





**Table 1** Acidity constants and rate constants for uncatalysed and acid-catalysed reactions of the conjugate acids of substituted tritylamines in aqueous perchloric acid containing 1–2% acetonitrile; ionic strength (NaClO<sub>4</sub>) = 1 mol dm<sup>-3</sup>, 25 °C<sup>a</sup>

Tritylamine	p <i>K</i> <sub>BH<sup>+</sup></sub> (% CH <sub>3</sub> CN)	<i>k</i> <sub>0</sub> /s <sup>-1</sup>	<i>k</i> <sub>H</sub> /dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup>
TrNH <sub>2</sub> , <b>1a</b>	9.2(16)	6.9 × 10 <sup>-5b</sup>	3.8 × 10 <sup>-5b</sup>
MMTrNHCH <sub>2</sub> CO <sub>2</sub> Me, <b>2b</b>	—	34.0	59.1
MMTrNHPh, <b>2c</b>	—	9.25	145
DMTrNH <sub>2</sub> , <b>3a</b>	9.5(28) <sup>c</sup>	3.49 × 10 <sup>-5d</sup>	1.2 × 10 <sup>-5d</sup>
DMTrNHPh, <b>3c,i</b>	8.9(39) <sup>e</sup>	41	37
DMTrNHC <sub>6</sub> H <sub>4</sub> Me, <b>3c,ii</b>	9.2(17) <sup>e</sup>	37	72
DMTrNHC <sub>6</sub> H <sub>4</sub> OMe, <b>3c,iii</b>	9.5(53) <sup>e</sup>	45	10
DMTrNHC <sub>6</sub> H <sub>4</sub> F, <b>3c,iv</b>	8.8(17) <sup>e</sup>	43	56
DMTrNHC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> , <b>3c,v</b>	9.3(87) <sup>e</sup>	38	23
DMTrNH( <i>p</i> -NO <sub>2</sub> Bn), <b>3d</b>	—	9	142
DMTrNHC <sub>3</sub> H <sub>7</sub> , <b>3e</b>	—	48	33
DMTrNHOMe, <b>3f</b>	—	0.20 <sup>f</sup>	1.3 <sup>f</sup>
TMTrNH <sub>2</sub> , <b>4a</b>	9.3(26) <sup>c</sup>	3.81 × 10 <sup>-4g</sup>	1.68 × 10 <sup>-4g</sup>
TMTrNH( <i>p</i> -NO <sub>2</sub> Bn), <b>4d</b>	—	5.8	118
TMTrNHC <sub>3</sub> H <sub>7</sub> , <b>4e</b>	9.7(26)	4.75	146
TMTrNHBn, <b>4g</b>	9.4(32)	4.9	138
TMTrNHC <sub>4</sub> H <sub>9</sub> , <b>4h</b>	9.7(36)	5.3	143
TMTrN(Me)Bn, <b>4i</b>	9.9(20)	5.7	128

<sup>a</sup> p*K*<sub>BH<sup>+</sup></sub> values of the bases, *i.e.* the p*K*<sub>a</sub> values of the corresponding alkylammonium ions,<sup>15</sup> were measured in acetonitrile–water solution, ionic strength 1.0 mol dm<sup>-3</sup> (NaClO<sub>4</sub>) at 21 °C; all arene substituents are at position 4. <sup>b</sup> 340 K, ionic strength (NaClO<sub>4</sub>) = 3.5 mol dm<sup>-3</sup>, 4% MeCN. <sup>c</sup> Ref. 9. <sup>d</sup> *k*<sub>0</sub> = 3.1 × 10<sup>-5</sup> s<sup>-1</sup> and *k*<sub>H</sub> = 1.6 × 10<sup>-5</sup> dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>,<sup>9</sup> from rate measurements made between 288 and 328 K, Δ*H*<sup>‡</sup> = 105 ± 5 and 126 ± 8 kJ mol<sup>-1</sup>, and Δ*S*<sup>‡</sup> = 21 ± 10 and 85 ± 15 J K<sup>-1</sup> mol<sup>-1</sup>, for *k*<sub>0</sub> and *k*<sub>H</sub>, respectively. <sup>e</sup> Ref. 12. <sup>f</sup> Ref. 16. <sup>g</sup> *k*<sub>0</sub> = 89 × 10<sup>-5</sup> s<sup>-1</sup> and *k*<sub>H</sub> = 50 × 10<sup>-5</sup> dm<sup>3</sup> mol<sup>-1</sup> s<sup>-1</sup>,<sup>9</sup> from rate measurements made between 288 and 328 K, Δ*H*<sup>‡</sup> = 97 ± 5 and 100 ± 5 kJ mol<sup>-1</sup>, and Δ*S*<sup>‡</sup> = 15 ± 10 and 19 ± 10 J K<sup>-1</sup> mol<sup>-1</sup>, for *k*<sub>0</sub> and *k*<sub>H</sub>, respectively.

