Proton Transfer Reactions of Triazol-3-ylidenes: Kinetic Acidities and Carbon Acid pK_a Values for Twenty Triazolium Salts in Aqueous Solution

Richard S. Massey,[a, c] Christopher J. Collett,[b, c] Anita G. Lindsay,[a] Andrew D. Smith[b]* and AnnMarie C. O'Donoghue[a]*

[a] *Department of Chemistry, Durham University, University Science Laboratories, South Road, Durham, DH1 3LE, UK*
E-mail: annmarie.odonoghue@durham.ac.uk

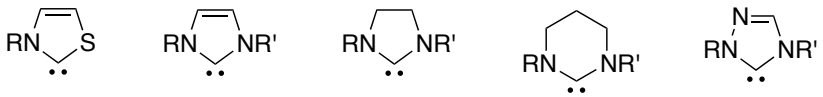
[b] *School of Chemistry, University of St Andrews, North Haugh, St Andrews KY16 9ST, UK*
E-mail: ads10@st-andrews.ac.uk

[c] *These authors contributed equally to this work.*

Abstract:

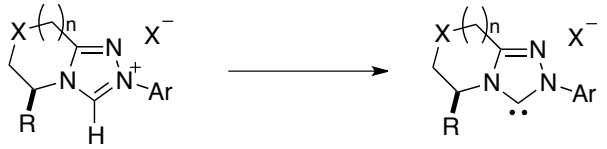
Second order rate constants have been determined for deuteroxide ion-catalyzed exchange of the C(3)-proton for deuterium, k_{DO} ($M^{-1}s^{-1}$), of a series of twenty triazolium salts in aqueous solution at 25 °C and ionic strength I = 1.0 (KCl). Evidence is presented that the rate constant for the reverse protonation of the triazol-3-ylidenes by solvent water is close to that for dielectric relaxation of solvent (10^{11} s^{-1}). This data enabled the calculation of carbon acid pK_a values in the range 16.6-18.5 for the twenty triazolium salts. pD-rate profiles for deuterium exchange of the triazolium salts reveal that protonation at nitrogen to give *dicationic* triazolium species occurs under acidic conditions, with estimates of pK_a^{N1} = -0.2-0.5.

Introduction Since the first isolation and characterisation of stable N-heterocyclic carbenes (NHCs), such species have come to prominence in various fields of chemistry.[1-12] Structural classes embodied within the NHC family include the thiazol-2-ylidenes **1**, imidazol-2-ylidenes **2** and imidazolin-2-ylidenes **3**, trihydropyrimidin-2-ylidenes **4** and triazol-3-ylidenes **5**. From the early seminal work of Breslow,[13] thiazol-2-ylidenes such as **1** have long been implicated as the catalytically active species in the benzoin condensation, however, until recently, applications beyond this C-C bond-forming reaction were relatively limited. In the last decade, NHCs have proven to be effective organocatalysts of a broad range of synthetic transformations. Initially based upon their established use in polarity reversal or Umpolung techniques,[5,10,14,15] methodologies have been developed for the generation and exploitation of azolium homoenolates[16] and enolates,[17] as well as acyl azolium[18] and α,β-unsaturated acylazoliums,[19] leading to remarkable reaction and product diversity within this field. Although many different NHC classes such as **1**-**3** have been employed in organocatalysis, the triazol-3-ylidenes **5** are the most often utilised. It is common in many synthetic transformations to generate the active NHC species *in situ* from the conjugate acid azolium ion precursor of the NHC by use of an appropriate base.[20] Remarkably, despite the widespread use of azolium ion precursors to NHCs in organocatalysis and elsewhere, there have been relatively few literature reports of the solution kinetic or thermodynamic Brønsted acidities of these pre-catalysts,[21-32] although there have been studies of NHC nucleophilicities[33] and gas phase proton affinities.[34-42] Washabaugh and Jencks reported on the C2-H/D exchange and aqueous pK_a values of a range of N-alkyl thiazolium ion analogues of thiamine, that are precursors to thiazol-2-ylidenes **1**.[27-29] Amyes *et al* reported aqueous pK_a values for the conjugate acids of N,N-dialkylimidazol-2-ylidenes **2** (R = R' = H or Me) and two benzoannelated variants.[22] We recently reported the kinetic acidities towards hydroxide ion, and the aqueous pK_a values, of a broad range of conjugate acid precursors to imidazol-2-ylidenes **2**, imidazolin-2-ylidenes **3** and trihydropyrimidin -2-ylidenes **4**.[24] In this paper, we report kinetic acidities and pK_a values in aqueous solution for a large series of synthetically relevant triazolium ion precursors to triazol-3-ylidenes **5**.



1 **2** **3** **4** **5**

A remarkably diverse range of triazol-3-ylidenes has been employed in organocatalytic transformations, with significant variations in both catalytic activities and reactivities being observed within this architecture. For example, *N*-pentafluorophenyl triazolium salts are generally the preferred precatalysts for benzoin and Stetter reaction processes,[43] while *N*-mesityl triazolium precatalysts show remarkably enhanced reactivity in NHC-catalysed processes involving enals.[44] Qualitative experiments by Bode and Mahatthananchai have shown that *N*-pentafluorophenyl triazolium salts are more acidic than the corresponding *N*-mesityl salts,[45] implicating that less of the corresponding active NHC is likely to be generated under typical reaction conditions. Further experimentation led them to elegantly ascribe the *N*-mesityl effect to irreversible initial addition of the NHC to the enal. Given these precedents, and the general interest in NHC-mediated catalysis using triazolium precatalysts, we aimed to quantify the effect of variation of the *N*-substituent, ring-size and substitution pattern within a series of chiral and achiral triazolium salt **6** precursors to singlet NHCs **7** upon their kinetic acidities and aqueous pK_a values (Scheme 1).



6 **7**

n = 0, 1; X = O, CH_2
R = H, alkyl
Ar = Ph, Mes, C_6F_5, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-CNC_6H_4
$X^- = Cl^-, BF_4^-$

Scheme 1. Substituent effects on kinetic acidities and pK_a values of triazolium salts.

Figure 1 illustrates the specific series of triazolium ions that we have studied and their chloride or tetrafluoroborate counterions (X^-). In each case, the second order rate constant for deuteroxide ion-catalyzed exchange of the C(3)-proton for deuterium, k_{DO} ($M^{-1}s^{-1}$) has been determined. Using these values, the carbon acid pK_a values for the

triazolium ions in aqueous solution have been calculated. To our knowledge, this is the first report of kinetic acidities and carbon acid pK_a values for a broad range of triazolium ions in any solvent. Analysis of the p*D*-rate profiles for deuterium exchange of triazolium ions **6** reveals distinct differences from analogous data for the deprotonations of the conjugate acid precursors to NHCs **1** – **4**. In particular, the data reveals that N(1) protonation to give dicationic triazolium ions can occur under relatively mild acidic conditions, where these species act as precursors to *monocationic* N-heterocyclic carbenes.

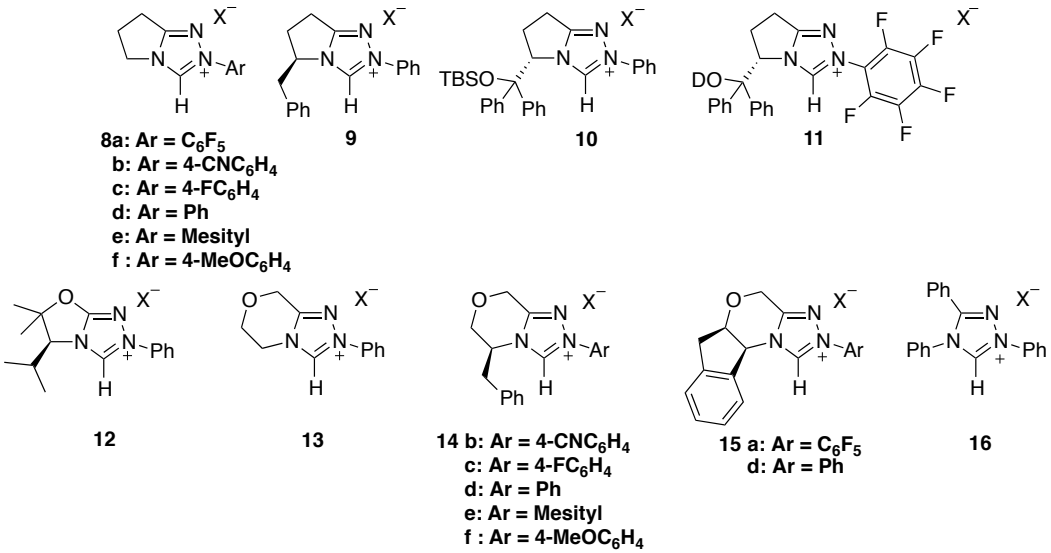


Figure 1. Series of achiral and chiral triazolium salts for which pK_a values in aqueous solution have been determined in this report.

Experimental Section

The syntheses of triazolium salts **8a-f**, **9-13**, **14b-f**, **15a-d** and **16-X**$^-$, the preparation of solutions, the determination of p*D*, and the NMR methods used to monitor deuterium exchange are described in the Supporting Information.

