# General acid–base catalysis in the reversible disproportionation reaction of *N*-chlorotaurine

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Third-order rate constants for the general base-catalysed reaction between *N*-chlorotaurine and its protonated form, $k_T^B$ ($M^{-2}$ $s^{-1}$), and for general acid catalysis of the reverse process, $k_T^{BH^+}$ ($M^{-2}$ $s^{-1}$), have been determined in aqueous solution at 25 °C and $I = 0.5$ M ($NaClO_4$). The slopes for the Brønsted correlations for the forward and the reverse reactions give $\beta = 0.55$ and $\alpha = 0.48$, respectively. These results suggest that a proton transfer is involved in the rate determining step of the reaction. The high acidity of protonated *N*,*N*-dichlorotaurine in aqueous solution rules out the possibility of a stepwise mechanism involving this species as an intermediate. We propose that disproportionation of *N*-chlorotaurine takes place by a concerted process, where proton and chlorine transfer occur simultaneously in the transition state. This mechanism differs from that found for the transfer of chlorine from a chloramine to an amine.

## Introduction

Taurine, 2-aminoethanesulfonic acid, is one of the most abundant free amino acids in mammalian tissue. It has been implicated in various functions in the body, one of which is to act as a trap for the HOCl produced by the myeloperoxidase–$H_2O_2$–$Cl^-$ system of leukocytes forming the long-lived oxidant *N*-chlorotaurine (TauNHCl), which is much less reactive and less toxic than HOCl. In acid media, or in an excess of hypochlorous acid, a second chlorine atom can be added to form *N*,*N*-dichlorotaurine ($TauNCl_2$). These reactions prevent the attack on cellular components by HOCl.[1–4] Although the presence of TauNHCl in intact cells has been demonstrated, its chemical characteristics and complete functions are not fully understood. A better knowledge of the reactivity of taurine and taurine chloramines may help us to better understand its physiological role.

The chemistry of *N*-halo compounds in aqueous solution has been recently reviewed by Armesto *et al.*[5] Aliphatic *N*-chloramines are formed by reaction of aqueous chlorine with the corresponding amine,[6–8] and are fairly stable in neutral or slightly basic media. However, they decompose in more basic conditions to give an aldehyde, ammonia and chloride ion as final reaction products.[9,10] In acid media *N*-chloramines disproportionate to give the corresponding *N*,*N*-dichloramines. These disproportionation reactions have been studied by several authors.[11–15] The mechanism proposed to account for the experimental observations involves the protonation of the monochloramine in a pre-equilibrium step and the subsequent reaction of the protonated chloramine with an unprotonated chloramine molecule to yield the corresponding dichloramine and amine (Scheme 1). The values of $pK_a$ for the conjugate

$$TauNH_2Cl^+ + H_2O \overset{K_a}{\rightleftharpoons} TauNHCl + H_3O^+$$

$$TauNHCl + TauNH_2Cl^+ \xrightarrow{k_2} TauNH_3^+ + TauNCl_2$$

**Scheme 1**

acids of *N*-chloramines that are obtained by the fit of the experimental data to the kinetic equation derived for Scheme 1 are in good agreement with those obtained spectrophotometrically.[11] Some of these authors have studied this reaction in the presence of buffer solutions and have found that the reaction is catalysed by the acid form of the buffer.[12,15] Different mechanisms have been proposed to account for the experimental rate law, including a pre-equilibrium formation of a hydrogen-bonded complex between the general acid and the chloramine followed by the reaction of this complex with a second chloramine molecule in the rate determining step.[15]

Therefore, in spite of these investigations, the mechanism by which *N*-chloramines yield *N*,*N*-dichloramines in aqueous solution remains unclear. In this work we report the results of a detailed kinetic study of the reversible disproportionation reaction of *N*-chlorotaurine. Our experimental observations are consistent with proton abstraction by a general base taking place in the slow step, and suggest a concerted mechanism in which deprotonation and chlorine transfer occur simultaneously in the transition state. The important physiological role played by taurine as an HOCl trap, forming *N*-chlorotaurine, adds interest to the present investigation.

## Experimental

### Materials

Hypochlorite stock solutions were prepared by bubbling chlorine gas through a 0.5 M NaOH solution, and their concentration was determined spectrophotometrically at 292 nm ($\varepsilon_{292} = 350$ $M^{-1}$ $cm^{-1}$).[16] Inorganic salts and organic chemicals were of the highest purity commercially available and were used as received.

