Rate–product correlations for concurrent nucleophilic displacements of halotriazines by hydroxide and alkoxides in water

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Rates and products of reactions of a fluorotriazine dye 1 with a range of alcohols (including tetrahydropyran-2-methanol, and α- and β-methylglucopyranoside and others given below) have been investigated in dilute aqueous solution at pH 11.2 and 25 °C by ion pair high performance liquid chromatography. The pseudo first-order rate constants when dissected, using product ratios, into contributions from the competing hydrolysis and alcoholysis reactions, show that the rates of hydrolysis are usually unchanged within experimental errors by addition of *ca.* 1% of the alcohols. However, hydrolysis rate constants are enhanced by addition of α- and β-methylglucopyranoside. Second-order constants, calculated from pK_a data (for propan-1-ol, methanol, ethane-1,2-diol, sorbitol, mannitol) for attack by alkoxide, decrease in the order of alcohols listed. Similar data for monosubstitutions of a dichlorotriazine dye 2 show that both rate constants and product ratios are strongly temperature dependent; the medium effect of additives (*e.g.* urea, salts) was also examined. A non-linear dependence of rate constant with alcohol concentration was observed for reaction of 2 with glucose, and several products were formed. The results illustrate the importance of mass law effects on the rates of these reactions.

Since the addition of hydroxide and alcohol to water generates alkoxide in a temperature-dependent equilibrium process [eqn. (1)], competitive alcoholysis and hydrolysis reactions in basic

$$HO^- + ROH \rightleftharpoons H_2O + RO^- \qquad (1)$$

media occur widely (*e.g.* ester hydrolysis and nucleophilic aromatic substitutions).[1] Alkoxide/hydroxide rate ratios vary greatly depending on the reaction conditions,[1] but more acidic alcohols increase the rates because more alkoxide ion is present at equilibrium. Also, even for reactions in predominantly aqueous solutions, addition of alcohols should in principle introduce an additional medium effect, which may be rate retarding.[2]

In neutral or weakly acidic aqueous media, the medium effect of small amounts of added alcohols on pseudo-first-order rate constants for hydrolyses in highly aqueous media has recently been investigated for benzoyltriazole, for which only a small amount of competing alcoholysis was observed and only hydrolysis was assumed to be significant.[3] In contrast, using a four-term rate law, we have established rate–product correlations for competing alcoholysis and hydrolysis of *p*-nitrobenzoyl[4] and *p*-nitrobenzenesulfonyl chloride[5] over the whole range of methanol- and ethanol-water mixtures by assuming that the reactions are third-order.

In basic aqueous media, competing alcoholysis and hydrolysis products were recently observed for cephalosporins (*e.g.* in aqueous chloroethanol).[6] For aqueous trifluoroethanol, although only hydrolysis products were stable under the reaction conditions, the expected linear relationship between pseudo-first-order rate constants and trifluoroethanol concentration was obtained.[6] In contrast, for hydrolyses of benzyl penicillins in aqueous glucose, rate constants varied non-linearly with glucose concentration (the products were not investigated).[7]

Our interest in the reactions of alcohols in basic aqueous media has arisen from an investigation of homogeneous models for the chemical selectivity of reactive dyes.[8] The use of dyes as probe molecules for investigating the reactivity of aqueous alcohols has the advantage that the dyes are readily soluble in water, and the reactions can readily be monitored by high performance liquid chromatography (HPLC). Typical reactive dyes function through a nucleophilic aromatic substitution reaction between a cellulose OH group on the fibre and a halotriazine linker unit to which the dye is already attached.[9,10] Both acid and base catalysis have been observed in the hydrolyses of chlorotriazines,[10–13] and in contrast to the expected stepwise nature of the $S_N(Ar)$ mechanism for nucleophilic aromatic substitution, it has been proposed recently that the reactions of substituted phenolates with a *p*-nitrophenoxytriazine may be concerted processes.[14]