Deuterium Exchange. All triazolium salts were rigorously dried before use in the deuterium exchange experiments. Typically, reactions were initiated by the addition of the reaction solution, containing internal standard (tetramethylammonium

deuteriosulfate) and buffer or DCl solution, directly to the triazolium salt. In general, the final substrate and internal standard concentrations in the reaction solutions were 5 - 10 mM and 0.5 - 1 mM, respectively. As triazolium salts **10-12**, **14b**, **15a** and **15d** were insoluble in D_2O, perdeuterated acetonitrile (33% v/v) was used as a co-solvent in the exchange reactions of these salts. All H/D exchange reactions were incubated at 25 ± 0.1 ºC in a thermostated water bath. p*D* values were recorded at the beginning and end of each reaction, and were found to be constant within error (± 0.03).

In general, the reaction progress was monitored over time by withdrawing aliquots (~750 μL) at timed intervals from a reaction solution (~ 10 mL). These aliquots were quenched to p*D* values 2-3 units below that of the reaction mixture by addition of 1 M DCl solution. The samples were either analysed immediately or placed in sealed bags containing calcium chloride and stored in the freezer for analysis at a later time. Reactions at lower p*D* values (< 1.5) were run directly in sealed NMR tubes thermostated at 25 ± 0.1 ºC, without the use of quenching. This was due to the inability to sufficiently quench the reaction through the lowering of p*D*.

Deuterium exchange was followed by ^{1}H NMR spectroscopy during the disappearance of 75-90% of the C(3)-proton signal of each substrate. There was no change in the integrated areas of signals due to all other protons of the triazolium salts **8-16-X**$^-$ during this period, and no additional signals appeared. Thus, there was no detectable hydrolysis or decomposition of any of the triazolium salt substrates under the reaction conditions. The observed pseudo-first-order rate constants for exchange of the C(3)-proton for deuterium, k_{ex} (s^{-1}), were obtained from the slopes of semilogarithmic plots of reaction progress against time according to eq 1. The values of f(s), the fraction of unexchanged substrate, were calculated from eq 2, where A_{C3H} and A_{std} are the integrated areas of the singlet due to the C(3)–H of the triazolium salt and the broad triplet at 3.3 ppm due to the methyl hydrogens of internal standard, tetramethylammonium deuterosulfate.

$$\ln f(s) = -k_{ex} t \qquad (1)$$

$$f(\mathrm{s}) = \frac{(A_{\mathrm{C3H}} / A_{\mathrm{std}})_{\mathrm{t}}}{(A_{\mathrm{C3H}} / A_{\mathrm{std}})_{0}} \quad (2)$$

Representative NMR spectra, all first order kinetic plots and tabulated k_{ex} data are included in the supporting information (Figures s1-s86, Tables s1-s24).

Results and Discussion

Deuterium Exchange Reactions

The deuterium exchange reactions of triazolium salts **8a-f-BF$_4^-$**, **9-Cl$^-$**, **13-BF$_4^-$**, **14c-f Cl$^-$** and **16-BF$_4^-$** were performed in fully aqueous solution at a range of p*D* values and at ionic strength, I = 1.0 (KCl). In all cases, C(3)-H/D exchange was too fast to monitor by ^{1}H NMR spectroscopy above p*D* 4.5 at 25 °C. As some of the deuterium exchange reactions were performed in acetic acid buffer solutions, the contribution of buffer species to the observed rate constant for exchange was assessed. For two representative azolium salts **8c-BF$_4^-$** and **8d-BF$_4^-$**, the effect of an increase in the total buffer concentration by 2.5-10-fold at a fixed buffer ratio resulted in no significant change in k_{ex} at 25 °C (see p S110-112 for results of experiments) once corrections were made for the slight changes in p*D* upon dilution of buffer at constant ionic strength. Buffer catalysis of exchange was also not significant in previous studies of the analogous deuterium exchange reactions of imidazolium, dihydroimidazolium and trihydropyrimidinium ion precursors to carbenes **2-4**.[22,24]

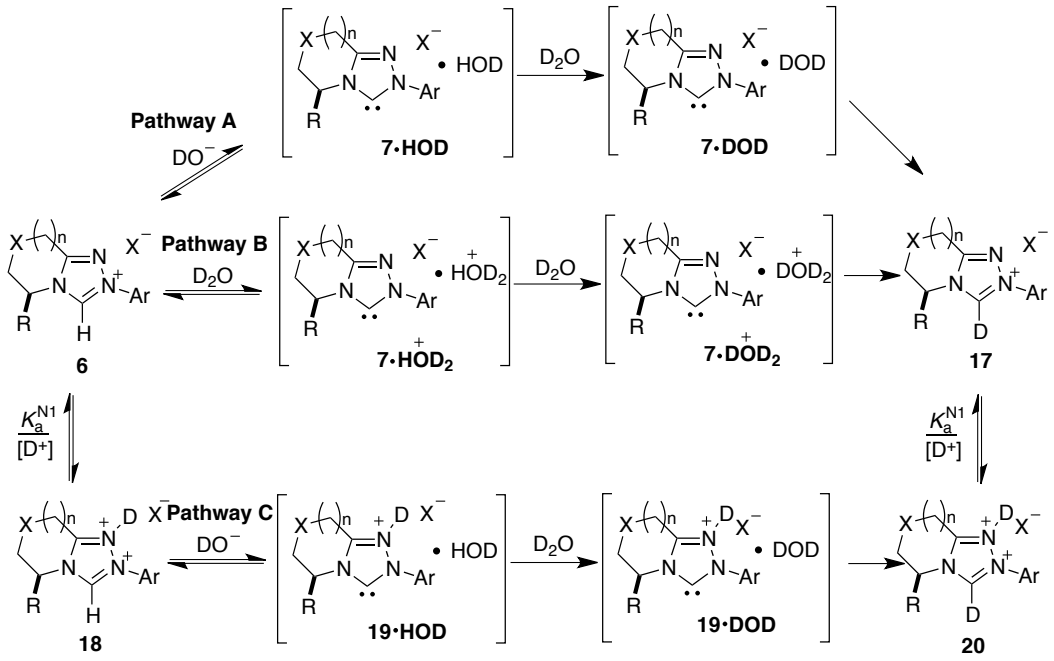
For the triazolium salts **8a-f-BF$_4^-$**, **9-Cl$^-$**, **13-BF$_4^-$**, **14c-f Cl$^-$** and **16-BF$_4^-$** studied in fully aqueous solution, values of k_{ex} increase with p*D* in the region from p*D* = 0 to 4.5. Figure 2 shows the p*D*–rate profiles of the values of k_{ex} for the deuterium exchange reactions of triazolium salts **8a-f-BF$_4^-$**. Analogous profiles for all salts in Figure 1 are included in the supporting information. The solid line through the data for triazolium salts **8b-f-BF$_4^-$** in Figure 2 shows the fit of the log k_{ex} - p*D* data to eq 3, which is derived from eq 4, where k_{DO} ($M^{-1}s^{-1}$) is the second-order rate constant for deuteroxide-catalyzed exchange, K_W = $10^{-14.87}$ [46] is the ion product of D_2O at 25 °C and γ_{DO} is the activity coefficient for deuteroxide ion under our experimental conditions. The good linear fits of the majority of the log k_{ex} – p*D* data for salts **8b-f-BF$_4^-$** to eq 3 is consistent with

deuteroxide-catalyzed exchange *via* Pathway A as the dominant mechanism for H/D-exchange (Scheme 2).

$$\log k_{ex} = \log\left(\frac{k_{DO}K_w}{\gamma_{DO}}\right) + pD \quad (3)$$

$$k_{ex} = k_{DO}[DO^-] \quad (4)$$

In Pathway A, deprotonation of the triazolium salt **6** by deuteroxide results in the formation of a complex **7.HOD** between NHC **7** and a molecule of HOD. Subsequent replacement of the molecule of HOD by bulk solvent DOD, followed by deuteration, leads to exchange product **17**. The deuteration step is effectively irreversible, as bulk solvent is present in large excess over substrate, thus k_{ex} reflects rate-limiting formation of solvent-equilibrated NHC **7.DOD** from the triazolium salt and deuteroxide ion.



Scheme 2. Potential competing pathways for deuterium exchange at C(3)-H of triazolium salts **6**.

Upon closer examination of the profiles for **8b-f-BF$_4^-$** in Figure 2, the dependencies of log k_{ex} on p*D* decreases for the 1-3 data points at the lowest p*D* values

and these points deviate upwards from the line of unit slope through the remaining log k_{ex} – p*D* data. As discussed in more detail below, the moderate deviation of these data points is likely due to the onset of additional competing pathways for H/D-exchange at lower p*D* values (Pathways B and/or C, Scheme 2). As a result, these data points were omitted from the fits to eq 3 in the determination of the k_{DO} values listed in Table 1. The log k_{ex} – p*D* data for triazolium salts **8d-Cl$^-$, 9-Cl$^-$, 13-BF$_4^-$, 14c-f-Cl$^-$** and **16-BF$_4^-$** in fully aqueous solution were analysed in a similar manner by fitting to eq 3 with the omission of the 1-4 data points at lower p*D* values that deviate upwards from the lines of unit slope through each set of data. Values of k_{DO} obtained by fitting the data for these salts to eq 3 (Table 1) agree well with those obtained as slopes of linear second order plots of the same range of k_{ex} values against deuteroxide concentration according to eq 4 (supporting information).

For pentafluorophenyl triazolium salt **8a-BF$_4^-$** (●), the altered dependence on p*D* is more marked and only the data points at the five highest p*D* values fit well to eq 3. In this case, the decreased dependence on p*D* is also followed by a downward break at the lowest p*D* values. This altered dependence on p*D* is not due to a medium effect as the ionic strength was constant for these measurements (I = 1.0 (KCl)). Extra data points were acquired in 1.24 and 2.0 M DCl (Figure 2, ○ on plot for **8a-BF$_4^-$**). Although the ionic strength is higher, these data points further support the existence of the downward break.

