The Influence of Borate Buffers on the Hydration Rate of Cyanohydrins: Evidence for an Intramolecular Mechanism

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The effects of borate buffers on the pseudo first-order rate constants for the hydration of hydroxyacetonitrile (**1**) have been examined in the pH range 8.6–10.3 at 80 °C. Kinetic results are compatible with a reaction of the neutral cyanohydrin with borate anion or any other kinetically equivalent mechanism. Cyanohydrin structural effects are consistent with a pathway involving the pre-equilibrium formation of a borate–substrate adduct, followed by a rate-determining intramolecular nucleophilic attack on the nitrile group. Phenylboronate ion has also been shown to act as an efficient catalyst, but it was not possible to detect any influence due to disubstituted borate ions. Thus, it is suggested that a trigonal borate anion actually acts as a nucleophile.

Hydration of some cyanohydrins has been found to be promoted in aqueous solutions of boric acid salts.[1,2] No information on the reaction mechanism has yet been published. However, it is reasonable to believe that the neighbouring hydroxy group plays a role in the course of the hydration on the grounds that several examples of borate catalysis have been reported for reactions involving hydroxylic compounds.[3–11]

In every case, the catalysis was attributed (i) to the ability of boric acid to form covalent adducts with alcohols reversibly, at a rate which is fast relative to the rates of many other reactions and (ii) to the efficiency of the subsequent intramolecular reaction.[12] Jencks considered this kind of behaviour as a model system in which the reacting groups are brought together in a similar manner to that occurring in enzymes.[13]

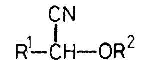
The most discussed example of borate catalysis has been the hydrolysis of phenyl salicylate; ground state activation,[5] transition state stabilization,[5,6] and nucleophilic catalysis[7,14] have been suggested as hypotheses in order to account for the borate efficiency. Strong evidence for the latter possibility was produced recently by Khan.[7] In addition, it is proposed that borate catalysis of the hydrolysis of 2-chloro alcohols,[4] hydroxythioesters,[10] and hydroxy-Schiff bases[9b] proceeds through the nucleophilic participation of a boron-bound hydroxy group.

Of course, a similar reaction path may account for the borate catalysis of cyanohydrin hydration, but one can suggest other explanations. Furthermore, involvement of the hydroxy group has not yet been demonstrated and substrate activation as a Lewis adduct of the nitrile and boric acid cannot be ruled out.

The present paper reports a kinetic study of the borate-catalysed hydration of hydroxyacetonitrile (**1**). In addition, results are presented about the influences of both substrate and catalyst structural effects in order to provide information concerning the reaction mechanism and the nature of active boron species.

Results and Discussion

Decomposition of Hydroxyacetonitrile.—Because of the alkaline pH of borate buffers, the reversible dissociation of cyanohydrins into carbonyl compounds and cyanide[15–18] was expected to take place. In order to carry out a kinetic study we selected hydroxyacetonitrile (**1**), which shows a high thermodynamic stability,[16] so as to avoid any alteration of pseudo first-order kinetics.

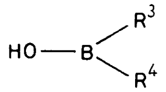


$$R^1\text{–}\overset{\displaystyle CN}{\overset{|}{C}}H\text{–}OR^2$$

(**1**) $R^1 = R^2 = H$

(**2**) $R^1 = Me, R^2 = H$

(**3**) $R^1 = R^2 = Me$



(**4**) $R^3 = Ph, R^4 = OH$

(**5**) $R^3 = R^4 = Ph$

Even in this case, unacceptable degrees of dissociation were obtained under the conditions used for the kinetic measurements [low concentrations of the substrate (**1**)], and the addition of some formaldehyde proved to be essential to shift the equilibrium.

The accurate prediction of the amount of dissociated hydroxyacetonitrile (**1**) required a knowledge of the value of the equilibrium constant K [equation (1)] for the stability of

$$K = \frac{[\text{HO-CH}_2\text{-CN}]}{[\text{HCHO}][\text{HCN}]} \qquad (1)$$

hydroxyacetonitrile at the temperature of the kinetic measurements (80 °C). The ionizations of both the substrate (K_a) and hydrogen cyanide (K_{HCN}) are known to alter the equilibrium[16] and a pH-dependent equilibrium constant was defined [equation (2)], and can be expressed according to equation (3).

$$K' = \frac{\{[\text{HO-CH}_2\text{-CN}] + [^-\text{O-CH}_2\text{-CN}]\}}{[\text{HCHO}]\{[\text{HCN}] + [\text{CN}^-]\}} \qquad (2)$$

$$K' = K\frac{1 + K_a/[\text{H}^+]}{1 + K_{\text{HCN}}/[\text{H}^+]} \qquad (3)$$

Measurements of the equilibrium constant K' were carried out, at 80 °C, using different pH values, by titration of the cyanide after the equilibrium had been reached in a dilute solution of hydroxyacetonitrile (10^{-3} mol dm^{-3}) and after freezing the equilibrium by acidification with acetic acid. The results are given in Table 1. Equation (3) adequately describes the observed behaviour and a least-squares treatment gave the value K = 8.2

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Table 1. Equilibrium constants for the stability of hydroxyacetonitrile (**1**) (initial concentration 1–5 × 10^{-3} mol dm^{-3}) at 80 °C, ionic strength 0.5 mol dm^{-3} (KNO_3).