unlikely to have had a significant effect, its proportion changed slightly as the ammonium salts were titrated against standard sodium hydroxide. The initial acidic pH of the solution for titration was chosen to minimise solvolytic deamination of the *N*-tritylalkyl- and *N*-tritylaryl-ammonium ions. Results are included in Table 1.

## Discussion

It is evident from the p*K*<sub>BH<sup>+</sup></sub> values of the substituted tritylamines, that the substrates in these deamination reactions under the acidic conditions of the kinetics experiments are actually the corresponding substituted tritylammonium cations.<sup>15</sup> Consequently, although *k*<sub>H</sub> is the rate constant of the real acid-induced reaction of the (substituted) ions, Tr–NH<sub>3</sub><sup>+</sup> (or Tr–NH<sub>2</sub>R<sup>+</sup>), *k*<sub>0</sub> corresponds to the hypothetical reaction of these ions at [H<sub>3</sub>O<sup>+</sup>] = 0. The insensitivity of the kinetics of deamination of TMTrNH<sub>2</sub> to the nature of the strong acid catalyst (Table 2) is in accord with previous studies using DMTrNH<sub>2</sub>, and is as expected for a specific acid-catalysed mechanism. The absence of a major solvent effect upon the rates of deaminations of both DMTrNH<sub>2</sub> and TMTrNH<sub>2</sub> shown in Tables 2 and 3 indicates that the choice of cosolvent need be guided only by solubility issues in deprotection reactions in synthesis.

Monomethoxytritylamine (MMTrNH<sub>2</sub>) is much less reactive than the dimethoxy- analogue,<sup>18</sup> and the parent tritylamine (TrNH<sub>2</sub>) is even less reactive. Furthermore, trityl and monomethoxytrityl carbenium ions are much less stable in aqueous solution than dimethoxy- and trimethoxy- analogues. Consequently, it was not possible to obtain reliable rate measurements on TrNH<sub>2</sub> and MMTrNH<sub>2</sub> under conditions (temperature, acidity, and ionic strength) comparable with those employed for dimethoxy- and trimethoxy- analogues. The similarity in the rate-enhancing effects of the extra 4-methoxy substituent between DMTrNH<sub>2</sub> and TMTrNH<sub>2</sub> upon both *k*<sub>0</sub> and *k*<sub>H</sub> (Table 1, a factor of about 30) suggests that the effect is upon the initial pre-equilibrium ionization (*k*<sub>1</sub>/*k*<sub>-1</sub>) rather than the subsequent *k*<sub>d</sub> and *k*<sub>a</sub> steps (Scheme 3). This is readily understood as the resonance effect of the extra methoxy substituent upon the stability of the dimethoxytrityl cation. The 4-methoxy substituent effect is much smaller, however, than the effect of

**Table 2** Effect of catalytic acids and solvent composition upon rate constants for uncatalysed (*k*<sub>0</sub>) and acid-catalysed (*k*<sub>H</sub>) reactions of 4,4',4''-trimethoxytritylammonium cation in aqueous solution at 298 K; ionic strength = 1 mol dm<sup>-3a</sup>

Acid (% cosolvent)	10 <sup>4</sup> <i>k</i> <sub>0</sub> /s <sup>-1</sup>	10 <sup>4</sup> <i>k</i> <sub>H</sub> /dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup>
HClO <sub>4</sub> (1% MeCN)	3.81 <sup>b</sup>	1.68 <sup>b</sup>
HCl (1% MeCN)	2.02	1.80
HBr (1% MeCN)	2.44	0.92
HNO <sub>3</sub> (1% MeCN)	2.44	1.21
HClO <sub>4</sub> (51% MeCN)	1.74	3.1
HClO <sub>4</sub> (78% MeCN)	2 <sup>c</sup>	5 <sup>c</sup>
HCl (60% AcOH)	8.6	3.6
HCl (95% AcOH) <sup>d</sup>	11	10

<sup>a</sup> The ionic strength was maintained constant with the sodium salt of the catalytic acid. <sup>b</sup> From Table 1. <sup>c</sup> These results are less precise due to the poorer quality of the linear correlation of *k*<sub>obs</sub> with [HClO<sub>4</sub>]. <sup>d</sup> Ionic strength not kept constant.

