Effects of amine–borane structure on the stoichiometry, rate and mechanism of reaction with hypochlorous acid: hydride oxidation versus B-chlorination

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Abstract

Various ring substituted benzylamine–boranes as well as α-methyl- and *N*-methylbenzylamine–borane undergo hydride oxidation and N-chlorination on reaction with NaOCl whereas *N,N*-dimethylbenzylamine–borane is subject to B-chlorination producing a mixture of amine chloroboranes. Results are consistent with previously established patterns of reactivity with alkyl- and non-aromatic heterocyclic secondary amine–boranes being subject to oxidation and their tertiary counterparts to B-chlorination. Current studies reveal the borane adducts of tertiary amines in the quinoline series to react via oxidative pathways. Ring or α-methyl substitution has a negligible effect on the rate of benzylamine–borane oxidation whereas N-methyl substitution causes a three-fold decrease. The benzylamine–borane reaction displays a modest substrate isotope effect ($k_{BH_3}/k_{BD_3} \cong 1.3$), a pronounced inverse solvent isotope effect ($k_{D_2O}/k_{H_2O} \cong 3$) and a pH dependence of rate that indicates saturation kinetics below pH 7.5. It is suggested that both oxidation and B-chlorination involve bimolecular rate-limiting attack of HOCl on amine–borane with different intimate mechanisms arising from correspondingly different activated complexes. A low reactivity of quinoline–monochloroborane with hypochlorite precludes the involvement of a chloroborane as a common intermediate in both processes. The activation free-energy for chlorination of trimethylamine–borane is higher than $\Delta G^{\ddagger}$ values obtained for oxidation of isoquinoline–borane and for a series of benzylamine–boranes. Activation enthalpies are relatively low for both processes. Unlike the chlorination reaction where the entropy term is negligible, $\Delta S^{\ddagger}$ for oxidation accounts for about 20–30% of the activation barrier. It is proposed that details of amine structure determine the mode of attack of amine–borane by HOCl with steric factors playing a dominant role.

Introduction

Results of previous investigations have shown reactions of hypochlorite with alkyl- and non-aromatic heterocyclic amine–boranes to proceed via pathways that are dependent on the structure of the amine component of the adduct, with secondary amine–boranes undergoing quantitative hydride oxidation followed by N-chlorination and tertiary amine–boranes undergoing B-chlorination [1, 2]. Equations (1) and (2) show, for systems investigated to date, the respective stoichiometries in terms of the molar ratio of HOCl to amine–borane: 4/1 for secondary amine–borane oxidation and 1:1 for tertiary amine–borane chlorination in which sequential subsequent chlorination steps are kinetically uncoupled from the initial reaction.

$$R_2NHBH_3 + 4HOCl \longrightarrow R_2NCl + B(OH)_3 + 3HCl + H_2O \quad (1)$$

$$R_3NBH_3 + HOCl \longrightarrow R_3NBH_2Cl + H_2O \quad (2)$$

Studies of solvent isotope effects and the pH dependence of rate suggest that, in both processes, hypochlorous acid is involved in an initial rate-determining attack on amine–borane. It has been speculated that the different reaction paths result from different four-centred transition-state configurations arising through attack of HOCl at the B–H bond of the adduct. Corresponding representations along with proposed stoichiometric mechanisms are shown in Schemes 1 and 2, respectively [1, 2]; however, the molecular details of the influence of structural change on mechanism and stoichiometry including the relative importance of steric versus electronic effects, is presently unknown. In an effort to gain further insight into such influences, investigations of hypochlorite interactions with amine–boranes containing aromatic components have been conducted and, in this paper, results obtained from studies of the reactivity of substituted benzylamine–boranes and quinoline–boranes are described.

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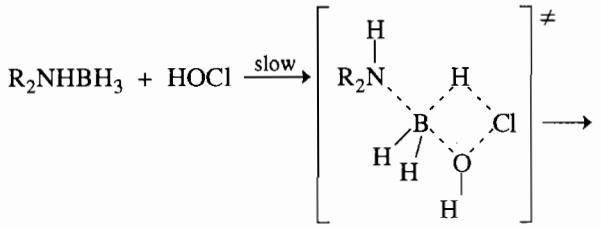


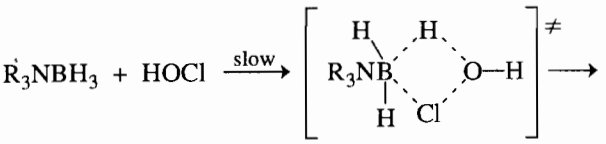
$$R_2NH + BH_2OH + HCl \quad (3)$$

$$BH_2OH + HOCl \xrightarrow{fast} BH(OH)_2 + HCl \quad (4)$$

$$BH(OH)_2 + HOCl \xrightarrow{fast} B(OH)_3 + HCl \quad (5)$$

$$R_2NH + HOCl \xrightarrow{fast} R_2NCl + H_2O \quad (6)$$

Scheme 1.



$$R_3NBH_2Cl + H_2O \quad (7)$$

Scheme 2.