Buffer basic component	pH	10^{-4} K'/dm^3mol^{-1} Found	Deviation[a]
HPO_4^{2-}	6.22	8.15	−0.01
HPO_4^{2-}	7.20	7.37	−0.13
N-Methylmorpholine	7.54	7.51	0.71
$B(OH)_4^-$	8.25	3.61	−0.19
$B(OH)_4^-$	8.35	3.02	−0.38
$B(OH)_4^-$	8.69	1.82	−0.21
CO_3^{2-}	8.50	2.64	−0.14
CO_3^{2-}	9.10	1.01	0.05

[a] Deviation from the data calculated from the value of $K = 8.2 \times 10^4$ dm^3 mol^{-1} by using equation (3); the value of $pK_{HCN} = 8.20$ was determined at 80.0 °C from R. M. Izatt, J. J. Christensen, R. T. Pack, and R. Bench, *Inorg. Chem.*, 1962, **1**, 828; $pK_a = 10.5$ was determined in the present work.

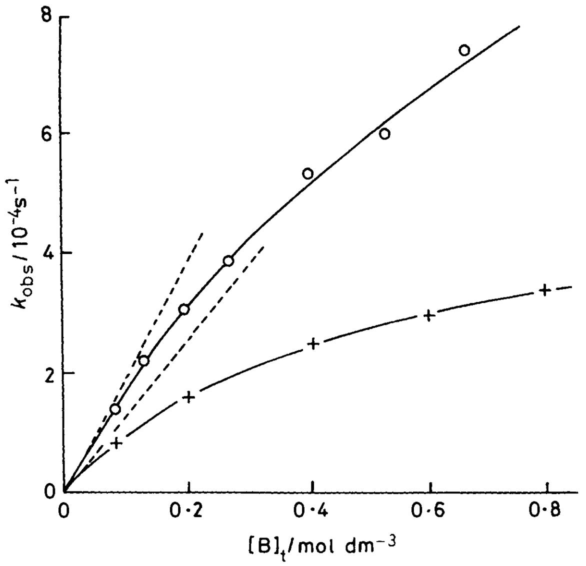

Figure 1. Dependence of the pseudo first-order rate constants for the hydroxyacetonitrile hydration on total borate buffer concentration at different theoretical buffer ratios: $[B(OH)_4^-]_t/[B(OH)_3]_t = 1$ (+), and 3 (○), at 80 °C, ionic strength 1 mol dm^{-3}. Hydroxyacetonitrile was stabilized by the addition of 5×10^{-3} and 1×10^{-2} mol dm^{-3} formaldehyde, respectively. Theoretical slopes (dashed lines) are calculated from $k_B = 2.5 \times 10^{-3}$ dm^3 mol^{-1} s^{-1} and equation (4).

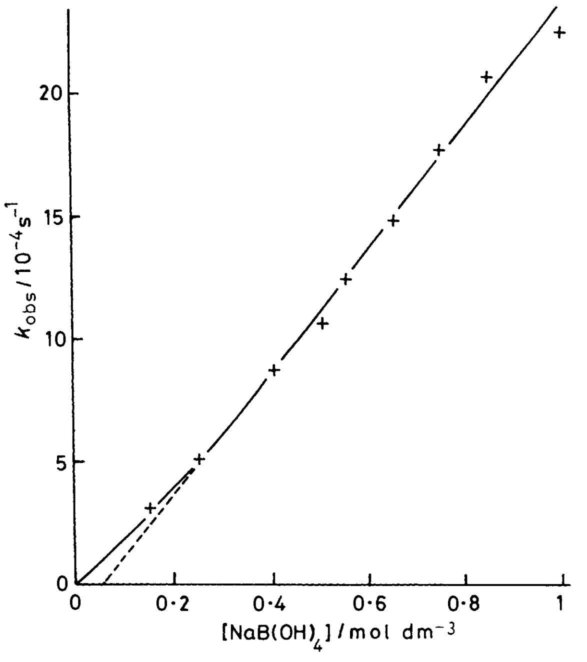

Figure 2. Dependence of the pseudo first-order rate constants for the hydroxyacetonitrile hydration on the concentration of sodium borate, at constant concentration of boric acid, $[B(OH)_3]_t = 0.05$ mol dm^{-3}, in the presence of 5×10^{-2} mol dm^{-3} formaldehyde, at 80 °C, ionic strength 1.0 mol dm^{-3}. The pH increased from 9.14 to 10.20 on increasing the sodium borate concentration from 0.15 to 1 mol dm^{-3}.