**Table 3** Effect of cosolvent upon rate constants for uncatalysed (*k*<sub>0</sub>) and perchloric acid-catalysed (*k*<sub>H</sub>) reactions of 4,4'-dimethoxytritylammonium cation in aqueous solution at 298 K; ionic strength (NaClO<sub>4</sub>) = 1 mol dm<sup>-3</sup>

Cosolvent	10 <sup>5</sup> <i>k</i> <sub>0</sub> /s <sup>-1</sup>	10 <sup>5</sup> <i>k</i> <sub>H</sub> /dm <sup>3</sup> mol <sup>-1</sup> s <sup>-1</sup>
1% MeCN <sup>a</sup>	3.49	1.2
60% AcOH	5.5	2.9
95% AcOH <sup>b</sup>	6	7

<sup>a</sup> It was shown that, under otherwise the same experimental conditions at 298 K, *k*<sub>obs</sub> increased only from 4.6 to 6.5 × 10<sup>-5</sup> s<sup>-1</sup> as the proportion of MeCN increased from 1 to 60%. <sup>b</sup> Ionic strength not kept constant.

an *N*-alkyl group (a factor of about 10<sup>6</sup> upon both *k*<sub>0</sub> and *k*<sub>H</sub> for DMTrNH<sub>2</sub>). Moreover, the rate-enhancements due to resonance of the second and third methoxy substituents virtually disappear in the *N*-alkyl derivatives, *i.e.* the *N*-alkyl has a levelling effect upon the rate-enhancing resonance effect of the second and third 4-MeO groups. Furthermore, comparisons of reactivities of mono-, di-, and tri-methoxy-substituted analogues with a common substituent on the

nitrogen, e.g.  $-\text{NH}-\text{Ph}$ , or  $-\text{NH}-\text{CH}_2\text{CO}_2\text{Me}$ ,<sup>9</sup> do not appear to follow any readily explicable pattern. Within the dimethoxytrityl series, however, all carbon-bonded *N*-substituents lead to similarly large rate enhancements (Table 1), and the alkoxy group of *N*-(dimethoxytrityl)-*O*-methylhydroxylamine has an effect smaller by a factor of only about 200 on  $k_0$  and 50 on  $k_{\text{H}}$  compared with the alkyl substituents. Replacement of an alkyl on the nitrogen by an alkoxy yields an  $\alpha$ -effect nucleofuge/nucleophile,<sup>19</sup> so there will be a higher proportion of internal return for the hydroxylamine, i.e.  $k_1/k_{-1}$  in Scheme 3 will be smaller, with an associated reduction in the overall rate constants,  $k_0$  and  $k_{\text{H}}$ , compared with the *N*-alkyl analogues.

We reported previously that the effect of substituents upon the base strengths of anilines,  $\rho(\sigma^-) = -2.9$ ,<sup>20</sup> is absent in *N*-tritylanilines;<sup>12</sup> moreover, all the *N*-tritylanilines we investigated were comparable as bases with simple alkylamines, i.e.  $\text{p}K_{\text{BH}^+} \text{ca. } 9$ . We ascribed this to steric inhibition of resonance between the lone pair on the nitrogen and the aryl residue and its *para*-substituents (if present). We now observe that  $k_0$  values for *N*-trityl(aryl)amines are generally higher than for *N*-trityl(alkyl)amines, but independent of the substituent in the arylamine ( $\rho = 0$  for  $k_0$ ), and  $k_{\text{H}}$  values are lower than for *N*-alkyl analogues, but again independent of the substituent in the arylamine ( $\rho = 0$  for  $k_{\text{H}}$ ). On the basis that arylamines are poorer nucleophiles and weaker bases than alkylamines,  $k_{-1}$  and  $k_{\text{a}}$  should be smaller for arylamines than for alkylamines, whereas  $k_1$  should be larger and  $k_{\text{d}}$  much the same. It follows (Scheme 3) that  $k_0$  should be larger for *N*-trityl(aryl)amines than *N*-trityl(alkyl)amines but  $k_{\text{H}}$  smaller as is observed (Table 1) but only by a factor of about 10 for  $k_0$  and even less for  $k_{\text{H}}$ . The absence of an effect by substituents in the aniline moiety upon both  $k_0$  and  $k_{\text{H}}$  is more intriguing and, like the origin of the massive rate enhancements caused by *N*-alkyl and *N*-aryl groups, is the subject of ongoing investigations.

