Saccharide-accelerated hydrolysis of boronic acid imines

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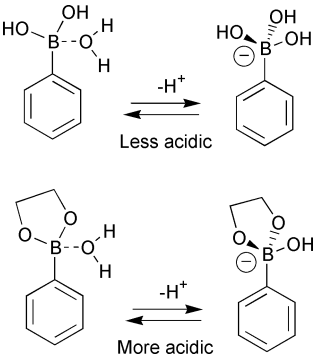
Twenty substituted *N*-benzylidineaniline derivatives have been synthesised and their kinetic behaviour investigated. The rate of hydrolysis of the boronic acid imines was found to be accelerated by added saccharide. Catalytic activity was only observed below the pK_a of the boronic acid. Altering the concentration or type of saccharide revealed a Brønsted-like linear free energy relationship, indicating that intramolecular general acid catalysis was operating. Structure–activity relationship studies demonstrated that the system's electronic demands were independent of the boronic acid moiety.

Introduction

The recognition of saccharides by boronic acids has received a significant amount of attention in recent years. The ability of boronic acid to bind rapidly and reversibly with 1,2- and 1,3-diols in competitive solvents has been used in the design of sensors for saccharides with read-out *via* photoinduced electron transfer (PET) fluorescence quenching, colorimetric and circular dichroism (CD) techniques.[1–3]

The effect of boric and boronic acid on the rate of hydrolysis of salicaldehyde-derived imines has been studied by Okuyama *et al.*,[4–6] and Rao and Philipp.[7] Both acids have the effect of enhancing the rate of hydrolysis of these imines. The effect of adding D-fructose was studied in the latter work, where it was found that the enhancement was removed on addition of the saccharide.

With these examples, the boronic acid is added, rather than being an integral part of the system. We decided to investigate how the Lewis acidity of integrated boronic acids affects the rate of hydrolysis of simple imines.[8] It has been known for over forty years that the boron atom in a boronic acid becomes more acidic when bound to a saccharide.[9] This is due to the reduction in the O–B–O bond angle from 120° in unbound boronic acid to approximately 108° when bound. This reduction in pK_a is the basis of many of the sensors developed, but its definition in this context is poorly defined. We feel it is best explained by considering the boronic acid to have a water molecule loosely associated to the boron atom. At high pH, the associated water is deprotonated and a tetrahedral boronate anion is formed. Saccharide binding enhances the Lewis acidity of the boron atom,[1,2] facilitating this deprotonation (Scheme 1).



Scheme 1 Qualitative description for the pK_a of boronic acid.

Results and discussion

Synthesis

Twenty imines were synthesised, these are split into two types depending on the side of substitution. Type I imines are substituted on the benzylidine ring and type II imines are substituted on the aniline ring (Fig. 1). The boronic acid derivatives were

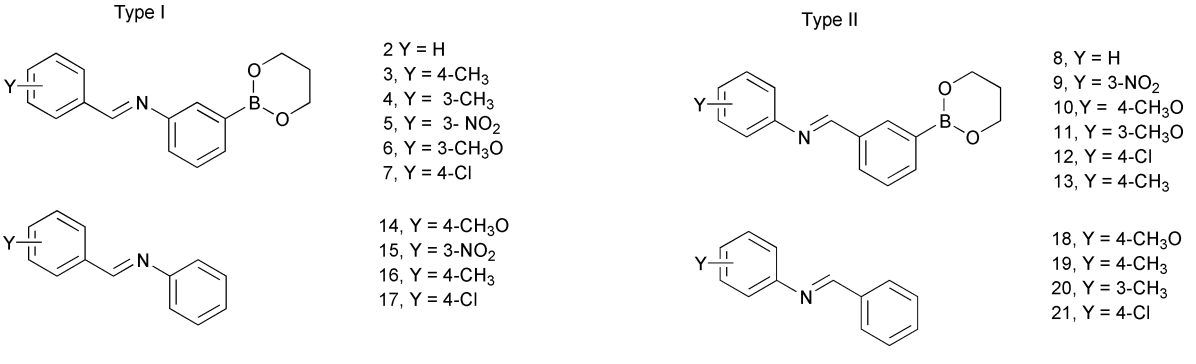


Fig. 1 The two types of imine, designated by substituted ring; Y = electron-donating or electron-withdrawing substituent.

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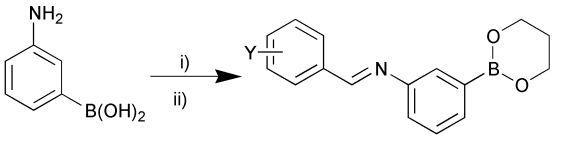
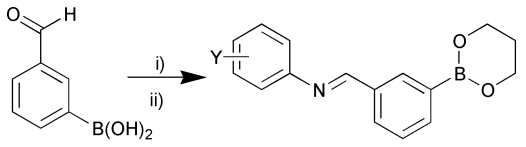


Scheme 2 Synthetic procedure for type I boronic acid imines. *Reagents and conditions*: (i) 1,3-propanediol, $HC(OMe)_3$, r.t., 2 h; (ii) $Y–C_6H_4CHO$, ethanol–C_6H_6, reflux in Dean–Stark apparatus, 24 h.



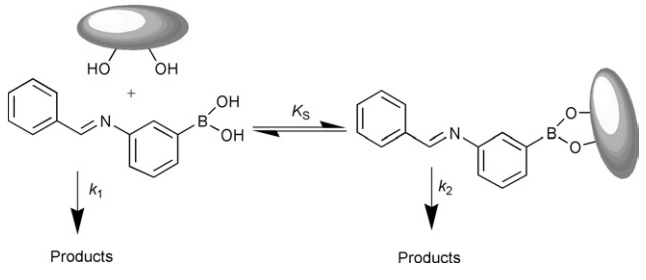
Scheme 3 Synthetic procedure for type II boronic acid imines. *Reagents and conditions*: (i) $Y–C_6H_4NH_2$, ethanol–C_6H_6, reflux in Dean–Stark apparatus, 24 h; (ii) 1,3-propanediol, ethanol–C_6H_6, reflux in Dean–Stark apparatus, 24 h.

synthesised according to Scheme 2 and Scheme 3. It was found that type I boronic acid imines could be conveniently formed from a common precursor, protected 3-aminobenzeneboronic acid. However, the protected precursor for type II imines, protected 3-formylbenzeneboronic acid, did not react as efficiently as the free acid. For this reason, the order of synthesis was reversed, with imine formation preceding protection by 1,3-propanediol. It should be noted that the protecting group was added for ease of characterisation of the target compounds and was chosen for its low binding constant (K_S)[10] with the boronic acid substrates, which should ensure rapid and complete displacement by added saccharide. Type I and II non-boronic acid imines were synthesised by condensation of the appropriate aldehyde and amine with azeotropic removal of water for 24 h.

Complexation catalysis mechanism

The system under investigation can currently be considered in the manner shown in Scheme 4. This *complexation catalysis* mechanism[11] is a simplification of the actual mechanism since it assumes no reversibility in either k_1 or k_2. However, the excess of water, acting as a reagent, compared to the low concentration of imine ensures that this is still a good description of the system under investigation. The saccharide does not have to involve itself chemically in the hydrolysis of imines but merely facilitates the reaction by providing a micro-environment which is different from that in the unbound state.

Uncomplexed boronic acid imines react to form products *via* the uncatalysed route described by k_1. In the presence of saccharides, boronic acids are bound with a binding constant K_S, resulting in the complexed boronic acid imine reacting to form products *via* the catalysed route described by k_2. This mechanism gives rise to eqn. 1, which describes the relationship between the three constants and how they affect the overall observed rate constant, k_{obs}. This equation is suitable when



Scheme 4 Proposed complexation catalysis mechanism.