10^4 dm^3 mol^{-1}. An appreciable difference is noticed between this value and the one ($K = 3.37$ 10^4 dm^3 mol^{-1}) which is deduced from the data given by Schlesinger and Miller.[16] However, that determination was dependent on a previous one concerning the lactonitrile stability[15] that seems unreliable based on a comparison with a later measurement.[17]

Kinetics of Hydroxyacetonitrile Hydration.—Figure 1 shows the dependence of the pseudo first-order rate constants for hydroxyacetonitrile hydration on total borate buffer concentration at constant buffer ratios, 1 and 3, at 80 °C and at a constant ionic strength of 1 mol dm^{-3} (KCl). The negative deviation to first-order dependence exhibited in Figure 1 must be related to the formation of polyborate ions,[19–23] as has often been observed previously for borate buffer catalysis.[24] The rise in pH (from 8.69 to 8.83 and from 9.06 to 9.35 for $R = 1$ and $R = 3$, respectively) with increasing total buffer concentration, unambiguously demonstrates the formation of polyborates.* There is a negligible contribution of the alkaline hydration of hydroxyacetonitrile, as attested by the extrapolation of the rate constants to zero buffer concentration. The stronger catalytic effect at high buffer ratio and the levelling off of the rate with increasing buffer concentration are indications of catalysis by monomeric borate ion, $B(OH)_4^-$. On the other hand, the inefficiency of boric acid itself was shown by the absence of hydration in aqueous boric acid.

In order to confirm that the buffer-active component is the borate ion, kinetic measurements were carried out under conditions restricting the formation of polyborate ions. Owing to the fact that the oligomers are made of both neutral and anionic boron entities, *i.e.* $B(OH)_4^-$ itself does not undergo polymerization,[19–23] rate constants were measured in solutions containing increasing concentrations of sodium borate (0.15–1 mol dm^{-3}) with a low and constant concentration of boric acid (0.05 mol dm^{-3}). When boric acid is used up by oligomer formation, further addition of sodium borate leads to monomeric borate ion. Figure 2 shows the dependence of the pseudo first-order rate constants for hydroxyacetonitrile hydration on the concentration of sodium borate under those conditions. A good agreement with a linear dependence is observed for borate concentrations in the range 0.25–1 mol dm^{-3}. However, experiments involving a pH-variation inevitably include a contribution from the hydroxide ion catalysed pathway of hydration,[25] for which the extent was shown to be restricted to

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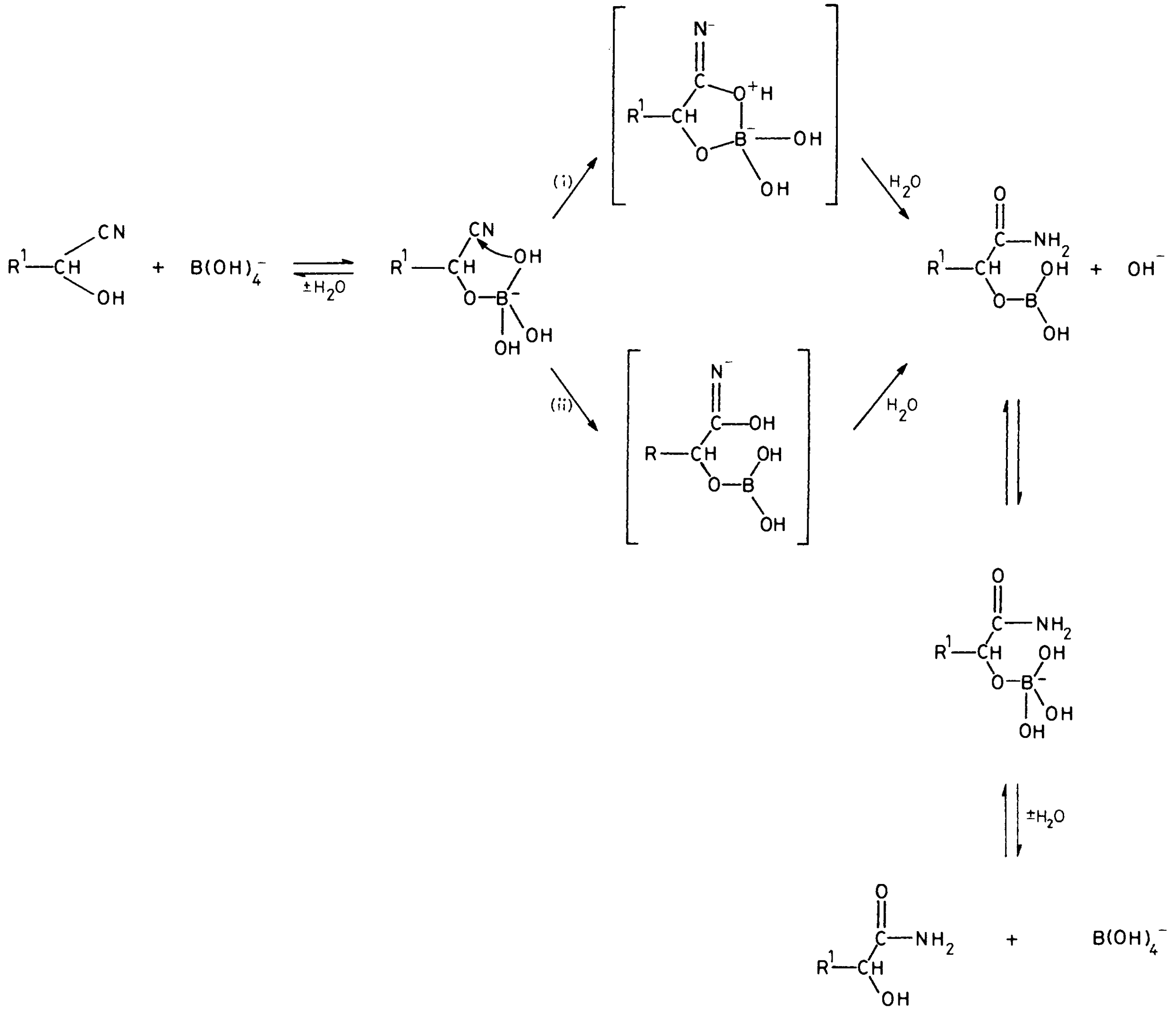
* An examination of the equilibrium constants for polyborate formation, calculated at 80 °C from previously reported data (ref. 20) showed that the deviation was consistent with the estimated concentrations of monomeric borate ion, but an accurate calculation of the composition of the medium is not possible because of the differences in ionic strength and of the questionable attribution of species according to later studies (refs. 21–23).