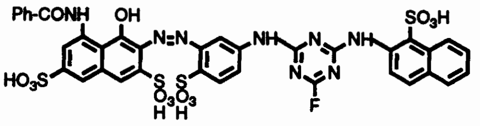
We now report rate and product data for two reactive dyes (**1** and **2**, abbreviated to DX) undergoing competing alcoholysis and hydrolysis in water, displacing one of the halides (X), to give monosubstitution products DOR and DOH respectively [eqn. (2)]. We also discuss the results in terms of rate–product

$$DX + RO^-/HO^- \longrightarrow DOR/DOH + X^- \qquad (2)$$

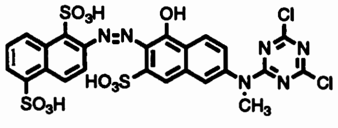
correlations (*i.e.* mass law effects) and the possible medium effects of added alcohols.

Results

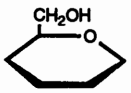
The selection of monofluorotriazine (**1**) and dichlorotriazine (**2**) reactive dyes as our substrates (DX) followed a screening process involving 15 candidates; the final choices for this investigation were based mainly on the requirements of convenient rates of hydrolyses at 25 °C with the formation of relatively stable products.[8b] The reaction conditions involved aqueous carbonate buffer to control the hydroxide concentration, low concentrations of added alcohol (typically *ca.* 0.1 M) leading to similar amounts of DOR and DOH, and very low concentrations of dye (*ca.* 3 × 10^{-4} M). Aqueous solutions of the following alcohols were investigated: methanol, propan-1-ol, ethane-1,2-diol, tetrahydropyran-2-methanol (**3**), α-methylglucopyranoside (**4**), β-methylglucopyranoside (**5**), sorbitol (**6**), mannitol (**7**) and glucose (**8**). As expected, mono-substitution [eqn. (2)] was observed and the reactions were accurately first-order.



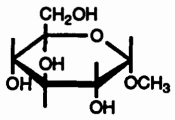
1
Fluorotriazine dye



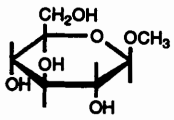
2
Dichlorotriazine dye



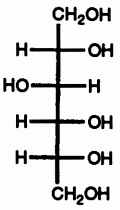
3
Tetrahydropyran-2-methanol



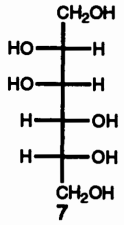
4
α-Methylglucopyranoside



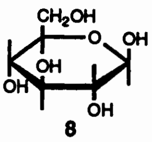
5
β-Methylglucopyranoside



6
D-Sorbitol



7
D-Mannitol



8
D-Glucose

Rate and product data were obtained from the integrated areas of chromatographic signals obtained by ion pair HPLC, as described elsewhere.[8] The most reliable pseudo-first-order rate constants (k_{obs}) were obtained from the constant for exponential decay in the concentration of the dye (k_{DX}), although appearance constants for DOH and DOR were also obtained.[8] Product ratios [P, eqn. (4)] were obtained from the linear plots of molar concentrations of DOR and DOH at various extents of reaction, a procedure which ensured that the product ratio was obtained before any of the products could decompose. First-order rate constants for the appearance of DOH (k_{DOH}) and DOR (k_{DOR}) were then obtained from the rate–product correlations given in eqns. (3) and (4). Values of

$$k_{obs} = k_{DX} = k_{DOH} + k_{DOR} \tag{3}$$

$$[DOR]/[DOH] = P = k_{DOR}/k_{DOH} \tag{4}$$

the rate constants k_{obs}, the product ratio (P) and the dissected rate constants (k_{DOH} and k_{DOR}) for **1** in solutions at pH 11.2, buffered using sodium carbonate, are given in Table 1.