NaOH solutions were standardised by titration with a gravimetrically prepared potassium hydrogen phthalate solution. $HClO_4$ solutions were standardised by using the titrated solutions of NaOH. Stock solutions of substituted acetate buffers were prepared by dissolving the corresponding substituted acetic acid (monochloroacetic acid, dichloroacetic acid, methoxyacetic acid or acetic acid) in $H_2O$, followed by the addition of an appropriate amount of NaOH to give buffer solutions at various acid:base ratios. Solutions of phosphate and hexafluoropropan-2-ol buffers were prepared by partial neutralisation of the acid form with NaOH.

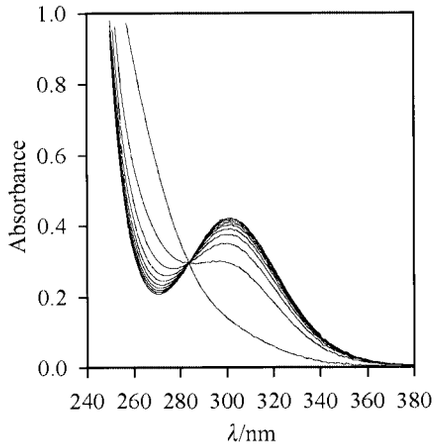


**Fig. 1** Typical absorption spectra for the reaction of disproportionation of *N*-chlorotaurine ($2.0 \times 10^{-3}$ M) at pH = 2.8 and 25 °C, showing the increase in absorbance at 301 nm due to the formation of *N*,*N*-dichlorotaurine. Scans were taken at 6 min intervals.

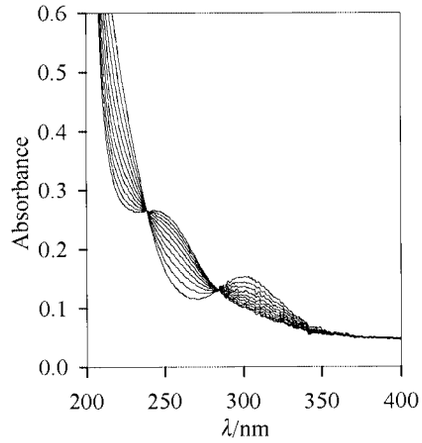


**Fig. 2** Spectra recorded every 6 min of the reaction of $TauNCl_2$ with $TauNH_2$, showing the loss of $TauNH_2$ ($\lambda_{max} = 301$ nm) and the formation of TauNHCl ($\lambda_{max} = 250$ nm). $[TauNCl_2]_o = 2.5 \times 10^{-4}$ M, $[TauNH_2] = 0.10$ M, pH = 7.1, $T = 25$ °C.

*N*-Chlorotaurine solutions were prepared daily by adding the appropriate amount of 0.14 M NaOCl to a 0.1 M taurine solution at pH 8–9, to give a final chloramine concentration of $1.0 \times 10^{-2}$ M. The formation of *N*,*N*-dichlorotaurine was negligible under these experimental conditions. The formation of *N*-chlorotaurine is a fast reaction and is complete within a few seconds of mixing.[6] The absorbance at 250 nm of a solution of *N*-chlorotaurine at pH = 9.31 decreased by less than 1% after 100 hours, showing that solutions of *N*-chloramine prepared following this procedure are stable for several days.

Solutions of *N*,*N*-dichlorotaurine were prepared immediately prior to use by disproportionation of *N*-chlorotaurine at pH 2–2.5 (Scheme 2).[17] The reaction was initiated by the addition

$$2TauNHCl + H_3O^+ \overset{K_d}{\rightleftharpoons} TauNCl_2 + TauNH_3^+ + H_2O$$

**Scheme 2**

of an adequate amount of acid to a solution of monochloramine ($2.5 \times 10^{-3}$ M), and was allowed to proceed for about 2 h. Formation of $TauNCl_2$ was quantitative under these conditions.

These solutions were reasonably stable and the observed decrease in the absorbance at 301 nm of a solution of *N*,*N*-dichlorotaurine at pH = 1.88 was less than 5% after 100 hours.

### Kinetic and equilibrium measurements

A Kontron Uvikon spectrophotometer was used to obtain UV-visible spectra and to measure rates of slow reactions. Faster reactions were studied using an Applied Photophysics DX17MV sequential stopped-flow spectrophotometer with an optical path length of 1 cm. All pH values were measured with a Radiometer PHM82 pH-meter equipped with a GK3401C combined glass electrode. The ionic strength was maintained at 0.5 M with $NaClO_4$ throughout. The temperature was kept at 25.0 ± 0.1 °C by circulating water from a thermostatted bath.