Scheme 1.

10% of the overall rate constant, or less, by comparative experiments in which an identical pH was attained by the addition of only KOH.[26] Ignoring that contribution, the pseudo first-order rate constant may be expressed as a function of the actual molarity of monomeric borate ion, according to the rate law of equation (4). $k_B = 2.5 \times 10^{-3}$ dm^3 mol^{-1} s^{-1} was

$$v = k_B[B(OH)_4^-][HO\text{-}CH_2\text{-}CN] \qquad (4)$$

taken as the asymptotic slope in Figure 2. Calculated initial slopes from that rate constant and equation (4) are drawn in Figure 1 and show good agreement with the extrapolation of experimental data to dilute borate buffers in which polymerization is negligible.

Mechanism for Borate Catalysis.—The rate law of equation (4) is consistent with a bimolecular reaction of hydroxyacetonitrile (**1**) with borate ion or any kinetically equivalent reaction. That is the case for the reaction mechanism in Scheme 1, which is derived from the previously reported mechanisms for borate or boric acid catalysed reactions of hydroxylic compounds.[3–11] According to Scheme 1, hydration occurs through the formation of a complex between the catalyst and the substrate and through a negatively charged transition state, which accounts for the rate law of equation (4). Two possibilities were previously suggested for the reaction of the functional group from the adduct: (i) nucleophilic attack by the hydroxy group of the adduct according to Khan[7] or, alternatively, (ii) the intramolecular transfer of the boron-co-ordinated hydroxide ion; this explanation has been preferred by Okuyama and his coworkers.[9–10] The application of both possibilities to the hydration of cyanohydrins is shown in Scheme 1. Each of them involves an intermediate containing a negatively charged nitrogen atom. Even though those species must be very unstable, their formation can be connected with the formation of similar ones, postulated in the course of the alkaline hydration of nitriles,[25] and better established during the base-catalysed cleavage of imido esters to nitriles.[27]

There is little direct evidence for the formation of borate adducts of monohydroxylic compounds in aqueous solution,[28] but diols[29–34] and hydroxy acids[29,31,35,36] are known to yield cyclic borate esters under similar conditions. Thus the hydroxy group of cyanohydrins is likely to add to boric acid even though low concentrations of the complex are obtained.

Further confirmation of the involvement of the adduct of cyanohydrins with borate ion comes from the examination of structural effects on the rates of hydration. In Table 2, lactonitrile (**2**) is shown to be hydrated about 20 times faster

Table 2. Comparison of the rate constants for the hydration of hydroxyacetonitrile (**1**), lactonitrile (**2**) and 2-methoxypropionitrile (**3**) in borax buffers at 80 °C.

$[B]_t$[a]/mol dm^{-3}	$10^4 k_{obs}$/dm^3 mol^{-1} s^{-1} (**1**)[b]	(**2**)[c]	(**3**)[c]
0.2	1.60	2.50	0.14
0.4	2.48	4.17	0.17
0.8	3.40	6.00	0.22

[a] Total buffer concentration. [b] Concentration 5.0×10^{-3} mol dm^{-3}, ionic strength 1 mol dm^{-3}. [c] Concentration 0.1 mol dm^{-3}, ionic strength 0.4 mol dm^{-3}.

than 2-methoxypropionitrile (**3**) in the presence of borax.* That enhancement gives an indication of the involvement of the hydroxy group in the catalytic pathway since the methylation must prevent the formation of any adduct from the nitrile (**3**) and since hydroxy and methoxy substituents are expected to exert similar inductive effects.[37]

In addition, higher catalytic rate constants were found for the lactonitrile hydration than for the reaction of hydroxyacetonitrile (Table 2) in contrast with the reduced electrophilic reactivity of the nitrile group expected from the electron-donating properties of the methyl substituent. This behaviour can be accounted for by a mechanism involving intramolecular steps if the highly favourable effect of substitution on the rates of ring closure reactions[12] is considered.

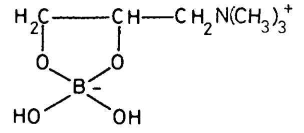
The effects of both *O*- and *C*-methylation of cyanohydrins are arguments in favour of a mechanism in which hydration takes place by an intramolecular nucleophilic reaction from the complex formed between boric acid and the substrate as shown in Scheme 1. However, those effects do not provide any indication for one of the mechanistic pathways in Scheme 1, or for any other equivalent pathway. The examination of the reactivity of substituted boron species has been carried out in order to get further insights into the course of the hydration mechanism.

