SHORT PAPER

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Oxidation of benzylamine by ClOH and *N*-chlorosuccinimide: a kinetic study†

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The reaction of benzylamine with *N*-chlorosuccinimide involves addition of the amine to electrophilic chlorine to yield *N*-chlorobenzylamine and not hydride abstraction at the α-carbon of the amine by the oxidant as proposed in the literature.

Keywords: benzylamine, N-chloroamines, N-chlorosuccinimide

It is well known that chlorinating agents react with amines in aqueous solution to yield unstable *N*-chloramines, which slowly decompose to form the corresponding aldehyde and ammonia.[1–4] It has also been established that the reaction involves the addition of the amine to electrophilic chlorine in the slow step. However, the oxidation of benzylamine by *N*-chlorosuccinimide (NCS) has been reported to follow a different mechanism.[5] It has been suggested that the reaction takes place by transfer of a hydride ion from the α–carbon of the amine to the oxidant in the rate-determining step. We would not have expected benzylamines to behave any differently from other aliphatic amines in their reaction with compounds containing electrophilic chlorine and therefore this report was surprising. This prompted us to carry out a kinetic investigation of the reaction of benzylamine with two common chlorinating agents, ClOH and NCS. Our results are consistent to a mechanism similar to that already proposed for other primary amines,[2,6] which involves the formation of *N*-chlorobenzylamine.

Experimental

N-chlorosuccinimide (Merck) was recrystallized from acetone. Aqueous solutions of ClO^- were prepared as described elsewhere.[7] Benzylamine (Merck) and all other chemicals were obtained from commercial sources and used as received. The reactions were followed by monitoring the disappearance of ClO^- at 292 nm or the formation of *N*-chlorobenzylamine at 240 nm using an Applied Photophysics DX.17MV sequential stopped-flow spectrofluorimeter. All the experiments were carried out at 25°C and a constant ionic strength of 0.5 M, maintained with $NaClO_4$. The concentration of benzylamine was always at least 10 times larger than that of the chlorinating agent (typically in the range $(0.5–5) \times 10^{-4}$ M). Values of the observed first-order rate constant, k_{obsd} (s^{-1}), were determined by fitting the absorbance-time data to the first-order integrated equation. The values of k_{obsd} were reproducible to ± 5 %. pH values were always measured at the end of the reaction using a Radiometer pHM82 pH-meter with a GK2401C combined glass electrode.

Results and discussion

The reaction between benzylamine and aqueous chlorine was found to be first-order with respect to the nucleophile. This was shown by the linear dependence of the observed rate constant, k_{obsd} (s^{-1}), on the concentration of the amine, $0.2–2 \times 10^{-2}$ M, in the presence of a 0.2 M phosphate buffer at pH 6.0 and 11.4. The increase in k_{obsd} on increasing the concentration of phosphate buffer from 2.5×10^{-2} to 0.1 M at pH 6.5 and $[BzA]_T$ = 1.0×10^{-3} M was less than 5%, showing that the reaction is not subject to general acid–base catalysis. Figure 1 shows that k_{obsd} goes through a maximum on increasing pH at constant benzylamine concentration. This kinetic behaviour is similar to that found for other amines and therefore supports the mechanism already proposed in the literature (see Scheme 1).[2,3,8]

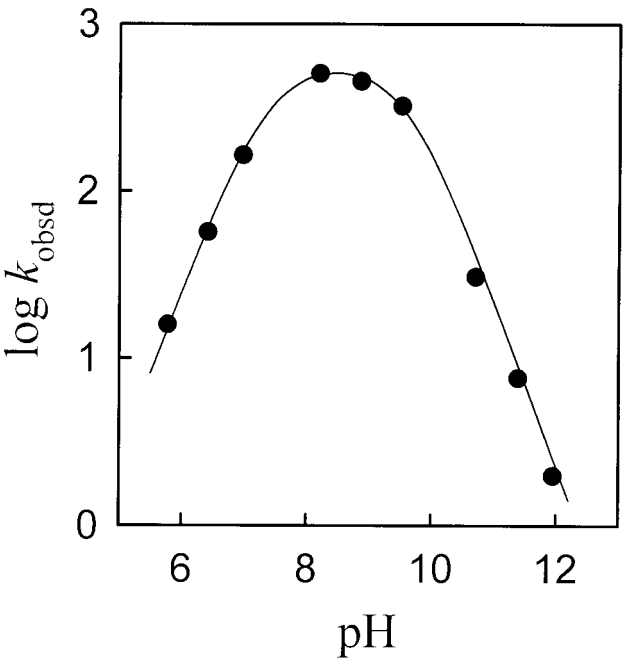
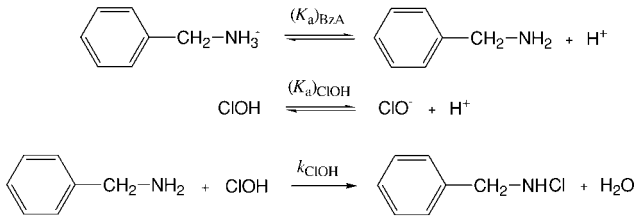


Fig. 1 pH-rate profile for the reaction between benzylamine (10^{-3} M) and ClOH in aqueous solution at 25°C and I = 0.5 M ($NaClO_4$).