The change in the dependence of log k_{ex} values on p*D* suggests competition from additional pathway(s) for deuterium exchange at lower p*D* values (Scheme 2). This could include a p*D*-independent mechanism for H/D exchange with deprotonation by solvent water rather than deuteroxide ion (Pathway B), which initially leads to intermediate **7.HOD$_2^+$**. As the log k_{ex} – p*D* data does not become completely p*D*-independent, the occurrence of Pathways A and B only, without allowing for protonation at N(1), are not sufficient to explain the data. Protonation of triazolium ion **6** at N(1) would decrease the fraction of monocationic substrate available for deuterium exchange *via* Pathways A and B, and could account for the continued decrease in log k_{ex} values with p*D*.[47] Additionally,

the initial protonation of the triazolium ion **6** at N(1) to give dicationic azolium ion **18** could be followed by deuteroxide-catalyzed exchange (Pathway C). In this mechanism, deprotonation by DO^- at C(3) would give a monocationic NHC-HOD complex **19.HOD**, and the subsequent formation of dicationic exchange product **20**.

Eq 5 allows for the additional dependence of pathway A on K_a^{N1}, the acidity constant for ionization at N(1), however, does not allow for pathway B or C. The log k_{ex} – p*D* data for triazolium salt **8a-BF$_4^-$** does not fit well at lower p*D* values to eq 5, which suggests that the combination of one or both of Pathways B and C, together with protonation at N(1), is required to account for the altered dependence of log k_{ex} on p*D* at lower p*D* values. Eqs 6 and 7 allow for the dependence of k_{ex} (s^{-1}) on Pathways A and B, or Pathways A and C, respectively, with protonation at N(1) at lower p*D* values in each case. In these kinetically indistinguishable equations, k_{D2O} (s^{-1}) is the first order rate constant for exchange *via* Pathway B, where deprotonation at C(3) is by solvent and k_{DO}' ($M^{-1}s^{-1}$) is the second order rate constant for deuteroxide-catalyzed C(3)-H/D exchange of the *N*-protonated azolium ion **18** *via* Pathway C.

$$\log k_{ex} = \log\left[\frac{K_a^{N1}\left(\left(\frac{k_{DO}K_w}{\gamma_{DO}}\right)10^{pD}\right)}{\left(K_a^{N1}+10^{-pD}\right)}\right] \tag{5}$$

$$\log k_{ex} = \log\left[\frac{K_a^{N1}\left(\left(\frac{k_{DO}K_w}{\gamma_{DO}}\right)10^{pD}\right)+\left(K_a^{N1}k_{D_2O}\right)}{\left(K_a^{N1}+10^{-pD}\right)}\right] \tag{6}$$

$$\log k_{ex} = \log\left[\frac{K_a^{N1}\left(\left(\frac{k_{DO}K_w}{\gamma_{DO}}\right)10^{pD}\right)+\left(\frac{k_{DO}'K_w}{\gamma_{DO}}\right)}{\left(K_a^{N1}+10^{-pD}\right)}\right] \tag{7}$$

The log k_{ex} – p*D* data for triazolium salt **8a-BF$_4^-$** fits well to eqs 6 and 7, which

confirms that Pathway A occurs at higher p*D* values and that one or both of Pathways B and C, together with protonation at N(1), could account for the data at lower p*D* values. On the basis of overall kinetic fitting to eqs 6 and 7, it is not possible to distinguish whether Pathway B or C, or both, occur at lower p*D*s. Owing to the two equations being kinetically indistinguishable, the log k_{ex} – p*D* data for triazolium salt **8a-BF$_4^-$** fit equally well overall to eqs 6 and 7. The solid line through the data for triazolium salt **8a-BF$_4^-$** in Figure 2 shows the fit to eq 6. Identical values of k_{DO} ($M^{-1}s^{-1}$), for deuterium exchange *via* Pathway A, are obtained from either fit and these are included in Table 1.

Assuming protonation at N(1) and either Pathway B or C, we can extract values for the other unknown constants in eqs 6 and 7. Consideration of the magnitude of kinetic constants obtained by assuming either extreme of Pathway B or C, enables us to probe the likelihood of either pathway and this will be discussed further below. Fitting to both equations yields identical values for K_a^{N1}, whereas assuming eq 6 or 7, respectively, the rate constants, k_{D2O} (s^{-1}) or k_{DO}' ($M^{-1}s^{-1}$) are obtained and these values are included in Table 2. The kinetic data in both Tables 1 and 2 will be discussed in the following sections.

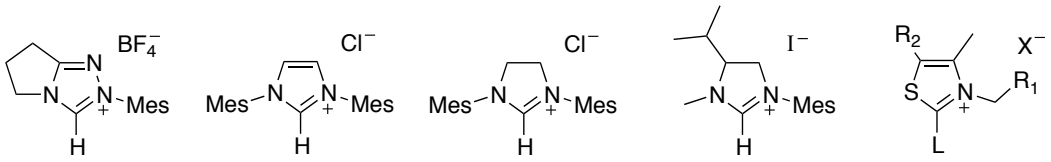
As chiral triazolium salts **10-12-BF$_4^-$**, **14b-Cl$^-$**, **15a-BF$_4^-$** and **15d-BF$_4^-$** were insoluble in D_2O, perdeuterated acetonitrile (33% v/v) was used as a co-solvent in the exchange reactions of these salts. The deuterium exchange reactions of triazolium salts **8a-BF$_4^-$** and **8d-BF$_4^-$** were studied both in D_2O, and in 2:1 D_2O:CD_3CN, so that the effect of acetonitrile co-solvent could be assessed. The appearance of the p*D*–rate profiles for **10-12-BF$_4^-$**, **14b-Cl$^-$**,and **15d-BF$_4^-$** in 2:1 D_2O:CD_3CN can also be explained by the occurrence of parallel pathways for deuterium exchange as in Scheme 2 (see supporting information for p*D*–rate profiles), however, the altered dependence of log k_{ex} values on p*D* occurs at higher p*D* values than for the salts studied in fully aqueous solution. The exchange data for the salts studied in in 2:1 D_2O:CD_3CN were fitted to eqs 6/7 rather than eq 3 in each case as this resulted in lower errors in k_{DO} values (Table 1). As discussed above for *N*-pentafluorophenyl salt **8a-BF$_4^-$** assuming either extreme of Pathways B or C, values for the constants k_{D2O} (s^{-1}) or k_{DO}' ($M^{-1}s^{-1}$) could be obtained and these are also

included for the salts studied in 2:1 D_2O:CD_3CN in Table 2.

The C(3)-H/D deuterium exchange reaction of the *N*-pentafluorophenyl triazolium salt **15a-BF$_4^-$** in 2:1 D_2O:CD_3CN was too fast to follow by ^{1}H NMR spectroscopy above p*D* 0.06. By contrast, the deuterium exchange reactions of all other triazolium salts in Figure 1 could be followed up to p*D* 3.5. For triazolium salt **15a-BF$_4^-$**, deuterium exchange data were acquired in 1-3 M DCl in 2:1 D_2O:CD_3CN (p*D*s ~ -0.42 – 0.06). The p*D*–rate profile of the values of k_{ex} for the deuterium exchange reaction for triazolium salt **15a-BF$_4^-$** (Figure s83) shows an increase in k_{ex} with p*D* in this range. This increase could either be due to deuteroxide catalysis of C(3)-H/D exchange for the triazolium salt **15a-BF$_4^-$** or the N1-deuterated conjugate acid. A plot of k_{ex} values for salt **15a-BF$_4^-$** against deuteroxide concentration (Figure s82) gave k_{DO}^* ($M^{-1}s^{-1}$) as its slope (Table 1).

Substituent Effects on Kinetic Acidities towards Deuteroxide Ion (k_{DO})

The kinetic acidities towards deprotonation of all triazolium ions by deuteroxide ion *via* Pathway A (k_{DO}, Table 1) are significantly higher than for analogous imidazolium,[22,24] 4,5-dihydroimidazolium[24] and thiazolium ions[27] studied in fully aqueous solution at 25 °C. As one representative comparison, the presence of the additional ring nitrogen increases the k_{DO} value for *N*-mesityl triazolium salt **8e-BF$_4^-$** by 1.3×10^3 and 4.4×10^3-fold, respectively, relative to the values for N,N-dimesitylimidazolium and 4,5-dihydroimidazolium salts **21** and **22** (k_{DO} = 4.08×10^4 $M^{-1}s^{-1}$ and 1.19×10^4 $M^{-1}s^{-1}$)[24]. A better measure of the true effect of the additional ring nitrogen atom can be gleaned by comparison with the k_{DO} value of 3.45×10^2 $M^{-1}s^{-1}$ for 1-mesityl-3-methyl-4-*i*propyl-4,5-dihydroimidazolium iodide **23**,[48] which has alkyl substituents at N(3) and C(4) as for triazolium ion **8e-BF$_4^-$**. The effect of the additional ring nitrogen is to increase k_{DO} by over 1.5×10^5-fold. The mechanism for deuterium exchange *via* Pathway A, involves the uphill deprotonation of the cationic triazolium ion by deuteroxide to give a solvent-equilibrated formally neutral carbene intermediate **7.DOD**. The presence of the additional electron-withdrawing ring nitrogen atom will destabilise the parent triazolium ion relative to the formally neutral transition state, thereby increasing the observed rate constant for exchange.