Experimental

Materials and methods

The benzylamines, trimethylamine–borane, tetrahydrofuran (THF), *p*-dioxane (99 + % purity) and the boron trifluoride–diethyl ether complex were obtained from Aldrich. $BF_3 \cdot Et_2O$ was distilled *in vacuo* to obtain a colorless liquid prior to its use in preparing tetrahydrofuran–borane *in situ*. Tetrahydrofuran was boiled under reflux over CaH_2 in a nitrogen atmosphere, then collected by decantation and refluxed over sodium and benzophenone and collected by distillation under dry N_2. Dioxane was boiled with aqueous HCl to remove acetal impurities. Upon cooling it was treated with KOH to neutralize the solution and after additional reflux treatment, again cooled and decanted and then allowed to reflux over CaH_2 under dry N_2. The cooled solvent was again decanted and collected by distillation from sodium and benzophenone in an N_2 atmosphere. Reagent grade benzene and toluene were obtained from Matheson, Coleman and Bell and dried over 4 Å molecular sieves before use. Hexane and diethyl ether were acquired from Aldrich and used without further purification.

Quinoline, isoquinoline, tetrahydrofuran–borane (THF – BH_3), sodium borodeuteride (listed as 98% $NaBD_4$) and deuterium oxide (> 99% isotopic purity) were obtained from Aldrich; sodium tetrahydridoborate, $NaBH_4$, from Morton International and 4-methylquinoline from Lancaster Syntheses Ltd. Sodium hypochlorite was obtained as an alkaline stabilized 5% aqueous solution from Mallinckrodt. Stock solutions were prepared by dilution with H_2O and analyzed iodometrically. Aliquot samples of stock solutions were then diluted with appropriate buffer solutions shortly before use in stoichiometry and kinetic studies. All inorganic salts were of reagent grade quality. Deionized water was re-distilled or passed through a Barnstead mixed-bed ion-exchange column to produce effluent of conductance corresponding to < 0.01 ppm of total salt measured as NaCl.

Elemental C, H and N analyses were carried out by Schwartzkopf Microanalytical Laboratory. Melting points were taken on a Mel-Temp apparatus and are uncorrected. UV–Vis spectra were recorded on a Perkin-Elmer model 552A double beam spectrophotometer and IR spectra on a Perkin-Elmer model 237 or Beckman IR-33 or model 4250 infrared spectrophotometer. Proton, ^{13}C and ^{11}B NMR spectra were recorded in $CDCl_3$ solution on a Varian XL-300 spectrometer at 299.94, 75.43 and 96.23 MHz, respectively, using Me_4Si as internal reference for ^1H and ^{13}C studies and $BF_3 \cdot Et_2O$ as external reference for ^{11}B spectra. All pH values were obtained using a Corning model 130 digital pH meter. The expressions 'pH' or 'operational pH' depict readings in aqueous dioxane solutions, e.g. 10% dioxane–90% H_2O. Stopped-flow spectrophotometric studies were carried out employing a Dionex D-110 spectrophotometer in conjunction with a Tektronix 5103N or model 2211 digital storage oscilloscope. Temperatures were controlled to ± 0.1 °C with circulated water using a Precision water bath.

Synthesis of amine–boranes

Preparative methods involved displacement of solvent from THF–BH_3 by free amine. Commercially available THF–BH_3 was utilized to prepare borane adducts of quinoline, 4-methylquinoline, isoquinoline, 4-methylbenzylamine and *N*,*N*-dimethylbenzylamine [3]. Other amine–boranes were prepared using THF–BH_3 generated *in situ* from $NaBH_4$ and $BF_3 \cdot Et_2O$ in tetrahydrofuran [4]. Characterization of each product was based on C, H and N analyses as well as IR and NMR spectra.

Quinoline–monochloroborane

Quinoline–borane was prepared as previously described from 5.2 ml (44 mmol) of quinoline and 80 ml (80 mmol) of 1 M THF–BH_3 [3]. Yield after recrystallization from benzene/hexane = 5.16 g (82% theory), m.p. 86–88 °C, lit. [3] 84–85 °C. IR spectrum (KBr pellet): ν(BH) 2255, 2360, 2380 cm^{-1}. A total of 4.96 g (0.0347 mol) of this compound and 125 ml of dry benzene were added to a 250 ml flask equipped with a gas inlet tube and an outlet tube connected to an

oil bubbler. Anhydrous HCl was bubbled through the solution for 2 h with stirring. Evolution of H_2 gas was accompanied by formation of a white precipitate. The crude product was collected by filtration, dissolved in benzene and re-precipitated by the addition of hexane. After a second recrystallization, a yield of 4.00 g (65% theory based on quinoline–borane) was obtained; m.p. 137 °C (dec.). IR (KBr): ν(B–H) 2365, 2395, 2460 cm^{-1}. ^{11}B NMR ($CDCl_3$, 20 °C): δ −2.65 (br t).