In Scheme 1, two of the three hydroxy groups that are attached to the boron atom in the complex are not directly involved during the reaction; then mono- and di-substituted borates are expected to display catalytic properties towards the hydration of cyanohydrins. The catalytic efficiency of monosubstituted species was clearly demonstrated by an experiment carried out with a buffer prepared from phenylboronic acid (**4**), at pH 9.1 (total buffer concentration = 0.15 mol dm^{-3}): that showed a substantial increase in the rate of lactonitrile hydration ($t_{\frac{1}{2}}$ = 15 min, at 80 °C) compared with a control experiment in the absence of catalyst (15% progress after 30 min).

In contrast with the behaviour of phenylboronate ion, the experiments carried out with disubstituted species, with the aim of detecting a catalytic activity towards cyanohydrin hydration, were unsuccessful.

(*a*) In methanol–water (1 : 1), the hydration of lactonitrile did not occur after 6 h at 80 °C and at pH 8.8 in the presence of diphenylborinic acid (**5**) (0.05 mol dm^{-3}), whereas 45% lactamide was obtained in a similar experiment using boric acid as catalyst.

(*b*) The addition of 2,3-dihydroxypropyl-*N*,*N*,*N*-trimethyl ammonium hydroiodide to a borate buffer was shown to give the cyclic complex (**6**), but led to a decrease in the rate constants for lactonitrile hydration consistent with the inefficiency of the borate ester (**6**).[38]

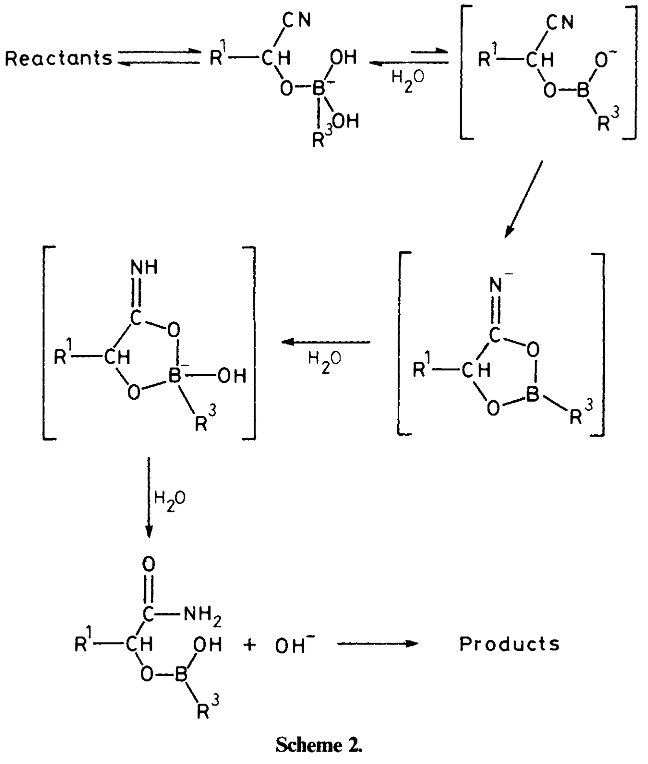


(**6**)

(*c*) In addition, the non-linear dependence in Figure 1 was attributed to the formation of unreactive polyborate ions. It is interesting to connect this with the structure of those oligomers[22] in which the tetrahedral boron, carrying the negative charge, is di- tri-, or tetra-substituted.

In every case, it is possible to find a particular explanation for the non-reactivity of disubstituted borate species. For the first one, it would be related to the steric hindrance due to the presence of two phenyl substituents. For the second one, the addition of 2,3-dihydroxypropyl-*N*,*N*,*N*-trimethylammonium ion would not only lead to the 1 : 1 complex (**6**) but mainly to the 2 : 1 complex in which boron is tetrasubstituted; however, this behaviour would contradict the reactivity observed previously for simple diols.[30,31] In the latter case the non-reactivity would be again related to steric hindrance or to the predominance of species containing tri- or tetra-substituted boron, which is in contradiction with the predominant formation of $B_3O_3(OH)_4^-$, that was concluded from studies on boric acid–borate solutions.[22,23]

However, it is possible to provide a general explanation in which the mechanism of hydration itself is the cause of the non-reactivity of disubstituted species. In Scheme 2, the cyclisation takes place from an highly nucleophilic borate trigonal ion. Contrary to the reactive complex involved in Scheme 1, this trigonal borate ion carries only one hydroxy group (R^3 = OH) that can be substituted, hence the pathway shown in Scheme 2 does not apply to disubstituted borate ions. There is no published data supporting the existence of the trigonal borate



Scheme 2.

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* The hydration of the nitrile (**3**) is attributed to the catalysis by hydroxide ion. As has been shown for methoxyacetonitrile, there is an increase in rate constant with increasing concentration of borate buffer at constant ionic strength as a result of the alteration of the hydroxide ion concentration due to the formation of polyborate ions and secondarily as a result of a medium effect (ref. 26).

species in solution. However, oxygen-ionized trigonal borate anions are known in the solid state for anhydrous crystalline borates,[39] and this leads us to suggest the formation of those species in solution through a minor pathway of ionization of oxygen-acids of boron. If this is true, a very small amount of the trigonal borate anion must be present in the medium, but this disadvantage is probably balanced by the high rate of cyclisation.