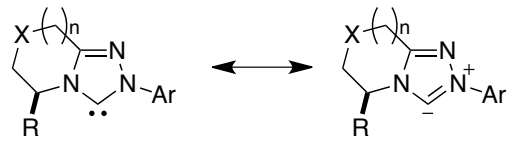
8e-BF$_4$$^-$ **21** **22** **23** **24**

The triazolium salts in Table 1 are also substantially more acidic than any thiazolium salt studied to date under similar reaction conditions, although the latter experiments have been limited to *N*-alkyl substituted examples.[27] We have measured a k_{DO} value of 3.28×10^5 $M^{-1}s^{-1}$ for thiazolium salt **24** (L = H; R_1 = Ph; R_2 = CH_2CH_2OD; X^- = Cl^-) under our experimental conditions in D_2O at 25 °C and I = 1.0 (KCl), which is at least 120-fold smaller than values for any of the triazolium ions in Table 1 (Supporting Information, pS72-S74). Washabaugh and Jencks reported similar k_{DO} values in the range 3.23×10^5 $M^{-1}s^{-1}$ – 2.14×10^6 $M^{-1}s^{-1}$ for the deuterium exchange reactions of a series of thiazolium salts **24** (L = H; R_1 = neutral alkyl or aryl; R_2 = H), in D_2O at 30 °C and I = 2.0 (NaCl).[27]

In contrast with the large 10^5-fold effect of the additional ring nitrogen, the result of varying the N-substituent on k_{DO} values is small. The span of kinetic acidities obtained by comparing k_{DO} values for all triazolium salts in Figure 1 is only 37-fold. The k_{DO} values change by only 16.2-fold across the series **8a-f-BF$_4$$^-$** from the most reactive *N*-pentafluorophenyl- to the least reactive 4-methoxyphenyltriazolium salt.[49] Within this series, our results agree with qualitative experiments by Bode and Mahatthananchai that suggested that the more electron withdrawing *N*-pentafluorophenyl triazolium salts are more acidic than the corresponding *N*-mesityl salts.[45] An even smaller *N*-aryl substituent effect on k_{DO} is observed across the morpholinyl series of triazolium salts **14c-f** in water. All of the series **14c-f** have higher k_{DO} values by 2.4-2.9-fold compared to analogous pyrrolidine-derived salts **8c-f** due to the presence of the electron withdrawing oxygen ring atom in the fused morpholinyl ring, however, the N-aryl substituent effect is less than 2-fold.

Similarly small N-aryl substituent effects were observed on k_{DO} values for the *N*,*N*-diarylimidazolium and 4,5-dihydroimidazolium series.[24] Despite having two *N*-aryl substituents, variation of these substituents (4-chlorophenyl, mesityl, 2,6-di-

*i*propylphenyl, 4-methoxyphenyl) only altered k_{DO} by less than 20-fold. The small effect of the N-aryl substituent in the imidazolium and dihydroimidazolium series was partly ascribed to the difficulty in achieving co-planarity of both aryl rings with the central imidazole or dihydroimidazole, however, this is not likely to be a major contributing factor for the triazolium salts in Figure 1 with just one N-aryl substituent. Alternatively, there could be a change in the nature of the transition state for proton transfer to deuteroxide, from resembling carbene **7** for more electron withdrawing N-aryl substituents to zwitterionic ylide **7'** as the substituent becomes more electron-donating. The alteration of charge density between species **7** and **7'**, depending on the electronic effect of the N-aryl substituent, could reduce the overall observed N-substituent effect.



7 **7'**

The effect of acetonitrile co-solvent on k_{DO} was assessed for triazolium salts **8a-** and **8d-BF$_4^-$**, which were studied both in 100% D_2O, and 2:1 D_2O:CD_3CN. The effect of the addition of acetonitrile co-solvent is a 5.4 fold increase in k_{DO} for **8d-BF$_4^-$** (Table 1). A small 1.2-fold increase is observed for **8a-BF$_4^-$** although the k_{DO} value in 2:1 D_2O:CD_3CN in this case is less accurate due to relatively few data points in the region of the p*D* profile due to Pathway A. Possible explanations for the observed increases in k_{DO} could be the decreased stabilities of the parent triazolium cations and the increased basicity of deuteroxide in the mixed solvent relative to fully aqueous solution.

As mentioned above, the deuterium exchange reaction of the *N*-pentafluorophenyl catalyst **15a-BF$_4^-$** in 2:1 D_2O:CD_3CN was too fast to measure above p*D* 0.06, and the estimated k_{DO}^* value of ~2×10^{13} $M^{-1}s^{-1}$in Table 1 is 25000-fold higher than the k_{DO} value for achiral analogue **8a-BF$_4^-$** in the same solvent. Both of these salts have a *N*-pentafluorophenyl substituent, however, differ by the fused ring systems attached to the central triazole. The value for k_{DO}^* for **15a-BF$_4^-$** is unfeasibly high and clearly exceeds

the bimolecular diffusional limit for small molecules in solution (~ 5×10^9 $M^{-1}s^{-1}$). This outcome is likely because the data for **15a-BF_4^-** is not adequately described by eq 4 alone. Given the small span of k_{DO} values of 37-fold for all other triazolium salts in Figure 1, this large rate enhancement of H/D exchange for **15a-BF_4^-** is surprising. By contrast, the k_{DO} value for the corresponding *N*-phenyl catalyst **15d-BF_4^-** is only 1.9-fold larger than for analogous achiral *N*-phenyl triazolium salt **8d-BF_4^-** in the same solvent and k_{ex} values could be acquired up to p*D* 3.8 in both cases. One possible explanation is a significantly higher pK_a^{N1} for **15a-BF_4^-** with the reaction of N-protonated **15a-BF_4^-** providing a greater contribution to k_{ex} at higher p*D*s than for the other triazolium salts. The N-protonated dicationic triazolium ions are predicted to have greater kinetic acidities towards deprotonation by deuteroxide ion than monocationic analogues (see k_{DO}' values in Table 2 and later discussion). UV-Vis spectrophotometric and NMR spectroscopic attempts at the determination of pK_a^{N1} in 2:1 D_2O:CD_3CN solutions were unsuccessful due to insufficient changes in the spectral data for **15a-BF_4^-** and other salts upon variation of p*D* (see pS113-115 supporting information). A higher pK_a^{N1} for **15a-BF_4^-** seems counter-intuitive as the electron withdrawing N-pentafluorophenyl group would be expected to decrease the basicity of N1. The recent crystal structure of an aza-Breslow intermediate analogue,[50] which was prepared from the *N*-(2,4,6)-tribromophenyl analogue of **15a-BF_4^-** and **15d-BF_4^-**, shows the non-planar orientation of the *N*-tribromophenyl substituent relative to the central triazole with one of the *ortho*-bromine atoms on this ring in close spacial proximity to N1. Protonation at N1 might decrease an unfavourable electrostatic interaction between the lone pair on N1 and those on the *ortho*-halogen atom. This could also be the case for *N*-pentafluorophenyltriazolium salt **15a-BF_4^-** and would account for a higher pK_a for N1-protonation. To the best of our knowledge, crystal structures of **15a-BF_4^-** and **15d-BF_4^-** have not been published.

Our suggestion of an increase in pK_a^{N1} for **15a-BF_4^-** due to the spacial influence of *ortho*-halogen atoms on the N-aryl ring on N1-basicity is supported by the significant difference between the p*D*-profile for **8a-BF_4^-** versus the other triazolium salts **8b-f-BF_4^-** in Figure 1. Of this series of triazolium salts, only the *N*-pentafluorophenyl triazolium salt **8a-BF_4^-** has *ortho*-halogen rather than hydrogen atoms on the *N*-aryl ring. The k_{DO} values for **8a-f-BF_4^-** only differ by 16.2 fold across the series and this reflects the electronic

effect of the *N*-aryl substituent. However, the onset of the altered dependence of log k_{ex} values on p*D* occurs at significantly higher p*D* values for **8a-BF$_4^-$** compared with the other triazolium salts **8b-f-BF$_4^-$**, which is possibly a result of a higher pK_a^{N1} for the former. For example, the onset of the altered dependence on p*D* occurs over 1 p*D* unit higher for *N*-pentafluorophenyl triazolium salt **8a-BF$_4^-$** compared with *N-para*-cyanophenyl salt **8b-BF$_4^-$**, however, their corresponding log k_{DO} values only differ by 0.3 units.

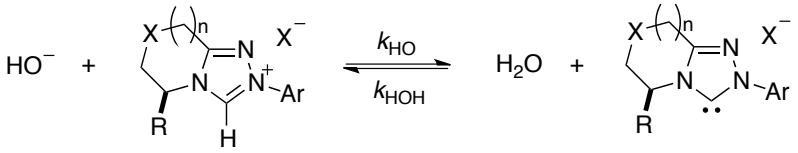
Effect of Counterion on Kinetic Acidities towards Deuteroxide Ion

The effect of a change in counterion on kinetic acidity could be assessed by comparing k_{DO} values for triazolium salt **8d** with two different counterions, X = BF_4^- and Cl^- in fully aqueous solution. A 1.2-fold increase in k_{DO} is observed upon changing from X = Cl^- to BF_4^-, which is just outside of the error range of these measurements. The small effect is unsurprising as the exchange reactions are performed using dilute millimolar solutions of the triazolium salts in a highly ionizing aqueous solvent at saturating ionic strength (I = 1.0 (KCl)). One could suggest different extents of assistance by the two counterions in the deprotonation step. However, general base catalysis by the more basic acetate ion is not significant, which would suggest that similar catalysis by the weakly basic tetrafluoroborate or chloride ions is unlikely in aqueous solution. By contrast, azolium cations and counter anions are known to form hydrogen bonds both in the solid state and in concentrated solutions in non-hydroxylic solvents, which often results in the observation of large anion effects.[51-56] Under the present fully aqueous conditions, hydrogen bonding with solvent clearly outcompetes any interactions between the triazolium cation and counteranion.