Isolation of N,N-dimethylbenzylamine–dichloroborane

A solution consisting of 0.509 g (3.42 mmol) of *N,N*-dimethylbenzylamine–borane in 100 ml dioxane was treated with 100 ml of an aqueous solution prepared from 20 ml (11 mmol) of stock NaOCl solution and 80 ml of carbonate buffer at pH 9.5. After about 3 min, four extractions were performed each utilizing 50 ml of diethyl ether. The combined ether fractions were washed once with H_2O and dried over anhydrous $MgSO_4$. Removal of ether *in vacuo* produced a yellow powder. Crude yield ≅0.2 g (27% theory); m.p. 137.5–139.5 °C. ^{11}B NMR ($CDCl_3$, 20 °C): δ 5.20 (br d). Recrystallization from toluene/hexane produced light yellow crystalline plates.

Stoichiometric and kinetic studies

All investigations were based on measured changes in NaOCl absorbance at 290 nm, or amine–borane between 225 and 240 nm. Determination of the molar equivalence of hypochlorite to amine–borane involved measurements of the absorbance decrease at 290 nm following the stopped-flow mixing of solutions. The initial reference absorbance was taken with a solution of given concentration of hypochlorite or amine–borane. The concentration of the second component was then varied over several experiments and the absorbance decrement, ΔA, determined as a function of its concentration. The maximum absorbance decrement occurred following the addition of a stoichiometrically equivalent, or excess, quantity of second component. Such spectrophotometric 'titrations' were carried out either on conventional or stopped-flow time scales. The success of the method is contingent on the absence of side reactions which are accompanied by changes in optical density and not kinetically decoupled from the initial reaction.

An iodometric method was also employed to study the stoichiometry of the hypochlorite quinoline–borane reaction wherein a known amount of quinoline–borane was added to a carbonate buffered solution at pH 9 containing excess NaOCl. Following a reaction time of ~1 min, the solution was acidified with 6 N H_2SO_4 and the remaining hypochlorite determined iodometrically. A subsequent plot of moles excess hypochlorite versus moles of amine–borane employed produced a straight line of slope equal to the negative of the molar ratio.

Stopped-flow kinetic studies involved measurements of reaction rates over several half-lives under pseudo-first-order or second-order conditions. In all cases, Beer's law was found to apply. In each experiment a buffered aqueous hypochlorite solution was mixed with amine–borane. Some studies were carried out in aqueous dioxane, to insure complete solubility of components. In such cases, the dioxane was contained in the solution of amine–borane at twice the concentration desired for the final reaction mixture. The ionic strength was controlled through the addition of NaCl.

Pseudo-first-order conditions were obtained by employing an excess of that reactant species for which an absorbance change was not followed. Pseudo-first-order rate constants, k_{obs}, were calculated from slopes of lines obtained from plots of ln A versus time and used to obtain second-order constants from a knowledge of the concentration of reactant employed in excess. In initial rate studies, ΔA was obtained under pseudo-first-order conditions as a function of time over finite time intervals in the early stages of reaction (~1 to 5%) in which the variation of optical density with time appears essentially linear. For chlorination reactions displaying an initial 1:1 stoichiometric ratio of OCl^- to amine–borane, rates of disappearance of amine–borane and hypochlorite were equal. By contrast, rapid consumption of greater quantities of hypochlorite accompanies disappearance of a mole of amine–borane (AB) in the oxidation of numerous primary and secondary amine–boranes where $-d[OCl^-]/dt = -4\ d[AB]/dt$, and, in the quinoline–borane series where $-d[OCl^-]/dt = -3\ d[AB]/dt$.

Second-order conditions involved use of amine–borane and hypochlorite in concentrations of comparable magnitude. For oxidation reactions involving 4:1 stoichiometry, second-order rate constants were obtained from plots of $[1/(b-4a)]\ \ln[b(a-x/4)/(a(b-x))]$ versus time where a and b represent initial concentrations of amine–borane and hypochlorite respectively, and x, the concentration of OCl^- consumed in time, t. As a rule, reported rate constants are the average of 2 or 3 determinations and are reproducible to ±10%.

Results and discussion

Analytical data for newly prepared amine–boranes and stoichiometric results are given in Tables 1 and 2 with a typical stopped-flow spectrophotometric titration of NaOCl with benzylamine–borane shown in Fig. 1. The 4/1 [NaOCl]/[amine–borane] ratios exhibited for *N*-methylbenzylamine–borane and the borane adducts of benzylamine and 2-methoxybenzylamine, are com-