[saccharide] $\gg$ [imine] and it should be noted that K in the equation is equal to the dissociation constant, quoted in units of M. The inverse of this value yields K_S, the binding constant, in units of M^{-1}.

$$k_{obs} = \frac{k_1 K + k_2[\text{saccharide}]}{K + [\text{saccharide}]} \quad (1)$$

Kinetic experiments

The conditions for the kinetic runs were chosen such that the system obeyed pseudo-first order reaction kinetics. Although this kinetic description was valid for the majority of compounds over the whole kinetic run, there were a number of anomalous compounds.† The absorption of these compounds increased initially before a maximum was passed, after which time their behaviour was pseudo-first order.

Saccharide dependence

The effect of different saccharide types and the effect of different concentrations of D-fructose with boronic acid imine **2** was explored. The observed rate constants and calculated pK_a for different saccharides and concentrations of D-fructose are given in Tables 2 and 3.

$$\log(K_c \cdot [P]_f + 1) = -\Delta pH$$
$$pK_a = 8.86 - \Delta pH \quad (2)$$

The concentration dependence of boronic acid imine **2** with D-fructose is shown in Fig. 2. This saturation curve is what one would expect if complexation catalysis were occurring and it indicates that binding of saccharide causes an increase in the rate of hydrolysis of the boronic acid imine **2**. Assuming a simple 1:1 binding event, the binding constant for the system can be calculated. The curve was fitted using eqn. (1) to give values for K_S of 340 M^{-1}, k_1 of 7.5×10^{-4} s^{-1} and k_2 of 2.15×10^{-3} s^{-1}, with an r value of 0.998.

Linear free energy relationship

Treating the intramolecular boronic acid in the same manner as a general acid of the same pK_a, we were able to obtain meaningful information by plotting a linear free energy relationship of the pK_a values from Tables 2 and 3 against the logarithm of the observed rate constant to give the Brønsted-like correlation shown in Fig. 3. The linear curve fit gave gradients of 0.245 and 0.242, with r values of 0.998 and 0.996, respectively. The linear free energy relationship shown in Fig. 3 suggests that the pK_a of the boronic acid moiety is influential in the enhancement in the observed rate of hydrolysis of

† Anomalous behaviour: certain compounds did not obey pseudo-first order kinetics for the whole of the experiment. These compounds (**5**, **9**, **15**, **17** and **21**) displayed an initial increase in absorption before assuming a normal first order decay curve. Reeves first noticed this phenomenon for **21**[12] and assigned it to the carbinolamine ether, formed when imines appended with electron-withdrawing substituents were stored in anhydrous alcohols, reverting back to the imine on introduction to aqueous conditions before being hydrolysed. This increase in the concentration of the absorbing species accounts for the observed initial increase in measured absorption. The kinetics of these compounds were analysed in two ways. In the first method, the period over which the absorption increased was ignored and only the data after the maximum was reached were used in the calculation of the rate constant. The second method involved the use of the kinetic modelling software Gepasi v3.21.[13–15] The reaction was defined as a consecutive two-step reaction, the first step being the conversion of the carbinolamine ether to the imine, and the second being the hydrolysis of the imine. The results of these two methods are shown in Table 1 and clearly show it was justified to ignore the induction period in the calculations, since the observed rate constants calculated by the Gepasi software were the same as the less rigorous pseudo-first order calculation.

Table 1 Rate constants for the decomposition of carbinolamine ether (k_{carb}) and subsequent imine hydrolysis (k_{obs}) applying pseudo-first order (P-FO) and Gepasi (Gep) methods

Compound		$k_{carb} \times 10^{-3}/s^{-1}$ (Gep)	$k_{obs} \times 10^{-4}/s^{-1}$ (Gep)	$k_{obs} \times 10^{-4}/s^{-1}$ (P-FO)
Non-boronic acids	**15**	6.3 ± 0.2	2.12 ± 0.07	2.13 ± 0.08
	17	47.7 ± 0.3	4.65 ± 0.17	4.64 ± 0.17
	21	69.5 ± 2.9	6.45 ± 0.03	6.45 ± 0.03
Boronic acids	**9**	7.3 ± 0.3	5.50 ± 0.08	5.41 ± 0.08
	5	10.0 ± 1.0	2.42 ± 0.05	2.58 ± 0.08
	9 + D-fructose	34.9 ± 1.7	16.50 ± 0.02	16.46 ± 0.07
	5 + D-fructose	35.1 ± 5.5	6.81 ± 0.11	6.81 ± 0.12

Table 2 Observed rate constants for the hydrolysis of **2** (4.0×10^{-5} M) in the presence of differing concentrations of D-fructose

[D-Fructose]/M	Rate constant $\times 10^{-4}/s^{-1}$	Calculated pK_a[a]
0	7.47 ± 0.09	8.86
0.001	10.91 ± 0.04	8.14
0.002	13.40 ± 0.10	7.88
0.003	14.45 ± 0.04	7.72
0.004	15.50 ± 0.04	7.60
0.005	16.17 ± 0.03	7.50
0.006	16.82 ± 0.07	7.43
0.007	17.70 ± 0.03	7.36
0.008	17.96 ± 0.11	7.31
0.009	18.28 ± 0.02	7.26
0.010	17.86 ± 0.06	7.21

[a] Manipulating data obtained for the boronic acid by Lorand and Edwards,[9] concentration values were converted into pK_a values. The equation used to obtain binding constants was rearranged to provide an equation which, given the known binding constants of phenylboronic acid with saccharides, afforded shifts in pK_a of the boronic acid. This method yielded the original values Lorand and Edwards would have worked from. The rearranged equation is shown in eqn. (2), where $[P]_f$ is the final concentration of saccharide, K_c is the binding constant, and the value 8.86 is the literature value for the pK_a of phenylboronic acid.

Table 3 Observed rate constants for the hydrolysis of **2** (5.0×10^{-5} M) in the presence of different polyols (0.01 M). Binding constants are from Lorand and Edwards[9]

Polyol	Rate constant $\times 10^{-4}/s^{-1}$	Binding constant/M^{-1}	Calculated pK_a[a]
D-Fructose	21.6	4370	7.21
Mannitol	18.1	2275	7.49
D-Galactose	11.9	276	8.29
D-Mannose	10.3	172	8.43
D-Glucose	10.1	110	8.54
1,3-Propanediol	8.5	0.88	8.86

[a] See footnote in Table 2.

the remote imine bond and that general acid catalysis is occurring. The value of the gradient would suggest an early, reactant-like transition state.[16]

pH dependence

To further probe this system, the pH dependence of **2** with and without D-fructose present was determined. As a control, *N*-benzylidineaniline was also examined. The results are shown in Fig. 4 and show a plateau region from pH 7 to 8.9 for

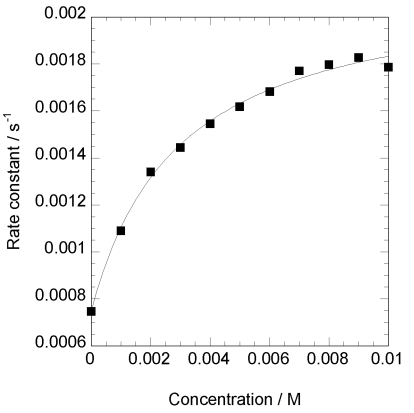


Fig. 2 Observed rate constant *vs.* [D-fructose] for the hydrolysis of **2** in 33% MeOH–66% H_2O, pH 7.77, observed at 320 nm.

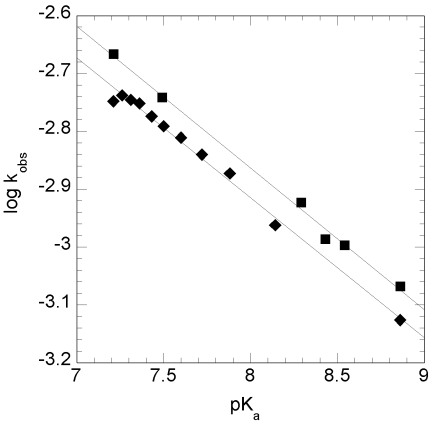


Fig. 3 Linear free energy relationship for **2** between the rate of imine hydrolysis and the pK_a of the boronic acid, calculated using eqn. (2).

compound **2** in the presence of 0.01 M D-fructose. The plateau region is indicative of an intramolecular process. Examples from the literature include the work of Kirby and Brown, who recently reported intramolecular general acid catalysis of the hydrolysis of dialkyl acetals of benzaldehyde,[17,18] and Okuyama *et al.* with the intramolecular general base catalysis of imines by tertiary amino groups.[19] An important point to note in the latter example is the observed Brønsted correlation between the pK_a of the tertiary amino group and the logarithm of the rate constant. This is due to the fact that the tertiary amino group is able to reach around and coordinate *via* a water molecule to the imine bond. This water molecule then deprotonates, the resultant hydroxide ion being delivered to the imine in an intramolecular fashion resulting in the observed general base catalysis.