The overall rate equation for this reaction, derived for Scheme 1, is given by equation (1):



Scheme 1

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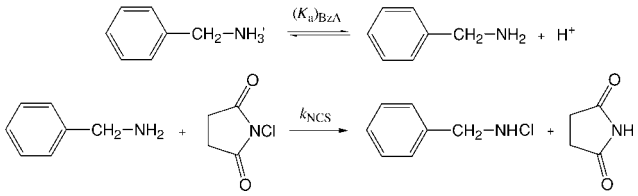
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

$$k_{obsd} = k_{ClOH}\ \frac{(K_a)_{BzA}\,[H^+]}{((K_a)_{BzA}+[H^+])((K_a)_{ClOH}+[H^+])}\ [BzA]_T \quad (1)$$

The solid line in Fig. 1 shows the good fit of the experimental results to this equation, which gives $(K_a)_{BzA} = (2.6 \pm 0.3) \times 10^{-10}$ M and $(K_a)_{ClOH} = (4.4 \pm 0.5) \times 10^{-8}$ M, in good agreement with literature values.[9,10] The value of $k_{ClOH} = (1.0 \pm 0.1) \times 10^8$/M/s is similar to those reported for the chlorination of other amines of similar pK_a.[3] The reaction was also studied at different temperatures in the range 15–45ºC. The values of k_{ClOH} were analysed according to the Eyring equation to obtain the activation parameters for chlorine transfer from ClOH to the amine ($\Delta H^{\ddagger}$ = (16 ± 3) /kJ/mol and $\Delta S^{\ddagger}$ = –(45 ± 10) /kJ/mol). The chlorination of amines by ClOH is characterised by $\Delta H^{\ddagger}$ values below the limit for diffusion-controlled reactions (20 kJ/mol).[2] This suggests that chlorine transfer may occur in more than one step, probably through the formation of a charge transfer complex between the amine and the chlorinating agent.

A similar investigation was carried out for the reaction between benzylamine and NCS. A plot of k_{obsd} against the total concentration of benzylamine, in the presence of a 0.2 M phosphate buffer at pH 6.9, was linear, showing that the reaction is first-order with respect to $[BzA]_T$. Experiments with different concentrations of buffer solution at constant pH ruled out catalysis by general acids or bases. The dependence of k_{obsd} on pH is shown in Fig. 2 and suggests that the unprotonated amine is the only reactive form of the nucleophile (see Scheme 2).



Scheme 2

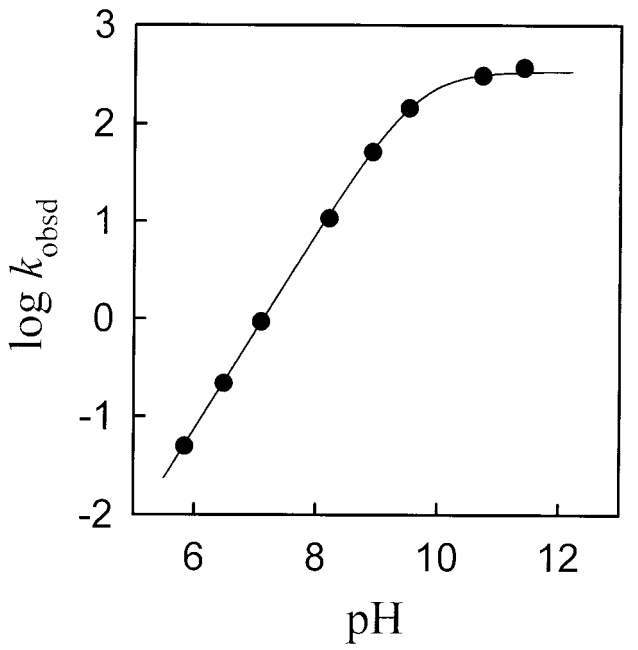
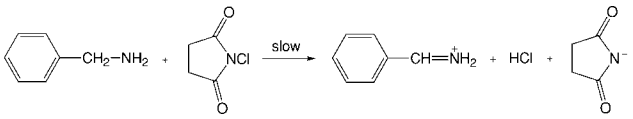


Fig. 2 pH-rate profile for the reaction between benzylamine (5×10^{-4} M) and NCS in aqueous solution at 25°C and I = 0.5 M ($NaClO_4$).

Values of (K_a)/M/$s_{BzA} = (2.23 \pm 0.02) \times 10^{-10}$ M and $k_{NCS} = (6.77 \pm 0.07) \times 10^5$ /M/s were obtained from the nonlinear least-squares fit of the experimental data to equation (2), derived for Scheme 2.

$$k_{obsd} = k_{NCS}\ \frac{(K_a)_{BzA}}{((K_a)_{BzA}+[H^+])}\ [BzA]_T \quad (2)$$

The experimental behaviour reported in this work for the chlorination of benzylamine closely resembles that found previously for other primary amines[6] and we conclude that the reaction takes place by nucleophile addition to the chlorinating agent to form *N*-chlorobenzylamine (see Schemes 1 and 2). In a previous study of the reaction of benzylamine with NCS, Banerji[5] found evidence in favour of a mechanism involving hydride abstraction at the α-carbon of the amine by the chlorinating agent in the slow step (Scheme 3).



Scheme 3

The second-order rate constant for reaction of benzylamine with NCS at 25 ºC obtained in this work is 10^8-fold larger than that reported by Banerji for the same reaction and is close to the value of $k_{NCS} = (6.3 \pm 0.4) \times 10^5$ $M^{-1}s^{-1}$ for glycine (pK_a = 9.8).[6] The large difference between these two values shows that the experimental data reported in the earlier work by Banerji probably corresponds to the slower decomposition of the *N*-chloramine formed in the fast reaction of benzylamine with NCS. It has been shown that the decomposition of *N*-chloramines in aqueous solution proceeds by an elimination mechanism, in which proton abstraction from the α-carbon of the amine by a general base is concerted with N–Cl bond cleavage.[4,7] The observation of catalysis by the neutral form of the amine and the fact that replacement of the α-hydrogens of benzylamine by deuterium slows the reaction by a factor of 6.2[5] are consistent with this mechanism.

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