TABLE 1. Analytical data for amine–boranes

Amine–borane	Yield[a] (%theory)	m.p.[b] (°C)	Analyses					
			Found			Theory (calculated)		
			C	H	N	C	H	N
Benzyl–	49	57–58.5	68.87	10.31		69.49	10.00	
N-Methylbenzyl–	68	67–68	70.80	10.07		71.17	10.45	
N,N-Dimethylbenzyl–	88	90–91	73.11	10.91		72.53	10.82	
4-Methylbenzyl–	64	114–115	71.56	10.58	10.18	71.17	10.45	10.37
2-Methoxybenzyl–	75	84–86	62.59	9.41	9.66	63.63	9.34	9.28
3-Methoxybenzyl–	71	91–92.5	64.44	9.24	9.16	63.63	9.34	9.28
4-Methoxybenzyl–	86	97–99.5	63.42	9.60	8.84	63.63	9.34	9.28
4-Chlorobenzyl–	55	119–120	53.87	7.12	8.84	54.09	7.13	9.01
α-Methylbenzyl–	82	91 (dec.)	70.41	10.22	10.16	71.17	10.45	10.37
4-Trifluoromethylbenzyl–	57	107–109	50.86	5.81	7.30	50.84	5.87	7.41
Quinoline-monochloro–	65	137 (dec.)	61.38	5.16	7.37	60.92	5.11	7.89
N,N-Dimethylbenzyldichloro–	27[c]	137.5–139.5	50.33	6.43	6.45	49.60	6.47	6.43

[a]After recrystallization. [b]Uncorrected. [c]Crude yield.

TABLE 2. Molar equivalence of hypochlorite to selected substrates; $t = 25$ °C

Substrate	Solvent (% dioxane–% H_2O)	'pH'	[NaOCl]/[Substrate][a]
Benzylamine	0.5–99.5	8.8	1.01[b]
Benzylamine–borane	1.0–99.0	8.8	4.01[b]
	0.5–99.5	8.9	4.10[c]
2-Methoxybenzylamine–borane	0.5–99.5	8.8	3.66[c]
N-Methylbenzylamine–borane	0.5–99.5	8.8	3.97[c]
N,N-Dimethylbenzylamine–borane	50.0–50.0	10.2	2.82[b]
	10.0–90.0	10.0	1.27[c]
Isoquinoline–borane	~1–99	8.8	3.13[c,d], 3.27[c]
Quinoline–borane	~5–95	<1	3.22[e]

[a]Molar ratio. [b]Conventional spectrophotometric measurement. [c]Stopped-flow spectrophotometric measurement. [d]Ref. 3. [e]Iodometric measurement.

parable to those observed with morpholine–borane and dimethylamine–borane where reaction is presumed to proceed via Scheme 1. The 1:1 stoichiometric equivalence of hypochlorite to benzylamine corresponds to N-chlorination. Comparable stoichiometry has been demonstrated in the reactions of hypochlorite with morpholine.

The rate law for the reaction of benzylamine–borane with hypochlorite in 10% dioxane–90% H_2O is given in eqn. (8)

$$-\mathrm{d[AB]}/\mathrm{d}t = -4[\mathrm{OCl^-}]_0/\mathrm{d}t = k_2[\mathrm{AB}][\mathrm{OCl^-}]_0 \qquad (8)$$

where $[\mathrm{OCl^-}]_0$ denotes total stoichiometric hypochlorite, i.e. $[\mathrm{HOCl}]+[\mathrm{OCl^-}]$. The hydrogen ion dependence of k_2 is shown in Table 3 and Fig. 2, with solvent and substrate isotope effects given in Table 4. The observed three-fold increase in rate in D_2O and the departure from a first-order dependence on hydrogen ion in the vicinity of the pK_a of HOCl strongly suggests a mechanism analogous to an A-1 pathway [7, 8] involving a rapid pre-equilibrium and subsequent oxidative attack of hypochlorous acid on amine–borane as depicted in Scheme 3.

$$\mathrm{H^+ + OCl^-} \overset{1/K_a}{\rightleftharpoons} \mathrm{HOCl} \qquad \text{(fast)} \qquad (9)$$

$$\mathrm{R_2NR'BH_3 + HOCl} \xrightarrow{k_r} \neq \qquad \text{(slow)} \qquad (10)$$

Scheme 3.

The kinetic consequence of Scheme 3, shown in eqn. (11),

$$\mathrm{Rate} \equiv -\mathrm{d[R_2NR'BH_3]}/\mathrm{d}t = k_r[\mathrm{R_2NR'BH_3}][\mathrm{HOCl}] \qquad (11)$$

is related to the observed rate eqn. (8), as shown in eqn. (12) wherein $k_2 = k_r[\mathrm{H^+}]/([\mathrm{H^+}]+K_a)$

$$\mathrm{Rate} = k_r[\mathrm{R_2NR'BH_3}][\mathrm{OCl^-}]_0[\mathrm{H^+}]/([\mathrm{H^+}]+K_a) \qquad (12)$$

The first-order dependence on hydrogen ion, evident at high pH, corresponds to the limiting case $K_a \gg [\mathrm{H^+}]$.