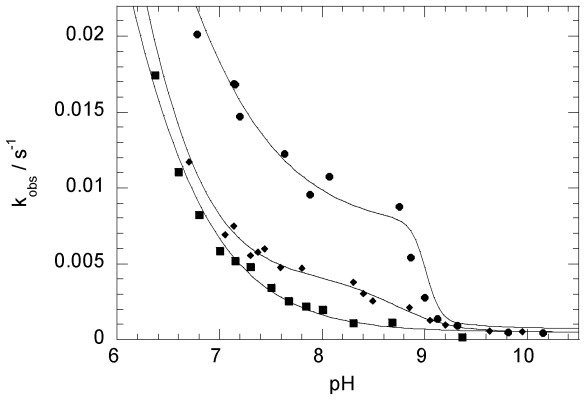
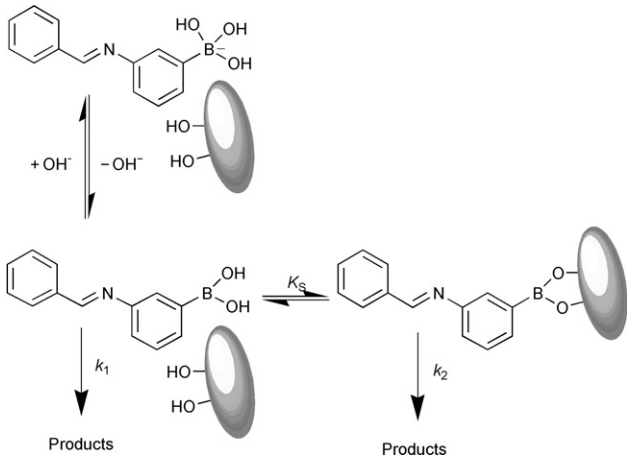


Fig. 4 Semi-logarithmic pH rate plot for the hydrolysis of selected imines: *N*-benzylidineaniline (■); compound **2** (◆); compound **2** in the presence of 0.01 M D-fructose (●).

The intramolecular process observed in the pH titration operates in the region pH 7 to 8.9, above which a rapid change in behaviour is observed. It should be noted that the pK_a of unbound phenylboronic acid is 8.86. This rapid drop-off in enhanced behaviour at the pK_a of the unbound boronic acid shows that the neutral trigonal species is the active form in the intramolecular process. Above pH 8.9, the boronic acid becomes inactive through the formation of a tetrahedral anionic boronate species. This can be represented by the complexation catalysis mechanism shown in Scheme 5. Binding D-fructose at a pH below the pK_a of the unbound boronic acid allows the intramolecular general acid catalytic pathway represented by k_2 to operate. At a pH above the pK_a of the unbound boronic acid, formation of the anionic tetrahedral species removes the neutral unbound boronic acid imine from the system and the catalytic pathway cannot be followed.



Scheme 5 Observed mechanism in the hydrolysis of boronic acid imines in the presence of saccharide at physiological pH.

The results presented here show that the mechanism of hydrolysis of boronic acid imines in the presence of saccharides proceeds by intramolecular general acid catalysis

Structure–activity relationship

To examine how the effect of the boronic acid pK_a was transmitted, a structure–activity relationship (SAR) study was performed. The behaviour of the twenty boronic and non-boronic acid imines was explored in the presence and absence of D-fructose. The results of our SAR experiments are shown in Table 4 for type I imines and in Table 5 for type II imines. The results are shown graphically in Fig. 5 for type I imines and in Fig. 6 for type II imines. Both the positive (ρ_{+ve}) and negative (ρ_{-ve}) gradients of the Hammett plots were obtained and are recorded in Table 6. The gradients of the data plotted in Fig. 5 and 6 give information about the electronic demands at the reaction centre. Both graphs show a discontinuity in the Hammett correlation, the downward break indicative of a change in the rate-determining step of the reaction.[20] One can see from further examination of the graphs that no effect was observed on the position of the changeover in the rate-determining step and that the reaction parameter ρ was the same within each type (I or II) regardless of saccharide interaction.

The structure–activity relationship studies indicate that the system's electronic demands are independent of the boronic acid moiety—irrespective of any saccharide interaction.

Structure–activity relationships of *N*-benzylidineaniline derivatives have been previously examined and a change in the rate-determining step of the reaction was observed, with the hydrogen-substituted compounds having the highest reactivity.[21,22] This was also observed in the hydrolysis of salicylidineanilines derivatives and a simplified reaction sequence has been used to explain this kinetic behaviour.[20] Based on the sequence proposed by Hoffmann; the first step involves addition of a proton to the imine nitrogen, the second, addition of water to the protonated imine and the third involves the decomposition of this species into the products of hydrolysis *via* the tetrahedral carbinolamine intermediate proposed by Jencks and co-worker[23,24] (Scheme 6).

For this mechanism, it has been shown that general acid catalysis can operate, in agreement with our findings.[22]

Kinetic isotope effect

The solvent deuterium kinetic isotope effect (KIE) was examined for a range of boronic and non-boronic acid imines in the presence of D-fructose, the results are displayed in Table 7. From these, it can be seen that both type I and II boronic acid imines have a significant KIE in the presence of

Table 4 SAR results for the hydrolysis of type I boronic and non-boronic acid imines in the presence and absence of D-fructose

Compound		σ Value	$k_{obs} \times 10^{-4}/s^{-1}$	$\log k_{obs}$	$k_{obs} \times 10^{-4}/s^{-1}$ (D-Fructose)	$\log k_{obs}$ (D-Fructose)
Boronic acids	**6**	−0.27	4.66 ± 0.04	−3.33	10.47 ± 0.05	−2.98
	3	−0.14	6.67 ± 0.04	−3.18	15.28 ± 0.03	−2.82
	4	−0.06	7.54 ± 0.13	−3.12	18.22 ± 0.05	−2.74
	2	0.00	7.47 ± 0.09	−3.13	17.86 ± 0.06	−2.75
	7	0.24	4.49 ± 0.02	−3.35	10.98 ± 0.04	−2.96
	5	0.71	2.58 ± 0.08	−3.59	6.81 ± 0.12	−3.17
Non-boronic acids	**14**	−0.27	4.31 ± 0.04	−3.37	—	—
	16	−0.14	6.32 ± 0.07	−3.20	—	—
	N-Benzylidineaniline	0.00	7.06 ± 0.12	−3.15	7.21 ± 0.04	−3.14
	17	0.24	4.64 ± 0.17	−3.33	—	—
	15	0.71	2.13 ± 0.08	−3.67	—	—

Table 5 SAR results for the hydrolysis of type II boronic and non-boronic acid imines in the presence and absence of D-fructose

Compound		σ Value	$k_{obs} \times 10^{-4}/s^{-1}$	$\log k_{obs}$	$k_{obs} \times 10^{-4}/s^{-1}$ (D-Fructose)	$\log k_{obs}$ (D-Fructose)
Boronic acids	**10**	−0.27	4.16 ± 0.03	−3.38	11.06 ± 0.06	−2.96
	13	−0.14	7.77 ± 0.01	−3.11	20.72 ± 0.13	−2.68
	8	0.00	9.87 ± 0.12	−3.01	26.00 ± 0.15	−2.59
	11	0.12	10.24 ± 0.09	−2.99	27.66 ± 0.12	−2.56
	12	0.24	7.17 ± 0.03	−3.14	18.94 ± 0.11	−2.72
	9	0.71	5.41 ± 0.08	−3.27	16.46 ± 0.07	−2.78
Non-boronic acids	**18**	−0.27	3.07 ± 0.04	−3.51	—	—
	19	−0.14	5.25 ± 0.19	−3.28	—	—
	20	−0.06	6.87 ± 0.04	−3.16	—	—
	N-Benzylidineaniline	0.00	7.06 ± 0.12	−3.15	7.21 ± 0.04	−3.14
	21	0.24	6.45 ± 0.03	−3.19	—	—