Conclusions

The present results provide several arguments supporting an intramolecular pathway for the borate catalysis of cyanohydrin hydration. This conclusion is in agreement with the mechanisms which have been previously proposed for the borate catalysis of the reactions of hydroxylic compounds.[3–11] The study of the activity of substituted borate ions allowed us to suggest an alternative pathway involving a trigonal borate anion. It cannot be ruled out that similar pathways apply to the reactions of other hydroxylic compounds, though the confirmation of this suggestion would require further investigation.

Experimental

UV spectra were obtained with an Aminco DW-2 spectrophotometer. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer. ^{1}H NMR spectra were obtained with a Varian EM-360L spectrometer. All chemical shifts are reported in ppm with tetramethylsilane and 3-trimethylsilylpropane-1-sulphonic acid sodium salt as internal references in organic and aqueous solutions, respectively. Measurements of pH at 80 °C were performed with a Tacussel Minisis 5000 pH-meter using a high temperature resistent Ingold 465 electrode and a closed jacketed cell thermostatted at 80 °C by circulating water. Potentiometric titrations were performed with a Tacussel Titrimax titrator. M.p.s were determined on a Büchi 510 apparatus. Calculations were performed with a Matra Datasystème Alcyane A6 microcomputer, using programs in basic Alcybaz.

Inorganic reagents were analytical grade and were used without further purification. $NaB(OH)_4$ solution (2 mol dm^{-3} stock solution) was prepared by direct reaction of NaOH and borax and was diluted as required. Phenyl boronic acid (Aldrich) was recrystallized from water before use. Diphenylboronic acid was obtained from the ethanolamine complex (Aldrich) by treatment with HCl and extraction with diethyl ether.[40] Formaldehyde aqueous solutions were prepared as previously described.[41]

Hydroxyacetonitrile and lactonitrile were distilled under vacuum in the presence of 2% H_3PO_4; $HOCH_2CN$, b.p. 69 °C/0.18 mmHg; $CH_3CH(OH)CN$, b.p. 94–97 °C/20 mmHg.

Lactamide was purchased commercially (Aldrich). Hydroxyacetamide was synthesized from hydroxyacetonitrile by the procedure of Becke, Fleig and Pässler[42] and was recrystallized from 100% EtOH, m.p. 115 °C (lit.,[43] 120 °C).

2-Methoxypropionamide was prepared by a stepwise procedure from methyl 2-bromopropionate. The starting material (23.3 g, 0.2 mol) was dropped into a stirred solution of sodium methoxide [obtained from Na (6 g) in MeOH (60 cm^3)] at 0 °C, and was allowed to stand for 80 min at room temperature. The reaction mixture was poured into diethyl ether (400 cm^3), washed with excess aqueous formic acid (0.24 mol) and with five 100 cm^3 portions of water. Ether was removed by distillation at atmospheric pressure. The liquid residue (22.5 g, 95%), dissolved in a minimum volume of MeOH, was saturated with anhydrous NH_3 (5.15 g, 0.3 mol) at -15 °C. The mixture was heated for 17 h at 110 °C in a closed vessel. The product was concentrated under reduced pressure, taken up in CH_2Cl_2 (200 cm^3), and washed with 10 cm^3 water. The organic layer was dried with sodium sulphate and the solvent was removed in a rotary evaporator. The solid residue was recrystallized from acetone–cyclohexane (14.8 g, 71%), m.p. 83–84 °C (lit.,[44] 84 °C); δ_H(60 MHz; $CDCl_3$) 1.43 (3 H, d, *J* 7 Hz, 2-Me), 3.45 (3 H, s, OMe), 3.78 (1 H, q, *J* 7 Hz, 2-H), and 6.70 (2 H, NH_2).

2-Methoxypropionitrile was prepared by dehydration of the amide (10 g, 0.097 mol) with excess thionyl chloride (14 cm^3, 0.194 mol) in chloroform (30 cm^3) heated to reflux. After 2 h, the solution was slowly added to a slurry of Na_2CO_3 (31.8 g, 0.3 mol) in water (50 cm^3) with vigourous stirring. The product was taken up in CH_2Cl_2 (170 cm^3) and washed with two 50 cm^3 portions of water. The organic layer was dried over sodium sulphate and the solvent was removed by distillation at atmospheric pressure. The distillation of the residue under reduced pressure gave pure 2-methoxypropionitrile (5.92 g, 72%), b.p. 54–56 °C/88–90 mmHg (lit.,[45] 114–117 °C/760 mmHg); δ_H(60 MHz; CCl_4) 1.53 (3 H, d, *J* 7 Hz, 3-Me), 3.48 (3 H, s, OMe), and 4.20 (1 H, q, *J* 7 Hz, 2-H).

Decomposition of Hydroxyacetonitrile at 80 °C.—Measurements were performed in buffered media from diluted hydroxyacetonitrile ($1–5 \times 10^{-3}$ mol dm^{-3}). The ionic strength was adjusted to 0.5 mol dm^{-3} with KNO_3. The solution (20–100 cm^3) was introduced into a stoppered flask and brought to 80 ± 0.1 °C in a thermostatted bath until equilibrium was reached (2–60 min). While hot, the equilibrium was quenched by adding excess acetic acid, then the solution was quickly cooled by immersion in an ice-bath. Addition of 2–5 cm^3 10^{-2} mol dm^{-3} $AgNO_3$ and potentiometric titration of excess Ag^+ with 10^{-2} mol dm^{-3} KCl allowed determination of the degree of dissociation of hydroxyacetonitrile.