Activation parameters for the forward reaction ( $K.k$ ) in Scheme 1 for  $\text{R} = \text{H}$ , have already been reported ( $\Delta H^\ddagger = 63 \text{ kJ mol}^{-1}$  and  $\Delta S^\ddagger = -19 \text{ J K}^{-1} \text{ mol}^{-1}$ ),<sup>7</sup> and are in accordance with a fast second-order catalytic mechanism (low  $\Delta H^\ddagger$  and modestly negative  $\Delta S^\ddagger$ ). This acid-catalysed cleavage of alcohols (and ethers) compares with the  $k_0$  reaction channel in the present investigation (Scheme 3), but with an important difference. In the  $k_0$  reaction channel of Scheme 3, the reactant is already protonated, so the reaction is essentially a first-order unimolecular reaction of an alkylammonium ion. Accordingly, there is no adverse translational component to the entropy of activation, as there is for the second-order bimolecular process, and there is no change in charge type as the reactant proceeds to the transition structure. In the absence of complicating differential solvation effects, therefore,  $\Delta S^\ddagger$  for the dissociative unimolecular mechanism should be modestly positive as is observed:  $\Delta S^\ddagger$  values for  $k_0$  for  $\text{DMTrNH}_2$  and  $\text{TMTTrNH}_2$  are 21 and  $15 \text{ J K}^{-1} \text{ mol}^{-1}$ , respectively. This entropy effect alone, of course, would lead to the deaminations being faster than the cleavage of ethers and alcohols at  $[\text{H}_3\text{O}^+] = 1 \text{ mol dm}^{-3}$ . The major cause, therefore, of the much faster cleavage of the C–O bonds in the protonated alcohols and ethers compared with cleavage of the C–N bond in the deamination of tritylammonium ions is the difference in enthalpies of activation (ca.  $63 \text{ kJ mol}^{-1}$  compared with ca.  $100 \text{ kJ mol}^{-1}$ ). There is no reaction channel in the cleavage of the alcohols (or ethers) corresponding to the acid-catalysed deamination. We see, however, that  $\Delta H^\ddagger$  values for this  $k_{\text{H}}$  process for both  $\text{DMTrNH}_2$  and  $\text{TMTTrNH}_2$  are virtually the same as for the uncatalysed  $k_0$  reactions.

## Experimental

Preparations of compounds have already been described.<sup>9,12</sup> Water was glass distilled and concentrations of stock solutions of perchloric acid were determined by titration against

standard sodium hydroxide which had been previously standardised against potassium hydrogen phthalate.

## Kinetics

The deamination reactions of the trityl-substituted ammonium cations occur in aqueous perchloric acid (containing 1–2% of acetonitrile to overcome solubility problems) to give equilibrium mixtures of the trityl cations and trityl alcohols. Trityl, 4,4'-dimethoxytrityl, and 4,4',4''-trimethoxytrityl cations absorb strongly at 432, 495, and 483 nm, respectively, and rates were measured by monitoring increases in absorbances at or close to these wavelengths. Conventional kinetics were measured using a Cecil 5502 double beam spectrophotometer controlled by an Elonex PC-433 and with the cell block thermostatted by water circulating from a Grant W6 water bath. The temperature was monitored with a platinum resistance thermometer in the cell block. Stopped-flow kinetics were carried out using an Applied Photophysics SX-17MV stopped-flow spectrofluorimeter at  $25 \pm 0.1 \text{ }^\circ\text{C}$ .<sup>14</sup> Rates of decomposition under acidic conditions were investigated under the usual pseudo first-order conditions. The observed pseudo first-order rate constants (averages of at least six runs) were plotted against  $[\text{H}_3\text{O}^+]$  to give the second-order catalytic constant from the gradient and the first-order rate constant for the uncatalysed reaction from the intercept.

## pK<sub>a</sub> Determinations

A pH titration method was used and has already been described.<sup>11</sup> A combined glass electrode coupled to a Metrohm 716 DMS Titrino automatic titrator was used to record the pH during the titration of the conjugated acid of the amine against standard sodium hydroxide. The reported  $\text{p}K_{\text{a}}$  values were optimised by fitting the experimental results to the appropriate sigmoidal equations derived from the Henderson–Hasselbach equation using a non-linear optimisation algorithm.

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