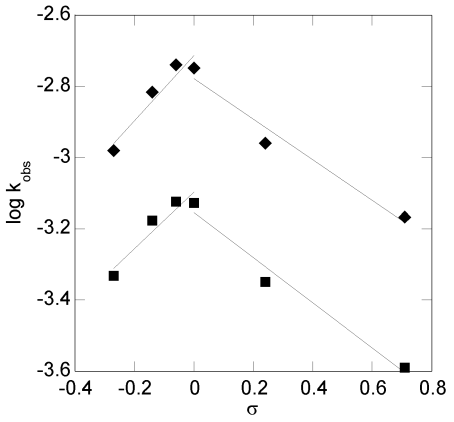
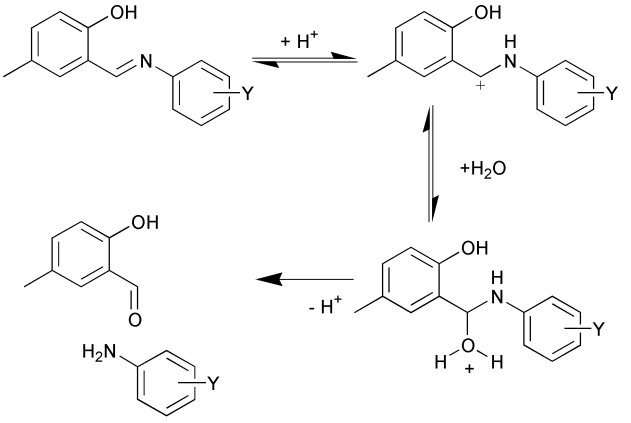


Fig. 5 Hammett plot for type I boronic acid imines at 20 °C; buffer solution only (■); buffer solution with 0.01 M D-fructose (◆).



Scheme 6 Kinetic description for the hydrolysis of *N*-(2-hydroxy-5-methylbenzylidine)aniline derivatives.[20]

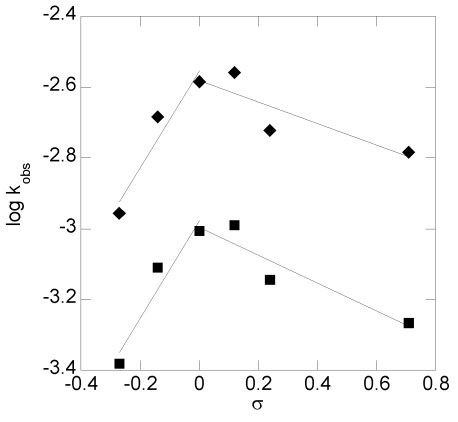


Fig. 6 Hammett plot for type II boronic acid imines at 20 °C; buffer solution only (■); buffer solution with 0.01 M D-fructose (◆).

Table 6 ρ Values obtained from the Hammett plots derived from the data in Tables 4 and 5

Compound type and conditions	ρ_{+ve}	ρ_{-ve}
Type I boronic acid	0.80	–0.63
Type I boronic acid + D-fructose	0.91	–0.57
Type I non-boronic acid	0.79	–0.73
Type II boronic acid	1.38	–0.39
Type II boronic acid + D-fructose	1.37	–0.30
Type II non-boronic acid	1.40	–0.16

Table 7 Solvent kinetic isotope effect for a range of boronic acid and non-boronic acid imines in the presence of 0.01 M D-fructose. Note: the apparent pH of solvents was equilibrated using a correction factor of pD = pH + 0.4

Compound	σ Value	Type	k_H/k_D
6	−0.27	I	2.30
10	−0.27	II	2.51
2	0.00	I	2.28
8	0.00	II	2.83
5	0.71	I	1.76
9	0.71	II	2.06
N-Benzylidineaniline	0.00	Control	1.30

D-fructose as compared with the non-boronic acid imine derivative *N*-Benzylidineaniline. In addition, type I imines display a smaller KIE than type II imines.

Conclusions

Intramolecular general acid catalysis should be dependent on the strength of the general acid involved, however there is little evidence to support this in the literature.[17,18,25] With boronic acid imines, we have shown that the strength of the *intramolecular* general acid controls the rate of hydrolysis. The strength of a boronic general acid (pK_a) can be varied by adding different amounts of saccharide (or indeed different types) without changing either the general acid or the gross structure of the molecule.

The acidity of the boron atom could be communicated to the imine bond *via* a proton-transfer mechanism through solvent water.[26–29] Only the neutral bound boronic acid has the ability to operate in this manner—above the pK_a of the free boronic acid the enhanced mechanism is lost and a purely intermolecular process takes over.

Experimental

General procedures

^1H and $\{^1H\}$-^{13}C NMR spectra were recorded on a Bruker AC-300 (300.13 and 75.47 MHz, respectively) spectrometer. All chemical shifts (δ) were recorded relative to tetramethylsilane as the internal standard. The multiplicities of the spectroscopic data are presented in the following manner: s = singlet; d = doublet; t = triplet; q = quintet; m = multiplet; br = broad signal. *J* Values are given in Hz. The $\{^1H\}$-^{13}C NMR spectra were subject to the polarisation enhancement that is nurtured during attached nucleus testing (PENDANT) technique,[30,31] resulting in primary and tertiary carbon atoms having a different phase to secondary and quaternary carbon atoms. The phase is presented in the following manner: (+) positive phase; (−) negative phase. Due to quadrapolar relaxation, carbon atoms attached directly to a boron atom were not observed in the spectra.

Electron impact (EI) mass spectra were recorded on a VG ProSpec mass spectrometer. Liquid secondary ion (LSI) mass spectra were recorded using a VG ZabSpec instrument. HRMS measurements were also obtained from either the VG ProSpec or VG ZabSpec spectrometers.

Elemental analyses were performed at the University of North London and the University of Birmingham.

Thin-layer chromatography (TLC) was carried out on precoated aluminium-backed silica gel plates supplied by Merck KGaA, Darmstadt, Germany (Silica Gel 60 F_{254}, thickness 0.2 mm, Art. 5554). Visualisation was achieved by UV light (254 nm).

Melting points were determined using a Gallenkamp melting point apparatus and are reported uncorrected.

All reagents and solvents were used as supplied by the Aldrich Chemical Co. Ltd., Lancaster Synthesis Ltd. and Fisher Scientific Ltd.

All kinetic measurements were performed on a Perkin-Elmer Lambda 20 UV/VIS spectrophotometer with data collected *via* the UV WinLab software package[32] on a PC running Microsoft NT v4. A thermostatted cell holder was fitted and connected to a Colora Kryo-Thermostat Wk 6, operating at 20 °C.

Stock solutions of imines were prepared in 5.00 cm^3 of HPLC methanol to a concentration of 0.0100 M. These were stored at 5 °C in the dark until required.

The pH 7.77 buffer was prepared according to literature procedures[33] as follows: 0.010000 M KCl, 0.002642 M KH_2PO_4 and 0.002642 M Na_2HPO_4 were prepared in a solution of HPLC methanol in deionised water (33% MeOH w/w) to give the appropriate buffer solution. This buffer solution was stored and dispensed under an N_2 atmosphere.

For experiments where the saccharide concentration rate dependence was studied, a stock solution of the highest saccharide concentration to be used was prepared in pH 7.77 buffer solution. Aliquots of this stock solution were then diluted with pH 7.77 buffer to give the weaker concentrations.