**Kinetics of disproportionation of TauNHCl.** Reactions were initiated by adding a volume of *N*-chlorotaurine solution at pH *ca.* 8.5 to a buffer solution at pH < 4 or to a solution of perchloric acid (0.01–0.50 M). The initial concentration of *N*-chlorotaurine, $[TauNHCl]_o$, was always $2.0 \times 10^{-3}$ M. Fig. 1 shows the spectral changes due to a decrease in the pH of a *N*-chlorotaurine solution from 8.5 to 2.8. The new absorption band at $\lambda_{max} = 301$ nm corresponds to the formation of *N*,*N*-dichlorotaurine. The kinetics of disproportionation of *N*-chlorotaurine to give *N*,*N*-dichlorotaurine were followed spectrophotometrically by monitoring the increase in absorbance at 301 nm. Fast disproportionation reactions of *N*-chlorotaurine in the presence of 0.1–0.5 M $HClO_4$ were studied using a stopped-flow spectrophotometer. An aqueous solution of *N*-chlorotaurine and a solution of $HClO_4$ were placed into the mixing syringes. These solutions were mixed in a 1:1 ratio to give a reaction mixture containing $2.0 \times 10^{-3}$ M *N*-chlorotaurine and the desired concentration of acid at $I = 0.5$ M ($NaClO_4$). Absorbance–time data were collected for at least four half-lives of the reaction. Values of the observed second-order rate constant, $(k_2)_{obsd}$ ($M^{-1}$ $s^{-1}$), for disproportionation of *N*-chlorotaurine were determined by the nonlinear least-squares fit of the data to the integrated second-order rate equation, eqn. (1), using SigmaPlot from Jandel Scientific.

$$A = A_\infty - \frac{(A_\infty - A_o)}{1 + 2[TauNHCl]_o\,(k_2)_{obsd}t} \qquad (1)$$

**Kinetics of the reaction of *N*,*N*-dichlorotaurine with taurine.** Reactions were initiated by adding a small volume of *N*,*N*-dichlorotaurine solution at pH 2–2.5, prepared as described above, to a buffered solution of taurine at pH 7–10. The initial concentration of *N*,*N*-dichloramine was always $2.5 \times 10^{-4}$ M. Spectra of the reaction mixture at pH = 7.1, recorded at different times after mixing, are shown in Fig. 2. The reaction leads to the disappearance of the absorption band due to *N*,*N*-dichlorotaurine ($\lambda_{max} = 301$ nm), which is replaced by a new band at $\lambda_{max} = 250$ nm corresponding to *N*-chlorotaurine. The reactions were followed spectrophotometrically by monitoring the change in absorbance at either 301 nm or 250 nm. The isolation method was used in all cases, with a taurine concentration at least 10-fold higher than the concentration of $TauNCl_2$. Values of the observed pseudo-first-order rate constant, $k_{obsd}$ ($s^{-1}$), were determined by the nonlinear least-squares fit of the absorbance–time data to the integrated first-order rate equation, eqn. (2), using SigmaPlot from Jandel Scientific.

$$A = A_\infty - (A_\infty - A_o)\exp(-k_{obsd}t) \qquad (2)$$

**Equilibrium of disproportionation.** The equilibrium constant for the disproportionation of *N*-chlorotaurine (see Scheme 2), $K_d$, was determined spectrophotometrically at 25 °C and $I = 0.5$ M ($NaClO_4$) by measuring the absorbance at 250 nm of equilibrium mixtures at different pH values. Reactions were initiated by the addition of a volume of *N*-chlorotaurine solution to a phosphate buffer at pH 1.8–9. The reaction mixtures were allowed to come to equilibrium overnight before making final pH and spectral measurements. Fig. 3 shows the dependence of the absorbance at 250 nm of equilibrium mixtures of *N*-chloro- and *N*,*N*-dichlorotaurine in the presence of a $10^{-3}$ M phosphate

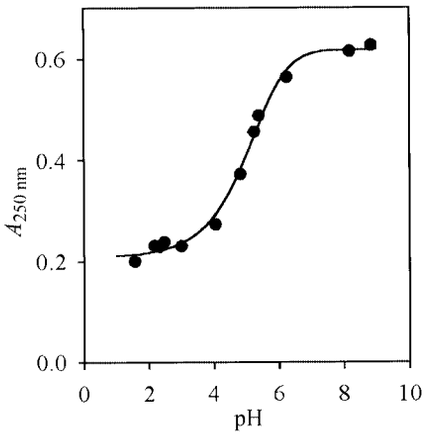


**Fig. 3** Determination of the equilibrium constant of disproportionation of *N*-chlorotaurine. $[TauNHCl]_o = 2.0 \times 10^{-3}$ M, $[TauNH_2] = 2.0 \times 10^{-2}$ M, $I = 0.5$ M ($NaClO_4$), $T = 25$ °C.