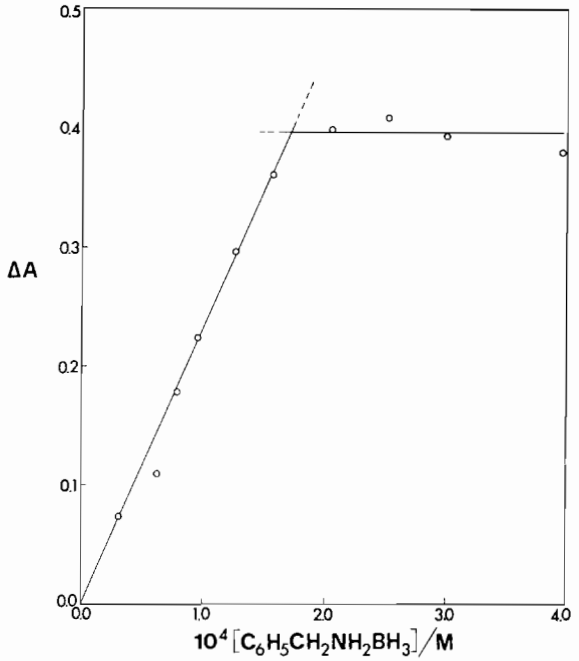


Fig. 1. Stopped-flow spectrophotometric titration of NaOCl with benzylamine–borane in 1% dioxane–99% H_2O (by volume); $t = 25$ °C; pH = 8.9; $[NaOCl]_0 = 7.09 \times 10^{-4}$ M; $[OCl^-]/[C_6H_5CH_2NH_2BH_3] = 4.10$.

TABLE 3. pH dependence of the rate of reaction of benzylamine–borane with sodium hypochlorite in 10% dioxane–90% H_2O (vol./vol.); $t = 25$ °C; $I = 0.10$ M

'pH'[a]	10^4[AB] (M)	10^4[NaOCl] (M)	$10^{-5}k_2$ (M^{-1} s^{-1})[b]
6.89	4.44	4.93	1.7
7.05	5.23	4.47	1.6
7.28	4.38	4.55	1.9
7.51	4.38	4.55	1.9
7.86	7.85	4.72	1.3
7.87	7.85	2.60	1.3
8.10	7.69	7.70	0.92
8.49	7.69	11.0	0.61
8.82	7.69	9.84	0.28
9.09	7.69	10.2	0.22
9.00	10.6	9.17	0.17
9.50	12.6	10.2	0.058
9.51	10.3	8.07	0.063
10.00	12.5	10.1	0.022
10.03	10.3	7.60	0.021
10.68	10.3	7.39	0.0044

[a]Phosphate buffer for pH 6.89–8.49; carbonate buffer for pH 8.82–10.68. [b]From second-order treatment: $-d[C_6H_5CH_2NH_2BH_3]/dt = k_2[C_6H_5CH_2NH_2BH_3][OCl^-]_0$.

The plateau region at lower pH is attributed to the onset of saturation kinetics where $[H^+] \gg K_a$.

Although $pK_a = 7.5$ for HOCl in aqueous solution [9], an operational pK_a of 7.65 in 10% dioxane–90% H_2O was obtained via titration of aqueous hypochlorite with standard HCl in this solvent system. Using this value and k_2 values obtained experimentally in the region of first-order hydrogen ion dependence (pH 8.5–10.7), a value $k_r = 4.8 \times 10^5$ M^{-1} s^{-1} (average of 9 points with average deviation $= 4 \times 10^4$) is calculated from eqns. (8) and (12). From this value of k_r and setting $K_a = 2.24 \times 10^{-8}$ M, values of k_2 may be calculated, again from eqns. (8) and (12), in the region of pH 6.9–8.5. Corresponding data are included in

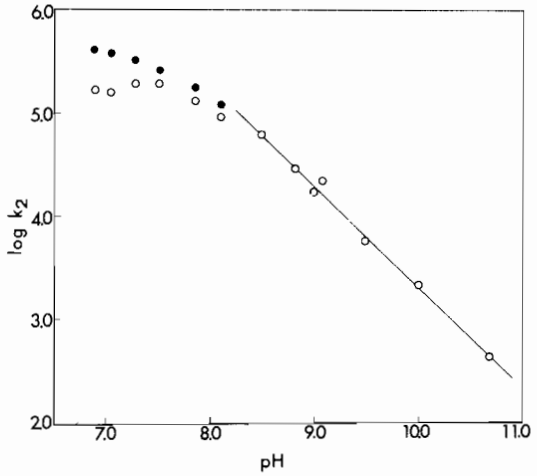


Fig. 2. pH dependence of k_2 for the reaction of benzylamine–borane with NaOCl in 10% dioxane–90% H_2O (by volume); $t = 25$ °C; $I = 0.10$ M, $k_2 = (-d[C_6H_5CH_2NH_2BH_3]/dt)/([C_6H_5CH_2NH_2BH_3][OCl^-]_0)$. ○, log k_2 (experimental). For pH = 8.5–10.7, $\log k_2 = -1.02$ pH + 13.4 ($r = -0.996$). ●, log k_2 (calculated from eqns. (8) and (12) using $k_r = 4.8 \times 10^5$ M^{-1} s^{-1} and $K_a = 2.24 \times 10^{-8}$ M).