For the pH dependence study, a 0.05 M NaCl stock solution was prepared, with or without D-fructose present. The pH was adjusted using dilute HCl and dilute NaOH, and pH values read on a Hanna Instruments HI 9321 microprocessor pH meter. Calibration of the pH meter was performed using Fisher Scientific Analytical Reagents buffer solutions. For pH measurements > pH 7, aqueous buffer solutions of pH 7.00 and 10.00 were used for calibration. For pH measurements < pH 7, aqueous buffer solutions of pH 4.00 and 7.00 were used for calibration.

The deuterated buffer solutions were made up as follows. 0.05 M NaCl was prepared in a solution of CH_3OD in D_2O (33% CH_3OD w/w) and stored under an N_2 atmosphere. The pH was measured and a correction factor of 0.4[11] was added to give an apparent pH of 8.12. For comparison, a non-deuterated buffer was made up as follows. 0.05 M NaCl was prepared in a solution of CH_3OH in H_2O (33% CH_3OH w/w) and stored under an N_2 atmosphere. The pH was measured and adjusted with 0.01 M NaOH to give an apparent pH of 8.04.

Kinetic measurements

1.25 cm^3 of an appropriate buffer solution was transferred by glass syringe into a quartz cuvette. This cuvette was placed within a thermostatted cuvette holder in the spectrophotometer and left for 10 min for temperature equilibration. After this time, 5 μL of a 0.0100 M stock solution of imine was introduced into the cuvette to give an initial imine concentration of 4.0×10^{-5} M. The cuvette was inverted three times to ensure mixing before being re-inserted into the spectrophotometer. UV WinLab[32] was used for data collection—this was started as soon as the sample chamber was closed. The period of time between introducing the analyte to the cuvette and beginning data collection was never more than 5 s. Data were collected for 1 h at intervals of 6 s to give a total of 601 data points. Data were recorded at an appropriate wavelength to study the disappearance of the imine absorption peak—this was usually 320 nm.

The data were analysed using Kaleidagraph 3.09, assuming pseudo-first order reaction kinetics to give rate constants.[34] The final absorption A_e was calculated by using the experimental data to fit an exponential curve of general formula $y = ae^{(bx)} + c$, with values of *a*, *b* and *c* calculated by the curve-fitting software. The value *c* represents the final absorption at infinite time, A_e. The curve-fitting software used the non-linear Levenberg–Marquardt algorithm[35,36] and reported the accuracy of the curve fit by the coefficient of determination, r^2. Usually r^2 was $\geqslant 0.99$, indicating a good fit of the data had been achieved. Typically, each experiment was repeated three times and the mean rate constant is reported with a standard deviation, represented by a ± value.

Where the absorption increased initially, indicating hydrolysis of the carbinolamine ether to form the imine, rate data were acquired after the maximum absorption had been passed. These rate constants were also calculated by applying the kinetic modelling software Gepasi v3.21.[13–15] The model was defined as being a two-step, irreversible consecutive reaction. The combined concentration of carbinolamine ether, imine and products was set to 4.0×10^{-5} M and the software varied both the starting concentrations of carbinolamine ether and imine, and also the kinetic rate constants k_1 and k_2 to fit the observed data. The optimisation method chosen was the Levenberg–Marquardt gradient descent method.[14,15,35–39] Typically, standard deviations of less than 1% were reported for the Gepasi kinetic rate constants. Acceptable convergence to a minimum was usually obtained after approximately 1000 iterations.

Synthesis

3-[1,3,2]Dioxaborinan-2-yl-phenylamine (1).[8] 3-Aminobenzeneboronic acid monohydrate (465 mg, 3.00 mmol) was dissolved in $HC(OMe)_3$ (20 cm^3) with stirring at room temperature. Propane-1,3-diol (250 mg, 3.00 mmol) was added, and the solution was stirred at room temperature for

2 h. The solvent was removed under reduced pressure to afford crude **1** as a light brown oil. Chloroform (10 cm^3) was added to redissolve the oil and then *n*-hexane (20 cm^3) was added. The light brown precipitate formed was removed by filtration. The filtrate solvent was removed under reduced pressure to afford the amine **1** (450 mg, 85% yield) as a white solid, mp 79–81 °C; δ_H (300 MHz, C^2HCl_3) 7.20–7.16 (2H, m, Ar-H), 7.12–7.08 (1H, m, Ar-H), 6.78–6.73 (1H, m, Ar-H), 4.15 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 3.80–3.40 (2H, br, Ar–NH_2), 2.04 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 146.3 (−), 128.0 (+), 124.9 (+), 120.4 (+), 117.6 (+), 61.8 (−), 27.3 (−); *m*/*z* (LSI) 177 (100%, $[M+H]^+$); R_f 0.32 (hexane–ethyl acetate, 1:1).

Benzylidene(3-[1,3,2]dioxaborinan-2-yl-phenyl)amine (2).[8] **1** (250 mg, 1.40 mmol) was dissolved in $HC(OMe)_3$ (3 cm^3) with stirring at room temperature. Benzaldehyde (160 mg, 1.50 mmol) was added and the reaction mixture was allowed to stir at room temperature for 60 h. The solvent was removed under reduced pressure to afford crude **2**. This oil was trituated with ether to afford **2** (329 mg, 88%) as a thick brown oil (Found: C, 72.36; H, 6.17; N, 5.38; $C_{16}H_{16}BNO_2$ requires: C, 72.49, H, 6.08, N, 5.28%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 308 (8544); ν_{max}/cm^{-1} 1631 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.44 (1H, s, N=CH), 7.87–7.81 (2H, m, Ar-H), 7.68–7.59 (2H, m, Ar-H), 7.51–7.45 (3H, m, Ar-H), 7.41–7.36 (1H, m, Ar-H), 7.34–7.29 (1H, m, Ar-H), 4.19 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, $C^2H_3O^2H$) 163.2 (+), 152.7 (−), 138.0 (−), 133.4 (+), 133.3 (+), 130.6 (+), 130.1 (+), 127.5 (+), 125.0 (+), 63.8 (−), 29.2 (−); *m*/*z* (LSI) 266 (100%, $[M+H]^+$).

(3-[1,3,2]Dioxaborinan-2-yl-phenyl)(4-methylbenzylidene)-amine (3). A solution of *p*-tolualdehyde (120 mg, 1.00 mmol) in absolute ethanol (5 cm^3) was added to a stirred solution of **1** (177 mg, 1.00 mmol) in absolute ethanol (20 cm^3). Benzene (2 cm^3) was added and the reaction vessel fitted with a Dean–Stark side-arm adapter filled with absolute ethanol. The reaction mixture was then stirred under reflux for 24 h, after which time the solution was allowed to cool and the solvent removed under reduced pressure. Recrystallisation of the crude product with petroleum ether (40–60) afforded **3** (256 mg, 92%) as a light brown microcrystalline solid, mp 79–80 °C (Found: C, 73.16; H, 6.67; N, 4.98; $C_{17}H_{18}BNO_2$ requires: C, 73.15; H, 6.50; N, 5.02%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 308 (13 820); ν_{max}/cm^{-1} 1618 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.45 (1H, s, N=CH), 7.85–7.74 (2H, m, Ar-H), 7.68–7.56 (2H, m, Ar-H), 7.44–7.26 (4H, m, Ar-H), 4.17 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 2.41 (3H, s, Ar–CH_3), 2.06 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 160.1 (+), 151.6 (−), 141.7 (−), 133.9 (−), 131.2 (+), 129.5 (+), 128.8 (+), 128.4 (+), 125.1 (+), 124.2 (+), 62.1 (−), 27.5 (−), 21.7 (+); *m*/*z* (EI) 279 (100%, M^+).

(3-[1,3,2]Dioxaborinan-2-yl-phenyl)(3-methylbenzylidene)-amine (4). Compound **4** was prepared according to the general procedure for the synthesis of **3**, except that *m*-tolualdehyde (120 mg, 1.00 mmol) was used in place of benzaldehyde to afford **4** (248 mg, 89%) as a light brown oil (HRMS found: M^+ *m*/*z* 279.1422; $C_{17}H_{18}BNO_2$ requires: *m*/*z* 279.1431); λ_{max} MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 307 (12 028); ν_{max}/cm^{-1} 1626 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.47 (1H, s, N=CH), 7.76 (1H, s, CH_3CCHC), 7.71–7.57 (3H, m, Ar-H), 7.45–7.25 (4H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 2.42 (3H, s, Ar–CH_3), 2.07 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 160.4 (−), 151.5 (+), 138.5 (+), 136.4 (+), 132.2 (−), 131.4 (−), 129.0 (−), 128.7 (−), 128.5 (−), 126.4 (−), 125.2 (−), 124.1 (−), 62.1 (+), 27.5 (+), 21.4 (−); *m*/*z* (EI) 279 (100%, M^+).