As reaction rates in neutral solutions are negligible, the likely nucleophiles in these reactions are hydroxide and alkoxide anions. If the pseudo-first-order rate constants, k_{DOR} and k_{DOH}, are assumed to be due to second-order processes, the second-order rate constants, k_{RO^-} and k_{HO^-}, are given by eqns. (5) and

$$k_{DOR} = k_{RO^-}[RO^-] \tag{5}$$

(6); the molar concentrations of alkoxide ([RO⁻], Table 2) were

$$k_{DOH} = k_{HO^-}[HO^-] \tag{6}$$

calculated from the pK_a of the alcohols in water at 25 °C (though not all were available), assuming a negligible medium effect. For the fluorotriazine **1**, additional measurements were made of the effect on the hydrolysis rate constants of varying the carbonate concentration (Table 3). Also, for the dichlorotriazine **2** in 1.5% methanol–water mixtures, the effects of added salts or cosolvents are shown in Table 4, and the effects of temperature are shown in Table 5.

Table 1 Effect of added alcohols on product ratios and rate constants ($k/10^{-4}$ s^{-1}) of the reactions of fluorotriazine **1** at 25.0 °C in 0.088 M sodium carbonate at pH 11.2

Alcohol[a]	k_{obs}[b]	P[c]	k_{DOR}[d]	k_{DOH}[d]
No added alcohol	0.46 ± 0.01	—	—	0.46 ± 0.01
Propan-1-ol	0.50 ± 0.01	0.09 ± 0.01	0.04 ± 0.01	0.46 ± 0.02
Methanol	0.69 ± 0.05	0.51 ± 0.01	0.23 ± 0.02	0.46 ± 0.03
3	0.67 ± 0.03	0.30 ± 0.01	0.15 ± 0.01	0.52 ± 0.03
Ethane-1,2-diol	0.83 ± 0.03	0.80 ± 0.01	0.37 ± 0.02	0.46 ± 0.02
4	1.31 ± 0.12	0.77 ± 0.03	0.57 ± 0.05	0.74 ± 0.07[e]
5	1.31 ± 0.09	0.72 ± 0.04	0.55 ± 0.04	0.75 ± 0.05[e]
6	2.34 ± 0.17	4.48 ± 0.03	1.91 ± 0.14	0.43 ± 0.03
7	2.40 ± 0.20	4.96 ± 0.20	2.00 ± 0.17	0.40 ± 0.04

[a] 0.132 M. [b] All values are an average of between two and five experiments using a particular alcohol. [c] Product ratio from eqn. (4) based on at least duplicated experiments. [d] First-order rate constants from eqns. (3) and (4). [e] Plots curve; lower values in the range 0.3–0.45 were also obtained (see text).

Table 2 Calculated second-order rate constants (k/dm^3 mol^{-1} s^{-1}) for reactions of fluorotriazine **1** with alcohols at 25 °C in 0.1 M sodium carbonate at pH 11.2

Alcohol[a]	pK_a	[RO⁻]/M	k_{RO^-}[b]	k_{HO^-}[c]
Water	15.74[d]	(1.60×10^{-3})[h]	—	0.029
Propan-1-ol	16.1[d]	1.66×10^{-6}	2.41	0.029
Methanol	15.09[d]	1.70×10^{-5}	1.35	0.029
	15.5[e]	6.61×10^{-6}	3.48	0.029
Ethane-1,2-diol	14.77[e]	3.56×10^{-5}	1.04	0.029
	14.59[f]	5.38×10^{-5}	0.69	0.029
Sorbitol	13.57[g]	5.63×10^{-4}	0.34	0.027
Mannitol	13.50[g]	6.62×10^{-4}	0.30	0.025
	13.29[d]	1.07×10^{-3}	0.19	0.025

[a] 0.132 M. [b] Second-order rate constant from eqn. (5). [c] Second-order rate constant from eqn. (6). [d] Ref. 2(*b*). [e] Ref. 15. [f] Ref. 16. [g] Ref. 17; values at 18.0 °C. [h] Hydroxide concentration.

Table 3 Effect of change in carbonate concentration and ionic strength on the rate of hydrolysis ($k/10^{-4}$ s^{-1}) of fluorotriazine **1** at 25.0 °C and pH 11.2

[Na_2CO_3]/M	[Na_2SO_4]/M	$k_{obs}/10^{-4}$ s^{-1}
0.10	—	0.61 ± 0.02
0.07	0.03	0.52 ± 0.02
0.005[a]	0.095	0.46 ± 0.02
0.05[a]	—	0.45 ± 0.02

[a] Solutions were set at pH 11.2 by addition of 0.1 M NaOH; the quench procedure (see Experimental section) was not used because problems were encountered with peak shapes (presumably the added sulfate interfered with the HPLC analyses).