TABLE 4. Isotope effects in the reaction of benzylamine–borane with hypochlorite in 10% aqueous dioxane; $t = 25$ °C, $I = 0.10$ M

pH	Substrate	$10^{-3}k_2$ (M^{-1} s^{-1})[a]	k_H/k_D
Substrate isotope effect			
9.00	$C_6H_5CH_2NH_2BH_3$	17.5	1.29
9.00	$C_6H_5CH_2NH_2BD_3$	13.6	
10.00	$C_6H_5CH_2NH_2BH_3$	2.07	1.31
10.00	$C_6H_5CH_2NH_2BD_3$	1.58	
pH(D)[b]	Solvent[c]	$10^{-3}k_2$ (M^{-1} s^{-1})[d]	k_{D_2O}/k_{H_2O}
Solvent isotope effect (for $C_6H_5CH_2NH_2BH_3$)			
9.50	H_2O	5.76	2.93
(9.47)	D_2O	16.9	
9.95	H_2O	2.24	2.94
(9.96)	D_2O	6.60	

[a]From second-order treatment; $-d[AB]/dt = k_2[AB][OCl^-]_0$; AB = amine–borane. [b]pD = pH + 0.41 [5, 6]. [c]10% Dioxane–90% H_2O (D_2O). [d]From second-order treatment: $d[C_6H_5CH_2NH_2BH_3]/dt = k_2[C_6H_5CH_2NH_2BH_3][OCl^-]_0$.

Fig. 2 to permit a comparison of experiment with theory.

It can be seen that the general kinetic pattern is compatible with the model although some digression is apparent below pH ~ 7.2. Some variation is undoubtedly due to experimental error. Also reduction potential data [9] yields $K_{eq} \sim 2.3 \times 10^3$ at 25 °C for the process $H^+(aq) + Cl^-(aq) + HOCl(aq) \rightarrow Cl_2(aq) + H_2O(l)$. Thus, some decline in rate may result from partial deterioration of HOCl at higher acidity. Although the digression is not fully understood, it appears that Scheme 3 does reflect the overall profile of the mechanism of reaction.

Although some insulation of the reactive site from electronic effects of ring substituents by the intervening methylene group is expected and, indeed, has been found in recent studies of benzylamine–borane *hydrolysis* where electronic effects of ring substituents are greatly reduced relative to effects observed in solvolysis of aniline–boranes [10, 11], the absence of a measurable effect here on oxidation rate with aromatic ring substitution or methyl substitution at the α-carbon (Table 5) suggests the absence of significant change in charge distribution on formation of the activated complex. Thus, the three- to four-fold decrease in rate with N-methyl substitution is speculatively attributed to steric inhibition in the transition state configuration.

Introduction of a second methyl group at nitrogen, however, leads to a change in stoichiometry from borane oxidation to B-chlorination as evidenced by isolation of the *N,N*-dimethylbenzylamine–dichloroborane adduct. This is attributed to a change in *intimate* mechanism associated with a different mode of attack of HOCl on substrate borane and seems typical of the reaction of tertiary amine–boranes. The variation of the experimentally determined $[OCl^-]_0$/[amine–borane] molar equivalence from unity (Table 2) is undoubtedly due to the formation of more highly chlorinated borane adducts within the time frame of absorbance measurements. This is not surprising in as much as previous studies have shown that, while initial chlorination of tertiary amine–boranes is retarded with increasing basicity, subsequent chlorination (of the monochloroborane) is pH independent [2]. Thus, at 'pH ~ 10', the formation of *N,N*-dimethylbenzylamine–monochloroborane is not rapid enough to be kinetically decoupled from successive chlorination processes. Second-order rate constants for chlorination of *N,N*-dimethylbenzylamine–borane are shown in Table 6.

TABLE 5. Rates of reaction of substituted benzylamine–boranes with hypochlorite in 10% dioxane–90% H_2O; $t = 25$ °C, 'pH' = 9.00, $I = 0.10$ M

Amine–borane	$10^{-4}k_2$ $(M^{-1}\ s^{-1})^a$
Benzyl–	1.7
2-Methoxybenzyl–	2.0
3-Methoxybenzyl–	1.7
4-Methoxybenzyl–	1.9
4-Methylbenzyl–	1.8
4-Trifluoromethylbenzyl–	1.6
4-Chlorobenzyl–	1.6
α-Methylbenzyl–	1.7
N-Methylbenzyl–	0.49

[a] $-d[AB]/dt = k_2[AB][OCl^-]_0$; AB = amine–borane.

Quinoline–borane and isoquinoline–borane represent interesting cases of tertiary amine adducts that react via the oxidative pathway. Rate data are given in Table 7. Spectrophotometric studies suggest a 3:1 molar equivalence of oxidant to substrate. The somewhat higher measured ratios appear indicative of side reactions involving the aromatic ring system. A 4:1 equivalence is ruled out since N-chlorination is precluded. Kinetic data and the pH dependence of the k_2 term show consistency with Scheme 3, however, the major argument for oxidation as opposed to B-chlorination emanates from studies of the reactivity of quinoline–monochloroborane in 50% aqueous dioxane. Here, a first-order decrease in chloroborane concentration is observed which is independent of added hypochlorite and acidity at 'pH' 8–12.5 (Table 8). Thus, B-chlorination cannot contribute to hypochlorite consumption in the quinoline–borane system. The quinoline–boranes undergo oxidative attack by HOCl and the disappearance of quinoline–monochloroborane in aqueous dioxane is due to its hydrolysis.