(3-[1,3,2]Dioxaborinan-2-yl-phenyl)(3-nitrobenzylidene)amine (5). Compound **5** was prepared according to the general procedure for the synthesis of **3**, except that 3-nitrobenzaldehyde (151 mg, 1.00 mmol) was used in place of benzaldehyde. Precipitation of the crude product from a chloroform solution with *n*-hexane afforded **5** (155 mg, 50%) as a bright yellow microcrystalline solid, mp 96–97 °C (Found: C, 61.87; H, 4.85; N, 8.88; $C_{16}H_{15}BN_2O_4$ requires: C, 61.97; H, 4.88; N, 9.03%. HRMS found: M^+ *m*/*z* 310.1111; $C_{16}H_{15}BN_2O_4$ requires: *m*/*z* 310.1125); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 314 (8630); ν_{max}/cm^{-1} 1623 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.73 (1H, s, N=CH), 8.58 (1H, s, Ar-H), 8.34–8.22 (2H, m, Ar-H), 7.72–7.60 (3H, m, Ar-H), 7.45–7.30 (2H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 157.0 (−), 150.2 (+), 148.7 (+), 138.1 (+), 134.1 (−), 132.3 (−), 129.8 (−), 128.6 (−), 125.5 (−), 125.0 (−), 124.3 (−), 123.5 (−), 62.1 (+), 27.4 (+); *m*/*z* (EI) 310 (100%, M^+).

{3-[(3-[1,3,2]Dioxaborinan-2-yl-phenylimino)methyl]phenyl}-methanol (6). Compound **6** was prepared according to the general procedure for the synthesis of **3**, except that *p*-anisaldehyde (136 mg, 1.00 mmol) was used in place of benzaldehyde. Recrystallisation of the crude product from petroleum ether (40–60) afforded **6** (170 mg, 57%) as a light cream microcrystalline solid, mp 62–63 °C (HRMS found: M^+ *m*/*z* 295.1373; $C_{17}H_{18}BNO_3$ requires: *m*/*z* 295.1380); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 315 (23 246); ν_{max}/cm^{-1} 1621 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.42 (1H, s, N=CH), 7.88–7.81 (2H, m, Ar-H), 7.66–7.55 (2H, m, Ar-H), 7.37 (1H, t, $^3J_{H-H}$ 7.3, Ar-H), 7.31–7.27 (1H, m, Ar-H), 7.01–6.94 (2H, m, Ar-H), 4.17 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 3.87 (3H, s, Ar–OCH_3), 2.07 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 162.2 (−), 159.5 (+), 151.7 (−), 131.0 (+), 130.5 (+), 129.4 (−), 128.4 (+), 125.1 (+), 124.1 (+), 114.2 (+), 62.1 (−), 55.4 (+), 27.5 (−); *m*/*z* (EI) 295 (100%, M^+).

(4-Chlorobenzylidene)(3-[1,3,2]dioxaborinan-2-yl-phenyl)-amine (7). Compound **7** was prepared according to the general procedure for the synthesis of **3**, except that 4-chlorobenzaldehyde (141 mg, 1.00 mmol) was used in place of benzaldehyde. Recrystallisation of the crude product from petroleum ether (40–60) afforded **7** (155 mg, 50%) as a bright yellow microcrystalline solid, mp 64–66 °C (HRMS found: M^+ *m*/*z* 299.0870. $C_{16}H_{15}BClNO_2$ requires: *m*/*z* 299.0884); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 319 (13 420); ν_{max}/cm^{-1} 1623 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.45 (1H, s, N=CH), 7.87–7.80 (2H, m, Ar-H), 7.68–7.62 (1H, m, Ar-H), 7.61–7.56 (1H, m, Ar-H), 7.47–7.41 (2H, m, Ar-H), 7.38 (1H, t, $^3J_{H-H}$ 7.4, Ar-H), 7.32–7.27 (1H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH_2), 2.07 (2H, q, $^3J_{H-H}$ 5.5, OCH_2CH_2); δ_C (75 MHz, C^2HCl_3) 158.5 (+), 151.0 (−), 137.2 (−), 134.9 (−), 131.6 (+), 129.9 (+), 129.0 (+), 128.5 (+), 125.0 (+), 124.1 (+), 62.1 (−), 27.5 (−); *m*/*z* (EI) 299 (100%, M^+).

(3-[1,3,2]Dioxaborinan-2-yl-benzylidene)-phenyl-amine (8).[8] Aniline (93.1 mg, 1.00 mmol) in absolute ethanol (5 cm^3) was added to a stirred solution of 3-formylbenzeneboronic acid (150 mg, 1.00 mmol) in absolute ethanol (20 cm^3). Benzene (2 cm^3) was added and the reaction vessel fitted with a Dean–Stark side-arm adapter filled with absolute ethanol. The reaction mixture was then stirred under reflux for 24 h. The solution was allowed to cool and the solvent removed under reduced pressure to afford a yellow oil. This oil was redissolved in absolute ethanol (20 cm^3) with stirring. To this, a solution of 1,3-propanediol (76 mg, 1.0 mmol) in absolute ethanol (5 cm^3) was added, followed by a small amount of benzene (2 cm^3). The mixture was heated to reflux under Dean–Stark conditions for 24 h, after which time the solution was allowed to cool and the solvent removed under reduced

pressure. Trituration with petroleum ether (40–60) afforded **8** (245 mg, 92%) as a thick brown oil (Found: C, 72.26; H, 6.18; N, 5.38; $C_{16}H_{16}BNO_2$ requires: C, 72.49, H, 6.08, N, 5.28%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 308 (11 352); ν_{max}/cm^{-1} 1627 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.48 (1H, s, N=CH), 8.24 (1H, s, Ar-H), 8.07–7.99 (1H, m, Ar-H), 7.92–7.86 (1H, m, Ar-H), 7.50–7.36 (3H, m, Ar-H), 7.26–7.19 (3H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 2.07 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 160.9 (+), 152.3 (−), 136.8 (−), 135.4 (+), 135.0 (+), 130.3 (+), 129.2 (+), 128.1 (+), 125.8 (+), 120.9 (+), 62.1 (−), 27.5 (−); m/z (LSI-MS) 266 (100%, $[M + H]^+$).

(3-[1,3,2]Dioxaborinan-2-yl-benzylidene)(3-nitrophenyl)amine (9). Compound **9** was prepared according to the general procedure for the synthesis of **8**, except that 3-nitroaniline (138 mg, 1.00 mmol) was used in place of aniline. Precipitation of the crude product from a chloroform solution with *n*-hexane afforded **9** (265 mg, 85%) as a bright yellow microcrystalline solid, mp 102–104 °C (Found: C, 61.84; H, 5.12; N, 9.08; $C_{16}H_{15}BN_2O_4$ requires: C, 61.97; H, 4.88; N, 9.03%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 256 (28 640); ν_{max}/cm^{-1} 1628 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.49 (1H, s, N=CH), 8.26 (1H, s, CCHCB), 8.12–7.98 (3H, m, Ar-H), 7.95–7.88 (1H, m, Ar-H), 7.58–7.44 (3H, m, Ar-H), 4.19 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 163.1 (+), 153.4 (+), 148.9 (+), 137.6 (−), 135.3 (−), 134.7 (−), 130.7 (−), 129.9 (−), 128.3 (−), 127.6 (−), 120.3 (−), 115.5 (−), 62.1 (+), 27.4 (+); m/z (EI) 310 (30%, M^+) 138 (100).