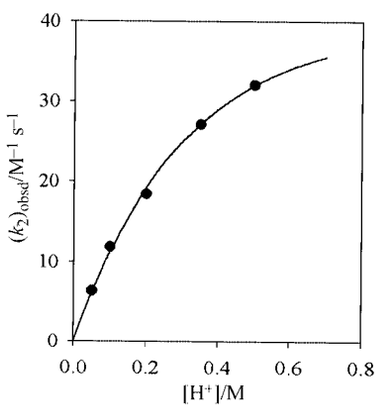


**Fig. 4** Influence of acid concentration on the observed second order rate constant of disproportionation of *N*-chlorotaurine. $[TauNHCl]_o = 2.0 \times 10^{-3}$ M, $I = 0.5$ M ($NaClO_4$), $T = 25$ °C.

buffer on pH. A relationship between the observed absorbance at 250 nm and the $H_3O^+$ concentration is given by eqn. (3),

$$A_{250\ nm} = A_{min} - \frac{b}{[H_3O^+]} + \left(\frac{b^2}{[H_3O^+]^2} + \frac{ab}{[H_3O^+]}\right)^{1/2} \quad (3)$$

where $a$ and $b$ are given by eqns. (4) and (5), respectively, $A_{min}$ is

$$a = 2[TauNHCl]_o(\varepsilon_{TauNHCl} - \varepsilon_{TauNCl_2}/2) \quad (4)$$

$$b = [TauNH_2]_T(\varepsilon_{TauNHCl} - \varepsilon_{TauNCl_2}/2)/(4K_d) \quad (5)$$

the minimum of absorbance at 250 nm, $[TauNHCl]_o$ is the initial concentration of *N*-chlorotaurine, $[TauNH_2]_T$ is the total concentration of taurine, and $\varepsilon_{TauNHCl}$ and $\varepsilon_{TauNCl_2}$ are the molar absorptivities of *N*-chloro- and *N*,*N*-dichlorotaurine, respectively. Values of $a = 0.82 \pm 0.02$, $b = (9.6 \pm 1.4) \times 10^{-7}$ and $A_{min} = 0.209 \pm 0.007$ were obtained by the nonlinear least-squares fit of the data to eqn. (3), using SigmaPlot from Jandel Scientific. A value of $K_d = (1.07 \pm 0.15) \times 10^6$ $M^{-1}$ was determined from these parameters and the known concentrations $[TauNH_2]_T$ and $[TauNHCl]_o$. The solid line in Fig. 3 shows the fit of the experimental data to eqn. (3).

## Results and discussion

### Disproportionation of TauNHCl

The influence of the concentration of hydronium ion on the second-order rate constant, $(k_2)_{obsd}$ ($M^{-1}\ s^{-1}$), for the disproportionation of *N*-chlorotaurine in water at 25 °C and $I = 0.5$ M ($NaClO_4$) was studied using a pH-jump technique, as described in the Experimental section. Fig. 4 shows a nonlinear dependence of $(k_2)_{obsd}$ on $[H_3O^+]$, which is similar to that found for other *N*-chloramines.[11,14,15] These results are consistent with the mechanism shown in Scheme 1, which involves a nucleophilic attack of the nitrogen atom of the neutral chloramine molecule on the chlorine atom of the *N*-protonated chloramine molecule. A relationship between the observed second-order rate constant $(k_2)_{obsd}$ and the concentration of $H_3O^+$, derived for Scheme 1, is given by eqn. (6), where $f_{TauNHCl}$ and $f_{TauNH_2Cl^+}$ are the fractions of neutral and protonated *N*-chlorotaurine, respectively.

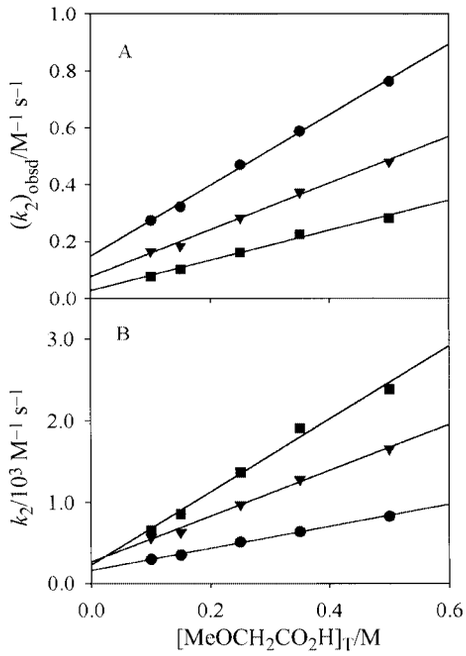


**Fig. 5** (A) Influence of the concentration of methoxyacetic acid–methoxyacetate buffers on the observed second order rate constant of disproportionation of *N*-chlorotaurine at 25 °C and $I = 0.5$ M ($NaClO_4$). ● pH = 2.98, ▼ pH = 3.48, ■ pH = 3.87. (B) Plot of $k_2$ (see text) against the total concentration of buffer for the data shown in plot (A).

