the chlorine reactivity is low and only small modifications in the parent compound's structure are expected under water treatment conditions.

During chlorination processes, HOCl is generally the major reactive species for the reaction with micropollutants. A pH dependence of organic and inorganic micropollutant transformation is commonly observed due to chlorine speciation in solution.

In the case of inorganic compounds, a fast transformation of ammonia, halides (Br^- and I^-), SO_3^{2-}, CN^-, NO_2^-, As(III) and Fe(II) by HOCl is reported whereas only a low chlorine reactivity with Mn(II) was shown in homogeneous solution. Chlorine reactivity usually results from an initial electrophilic attack of HOCl on inorganic compounds. A similar intermediate of XCl type is proposed during chlorination of X = (halides, SO_3^{2-}, CN^-, NO_2^- or As(III)). In the case of ammonia and halides, reactive transformation products which can induce further oxidation reactions are formed.

For the reaction of chlorine with organic compounds, second-order rate constants can vary over more than 10 orders of magnitude. Oxidation, addition and electrophilic substitution reactions of chlorine with organic compounds are reported in literature. Addition and oxidation reactions are typically slow. Only electrophilic attacks of chlorine on the organic compounds are usually fast enough to be significant. Consequently, chlorine is highly selective towards organic compounds and its reactivity is commonly limited to particular sites (such as amine and reduced sulfur functional groups or activated aromatic systems). During chlorination processes, small modifications in the micropollutant structure are expected.

For inorganic and organic compounds, linear structure–activity relationships can be proposed based on the electron-donor/acceptor characteristics, structural analogy and from the expected chlorination mechanisms. Considering the known chlorine reactivity with the main functional groups, an estimation of the order of magnitude of chlorination reaction rate constants can be carried out. Such estimations were shown to be in agreement with literature data for numerous pharmaceuticals and endocrine disruptors. However, due to more complex chemical structures, such estimations are more difficult to be obtained in the case of certain heterocycles or cyanotoxins. Finally, for compounds with an electrophilic ozone and chlorine attack on the aromatic ring, a good linear correlation between chlorination and ozonation rate constants was observed. For a given compound, rate constants of ozonation are about four orders of magnitude higher than those for chlorination.

In summary, significant information on chlorine reactivity with the main classes of organic and inorganic compounds is available in literature. It allows a good understanding of chlorine reactivity with numerous micropollutants. However, some gaps in knowledge were also identified. For example, information on chlorine reactions with heterocyclic structures is scarce. Similarly, because chlorine reactions with double bonds of the matrix water components could be observed under certain water treatment conditions, further studies on chlorination of olefins should be performed. Finally, bromination and iodination was sometimes shown to be highly significant in bromide- and/or iodide-containing waters because the corresponding reactions with HOBr and HOI are often orders of magnitude faster than those with HOCl.

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