{4-[(3-[1,3,2]Dioxaborinan-2-yl-benzylidene)amino]phenyl}-methanol (10). Compound **10** was prepared according to the general procedure for the synthesis of **8**, except that *p*-anisidine (123 mg, 1.00 mmol) was used in place of aniline. Precipitation of the crude product from a chloroform solution with *n*-hexane afforded **10** (247 mg, 83%) as a light brown microcrystalline solid, mp 83–85 °C (HRMS found: M^+ m/z 295.1371; $C_{17}H_{18}BNO_3$ requires: m/z 295.1380); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 330 (15 200); ν_{max}/cm^{-1} 1620 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.49 (1H, s, N=CH), 8.20 (1H, s, CCHCB), 8.05–7.98 (1H, m, Ar-H), 7.89–7.82 (1H, m, Ar-H), 7.44 (1H, t, $^3J_{H-H}$ 7.7, Ar-H), 7.28–7.22 (2H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 3.83 (3H, s, Ar–OCH_3), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 158.9 (+), 158.1 (−), 145.1 (−), 136.4 (+), 135.6 (−), 134.8 (+), 130.0 (+), 128.1 (+), 122.2 (+), 114.4 (+), 62.0 (−), 55.5 (+), 27.4 (−); m/z (EI) 295 (100%, M^+).

{3-[(3-[1,3,2]Dioxaborinan-2-yl-benzylidene)amino]phenyl}-methanol (11). Compound **11** was prepared according to the general procedure for the synthesis of **8**, except that *m*-anisidine (123 mg, 1.00 mmol) was used in place of aniline. The product **11** (266 mg, 90%) was afforded as a light yellow oil (Found: C, 69.35; H, 6.26; N, 4.80; $C_{17}H_{18}BNO_3$ requires: C, 69.18; H, 6.15; N, 4.75%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 306 (9550); ν_{max}/cm^{-1} 1626 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.47 (1H, s, N=CH), 8.22 (1H, s, CCHCB), 8.07–7.98 (1H, m, Ar-H), 7.92–7.85 (1H, m, Ar-H), 7.45 (1H, t, $^3J_{H-H}$ 7.7, Ar-H), 7.33–7.25 (1H, m, Ar-H), 6.85–6.75 (3H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 3.84 (3H, s, Ar–OCH_3), 2.07 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 161.0 (−), 160.3 (+), 153.7 (+), 136.8 (−), 135.3 (+), 135.0 (−), 130.3 (−), 129.9 (−), 128.1 (−), 112.9 (−), 111.8 (−), 106.6 (−), 103.9 (−), 62.1 (+), 55.4 (−), 27.5 (+); m/z (EI) 295 (75%, M^+), 123 (100).

(4-Chlorophenyl)(3-[1,3,2]dioxaborinan-2-yl-benzylidene)-amine (12). Compound **12** was prepared according to the general procedure for the synthesis of **8**, except that 4-chloroaniline (128 mg, 1.00 mmol) was used in place of aniline. Trituration with petroleum ether (40–60) afforded **12** (208 mg, 69%) as a creamy yellow microcrystalline solid, mp 82–84 °C (Found: C, 64.07; H, 5.01; N, 4.60; $C_{16}H_{15}BClNO_2$ requires: C, 64.15; H, 5.05; N, 4.68%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 302 (9648); ν_{max}/cm^{-1} 1621 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.43 (1H, s, N=CH), 8.22 (1H, s, CCHCB), 8.05–7.96 (1H, m, Ar-H), 7.92–7.85 (1H, m, Ar-H), 7.45 (1H, m, Ar-H), 7.38–7.31 (2H, m, Ar-H), 7.18–7.11 (2H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 161.7 (+), 150.3 (−), 137.1 (+), 135.0 (+), 134.8 (−), 131.4 (−), 130.3 (+), 129.2 (+), 128.1 (+), 122.2 (+), 62.0 (−), 27.3 (−); m/z (EI) 299 (100%, M^+).

(3-[1,3,2]Dioxaborinan-2-yl-benzylidene)-*p*-tolylamine (13). Compound **13** was prepared according to the general procedure for the synthesis of **8**, except that *p*-toluidine (107 mg, 1.00 mmol) was used in place of aniline. Crude **13** was dissolved in *n*-hexane to remove a small amount of orange solid. The solution was then concentrated under reduced pressure to afford **13** (225 mg, 81%) as a clear oil (Found: C, 73.05; H, 6.38; N, 4.96; $C_{17}H_{18}BNO_2$ requires: C, 73.15; H, 6.50; N, 5.02%); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 315 (11 605); ν_{max}/cm^{-1} 1625 (st, C=N); δ_H (300 MHz, C^2HCl_3) 8.48 (1H, s, N=CH), 8.22 (1H, s, CCHCB), 8.07–7.99 (1H, m, Ar-H), 7.91–7.84 (1H, m, Ar-H), 7.45 (1H, t, $^3J_{H-H}$ 7.4, Ar-H), 7.23–7.11 (4H, m, Ar-H), 4.18 (4H, t, $^3J_{H-H}$ 5.5, OCH_2CH$_2$), 2.37 (3H, s, Ar–CH_3), 2.08 (2H, q, $^3J_{H-H}$ 5.5, OCH$_2$CH_2); δ_C (75 MHz, C^2HCl_3) 160.1 (+), 149.7 (−), 136.6 (+), 135.7 (−), 135.6 (−), 134.9 (+), 130.2 (+), 129.8 (+), 128.1 (+), 120.9 (+), 62.1 (−), 27.5, (−) 21.1 (+); m/z (EI) 279 (73%, M^+), 106 (100).

(4-Phenyliminomethylphenyl)methanol (14). *p*-Anisaldehyde (136 mg, 1.00 mmol) in absolute ethanol (5 cm^3) was added to a stirred solution of aniline (93.1 mg, 1.00 mmol) in absolute ethanol (20 cm^3). Benzene (2 cm^3) was added and the reaction vessel was fitted with a Dean–Stark side-arm adapter filled with absolute ethanol. The reaction mixture was then stirred under reflux for 24 h. The mixture was allowed to cool and then concentrated under reduced pressure to afford crude **14** as a creamy yellow solid. The crude product was recrystallised from the minimum amount of petroleum ether (40–60) to afford **14** (168 mg, 79%) as a white microcrystalline solid, mp 56–58 °C [lit. 58–60 °C][40] (HRMS found: M^+ m/z 211.1001; $C_{14}H_{13}NO$ requires: m/z, 211.0997); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 309 (23 272); δ_H (300 MHz, $C^2H_3O^2H$) 8.44 (1H, s, N=CH), 7.86 (2H, m, Ar-H), 7.45–7.33 (2H, m, Ar-H), 7.28–7.15 (3H, m, Ar-H), 7.18–6.99 (2H, m, Ar-H), 3.86 (3H, s, Ar–OCH_3); δ_C (75 MHz, C^2HCl_3) 162.3 (−), 159.8 (+), 152.4 (−), 130.6 (+), 129.3 (−), 129.2 (+), 125.6 (+), 120.9 (+), 114.2 (+), 55.5 (+); m/z (EI) 211 (100%, M^+).

(3-Nitrobenzylidene)phenylamine (15). Compound **15** was synthesised according to the general procedure for the synthesis of **14**, except 3-nitrobenzaldehyde (151 mg, 1.0 mmol) was used in place of *p*-anisaldehyde. Recrystallisation from petroleum ether (40–60) afforded **15** (120 mg, 53%) as a bright yellow microcrystalline solid, mp 62–63 °C (HRMS found: M^+ m/z 226.0749; $C_{13}H_{10}N_2O_2$ requires: m/z 226.0742); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 310 (9670); ν_{max}/cm^{-1} 1616 (st, C=N); δ_H (300 MHz, $C^2H_3O^2H$) 8.77 (1H, t, $^3J_{H-H}$ 1.8, Ar-H), 8.67 (1H, s, N=CH), 8.37–8.31 (1H, m, Ar-H), 8.32–8.26 (1H, m, Ar-H), 7.73 (1H, m, Ar-H), 7.45–7.38 (2H, m, Ar-H), 7.33–7.26 (3H, m, Ar-H); δ_C (75 MHz, C^2HCl_3) 157.2 (+), 150.9 (−), 148.7 (−), 137.9 (−), 134.2 (+), 129.8 (+), 129.4 (+), 126.9 (+), 125.6 (+), 123.5 (+), 121.0 (+); m/z (EI) 226 (100%, M^+).