Temperature dependent studies further support the proposal that oxidation and chlorination result from different modes of HOCl attack at the respective amine–boranes, as opposed to a single mode of attack to form the monochloroborane with the ultimate stoichiometry dependent on the subsequent fate of this intermediate. Variations of second-order rate constants between 18° and 34° for five substrates are given in Table 9 along with corresponding activation parameters. Activation enthalpies and entropies are interpreted as composite parameters in accordance with Scheme 3. Isoquinoline–borane and the benzylamine adducts are known to undergo hydride oxidation whereas trimethylamine–borane is subject to B-chlorination. Differences in magnitude of activation parameters as well as marked differences in relative importance of ΔH^* and ΔS^* terms argue against a common transition state configuration for rate-limiting steps.

The calculated free-energy of activation for oxidative attack by HOCl on amine–borane is low in comparison to that observed for other amine–borane solution reactions, e.g. ~1/4 to 1/3 of that observed for acid-catalyzed and acid-independent solvolysis [11]. The entropy term accounts for 20–30% of the free energy of activation and a small enthalpy term suggests the

TABLE 6. Rate of reaction of *N,N*-dimethylbenzylamine–borane with hypochlorite in 50% aqueous dioxane; $t = 25$ °C, 'pH' = 10.04, $I = 0.054$ M

10^3[NaOCl] (M)	10^3[AB] (M)	-10^2d[NaOCl]/dt (M s^{-1})	k_2[a] (M^{-1} s^{-1})	k_{obs}[b] (s^{-1})	k_2[c] (M^{-1} s^{-1})
0.758	29.6	6.19	276	9.42	318
	42.0	8.41	264	14.0	333
	49.8	10.5	278	18.4	369
1.72	29.6	17.6	345	8.90	301
	42.0	18.3	254	11.0	262
	49.8	20.5	240	14.1	283
2.26	29.6	27.7	414	14.1	475
	42.0	37.3	393	20.4	486
	49.8	46.9	417	23.1	464
Average k_2 values			320		366

[a]From initial rate treatment: $k_2 = (-\text{d[NaOCl]/d}t)/([\text{NaOCl}][\text{AB}])$. [b]From pseudo-first-order treatment: $k_{obs} = -\text{d ln[NaOCl]/d}t$. [c]$k_2 = k_{obs}/[\text{AB}]$; AB = amine–borane.

TABLE 7. Rates of reaction of hypochlorite with substrates in the quinoline–borane series; solvent = 0.25% dioxane–99.75% H_2O, $t = 25$ °C

Quinoline–borane				
pH	9.1	10.4	11.0	
k_2 (M^{-1} s^{-1})[a]	4580[b]	218[b]	59[b]	
4-Methylquinoline–borane				
pH	8.9	10.4	11.0	
k_2 (M^{-1} s^{-1})	17500[c]	442[c]	109[c]	
Isoquinoline–borane				
pH	9.3	9.9	10.4	11.1
k_2 (M^{-1} s^{-1})	5900[b]	977[c]	430[b,d]	97[c], 106[c,e]

[a]$k_2 = -(\text{d[AB]/d}t)/[\text{AB}][\text{OCl}^-]_0$; AB = amine–borane. [b]Average of 5 determinations. [c]Average of 4 determinations. [d]0.6% dioxane–99.4% H_2O. [e]25% dioxane–75% H_2O.

TABLE 8. Rate of disappearance of quinoline–monochloroborane in 50% aqueous dioxane at 25 °C

'pH'	10^5[AB] (M)	10^4[NaOCl] (M)	k_{obs}[a] (s^{-1})	k_{obs}[b] (s^{-1})
12.56[c]	3.18	0.0	1.31	
12.56	3.18	2.6	1.44	1.40
12.54	3.18	13	1.42	1.61
8.02[d]	2.25	0.0	1.43	1.57
8.02	2.25	5.3	1.23	1.39
8.02	2.25	16	1.49	1.32

[a]$k_{obs} = -\text{d ln}([C_9H_7NBH_2Cl])/\text{d}t$. [b]From initial rate measurements. [c]$I = 0.123$ M. [d]$I = 0.147$ M.

absence of great demand for bond cleavage in the transition state.

A four-center transition-state configuration leading to borane oxidation (Scheme 1) seems consistent with activation parameters and the absence of significant effects of ring or α-methyl substitution. Similar four-center transition state configurations involving addition of boron and boron-bonded hydrogen across functionalized groups have been invoked [12–15] and such a model is also consistent with the small substrate isotope effect which is comparable to that reported in previous studies of amine–borane reactions in which the rate-determining step is thought to involve attack at the B–H bond [15–17]. It seems unlikely here that significant loss of the B–H stretching vibration is occurring in the activated complex.