Estimation of pK_a

The carbon acid pK_a values for triazolium salts **6** in water may be obtained from the rate constants for deprotonation by hydroxide ion (k_{HO}) and for the reverse protonation of NHC **7** by water (k_{HOH}) according to eq 8 derived for Scheme 3.[22,24] In eq 8, K_w is the equilibrium constant for autoionization of water. Values for k_{HO} ($M^{-1}s^{-1}$) for deprotonation of triazolium ions **6** at C(3) by hydroxide ion can be calculated from

corresponding experimental k_{DO} values for deuteroxide-catalyzed C(3)-H/D exchange *via* Pathway A (Scheme 2).

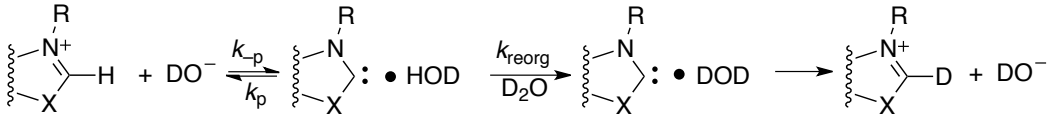


Scheme 3. Ionization of triazolium ion salt **6** at C(3) to yield NHCs **7**.

$$pK_a = pK_w + \log \frac{k_{HOH}}{k_{HO}} \tag{8}$$

Evidence was presented in earlier work by Amyes *et al*[22] and us[24] supporting the hypothesis that the reverse protonation of imidazol-2-ylidenes **2**, imidazolin-2-ylidenes **3** and trihydropyrimidin -2-ylidenes **4** is limited by reorganization of solvent, and occurs with a limiting rate constant of $k_{HOH} = 1 \times 10^{11}$ s^{-1}. The k_{ex} values for deuterium exchange at C(2) of the corresponding imidazolium, 4,5-dihydroimidazolium and trihydropyrimidinium ions were found to be unaltered by an increase in the concentration of acetate, phosphate or quinuclidine buffers at fixed p*D* values in D_2O solution. The absence of detectable general base catalysis of exchange strongly supports the conclusion that solvent reorganization is the rate-limiting step in the overall deuterium exchange mechanism in the presence of deuteroxide, which involves the replacement of the initially formed HOD molecule by a molecule of bulk D_2O *via* dielectric relaxation of solvent (k_{reorg}, Scheme 4). Thus, in the overall mechanism for deuterium exchange, non-rate limiting proton transfer to deuteroxide ion from the imidazolium, 4,5-dihydroimidazolium or trihydropyrimidinium ion is followed by irreversible solvent reorganization due to the large dilution of the molecule of HOD by bulk solvent. In this case, general base catalysis of exchange is not possible because there is no mechanism by which buffer bases can lower the barrier to the physical transport step that limits the exchange of HOD for D_2O. Therefore the microscopic reverse protonation of the corresponding NHCs **2-4** by water is also limited by reorganization of solvent and a limiting rate constant of $k_{HOH} = k_{reorg} = 1 \times 10^{11}$ s^{-1} for the dielectric relaxation of

water[57,58] could be assumed. In related studies, the rate of proton transfer from neat alcohol solvents to singlet diphenylcarbene has been shown by femtosecond transient absorption spectroscopy to be controlled by solvent reorganization.[59]



Scheme 4. Mechanism for deuteroxide-catalyzed azolium ion H/D-exchange.

Washabaugh and Jencks reported rate constants for C(2)-hydron exchange catalyzed by deuteroxide ion for a range of thiazolium ions **24** (L = H, D or T; R_1 = Me, Ph, CN; R_2 = H).[27-29] These reactions showed primary kinetic isotope effects that increase over the range $(k_H/k_T)_{obs}$ = 2.9-14.7 with increasing acidity of the thiazolium ion.[29] These varying primary kinetic isotope effects, and the observation of significant deviations of $(k_D/k_T)_{obs}$ and $(k_H/k_T)_{obs}$ values from the Swain-Schaad relationship, shows that there is significant internal return of the transferred hydron to the thiazolyl carbene from water.[29] This is consistent with an Eigen mechanism[60] for proton transfer (Scheme 4), in which both proton transfer (k_p) and reorganization of the NHC.water complex (k_{reorg}) are partially rate-limiting, and a small intrinsic barrier for proton transfer.[29] The extent of internal return (k_p/k_{reorg} ~ 3.3) was largest for the least acidic thiazolium ion **24** (R_1 = Me; R_2 = H) with $k_{DO} = 4.27 \times 10^5$ $M^{-1}s^{-1}$ and pK_a = 18.9 at 30 °C and ionic strength 2.0 M (NaCl). For the more acidic *N*-cyanomethylthiazolium ion **24** (R_1 = CN; R_2 = H) with $k_{DO} = 4.62 \times 10^7$ $M^{-1}s^{-1}$ and pK_a = 16.9, the internal return ratio decreases to k_p/k_{reorg} ~ 0.3.

For the structurally similar imidazolium, 4,5-dihydroimidazolium and trihydropyrimidinium ions, values of k_{DO} ($M^{-1}s^{-1}$) at 25 °C and ionic strength 1.0 M (KCl) range from 3.92×10^5 $M^{-1}s^{-1}$ to 6.15×10^{-4} $M^{-1}s^{-1}$,[24] which are 1.1 - 6.9 × 10^8 fold smaller than corresponding values for the thiazolium ion **24** (L=H; R_1 = Me; R_2 = H) for which solvent reorganization is largely rate-limiting (k_p/k_{reorg} ~ 3.3). Therefore, relative to their azolium ion ground state, imidazol-2-ylidenes **2**, imidazolin-2-ylidenes **3** and trihydropyrimidin-2-ylidenes **4** should be less stable than the corresponding thiazol-2-ylidenes, and so their protonation by water should be even more limited by the solvent

reorganization step ($k_p >> k_{reorg}$).

The k_{DO} values in Table 1 for triazolium salts **8a-f-BF$_4^-$**, **9-Cl$^-$**, **13-BF$_4^-$**, **14c-f Cl$^-$** and **16-BF$_4^-$** in aqueous solution at 25 °C and ionic strength 1.0 M (KCl) range from 4.20×10^7 $M^{-1}s^{-1}$ to 6.82×10^8 $M^{-1}s^{-1}$, and are no greater than 14.7-fold different from the value determined for the N-cyanomethylthiazolium salt **24** (R_1 = CN; R_2 = H) under similar reaction conditions ($k_{DO} = 4.62 \times 10^7$ $M^{-1}s^{-1}$). For thiazolium ions **24**, the change of N-substituent from methyl to cyanomethyl increases k_{DO} by 109-fold, and the internal return ratio, k_p/k_{reorg}, decreases by 10-fold from 3.3 to 0.3. Therefore, the k_p/k_{reorg} values for triazolium salts **8**, **9a-f**, **10**, **14** and **15c-f** are expected to be the same, or at most 2-fold lower, than for the *N*-cyanomethylthiazolium salt **24** (R_1 = CN; R_2 = H). On this basis, rate constants for protonation of the corresponding triazolylidenes **7** by water should be the same, and no more than ~6-fold lower than, the rate constant for reorganization of solvent ($k_{reorg} = 1 \times 10^{11}$ s^{-1}).

Although the k_p/k_{reorg} ratios clearly illustrate that re-protonation of thiazolylidenes and solvent reorganization occur at similar rates, Washabaugh and Jencks state that the extent of internal return should be interpreted conservatively because the errors are ± 30% or more.[29] For the determination of a pK_a value for *N*-cyanomethylthiazolium salt **24** (R_1 = CN; R_2 = H) using eq 8, these authors have assumed the limiting k_{HOH} value for the protonation of the *N*-cyanomethylthiazolylidene by water.[27] For the determination of triazolium ion pK_as, we have also assumed that the re-protonation of triazolylidenes **7** is limited by reorganization of solvent and that $k_{HOH} = k_{reorg} = 1 \times 10^{11}$ s^{-1}. Furthermore, significant general base catalysis of exchange was not observed for two representative salts **8c-** and **8d-BF$_4^-$**, which have larger k_{DO} values than for the N-cyanomethylthiazolium salt **24** (R_1 = CN; R_2 = H). It was not possible to probe for buffer catalysis of exchange in the case of triazolium salts more acidic than **8c-BF$_4^-$**, as deuterium exchange in acetic acid buffers was too fast to monitor by ^{1}H NMR spectroscopy. The absence of significant general base catalysis of exchange supports the conclusion that re-protonation of triazolylidenes and solvent reorganization occur at the same rate.

For the triazolium salts studied in 2:1 D_2O:CD_3CN, the same value of $k_{HOH} = k_{reorg} = 1 \times 10^{11}$ s^{-1} has been assumed for the reverse protonation of the corresponding NHCs by water. To our knowledge, rate constants for dielectric relaxation of acetonitrile-water mixtures have not been determined to date. The dielectric relaxation of pure acetonitrile is only 2.5-fold slower than water at 25 °C, and added electrolytes have been shown to increase this value by up to 2-fold.[61] As 2:1 D_2O:CD_3CN solutions are largely aqueous, it is reasonable to assume that the rate constant for solvent reorganization by dielectric relaxation of solvent is similar to that in fully aqueous solution.