$$(k_2)_{obsd} = k_2 f_{TauNHCl} f_{TauNH_2Cl^+} = \frac{k_2 K_a [H_3O^+]}{(K_a + [H_3O^+])^2} \quad (6)$$

The solid line in Fig. 4 corresponds to the fit of the experimental data to eqn. (6), which gives a value of $K_a = (1.14 \pm 0.09)$ M for the acidity constant of the conjugate acid of *N*-chlorotaurine, and $k_2 = (1.51 \pm 0.07) \times 10^2$ $M^{-1}\ s^{-1}$ for the second-order rate constant for disproportionation of *N*-chlorotaurine. As far as we know the value of the $pK_a$ of *N*-chlorotaurine has not been measured but the value close to zero obtained in our study is similar to that of *N*-chloramines derived from amines of basicity similar to taurine.[18,19]

The results of experiments at different concentrations of taurine show that the observed second-order rate constant $(k_2)_{obsd}$ does not depend on [taurine] and indicate that the reaction is not reversible under these experimental conditions.

To investigate whether this reaction is subject to general acid or general base catalysis, we carried out experiments at constant pH in methoxyacetic acid–methoxyacetate buffers of different acid–base ratios. Fig. 5A shows linear plots of the observed second-order rate constants for disproportionation against the total concentration of buffer. The slopes of the lines increase with the fraction of buffer in the acid form and this behaviour shows that the reaction is subject to general acid catalysis. However, the reaction involves a neutral and a protonated *N*-chlorotaurine molecule and therefore $(k_2)_{obsd}$ depends on the fractions of *N*-chlorotaurine in the neutral and protonated forms as shown by eqn. (6). Plots of $k_2 = (k_2)_{obsd}/(f_{TauNHCl} f_{TauNH_2Cl^+})$ against the total concentration of methoxyacetate buffer (Fig. 5B) show that the amount of catalysis

**Table 1** Third order rate constants, $k_T^B$, for the reaction between *N*-chlorotaurine and its protonated form catalysed by general bases in aqueous solution at 25 °C and $I = 0.5$ M ($NaClO_4$)

| Base | $pK_{BH}$ [a] | $k_T^B/M^{-2}\,s^{-1}$ |
|---|---|---|
| $H_2O$ | −1.74 | 2.72 ± 0.12 |
| $Cl_2CHCO_2^-$ | 1.26 | (3.6 ± 0.4) × $10^2$ |
| $ClCH_2CO_2^-$ | 2.70 | (1.65 ± 0.03) × $10^3$ |
| $CH_3OCH_2CO_2^-$ | 3.45 | (5.9 ± 0.2) × $10^3$ |
| $CH_3CO_2^-$ | 4.60 | (2.41 ± 0.11) × $10^4$ |

[a] $pK_a$ values at 25 °C and $I = 0.5$ M ($NaClO_4$) determined from the pH of partially neutralised solutions.

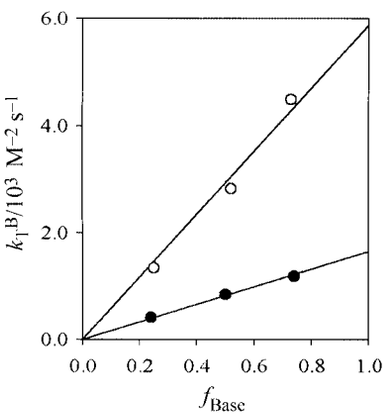


**Fig. 6** Plot of the third order rate constant of disproportionation of *N*-chlorotaurine against the fraction of buffer in the basic form. ● Monochloroacetic acid–monochloroacetate buffer, ○ methoxyacetic acid–methoxyacetate buffer.

observed increases with increasing fraction of buffer in the basic form. To further confirm these experimental observations, we carried out experiments in the presence of other substituted acetate buffers, always obtaining a linear dependence of $k_2$ on the total concentration of buffer. These results suggest that proton abstraction by a general base is involved in the rate determining step, as shown in Scheme 3. The rate law derived for this Scheme is given by eqn. (7), where $k_T^B$ is the third-order

$$-\frac{d[TauNHCl]_T}{dt} = 2(k_2^o + k_T^B[B])f_{TauNHCl^+}f_{TauNHCl_2Cl^+}[TauNHCl]_T^2 \quad (7)$$

rate constant for the base-catalysed reaction between TauNHCl and $TauNH_2Cl^+$.