(4-Methylbenzylidene)phenylamine (16). Compound **16** was synthesised according to the general procedure for the synthesis of **14**, except *p*-tolualdehyde (120 mg, 1.0 mmol) was used in place of *p*-anisaldehyde. Recrystallisation from petroleum ether (40–60) afforded **16** (163 mg, 83%) as a white solid, mp 43–44 °C [lit. 44–45 °C][23] (HRMS found: M^+ m/z 195.1052; $C_{14}H_{13}N$ requires: m/z 195.1048); λ_{max} (HPLC MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 304 (16 635); δ_H (300 MHz, $C^2H_3O^2H$) 8.49 (1H, s, N=CH), 7.85–7.76 (2H, m, Ar-H), 7.45–7.16 (7H, m, Ar-H), 2.40 (3H, s, Ar–CH_3); δ_C (75 MHz, C^2HCl_3) 160.4 (+), 152.3 (−), 141.9 (−), 133.7 (−), 129.6 (+), 129.2 (+), 128.9 (+), 125.8 (+), 121.1 (+), 21.7 (+); m/z (EI) 195 (100%, M^+).

(4-Chlorobenzylidene)phenylamine (17). Compound **17** was synthesised according to the general procedure for the synthesis of **14**, except 4-chlorobenzaldehyde (141 mg, 1.0 mmol) was used in place of *p*-anisaldehyde. Recrystallisation from petroleum ether (40–60) afforded (175 mg, 81%) as a white solid, mp 62–63 °C [lit. 60–62 °C][23] (Found: C, 72.55; H, 4.44; N, 6.65; $C_{13}H_{10}ClN$ requires: C, 72.39; H, 4.67; N, 6.49%; HRMS found: M^+ m/z 215.0507; $C_{13}H_{10}ClN$ requires: m/z 215.0502); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 309 (12 257); δ_H (300 MHz, C^2HCl_3) 8.42 (1H, s, N=CH), 7.89–7.81 (2H, m, Ar-H), 7.49–7.36 (4H, m, Ar-H), 7.29–7.18 (3H, m, Ar-H); δ_C (75 MHz, C^2HCl_3) 158.8 (+), 151.7 (−), 137.4 (−), 134.8 (−), 130.0 (+), 129.3 (+), 129.1 (+), 126.3 (+), 121.0 (+); m/z (EI) 215 (100%, M^+).

[4-(Benzylideneamino)phenyl]methanol (18). *p*-Anisidine (123 mg, 1.00 mmol) in absolute ethanol (5 cm^3) was added to a stirred solution of benzaldehyde (106 mg, 1.00 mmol) in absolute ethanol (20 cm^3). Benzene (2 cm^3) was added and the reaction vessel was fitted with a Dean–Stark side-arm adapter filled with absolute ethanol. The reaction mixture was then stirred under reflux for 24 h. The mixture was allowed to cool and then concentrated under reduced pressure to afford crude **18** as an off-white solid. The crude product was recrystallised from the minimum amount of petroleum ether (40–60) to afford **18** (131 mg, 62%) as a white microcrystalline solid, mp 69–70 °C [lit. 70–71 °C][41] (HRMS found: M^+ m/z 211.0999; $C_{14}H_{13}NO$ requires: m/z 211.0997); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 330 (16 952); δ_H (300 MHz, $C^2H_3O^2H$) 8.56 (1H, s, N=CH), 7.93–7.86 (2H, m, Ar-H), 7.51–7.45 (3H, m, Ar-H), 7.30–7.23 (2H, m, Ar-H), 6.99–9.93 (2H, m, Ar-H), 3.81 (3H, s, Ar–OCH_3); δ_C (75 MHz, C^2HCl_3) 158.5 (+), 158.3 (−), 144.9 (−), 136.5 (−), 131.1 (+), 128.8 (+), 128.6 (+), 122.3 (+), 114.4 (+), 55.5 (+); m/z (EI) 211 (80%, M^+), 196 (100, $[M - CH_3]^+$).

Benzylidene-*p*-tolylamine (19). Compound **19** was synthesised according to the general procedure for the synthesis of **18**, except *p*-toluidine (107 mg, 1.00 mmol) was used in place of *p*-anisidine, to afford **19** (148 mg, 76%) as a brown oil (HRMS found: M^+ m/z 195.1056; $C_{14}H_{13}N$ requires: m/z 195.1048); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 315 (8900); δ_H (300 MHz, $C^2H_3O^2H$) 8.49 (1H, s, N=CH), 7.91–7.83 (2H, m, Ar-H), 7.50–7.43 (3H, m, Ar-H), 7.22–7.10 (4H, m, Ar-H), 2.33 (3H, s, Ar–CH_3); δ_C (75 MHz, C^2HCl_3) 159.7 (+), 149.5 (−), 136.4 (−), 135.9 (−), 131.3 (+), 129.9 (+), 128.8 (+), 121.0 (+), 21.2 (+); m/z (EI) 195 (100%, M^+).

Benzylidene-*m*-tolylamine (20). Compound **20** was synthesised according to the general procedure for the synthesis of **18**, except *m*-toluidine (107 mg, 1.00 mmol) was used in place of *p*-anisidine, to afford **20** (174 mg, 89%) as a light brown oil (HRMS found: M^+ m/z 195.1039; $C_{14}H_{13}N$ requires: m/z 195.1048); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 311 (9602); ν_{max}/cm^{-1} 1629 (st, C=N); δ_H (300 MHz, $C^2H_3O^2H$) 8.50 (1H, s, N=CH), 7.93–7.86 (2H, m, Ar-H), 7.52–7.45 (3H, m, Ar-H), 7.30–7.23 (1H, m, Ar-H), 7.09–6.99 (3H, m, Ar-H), 2.36 (3H, s, Ar–CH_3); δ_H (300 MHz, C^2HCl_3) 8.49 (1H, s, N=CH), 8.01–7.93 (2H, m, Ar-H), 7.55–7.49 (3H, m, Ar-H), 7.39–7.31 (1H, m, Ar-H), 7.15–7.07 (3H, m, Ar-H), 2.45 (3H, s, Ar–CH_3); δ_C (75 MHz, C^2HCl_3) 160.4 (+), 152.3 (−), 139.2 (−), 136.5 (−), 131.6 (+), 129.3 (+), 129.0 (+), 127.0 (+), 121.9 (+), 118.2 (+), 21.7 (+); m/z (EI) 195 (100%, M^+).

Benzylidene(4-chlorophenyl)amine (21). Compound **21** was synthesised according to the general procedure for the synthesis of **18**, except 4-chloroaniline (128 mg, 1.00 mmol) was used in place of *p*-anisidine. Recrystallisation from petroleum ether (40–60) afforded **21** (70.8 mg, 33%) as a white solid, mp 59–60 °C [lit. 61–61.5 °C][41] (Found: C, 72.40; H, 4.75; N, 6.56; $C_{13}H_{10}ClN$ requires: C, 72.39; H, 4.67; N, 6.49%; HRMS found: M^+ m/z 215.0492; $C_{13}H_{10}ClN$ requires: m/z 215.0502); λ_{max} (MeOH)/nm (ε/dm^3 mol^{-1} cm^{-1}) 311 (11 456); δ_H (300 MHz, C^2HCl_3) 8.43 (1H, s, N=CH), 7.92–7.86 (2H, m, Ar-H), 7.52–7.45 (3H, m, Ar-H), 7.39–7.32 (2H, m, Ar-H), 7.19–7.12 (2H, m, Ar-H); δ_C (75 MHz, C^2HCl_3) 160.8 (+), 150.5 (−), 136.0 (−), 131.7 (+), 131.5 (−), 129.3 (+), 128.9 (+), 122.3 (+); m/z (EI) 215 (100%, M^+).

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