Values for k_{HO} ($M^{-1}s^{-1}$) for deprotonation of triazolium salts **8-16** at C(3) by hydroxide ion could then be calculated from corresponding k_{DO} values using a secondary solvent isotope effect of $k_{DO}/k_{HO} = 2.4$[62] for proton transfer that is largely limited by solvent reorganization. These k_{HO} values may be combined in eq 8 with the rate constant for the reverse protonation of the NHC by water using $k_{HOH} = 1 \times 10^{11}$ s^{-1}. The resulting pK_a values for all triazolium salts are listed in Table 1 and range from 16.6 – 18.5. For those salts with k_{DO} values ≤ 8.66×10^7 $M^{-1}s^{-1}$ in fully aqueous solution, the value for *N*-(4-fluorophenyl-)-triazolium salt **8c-BF_4^-**, the error in pK_a is ≤ 0.08 units (supporting information pS109-110). General base catalysis of C(3)-H/D-exchange was not significant for **8c-BF_4^-**, which strongly supports the claim that $k_{HOH} = k_{reorg}$ for this and less reactive salts. For salts with k_{DO} values greater than for **8c-BF_4^-**, deuterium exchange reactions in buffers were too fast to enable assessment of the presence/absence of general base catalysis of exchange. As discussed above, in these cases k_{HOH} could be up to ~six-fold lower than k_{reorg} and the true pK_a values could be up to one unit lower than the values quoted in Table 1.

This small span of pK_a values reflects the small substituent effects on kinetic acidities towards deuteroxide ion as the same k_{HOH} value for reprotonation is used in each case. By contrast, the pK_a values for the triazolium salts are 5 units lower than for analogous imidazolium salts, which demonstrates the large influence of the extra ring nitrogen atom on acidity.

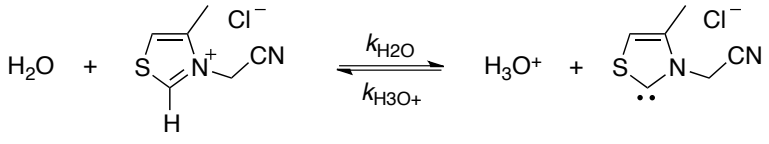
Additional Pathways for Deuterium Exchange

One of the notable effects of the additional ring nitrogen of the triazolium ions **6** is the change in dependence of log k_{ex} values on p*D* as the acidity of the medium is increased. Analogous exchange reactions of the significantly less reactive *N*,*N*-disubstituted imidazolium, dihydroimidazolium and trihydropyrimidinium ions show just a single region in the p*D*–rate profiles, which involves an increase in log k_{ex} with p*D*, and is consistent with deuteroxide-catalyzed exchange *via* Pathway A only. Washabaugh and Jencks observed the onset of a clear p*D*-independent region in the p*D*–rate profile for C(2)-proton exchange of thiazolium salt **24** (L=H; R_1 = 2-methyl-4-aminopyrimidinyl; R_2 = CH_2CH_2OD; X^- = Cl^-) but only in 2-4 M DCl solution at D_0 values less than –1.0.[27] This was ascribed to p*D* independent C(2)-H/D exchange by a mechanism analogous to Pathway B in Scheme 1, and a value of $k_{D2O} = 1.5 \times 10^{-8}$ s^{-1} was estimated. Similarly, the onset of a p*D*-independent region was observed for the 3-cyanomethyl-4-methylthiazolium salt **24** (R_1 = cyano; R_2 = H; X^- = Cl^-) in 0.8-2.7 M DCl yielding $k_{D2O} = 9.4 \times 10^{-8}$ s^{-1}.[28] Further decreases in log k_{ex} values for this salt were observed in DCl solutions of greater than 5 M and this was ascribed to modest acid inhibition of ionization in strong acid media because of acidity function effects.[28] The large increase in the activity of hydronium ion in strong acid solutions (> 1 M) would be expected to shift the equilibrium in Scheme 5 to the left.

The continued decrease in the log k_{ex} data for **8a-BF_4^-** in aqueous solution at lower p*D* values is not likely due to acidity function effects as these measurements were conducted in more dilute DCl solutions (< 1M DCl). Furthermore, such acid inhibition effects would be expected to be similar for the closely related thiazolium and triazolium carbon acids and further decreases in log k_{ex} values are only observed for DCl concentrations greater than 5 M in the former case.

Washabaugh and Jencks calculated a pK_a value of 16.9 for the 3-cyanomethyl-4-methylthiazolium salt **24** (L = H; R_1 = cyano; R_2 = H; X^- = Cl^-) in aqueous solution at 30 °C by application of eq 8 using $k_{DO} = 4.68 \times 10^7$ $M^{-1}s^{-1}$, k_{DO}/k_{HO} = 2.4, and by assuming reprotonation of the thiazolyl carbene is at the diffusional limit.[27] Using the p*D*-

independent value of k_{D2O} = 9.4 × 10^{-8} s^{-1}, they obtained the same pK_a value by application of eq 9, derived for Scheme 5, using an experimental value of k_{H2O}/k_{D2O} = 2.6 and by assuming that reprotonation of the thiazolyl carbene by hydronium ion is also diffusion controlled (k_{H3O+} = 2 × 10^{10} $M^{-1}s^{-1}$).[27] The excellent agreement obtained using two different kinetic estimations of pK_a strongly supports the assignment of the p*D*-independent region to a mechanism analogous to Pathway B (Scheme 2).



24

(L = H; R_1=CN; R_2=H; X=Cl)

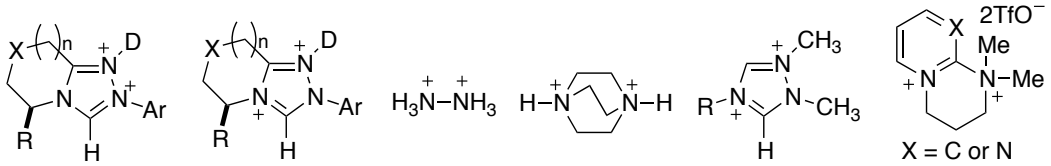
Scheme 5. Ionization of thiazolium salts **24** at C(2) to yield corresponding thiazolyl carbenes.

$$pK_a = -\log \frac{k_{H2O}}{k_{H3O+}} \qquad (9)$$

By contrast the C(3)-carbon acid pK_a value in aqueous solution calculated for the triazolium salt **8a-BF_4^-** obtained by application of eq 9 using the k_{D2O} value in Table 2, with the same assumptions as Washabaugh and Jencks, is 2.5 units lower than when estimated using eq 8. Similar decreases of 12.6-3.3 units in C(3)-carbon acid pK_a values calculated using eq 8 and 9 are obtained for the other salts listed in Table 2, and these differences are most likely due to over-estimation of k_{D2O} values. As the p*D*-rate profiles do not become p*D*-independent for any of the triazolium ions, the fitting of data to eq 6 will likely over-estimate the k_{D2O} values, resulting in subsequent under-estimation of the C(3)-carbon acid pK_as. In addition, as full N(1)-protonation is not observed, which would be evident from the levelling of log k_{ex} values at higher acid concentrations, the errors in the K_a^{N1} values in Table 2 from the fits to eq 6/7 are relatively high (up to ± 50%). These relatively large errors in the K_a^{N1} values will also influence the magnitude of the k_{D2O} value. Further support of k_{D2O} overestimation comes from a comparison of deuterium exchange data for the *N*-pentafluorophenyltriazolium salt **8a-BF_4^-** (Tables 1

and 2) and the 3-cyanomethyl-4-methylthiazolium salt **24** (R_1 = cyano; R_2 = H; X = Cl^-) studied by Washabaugh and Jencks. The k_{DO} value for **8a-BF$_4^-$** is higher by 14.7-fold than the corresponding value for the thiazolium salt **24** whereas the calculated k_{D2O} value is higher by over 5000-fold. Although the anomalously large k_{D2O} values could be a result of unavoidable error in the fitting to eq 6, one could also surmise that these observations infer that Pathway B is not significant and Pathway C instead dominates.

As mentioned previously, the appearance of the p*D*-rate profile for triazolium salt **8a-BF$_4^-$** at lower p*D* values requires that protonation at N(1) occurs. If protonation at N(1) did not occur then either the log k_{ex} data would continue to linearly decrease at lower p*D*s for exchange *via* Pathway A or levelling would occur for exchange *via* Pathway B as was observed for thiazolium ions **24**. Protonation at N(1) and the combination of one, or both, of Pathways B and C are required to explain the kinetic data. The fitting of log k_{ex} – p*D* data for triazolium salt **8a-BF$_4^-$** to eq 6 or 7 yields an estimate of pK_a^{N1} ~ -0.2. Fitting of data for the other triazolium salts **10-12-BF$_4^-$**, **14b-Cl$^-$,** and **15d-BF$_4^-$** yields similar pK_a^{N1} values in the range -0.2-0.5. There is no available literature pK_a value for the dicationic parent triazolium ion in water, however, aqueous pK_a values of -1 and 2.21, respectively, have been determined for the dicationic hydrazinium ion **25**[63] and DABCO-2H$^+$ **26**[64], which bracket the values determined in this work. The charge separation in triazolium ion **18**, when drawn alternatively as **18'**, is similar to diprotonated-DABCO **26**, although the former involves protonation at sp^2 rather than sp^3nitrogen. Furthermore, there have been two literature reports of the syntheses and spectral characterisation of trialkylated triazolium ions **27** (R = Me or ^{i}Pr)[65,66] with triflate or tetrafluoroborate counterions, which also support the existence of dicationic triazolium ions **18**/**18'** under acidic conditions. Dicationic amidinium ions **28** have been prepared by Murphy and co-workers, which proved to be more reactive as methylating agents than dimethylsulfate.[67] Furthermore, recent work by Keitz *et al* implicates Brønsted acid protonation of the unsubstituted triazole nitrogen of a 1,2,3-triazolylidene bound to a ruthenium catalyst in the protonolysis of the Ru-carbene bond in the generation of the metathesis-active species.[68]