Observed third-order rate constants, $(k_T^B)_{obsd}$ ($M^{-2}\,s^{-1}$), for the buffer-catalysed reaction were obtained as the slopes of the linear plots of $k_2$ against the total concentration of the acidic and basic forms of the buffer according to eqn. (8), where $k_2^o$

$$k_2 = k_2^o + (k_T^B)_{obsd}[buffer] \quad (8)$$

($M^{-1}\,s^{-1}$) is the second-order rate constant for the solvent-catalysed reaction at the pH of the experiment.

Values of $k_T^B$ ($M^{-2}\,s^{-1}$) for catalysis of the reaction by the basic form of the buffer were obtained, as the slopes of plots of $(k_T^B)_{obsd}$ against the fraction of buffer in the basic form, $f_B$, (see Fig. 6), or as the average of the values of $(k_T^B)_{obsd}/f_B$, and are summarised in Table 1. The values of $k_2^o$, obtained as the intercepts of plots of $k_2$ against [buffer] at pH ≤ 3, do not depend on pH and a value of $k_2^{H_2O} = (1.7 \pm 0.3) \times 10^2\ M^{-1}\,s^{-1}$ for the water-catalysed reaction between TauNHCl and $TauNH_2Cl^+$ was obtained as the average of the values of the intercepts for experiments at pH ≤ 3. This value is in good agreement with that determined in the absence of buffers. A slight increase in the value of $k_2^o$ with increasing pH was observed at pH > 3, probably due to the onset of catalysis by hydroxide ion. However, the large error associated with the values of $k_2^o$ did not allow us to determine an accurate value of the catalytic constant for the $HO^-$-catalysed reaction.

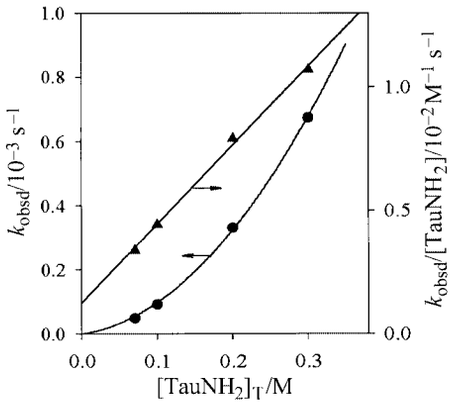


**Fig. 7** Influence of taurine concentration upon the observed first order rate constant of the reaction of $TauNCl_2$ with $TauNH_2$ (filled circles), $[TauNCl_2]_o = 2.5 \times 10^{-4}$ M, pH = 8.48. Filled triangles stand for the linear plot of $k_{obsd}/[TauNH_2]$ against $[TauNH_2]_T$.

$$TauNH_2Cl^+ + H_2O \overset{K_a}{\rightleftharpoons} TauNHCl + H_3O^+$$

$$B + TauNHCl + TauNH_2Cl^+ \underset{k_{-2}^o + k_T^{BH^+}[BH^+]}{\overset{k_2^o + k_T^B[B]}{\rightleftharpoons}} TauNH_2 + TauNCl_2 + BH^+$$

**Scheme 3**

### Reaction of *N*,*N*-dichlorotaurine with taurine

A kinetic study of the reverse process, the reaction of $TauNCl_2$ with $TauNH_2$ (Scheme 3), was carried out in the presence of taurine buffers of different concentrations at constant pH. Fig. 7 shows a greater than first-order dependence of the observed pseudo-first order rate constant for this reaction, $k_{obsd}$ ($s^{-1}$), on the total concentration of buffer. Plots of $k_{obsd}/[TauNH_2]_T$ against $[TauNH_2]_T$ are linear (see Fig. 7) and suggest that the rate equation has the form $k_{obsd} = a[TauNH_2]_T + b[TauNH_2]_T^2$.

Since a general base is involved in the slow step of the disproportionation reaction of TauNHCl (forward reaction in Scheme 3), the microscopic reversibility principle requires that protonation by a general acid should take place in the reverse process. The following rate equation was derived for Scheme 3, where $[TauNH_2]$ is the concentration of taurine in the basic form, $k_{-2}^o$ ($M^{-1}\,s^{-1}$) is the second-order rate constant for the solvent-catalysed reaction and $k_T^{BH^+}$ ($M^{-2}\,s^{-1}$) is the third-order rate constant for catalysis of the reaction by the acid form of the buffer. If the reaction is catalysed by $TauNH_3^+$ as a general acid, eqn. (9) transforms into eqn. (10), where $f_{TauNH_3^+}$ is the fraction of taurine present in the protonated form.

$$k_{obsd} = [TauNH_2](k_{-2}^o + k_T^{BH^+}[BH^+]) \quad (9)$$

$$\frac{k_{obsd}}{[TauNH_2]} = k_{-2}^o + k_T^{TauNH_3^+}f_{TauNH_3^+}[TauNH_2]_T \quad (10)$$