Acid Dissociation of Hydroxyacetonitrile at 80 °C.—An approximate value $pK_a = 10.5 \pm 0.1$ was given by the pH of a solution in which the cyanohydrin (0.4 mol dm^{-3}) was supposed to be 50% ionized. That was achieved by addition of NaOH (0.2 mol dm^{-3}). The ionic strength was adjusted to 0.5 mol dm^{-3} (KNO_3) and the addition of formaldehyde (2.5×10^{-2} mol dm^{-3}) was expected to reverse the decomposition of the cyanohydrin. A calculation of the actual composition of the solution using equations (2) and (3) showed that the formation of cyanide ion only caused the pH to change by 0.05 units.

Kinetics of the Hydration of Hydroxyacetonitrile.—In the presence of borate buffer, the preparative scale hydration of the nitrile (**1**) (0.2–0.5 mol dm^{-3}) was shown to give hydroxyacetamide in 40% yield, due to the formation of polymers.[1] When the reaction was followed by monitoring the UV absorption of the amide at 220 nm, the side-reactions were shown to be connected with the appearance of an absorption at 240 nm when the initial concentration was in the range 0.02–0.1 mol dm^{-3}. The decrease in the relative extent of absorption at 240 nm compared with that of the amide, as the initial concentration of the nitrile (**1**) was decreased, confirmed that side-reactions occurred through a polycondensation of the reactant. That is, side-reactions were more than first order with respect to the nitrile (**1**). The disappearance of the absorption corresponding to side-products, when initial concentration was $< 10^{-2}$ mol dm^{-3}, allowed us to make a kinetic study of the hydration of the nitrile (**1**) by UV spectrophotometry. The hydration of the nitrile (**1**), 5×10^{-3} mol dm^{-3}, was followed by monitoring the increase in absorbance at 220 nm in a stoppered jacketed cell which was carefully thermostatted at 80 ± 0.1 °C. The reactions were initiated by the addition of the reactant to the pre-heated solution. The added concentrations of formaldehyde (5×10^{-3}–5×10^{-2} mol dm^{-3}) were calculated using equations (2) and (3) in order to limit the degree of decomposition of the nitrile (**1**) to the maximum value of 2%. Excess formaldehyde (up to 0.2 mol dm^{-3}) did not alter the rates even though it increased optical densities because of the equilibrium formation of *N*-methylolamide.[46] The ionic strength was maintained constant at 1 mol dm^{-3} by the addition of potassium chloride. Kinetic runs were followed for at least three half-lives. Pseudo first-order rate constants were determined from a non-linear least-squares procedure according to equation (5)

$$\text{o.d.} = A + B\exp(-k_{\text{obs}}\,t), \qquad (5)$$

where A, B, and k_{obs} are adjustable parameters.

Kinetics of the Hydrations of Lactonitrile and 2-Methoxypropionitrile.—The disappearance of the nitrile (0.1 mol dm^{-3}) was followed by NMR spectroscopy, by integration of the corresponding signals of the reactant and product. The product was identified by comparison of NMR chemical shifts with the pure amide. The ionic strength was maintained constant at 0.4 mol dm^{-3}. Samples of solution (5 cm^3), in stoppered tubes, were introduced in a water bath thermostatted at 80 ± 0.1 °C. After varying lengths of time, samples were removed and quickly cooled in an ice-bath for NMR analysis. Pseudo first-order rate constants were determined from a weighed least-squares procedure[47] according to equation (6) where y is the mole fraction of the unchanged nitrile. The weighting factor $w = y^2$ was used.

$$\ln y = a - k_{\text{obs}}\,t \qquad (6)$$

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References

1 J. Jammot, R. Pascal, and A. Commeyras, *Tetrahedron Lett.*, 1989, 563.

2 M. Wechsberg and R. Schoenbeck, E.P. 0, 006, 140/1980.

3 H. G. Peer, *Recl. Trav. Chim. Pays-Bas*, 1960, **79**, 825.

4 (*a*) R. L. Letsinger, S. Dandegaonker, W. J. Vullo, and J. D. Morrison, *J. Am. Chem. Soc.*, 1963, **85**, 2223; (*b*) R. L. Letsinger and J. D. Morrison, *ibid.*, 1963, **85**, 2227.

5 B. Capon and B. C. Ghosh, *J. Chem. Soc. B*, 1966, 472.

6 D. W. Tanner and T. C. Bruice, *J. Am. Chem. Soc.*, 1967, **89**, 6954.

7 M. N. Khan, *J. Mol. Catal.*, 1987, **40**, 195.

8 J. Hoffmann and V. Sterba, *Collect. Czech. Chem. Commun.*, 1972, **37**, 2043.

9 (*a*) H. Matsuda, H. Nagamatsu, T. Okuyama, and T. Fueno, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 500; (*b*) H. Nagamatsu, T. Okuyama, and T. Fueno, *ibid.*, 1984, **57**, 2502, 2508.