18 **18'** **25** **26** **27** **28**

Table 2 additionally includes estimates of second order rate constants, k_{DO}' ($M^{-1}s^{-1}$) for deuteroxide-catalyzed exchange of the C(3)-H of N-protonated triazolium ions **8a-BF_4^-**, **10-12-BF_4^-**, **14b-Cl^-**, and **15d-BF_4^-** obtained by fitting the log k_{ex} – pD data for the relevant salts to eq 7 with the assumption that only Pathways A and C occur. Bimolecular diffusion of small molecules in solution has an associated rate constant of $k_d = 5 \times 10^9$ $M^{-1}s^{-1}$, and in the case of facilitated diffusion, as observed for hydronium ion, $k_d = 2 \times 10^{10}$ $M^{-1}s^{-1}$. In general, bimolecular rate constants should not exceed these diffusional limits. The k_{DO}' value estimated for triazolium salt **8a-BF_4^-** is just greater than these limits, however, allowing for the errors in both k_{DO}' and K_a^{N1} could be considered as diffusion-limited. This observation is not unreasonable as the dicationic salts would be expected to have similar or greater kinetic acidities than monocationic analogues which have k_{DO} values in the range 10^7-10^8 $M^{-1}s^{-1}$ in aqueous solution. All except one of the other estimated k_{DO}' values in Table 2 for **10-12-BF_4^-**, **14b-Cl^-**, and **15d-BF_4^-** studied in 2:1 D_2O:CD_3CN are significantly greater than the limiting diffusional rate constant and cannot be rationalized as diffusion-limited within errors arising from the fitting process. Thus, the occurrence of Pathway C can clearly be excluded for these salts studied in 2:1 D_2O:CD_3CN, however is still a possibility for **8a-BF_4^-**.

Using the estimated k_{DO}' value for **8a-BF_4^-** in Table 2 obtained with the assumption that only Pathways A and C occur, and, by application of eq 8 as described above, a C(3)-H carbon acid pK_a value of 14.9 may be predicted for the N(1)-protonated dicationic triazolium ion **8a-BF_4^-**. This predicted value is lower by 1.7 units than the corresponding carbon acid pK_a in Table 1 for the monocationic triazolium ion in aqueous solution. Thus, the predicted kinetic and thermodynamic acidities of the dicationic triazolium precursors **18** to monocationic NHCs **19** are the highest observed to date compared to other NHC families **1-5**.

In conclusion, studies of the proton transfer reactions of a range of triazolyl carbenes indicate that triazolium precatalysts are more acidic by 5 p*K* units than analogous imidazolium and 4,5-dihydroimidazolium architectures. Our results show that the incorporation of electron withdrawing N-aryl substituents on the triazolium ring, and an electronegative oxygen atom within the fused ring, increase the kinetic acidity (k_{DO}) and decrease the pK_a. The presence of the additional ring nitrogen atom in triazolium ions compared with imidazolium and thiazolium counterparts results in an altered dependence of first order rate constants for deuterium exchange on p*D* under acidic conditions. The data requires that protonation at N(1) occurs to give *dicationic triazolium ions* at lower p*D* values with estimates of pK_a^{N1} = -0.2-0.5. Our results suggest that the presence of an *ortho*-halogen on the N-aryl substituent could potentially increase pK_a^{N1} and work in our laboratories is focused on acquiring additional proof of this hypothesis. Assuming the occurrence of deuteroxide catalyzed exchange for these N-protonated dicationic triazolium ions, we have also estimated C(3)-H pK_a values that are at least 2 units lower than for the non-protonated monocationic analogues. Work from our laboratories is also directed toward the implications of these more acidic dicationic triazolium species in catalysis, and their use in the possible extension of NHC-mediated transformations.

References

(1) Alder, R. W.; Blake, M. E.; Chaker, L.; Harvey, J. N.; Paolini, F.; Schutz, J. *Angew. Chem. Int. Ed.* **2004**, *43*, 5896.
(2) Arduengo, A. J. *Acc. Chem. Res.* **1999**, *32*, 913.
(3) Bourissou, D.; Guerret, O.; Gabbai, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39.
(4) de Fremont, P.; Marion, N.; Nolan, S. P. *Coord. Chem. Rev.* **2009**, *253*, 862.
(5) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606.
(6) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117.
(7) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290.
(8) Kirmse, W. *Angew. Chem. Int. Ed.* **2004**, *43*, 1767.
(9) Kuhl, O. *Chem. Soc. Rev.* **2007**, *36*, 592.
(10) Marion, N.; Diez-Gonzalez, S.; Nolan, S. P. *Angew. Chem. Int. Ed.* **2007**, *46*, 2988.
(11) Perry, M. C.; Burgess, K. *Tetrahedron-Asymmetry* **2003**, *14*, 951.
(12) Vignolle, J.; Cattoen, X.; Bourissou, D. *Chem. Rev.* **2009**, *109*, 3333.
(13) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.

(14) Campbell, C. D.; Duguet, N.; Gallagher, K. A.; Thomson, J. E.; Lindsay, A. G.; O'Donoghue, A. C.; Smith, A. D. *Chem. Commun.* **2008**, 3528.
(15) Glorius, F.; Hirano, K. In *Organocatalysis* 2008; Vol. 2, p 159.
(16) For reviews see: (a) Nair, V.; Vellalath, S.; Babu B. P. *Chem. Soc. Rev.* **2008**, *37*, 2691. (b) Nair, V.; Menon, R. S.; Biju, A. T.; Sinu, C. R.; Paul, R. R.; Jose, A.; Sreekumar, V. *Chem. Soc. Rev.* **2011**, *40*, 5336. For selected examples see: (a) Burstein, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205. (b) Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370. (c) Chan, A.; Scheidt, K. A. *Org. Lett.* **2005**, *7*, 905. (d) He, M.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3131. (e) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2007**, *129*, 5334. (f) Phillips, E. M.; Reynolds, T. E.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2416. (g) Chan, A.; Scheidt, K. A. *J. Am. Chem. Soc.* **2008**, *130*, 2740. (h) Rommel, M.; Fukuzumi, T.; Bode, J. W. *J. Am. Chem. Soc.* **2008**, *130*, 17266. (i) Liu, Q.; Rovis, T. *Org. Lett.* **2009**, *11*, 2856. For the use of α'-hydroxyenones as α,β-unsaturated aldehyde surrogates see Chiang, P.-C.; Rommel, M.; Bode, J. W. *J. Am. Chem. Soc.* **2009**, *131*, 8714.
(17) For selected examples see: (a) Zhang, Y. R.; He, L.; Wu, X.; Shao, P. L.; Ye, S. *Org. Lett.* **2008**, *10*, 277. (b) Lv, H.; Zhang, Y.-R.; Huang, X.-L.; Ye, S. *Adv. Synth. Catal.* **2008**, *350*, 2715. (c) He, L.; Lv, H.; Zhang, Y.-R.; Ye, S. *J. Org. Chem.* **2008**, *73*, 8101. (d) Zhang, Y.-R.; Lv, H.; Zhou, D.; Ye, S. *Chem. Eur. J.* **2008**, *14*, 8473. (e) Wang, X-N.; Shao, P-L.; Lv, H.; Ye, S. *Org. Lett.* **2009**, *11*, 4029. (f) Huang, X.-L.; He, L.; Shao, L. P.-L.; Ye, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 192. (g) Lv, H.; You L.; Ye, S. *Adv. Synth. Catal.* **2009**, *351*, 2822. (h) Wang, X.-N. Lv, H. Huang, X.-L. Ye, S. *Org. Biomol. Chem.* **2009**, *7*, 346. (i) Lv, H.; Chen, X.-Y.; Sun, L.-H.; Ye, S. *J. Org. Chem.* **2010**, *75*, 6973. (j) Shao, P.-L.; Chen, X.-Y.; Ye, S. *Angew. Chem., Int. Ed.* **2010**, *49*, 8412. (k) Duguet, N.; Campbell, C. D.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2008**, *6*, 1108; (l) Concellón, C.; Duguet, N.; Smith, A. D. *Adv. Synth. Cat.* **2009**, *351*, 3001. (m) Duguet, N.; Donaldson, A.; Leckie, S. M.; Douglas, J.; Shapland, P.; Brown, T. B.; Churchill, G.; Slawin, A. M. Z.; Smith, A. D. *Tetrahedron: Asymmetry*, **2010**, *21*, 582. (n) Duguet, N.; Donaldson, A.; Leckie, S. M.; Kallström, E. A.; Campbell, C. D.; Shapland, P.; Brown, T. B.; Slawin, A. M. Z.; Smith, A. D. *Tetrahedron: Asymmetry*, **2010**, *21*, 601. (o) Douglas, J.; Ling, K.; Concellon, C.; Slawin, A. M. Z.; Churchill, G.; Smith, A. D. *Eur. J. Org. Chem.*, **2010**, 5863. (p) Reynolds, J. T.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 16406. (q) Vora, H. U.; Rovis, T. *J. Am. Chem. Soc.* **2010**, *132*, 2860. (r) He, M.; Uc, G. J.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 15088. (s) Kaeobamrung, J.; Kozlowski, M. C.; Bode, J. W. *Proc. Nat. Acad. Sci.* **2010**, *107*, 20661. (t) Kobayashi, S.; Kinoshita, T.; Uehara, H.; Sudo, T.; Ryu, I. *Org. Lett.* **2009**, *11*, 3934. (u) Kawanaka, Y.; Phillips, E. M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 18028. (v) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418. (w) Phillips, E. M.; Wadamoto, M.; Chan, A.; Scheidt, K. A. *Angew. Chem. Int. Ed.* **2007**, *46*, 3107. (x) Li, Y.; Wang, X-Q.; Zheng, C.; You, S-L.