Kinetic data for reaction of **2** with glucose are shown in Fig. 1, and the dependence of the integrated areas of chromatographic peaks for products is shown in Fig. 2.

Discussion

The progress of reactions is often monitored by a simple procedure such as appearance or disappearance of acid or base, or of a UV–VIS signal, for the whole reaction mixture and derived rate constants are often correlated with reaction variables such as concentrations, pH, solvent properties and substituent constants. Although rate–product correlations require considerably more experimental data, they provide additional information

Table 4 Effect of additives on product ratios and rate constants ($k/10^{-4}\ s^{-1}$) of reactions of dichlorotriazine **2** in 1.5% v/v MeOH–water solutions at 25 °C in 0.017 M sodium carbonate at pH 11.0

Additive[a]	$k_{obs}/10^{-4}\ s^{-1}$	P[b]	k_{DOR}[c]/ $10^{-4}\ s^{-1}$	k_{DOH}[c]/ $10^{-4}\ s^{-1}$
No Additive	9.40	3.11 ± 0.08	7.11	2.29
NaCl	1.35	2.73 ± 0.07	0.99	0.36
CH_3CN	1.48	3.36 ± 0.05	1.14	0.34
Urea	1.52	2.95 ± 0.03	1.14	0.38
Bu_4N^+Br-	30.8	3.04 ± 0.13	23.2	7.63

[a] 10% w/v. [b] Product ratio from eqn. (4). [c] First-order rate constants from eqns. (3) and (4).

Table 5 Effect of temperature on product ratios and rate constants ($k/10^{-4}\ s^{-1}$) of reactions of dichlorotriazine **2** in 1.5% v/v MeOH–water solutions containing 0.017 M sodium carbonate at pH 11.0

T/°C	$k_{obs}/10^{-4}\ s^{-1}$	P[a]	k_{DOR}[b]$/10^{-4}\ s^{-1}$	k_{DOH}[b]$/10^{-4}\ s^{-1}$
0.0	0.61	5.36 ± 0.29[c]	0.51	0.096
10.0	1.72	4.26 ± 0.07	1.39	0.33
20.0	5.93	3.51 ± 0.10	4.62	1.31
25.0	10.1	2.99 ± 0.12	7.57	2.53
35.0	30.0	2.09 ± 0.10	20.3	9.7
50.0	96.8	1.46 ± 0.04[d]	57.5	39.2
60.0	229	1.12 ± 0.04	121	108

[a] Product ratio from eqn. (4). [b] First-order rate constants from eqns. (3) and (4). [c] Average of five measurements. [d] Average of three measurements.

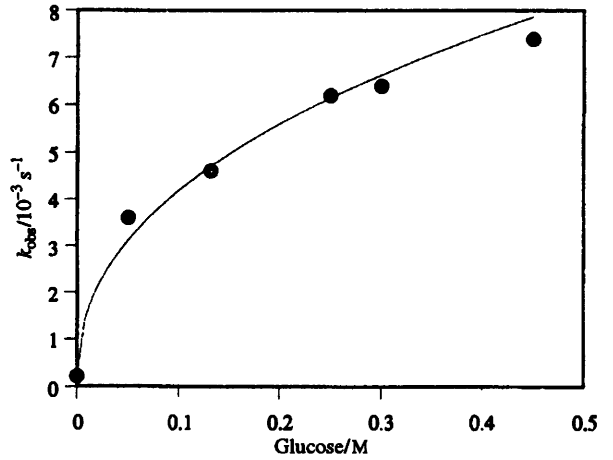


Fig. 1 First-order rate constants for decomposition of dichlorotriazine **2** in aqueous glucose at pH 11.0 and 25 °C