Fig. 8 shows plots of $k_{obsd}/[TauNH_2]$ against $[TauNH_2]_T$ for the reaction of *N*,*N*-dichlorotaurine with taurine in buffered solutions at different pH values. Values of $k_{-2}^o$, obtained from the intercepts of these plots, increase with decreasing pH. The linear dependence of $k_{-2}^o$ on $[H_3O^+]$ (not shown) gives $k_{-2}^{H_2O} = (7.9 \pm 0.5) \times 10^{-4}\ M^{-1}\,s^{-1}$ for the water-catalysed reaction and $k_T^{H_3O^+} = (1.6 \pm 0.2) \times 10^5\ M^{-2}\,s^{-1}$ for catalysis of this reaction by $H_3O^+$ (see eqn. (11)). A value of $k_T^{TauNH_3^+} =$

$$k_{-2}^o = k_{-2}^{H_2O} + k_T^{H_3O^+}[H_3O^+] \quad (11)$$

**Table 2** Third order rate constants, $k_T^{BH}$, for chlorination of taurine by *N*,*N*-dichlorotaurine catalysed by general acids in aqueous solutions at 25 °C and $I = 0.5$ M ($NaClO_4$)

| Acid | $pK_{BH}$ [a] | $k_T^{BH}/M^{-2}\ s^{-1}$ |
|---|---|---|
| $H_3O^+$ | −1.74 | $(1.6 \pm 0.2) \times 10^5$ |
| $CH_3CO_2H$ | −4.60 | $90 \pm 2$ |
| $H_2PO_4^-$ | −6.73 | $10.9 \pm 0.3$ |
| $(CF_3)_2CHOH$ | −9.30 | $0.326 \pm 0.010$ |
| $^-O_3S(CH_2)_2NH_3^+$ | −9.06 | $(3.5 \pm 0.3) \times 10^{-2}$ |
| $H_2O$ | −15.74 | $(1.42 \pm 0.09) \times 10^{-5}$ |

[a] $pK_a$ values at 25 °C and $I = 0.5$ M ($NaClO_4$) determined from the pH of partially neutralised solutions.

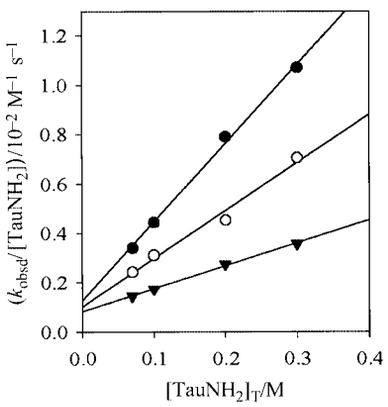


**Fig. 8** Plots of $k_{obsd}/[TauNH_2]$ against $[TauNH_2]_T$ for the reaction of *N*,*N*-dichlorotaurine with taurine in buffered solutions at different pH values, ● pH = 8.48, ○ pH = 8.96, ▼ pH = 9.36.

$(3.5 \pm 0.3) \times 10^{-2}\ M^{-2}\ s^{-1}$ was determined by plotting the slopes of the plots in Fig. 8 against $f_{TauNH_3^+}$.

Catalysis by acetic acid was investigated at pH = 9.0 in the presence of a 0.1 M taurine buffer. The reaction was also studied in phosphate and hexafluoropropan-2-ol buffer solutions containing 0.05 M taurine at pH = 7.2 and 9.2, respectively. In all cases the observed pseudo-first order rate constant, $k_{obsd}$, shows a linear dependence on $[BH^+]$, consistent with eqn. (9). Values of the catalytic constants for these general acids were obtained from the slopes of plots of $k_{obsd}$ against $[BH^+]$ and the concentration of unprotonated taurine. The values for these catalytic constants are summarised in Table 2.

The values of the rate constants for the water-catalysed reaction between *N*-chlorotaurine and its protonated form, $k_2^{H_2O}$, and for the reverse reaction catalysed by $H_3O^+$, $k_T^{H_3O^+}$, can both be used to calculate the equilibrium constant for the reaction shown in Scheme 3. The value of this equilibrium constant is $k_2^{H_2O}/k_T^{H_3O^+} = (1.1 \pm 0.2) \times 10^{-3}$ M. This value can be combined with $K_a = 8.71 \times 10^{-10}$ M and $K_a = 1.14$ M for the acidity constants of protonated taurine and *N*-chlorotaurine, respectively, to obtain a value of $K_d = (1.1 \pm 0.2) \times 10^6\ M^{-1}$ for the equilibrium constant of the reaction in Scheme 2. This value is in good agreement with that determined spectrophotometrically.