For trimethylamine–borane chlorination; however, the activation barrier is predominantly defined by the enthalpy term. Previous studies have shown B-chlorination rates to be very similar for borane adducts of trimethylamine, triethylamine, *N*-methylmorpholine and quinuclidine [2]. From Scheme 3, k_r values in the order of 10^5 M^{-1} s^{-1} are calculated for each of these adducts. Similar values emerge from studies in 12.5% dioxane–87.5% H_2O and, from data of Table 6, a value $k_r = 1.1 \times 10^5$ M^{-1} s^{-1} is calculated for *N,N*-dimethylbenzylamine–borane in 50% aqueous dioxane. For these substrates and under the conditions employed, there is very little effect on rate resulting from changes in structure or dioxane–water content of the solvent. Although details of differences in the *intimate* mechanisms of oxidation and chlorination reactions are not fully understood, chlorination appears to be subject to a somewhat higher free energy of activation.

In the quinoline–borane series the oxidation rate is enhanced by about a factor of two upon introduction of a methyl group at the 4 position. This may reflect a modest inductive effect transmitted through the conjugated system to the nitrogen atom. The three-fold decrease in rate accompanying substitution of the electron donating methyl group for hydrogen at nitrogen in benzylamine–borane, however, suggests that, in general, steric interactions may be more important. Al-

TABLE 9. Temperature dependent data from reactions of amine–boranes with NaOCl in 10% dioxane–90% H_2O; $I = 0.10$ M

Amine–borane		$k_2 \times 10^3$ (M^{-1} s^{-1})[a] at t (°C)					$\Delta H_{ex}^{\neq}$ [b] (kcal/mol)	$\Delta S_{ex}^{\neq}$ [b] cal/(mol K)	$\Delta H_r^{\neq}$ [c] (kcal/mol)	$\Delta S_r^{\neq}$ [d] cal/(mol K)
	t (°C) =	17.9	21.6	27.7	30.6	34.3				
Benzyl–[e]		1.93	2.06	2.36	2.46	2.59	2.7	−34.3	6.6	−9.5
α-Methylbenzyl–[e]		1.97	2.50	2.77	2.88	3.04	3.7	−30.5	7.6	−5.7
2-Methoxybenzyl–[e]		2.05	2.36	2.65	2.82	2.93	3.3	−32.1	7.2	−7.3
	t (°C) =	18.4	21.7	25.3	29.8	32.6				
Isoquinoline–[f]		6.87	7.68	8.49	8.81	9.32	3.0	−30.3	6.9	−9.2
	t (°C) =	18.3	20.9	23.6	27.7	31.4				
Trimethylamine–[f]		1.07	1.19	1.36	1.57	1.88	7.0	−20.9	10.9	+0.2

[a] $k_2 = -\mathrm{d}[\text{amine–borane}]/([\text{amine–borane}][OCl^-]_0\,\mathrm{d}t)$. [b] From $\ln k_2/T$ vs. $1/T$. [c] $\Delta H_r^{\neq} = \Delta H_{ex}^{\neq} + \Delta H_a^{\circ}$; $\Delta H_a^{\circ} = 3.9$ kcal/mol (calc. from ref. 9). [d] $\Delta S_r^{\neq} = \Delta S_{ex}^{\neq} + \Delta S_a^{\circ} - R \ln[H^+]$; $\Delta S_a^{\circ} = -21$ cal/(mol K) (calc. from ref. 9). [e] pH' = 10.0 [f] pH' = 9.2.

though hydrogen bonding involving nitrogen-bonded hydrogen in secondary amine adducts may contribute to the stabilization of the transition state configuration for oxidation, relative reactivities of quinoline– and isoquinoline–boranes probably offer greater support for a steric argument. Here, the greater rate of oxidation of isoquinoline–borane may reflect the absence of steric hinderance of the peri-hydrogen atom. A similar trend in hydrolysis rates has been attributed to the relative importance of peri-hydrogen steric interactions [3].

We suggest, then, that steric factors are critical in determining whether the oxidation or chlorination pathway is followed. As aromatic substrates, quinoline– and isoquinoline–borane display a planar environment at nitrogen rather than the distorted tetrahedral configuration existent in alkyl and non-aromatic heterocyclic tertiary amine–boranes. That quinoline– and isoquinoline–boranes undergo oxidation may be due to the absence of steric hindrance to the achievement of the appropriate (4-center or other) transition state configuration. Thus, steric considerations permitting, the oxidative pathway is favored. However, steric crowding is presumably sufficient in non-aromatic *tertiary* amine–boranes, where nitrogen exists in tetrahedral coordination, to inhibit the oxidative mechanism and favor the chlorination pathway.

The comparable activation entropy terms observed for oxidation of isoquinoline–borane and boranes in the benzylamine series may also suggest that, given structural features which permit attainment of a transition state configuration leading to oxidation, the spatial barrier to its formation becomes relatively independent of structure. In any event, it seems clear that the stoichiometric outcome of the reaction of amine–borane with hypochlorite is dependent on the particular mode of attack by HOCl which is determined by structural features in the amine portion of the adduct and that steric factors play the dominant role.

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