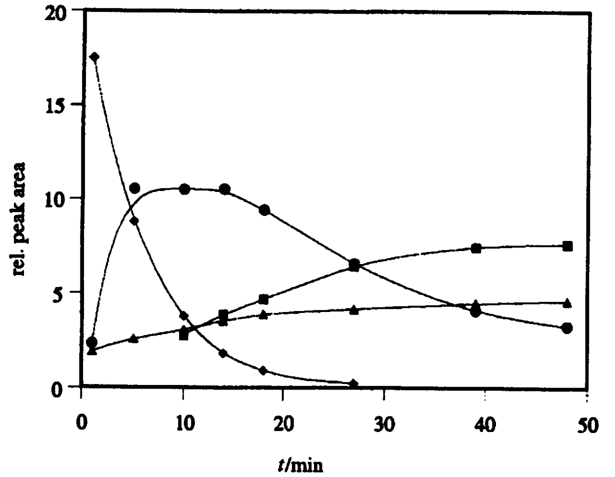


Fig. 2 Relative peak areas of HPLC chromatograms as a function of time for decomposition of dichlorotriazine **2** (◆) in aqueous glucose at pH 11.0 and 25 °C; the product peak marked (▲) corresponds to the displacement of one of the two chlorine substituents by OH, and the other two peaks are products derived from attack by glucose

about competing pathways. Many reactions in alkaline aqueous media are assumed to be bimolecular and second-order rate constants are quoted. However, it is possible that the alkoxide/hydroxide acts as base rather than as nucleophile and deprotonates a water molecule adjacent to the reaction site. Addition of alcohol to basic media giving alkoxide might then lead to enhanced rates of hydrolysis, in addition to the alcoholysis expected for a second-order mechanism. The presence of an extra reaction pathway (such as alkoxide-assisted hydrolysis) can be investigated using rate-product correlations, as shown below.

If we assume that the rate enhancement of added alcohol leads only to the alcoholysis product DOR, and if there is no medium effect of added alcohol, the same numerical value of k_{DOH} should be applicable whether or not alcohol is present. The results (Table 1) show that k_{DOH} is almost constant [$(0.46 \pm 0.06) \times 10^{-4}\ s^{-1}$], possibly within experimental errors for propanol, methanol, tetrahydropyran-2-methanol, ethane-1,2-diol, sorbitol and mannitol. Consequently, for the alcohols listed, we have established that there is a satisfactory overall rate–product correlation for competing hydrolysis and alcoholysis of the reactive dye **1**.

The trend of the results (Table 1) is such that there may be slight tendency for the higher molecular weight alcohols **3**, **6** and **7** to give values of k_{DOH} outside the typical range of 0.43–0.46, as might be expected if a small effect due to the medium were superimposed on the observed trends. Although the polyols (**6** and **7**) tend to give lower results (0.40 ± 0.04), and the more hydrophobic alcohol (**3**) gives a higher value (0.52), the effects are small. When the results for **3** were repeated in another batch of aqueous sodium carbonate, identical values for k_{DOH} of $0.61 \times 10^{-4}\ s^{-1}$ were obtained both in the presence and absence of alcohol; hence, there is no clear evidence that medium effects significantly complicate the rate–product correlation.

However, calculated values of k_{DOH} (Table 1) are significantly enhanced for α- and β-methylglucopyranoside (**4** and **5**). A cause of uncertainty in these results is that a plot of [DOR] *vs.* [DOH] becomes non-linear after 50–70% reaction, after which there is upward curvature of the plot leading to higher values of P [eqn. (4)]. Curved plots were not obtained in our previous studies of the reactions of α- and β-methylglucopyranoside with the dichlorotriazine **2**.[8a] Also, the hydrolysis product (DOH) is stable under the reaction conditions and the increase in P at higher extents of reaction appears to be due to a change in the kinetic product ratio as the reaction proceeds towards completion. Higher values of P, as observed towards the end of the reaction, would improve the rate–product correlation. Nevertheless, our best estimates of P (Table 1) are calculated from duplicated linear plots ($r = 0.99$) over the first 70% of reaction, but in three other experiments even lower values of P (in the range 0.35–0.47) were observed for the first 50% reaction. As the best values of k_{DOH} for **4** and **5** (0.74 and 0.75, respectively, Table 1) are significantly higher than the expected value of 0.46, there are deviations from the expected rate–product correlation [eqns. (3) and (4)], consistent with an additional rate-enhancing contribution to the rate law from alkoxide-assisted hydrolysis.