### Brønsted relationships

Fig. 9 shows Brønsted correlations of rate constants for the reaction between TauNHCl and $TauNH_2Cl^+$ catalysed by substituted acetates, $k_T^B$ (circles), and the reverse reaction of *N*,*N*-dichlorotaurine with taurine catalysed by general acids, $k_T^{BH^+}$ (triangles), with the $pK_a$ of the catalyst, $pK_{BH}$. The data are correlated by lines of slope $\beta = 0.55 \pm 0.03$ and $\alpha = 0.48 \pm 0.03$, respectively. The open circle corresponds to the rate constant for the reaction between *N*-chlorotaurine and its protonated form catalysed by $H_2O$ and the open triangles to the rate constants for catalysis of the reverse reaction by $H_3O^+$ and $H_2O$ acting as an acid. Values of the third-order rate constants for the water-catalysed reactions were calculated by dividing $k_2^o$ and $k_{-2}^o$ by 55.5 M. The deviations of the points for $H_2O$ from the correlation lines are usual in this kind of plot.[20] The sum of the Brønsted exponents gives $\alpha + \beta = 1.03 \pm 0.04$, which is in good agreement with the value of 1.00 expected for the dependence of the logarithm of the overall equilibrium constant on the $pK_a$ of the catalyst.[21]

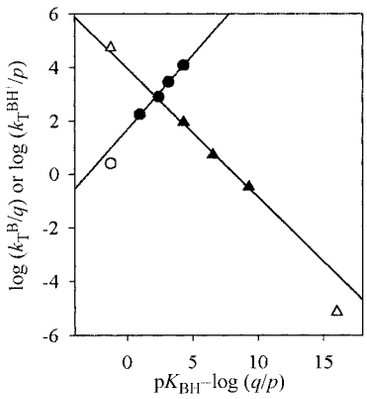


**Fig. 9** Brønsted plots for the base-catalysed reaction of disproportionation of *N*-chlorotaurine (circles) and for the acid-catalysed reverse reaction of *N*,*N*-dichlorotaurine with taurine (triangles).

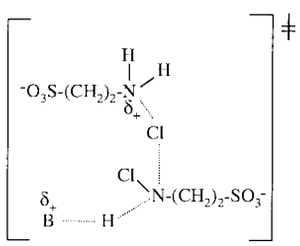


**Fig. 10** Proposed transition state for disproportionation of *N*-chlorotaurine.

The fact that the reaction between *N*-chlorotaurine and its protonated form is subject to general base catalysis suggests that a proton transfer takes place in the slow step. These experimental results would be consistent with a stepwise mechanism involving a fast equilibrium reaction to give the protonated *N*,*N*-dichlorotaurine as an intermediate followed by a slow proton transfer to the medium. However, protonated dichloramines must be extremely acidic. It is known that the $pK_a$s of protonated *N*-chloramines are *ca.* 10 p*K* units lower than those of the corresponding protonated amines and literature values for different chloramines are close to 0.[19,22] Assuming that substitution of a second hydrogen atom for a chlorine has a similar effect, the estimated $pK_a$ of the protonated *N*,*N*-dichlorotaurine would be *ca.* −10. Therefore, its deprotonation in aqueous solution should be, according to Eigen's theory,[23] a diffusion-controlled reaction. These arguments suggest that the proposed intermediate is too unstable to have a significant lifetime in aqueous solution and support a concerted mechanism, in which deprotonation of a neutral chloramine molecule occurs simultaneously with chlorine transfer.

The observed value of the Brønsted slope, $\beta = 0.55$, shows that the proton is about half transferred to the catalyst in the transition state (Fig. 10). Unfortunately, our experimental results do not provide a measure of the extent of chlorine transfer in the transition state for disproportionation of *N*-chlorotaurine and therefore we do not have any information on whether or not these two processes, proton and chlorine transfer, occur synchronously along the reaction coordinate.[24,25]

The mechanism proposed for this reaction differs from that found for chlorine transfer from a chloramine to an amine.[26] The latter involves a fast protonation of the chloramine in a fast

pre-equilibrium step followed by nucleophilic attack of the amine at chlorine in the slow step (Scheme 4).

$$RNH_2Cl^+ + H_2O \overset{K_a}{\rightleftharpoons} RNHCl + H_3O^+$$

$$R'NH_2 + RNH_2Cl^+ \xrightarrow[\text{slow}]{k_2} R'NH_2Cl^+ + RNH_2$$

**Scheme 4**

This reaction yields a protonated chloramine of $pK_a$ much higher than that of a protonated *N*,*N*-dichloramine, which can therefore exist as a real intermediate in aqueous solution. The low stability of protonated *N*,*N*-dichloramines towards proton loss to the solvent is responsible for the enforced concerted mechanism for disproportionation of chloramines.[27]

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