10 T. Okuyama, H. Nagamatsu, and T. Fueno, *J. Org. Chem.*, 1981, **46**, 1336.

11 F. J. Perez and H. N. Niemeyer, *Heterocycles*, 1986, **24**, 13.

12 A. J. Kirby, *Adv. Phys. Org. Chem.*, 1980, **17**, 183; L. Mandolini, *ibid.*, 1986, **22**, 1; M. I. Page and W. P. Jencks, *Gazz. Chim. Ital.*, 1987, **117**, 455.

13 W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, p. 30.

14 Ref. 13, p. 32.

15 W. F. Yates and R. L. Heider, *J. Am. Chem. Soc.*, 1952, **74**, 4153.

16 G. Schlesinger and S. L. Miller, *J. Am. Chem. Soc.*, 1973, **95**, 3729.

17 M. Béjaud, L. Mion, and A. Commeyras, *Bull. Soc. Chim. Fr.*, 1976, 233.

18 W. M. Ching and R. G. Kallen, *J. Am. Chem. Soc.*, 1978, **100**, 6119.

19 J. O. Edwards, *J. Am. Chem. Soc.*, 1953, **75**, 6151; N. Ingri, G. Lagerstroem, M. Frydman, and L. G. Sillen, *Acta Chem. Scand.*, 1957, **11**, 1034; N. Ingri, *ibid.*, 1962, **16**, 439; 1963, **17**, 573, 581; R. K. Momii and N. H. Nachtrieb, *Inorg. Chem.*, 1967, **6**, 1189.

20 R. E. Mesmer, C. F. Baes, and F. H. Sweeton, *Inorg. Chem.*, 1972, **11**, 537.

21 H. D. Smith, Jr., and R. J. Wiersema, *Inorg. Chem.*, 1972, **11**, 1152.

22 L. Maya, *Inorg. Chem.*, 1976, **15**, 2179.

23 M. Maeda, *J. Inorg. Nucl. Chem.*, 1979, **41**, 1217.

24 Ref. 13, p. 470.

25 P. L. Compagnon and M. Miocque, *Ann. Chim. (Paris)*, 1970, **5**, 11.

26 J. Jammot, R. Pascal, and A. Commeyras, unpublished work.

27 H. F. Gilbert and W. P. Jencks, *J. Am. Chem. Soc.*, 1979, **101**, 5774.

28 T. L. Paal, *Acta Chim. Acad. Sci. Hung.*, 1980, **103**, 193.

29 M. Bartusek, *Scr. Fac. Sci. Nat. Univ. Purkynianae Brno.*, 1977, **7**, 65.

30 R. Pizer and L. Babcock, *Inorg. Chem.*, 1977, **16**, 1677; L. Babcock, and R. Pizer, *ibid.*, 1983, **22**, 174.

31 M. van Duin, J. A. Peters, A. P. G. Kieboom, and H. van Bekkum, *Tetrahedron*, 1984, **40**, 2901; 1985, **41**, 3411.

32 M. Makkee, A. P. G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 1985, **104**, 230.

33 J. G. Dawber, *J. Chem. Soc., Faraday Trans. 1*, 1987, **83**, 771.

34 J. F. Verchere and M. Hlaibi, *Polyhedron*, 1987, **6**, 1415; J. F. Verchere and J. P. Sauvage, *Bull. Soc. Chim. Fr.*, 1988, 263; S. Chapelle and J. F. Verchere, *Tetrahedron*, 1988, **44**, 4469.

35 S. Friedman, B. Pace, and R. Pizer, *J. Am. Chem. Soc.*, 1974, **96**, 5381; R. Pizer and R. Slezer, *Inorg. Chem.*, 1984, **23**, 3023.

36 M. van Duin, J. A. Peters, A. P. G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 1986, **105**, 488; M. van Duin, J. A. Peters, A. P. G. Kieboom, and H. van Bekkum, *J. Chem. Soc., Perkin Trans. 2*, 1987, 473.

37 M. Charton, *J. Org. Chem.*, 1964, **29**, 1222.

38 J. Jammot, Thesis, University of Montpellier, II, 1988.

39 F. A. Cotton and G. Wilkinson, 'Advanced Inorganic Chemistry,' Wiley, New York 1980, p. 296.

40 R. L. Letsinger and I. Skoog, *J. Am. Chem. Soc.*, 1955, **77**, 2491.

41 R. Pascal, A. Rousset, and A. Commeyras, *Nouv. J. Chim.*, 1989, **13**, 205.

42 F. Becke, H. Fleig, and P. Pässler, *Liebigs Ann. Chem.*, 1971, **749**, 198.

43 A. Schmuck, *Biochem. Z.*, 1924, **147**, 193.

44 R. G. Ault, N. N. Haworth, and E. L. Hirst, *J. Chem. Soc.*, 1934, 1722.

45 K. Utimoto, Y. Wakabayashi, T. Horiie, M. Inoue, Y. Shishiyama, M. Obayashi, and H. Nozaki, *Tetrahedron*, 1983, **39**, 967.

46 G. A. Crowe and C. C. Lynch, *J. Am. Chem. Soc.*, 1950, **72**, 3622; J. Ugelstad and J. J. de Jonge, *Recl. Trav. Chim. Pays-Bas*, 1957, **76**, 919.

47 R. de Levie, *J. Chem. Educ.*, 1986, **63**, 10.

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