The calculated second-order hydrolysis rate constants (k_{HO^-}, Table 2) parallel the values of k_{DOH} (Table 1), and the much larger values of k_{RO^-} tend to decrease as the pK_a decreases. Sorbitol and mannitol (**6** and **7**) give high values of P and correspondingly high values for k_{DOR} (Table 1), but values of k_{RO^-} are low (Table 2). Although the reliability of the necessary pK_a data is not always clear, and two values are given in several cases in Table 2, the increase in k_{obs} for the polyhydric alcohols (Table 1) is due to an increase in the amount of alkoxide ion present at equilibrium. The high rate ratio k_{MeO^-}/k_{HO^-} of *ca.* 100 (Table 2) parallels the values of 49 for 2-fluoro-5-nitropyridine and of 22 for 2-fluoro-3-nitropyridine in water at 25 °C.[1]

Additional complexities in the rate law are illustrated for the reactions of the dichlorotriazine dye **2** with glucose (Fig. 1), which provides a further example[7] of the inhibition by glucose of the reactivity of the glucose anion, presumably because a dimeric species is formed.[7] Our chromatographic studies (Fig. 2) show an example where **2** reacts over a period of 50 min, with the dominant kinetic product being formed after 15 min, this product being one of several products present after 30 min (we separated five products[8b] but only three are shown in Fig. 2 for simplicity). Presumably, the formation of the initial product involves reaction of the hemiacetal oxyanion,[7] and the formation of such a major product must make the main contribution to the rate enhancement caused by the addition of glucose to the water. However, product ratios depend strongly on reaction times; after 3 h there are seven products with the main product being the hydroxychloro compound (DOH, the product of mono-hydrolysis). Consequently, it is conceivable that a rate law effect due to the hemiacetal anion could appear to be a medium effect on hydrolysis, although such an effect is less likely in neutral or acidic solutions.[18]

The effect of ionic strength and the possibility of general base catalysis by carbonate was investigated using mixtures of sodium carbonate and sodium sulfate. The results (Table 3) show that hydrolysis rates are slightly suppressed by halving the amount of carbonate but at constant ionic strength, with sodium sulfate replacing sodium carbonate, a twenty fold reduction in carbonate concentration lowered the hydrolysis rate constant by only 20%. Hence, general base catalysis by carbonate appears to be relatively unimportant. Buffer catalysis by phosphate was observed in related work on the hydrolysis of the monochlorotriazine, atrazine, and a third-order hydrolysis mechanism was proposed.[13]

The effects of cosolvents and of further added salts were investigated briefly using the dichlorotriazine dye **2** and methanol as a probe alcohol. There is a very small effect on DOMe/DOH product ratios (Table 4), and as expected for a diluent, additives tend to reduce the rate constants (*e.g.* for NaCl, acetonitrile and urea). However, preliminary studies indicate that tetrabutylammonium bromide has a strong rate-enhancing effect.

Methanol in highly aqueous media was also used to investigate the effect of temperature on product ratios for the dichlorotriazine dye **2**. The five-fold decrease in product ratio (DOMe/DOH) with an increase in temperature from 0 to 60 °C (Table 5) is as expected for a reaction in which the hydroxide–alkoxide equilibrium [eqn. (1)] is dominant.[1,2]

Conclusions

Constant values of k_{DOH} for aqueous propanol, methanol, ethanediol, mannitol and sorbitol (Table 1) are derived from the rate–product correlation for competing displacements of a fluorotriazine **1** by hydroxide and alkoxide. Hence, from the value of k_{DOH} for hydrolyses in the absence of alcohols and the product ratio (P) in the presence of alcohols, values of k_{DOR} could be predicted from eqn. (4) and values of k_{obs} could then be obtained from eqn. (3). The results imply that the addition of small concentrations (< 0.2 M) of these alcohols to water has a small or negligible rate-retarding effect on the rate of hydrolysis, and are consistent with competing bimolecular reactions. In contrast, values of k_{DOH} are enhanced by addition of α- and β-methylglucopyranoside; these and other published[2,8] reports of rate enhancements by added alcohols, suggest the possibility that there may be contributions from third-order reactions in which an additional pathway for hydrolysis occurs when alkoxide (acting as a base) activates a water molecule (acting as a nucleophile).

The lack of stability of the products for the dichlorotriazines, particularly in aqueous glucose (Fig. 2), illustrates the need to monitor product formation as the reaction proceeds to try to ensure that the primary products are observed. We expect that such experiments will uncover significant mass law contributions to the rate effects of added alcohols in water and if so, additional rate-law terms would need to be taken into account before the medium effect of the added alcohols or carbohydrates can be deduced.

Experimental

Materials

The dyes, fluorotriazine **1** and dichlorotriazine **2**, were available from the Zeneca Fine Chemicals collection. For HPLC, the methanol was AR grade (Fisons) and tetrabutylammonium bromide was 98+% (Lancaster Synthesis Ltd.). Propan-1-ol and D-mannitol (mp 164.8–165.6 °C; lit.,[19] 166 °C) were BDH GPR grade. D-Sorbitol (99+%, mp 97.4–98.3 °C; lit.,[20] 97 °C) and methyl β-D-glucopyranoside hemihydrate (99%, mp 112.8–114.9 °C; lit.,[19] 115–116 °C) were from Aldrich. Methyl α-D-glucopyranoside (mp 165.8–166.8 °C; lit.,[19] 168 °C) was from an unknown source. D-Glucose was BDH AR grade, mp 148–150.5 °C; lit.,[20] 146 °C. Ethane-1,2-diol (BDH) and tetrahydropyran-2-methanol (98%, Aldrich) were distilled before use; the latter contained acidic impurities which were treated with solid sodium carbonate prior to distillation. All other chemicals were used without further purification. Sodium carbonate ('anhydrous', Fisons and BDH) were titrated with HCl (Radiometer RTS 822 recording titration system) to determine the moisture content.

Analytical methods

Products were analysed by ion pair reversed phase HPLC at 40 °C. The chromatography columns were 15 cm × 1/4″ Spherisorb S5 ODS2, typically eluted with *ca.* 50–60% methanol–water containing 0.01 M tetrabutylammonium bromide. Detection was at 537 nm for the fluorotriazine **1** and at 488 nm for the dichlorotriazine **2**. Typical absorbance values were 0.2. With a flow rate of eluent of 2.0 ml min^{-1}, typical retention times were 5–30 min under isocratic conditions. Optimum performance of the column required prior elution with eluent for 1 h to attach reproducibly the tetrabutylammonium ions to the column.

The HPLC equipment comprised a Rheodyne 7125 injection valve, a Waters M-45 pump, a Spectromonitor detector 3200 and a Hewlett Packard 3394A integrator.

Kinetic methods

An aqueous solution, containing sodium carbonate (9.2 g l^{-1}, 0.088 M, pH 11.2) and a weighed amount of the model alcohol, were made up to 50 ml, and were then thermostatted at 25.0 °C for at least 10 min before reaction was initiated by pouring the solution onto a weighed amount of dye in a vessel also thermostatted at 25 °C. The flask was then immediately shaken rapidly before 1 ml aliquots were withdrawn at suitable time intervals and were quenched with 1 M HCl (four drops for studies of **1** at pH 11.2 and one drop for **2** at pH 11.0) and three drops of pH 7 buffer. Quenched samples were stored in an ice bath before HPLC analyses of quenched solutions were carried out (usually within 3 h); control experiments established the stability of the reactants and products in quenched solutions (the pH after quench was 6.5).

Calculations were carried out as described below, using the LSKIN first-order kinetics program,[21] adapted for use on a PC by Dr M. S. Garley (Swansea). The number of data points used for the calculations of rate constants was typically about 10, including the theoretical infinity area of zero for complete decomposition of substrate.

Acknowledgements

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