Chem. Commun. **2009**, 5823. (y) Lv, H.; Mo, J.; Fang, X.; Chi, Y. R. *Org. Lett.* **2011**, *13*, 5366. (z) Ling, K. B.; Smith, A. D. *Chem. Commun.* **2011**, *47*, 373.

(18) For selected examples see: (a) Bakhtiar, C.; Smith, E. H. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 239. (b) Grasa, G. A.; Kissling, R. M.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 3583. (c) Grasa, G. A.; Güveli, T.; Singh, R.; Nolan, S. P. *J. Org. Chem.* **2003**, *68*, 2812. (d) Connor, E. F.; Nyce, G. W.; Myers, M.; Möck, A.; Hedrick, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 914. (e) Nyce, G. W.; Lamboy, J. A.; Connor, E. F.; Waymouth, R. M.; Hedrick, J. L. *Org. Lett.* **2002**, *4*, 3587. (f) Nyce, G. W.; Glauser, T.; Connor, E. F.; Möck, A.; Waymouth, R. M.; Hedrick, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 3046. (g) Suzuki, Y.; Yamauchi, K.; Muramatsu, K.; Sato, M. *Chem. Commun*. **2004**, 2770. (h) Kano, T.; Sasaki, K.; Maruoka, K. *Org. Lett.* **2005**, *7*, 1347. (i) Suzuki, Y.; Muramatsu, K.; Yamauchi, K.; Morie, Y.; Sato, M. *Tetrahedron* **2006**, *62*, 302. (j) Movassaghi, M.; Schmidt, M. A. *Org. Lett*. **2005**, *7*, 2453. (k) Schmidt, M. A.; Müller, P.; Movassaghi, M. *Tetrahedron Lett*. **2008**, *49*, 4316. (l) Thomson, J. E.; Rix, K.; Smith, A. D. *Org. Lett*. **2006**, *8*, 3785. (m) Thomson, J. E.; Campbell, C. D.; Concellón, C.; Duguet, N.; Rix, K.; Slawin, A. M. Z.; Smith, A. D. *J. Org. Chem.* **2008**, *73*, 2784. (n) Thomson, J. E.; Kyle, A. F.; Concellón, C.; Gallagher, K. A.; Lenden, P.; Morrill, L. C.; Miller, A. J.; Joannesse, C.; Slawin, A. M. Z.; Smith, A. D. *Synthesis*, **2008**, *40*, 2805. (o) Thomson, J. E.; Kyle, A. F.; Ling, K. B.; Smith, S. R.; Slawin, A. M. Z.; Smith, A. D. *Tetrahedron*, **2010**, *66*, 3801. (p) Campbell, C. D.; Collett, C. J.; Thomson, J. E.; Slawin, A. M. Z.; Smith, A. D. *Org. Biomol. Chem.* **2011**, *9*, 4205. (q) Campbell, C. D.; Concellón, C.; Smith, A. D. *Tetrahedron: Asymmetry*, **2011**, *22*, 797. (r) Smith, A. D. *Synthesis*, **2012**, *44*, 1182. (s) Rovis, T. *Adv. Synth. Cat.* **2012**, *354*, 1617.

(19) For selected examples see: (a) Ryan, S. J.; Candish, L.; Lupton, D. W. *J. Am. Chem. Soc.* **2009**, *131*, 14176. (b) Mahatthananchai, J.; Zheng, P.; Bode, J. W. *Angew. Chem. Int. Ed.* **2011**, *50*, 1673. (c) Zhu, Z.-Q.; Xiao J.-C. *Adv. Synth. Catal.* **2010**, *352*, 2455. (d) De Sarkar, S.; Studer, A. *Angew. Chem. Int. Ed.* **2010**, *49*, 9266. (e) Guin, J.; De Sarkar, S.; Grimme, S.; Studer, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 8727. (f) Rong, Z.-Q.; Jia, M.-Q.; You, S.-L. *Org. Lett.* **2011**, *13*, 4080. (g) Zhu, Z.-Q.; Zheng, X.-L.; Jiang, N.-F.; Wang, X.; Xiao, J.-C. *Chem. Commun.* **2011**, *47*, 8670.

(20) Limited examples of NHC-catalysed processes proceeding without added base have been reported. See: (a) Ciganek, E. *Synthesis*, **1995**, 1311. (b) Kaeobamrung, J.; Mahatthananchai, J.; Zheng, P.; Bode, J. W. *J. Am. Chem. Soc.* **2010**, *132*, 8810. (c) Zhu, Z.-Q.; Zheng, X.-L.; Jiang, N.-F.; Wang, X.; Xiao, J.-C. *Chem. Commun*. **2011**, *47*, 8670.

(21) Alder, R. W.; Allen, P. R.; Williams, S. J. *Chem. Commun.* **1995**, 1267.

(22) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Toth, K. *J. Am. Chem. Soc.* **2004**, *126*, 4366.

(23) Chu, Y.; Deng, H.; Cheng, J. P. *J. Org. Chem.* **2007**, *72*, 7790.

(24) Higgins, E. M.; Sherwood, J. A.; Lindsay, A. G.; Armstrong, J.; Massey, R. S.; Alder, R. W.; O'Donoghue, A. C. *Chem. Commun.* **2011**, *47*, 1559.
(25) Kim, Y. J.; Streitwieser, A. *J. Am. Chem. Soc.* **2002**, *124*, 5757.
(26) Magill, A. M.; Cavell, K. J.; Yates, B. F. *J. Am. Chem. Soc.* **2004**, *126*, 8717.
(27) Washabaugh, M. W.; Jencks, W. P. *Biochemistry* **1988**, *27*, 5044.
(28) Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 674.
(29) Washabaugh, M. W.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 683.
(30) Bordwell, F. G.; Satish, A. V. *J. Am. Chem. Soc.* **1991**, *113*, 985.
(31) Guthrie, J. P.; O'Ferrall, R. A. M.; O'Donoghue, A. C.; Waghorne, W. E.; Zrinski, I. *J. Phys. Org. Chem.* **2003**, *16*, 582.
(32) Pezacki, J. P. *Can. J. Chem.* **1999**, *77*, 1230.
(33) Maji, B.; Breugst, M.; Mayr, H. *Angew. Chem. Int. Ed.* **2011**, *50*, 6915.
(34) Bouffard, J.; Keitz, B. K.; Tonner, R.; Guisado-Barrios, G.; Frenking, G.; Grubbs, R. H.; Bertrand, G. *Organometallics* **2011**, *30*, 2617.
(35) Gronert, S.; Keeffe, J. R.; O'Ferrall, R. A. M. *J. Org. Chem.* **2009**, *74*, 5250.
(36) Gronert, S.; Keeffe, J. R.; O'Ferrall, R. A. M. *J. Am. Chem. Soc.* **2011**, *133*, 3381.
(37) Kassaee, M. Z.; Shakib, F. A.; Momeni, M. R.; Ghambarian, M.; Musavi, S. M. *J. Org. Chem.* **2010**, *75*, 2539.
(38) Lai, C. L.; Guo, W. H.; Lee, M. T.; Hu, C. H. *J. Organomet. Chem.* **2005**, *690*, 5867.
(39) Lee, M. T.; Hu, C. H. *Organometallics* **2004**, *23*, 976.
(40) Lo, R.; Ganguly, B. *Chem. Commun.* **2011**, *47*, 7395.
(41) Tian, Z. X.; Kass, S. R. *Int. J. Mass Spec.* **2007**, *267*, 288.
(42) Huber, S. M.; Heinemann, F. W.; Audebert, P.; Weiss, R. *Chem. Eur. J.* **2011**, *17*, 13078.
(43) For select examples see: (a) Kerr, M. S.; Read de Alaniz, J.; Rovis, T. *J. Org. Chem.* **2005**, *70*, 5725. (b) Kerr, M. S.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 8876. (c) Baragwanath, L.; Rose, C. A.; Zeitler, K.; Connon S. J. *J. Org. Chem.* **2009**, *74*, 9214. For the effect of different aryl substituents on triazolium salts for the intramolecular Stetter reaction see Rovis, T. *Chem. Lett.* **2008**, *37*, 2.
(44) For select examples see: (a) Sohn, S. S.; Bode, J. W. *Org. Lett.* **2005**, *7*, 3873. (b) He, M.; Struble, J. R.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 8418. (c) Struble, J. R.; Bode, J. W. *Org. Synth.*, **2010**, *87*, 362.
(45) Mahatthananchai, J.; Bode, J. W. *Chem. Sci.* **2012**, *3*, 192.
(46) Covington, A. K.; Robinson, R. A.; Bates, R. G. *J. Phys. Chem.* **1966**, *70*, 3820.
(47) We are assuming that N1 is the atom of highest proton affinity on the monocationic 1,2,4-triazolium salt. Previous density functional calculations for 1,2,3-triazolylidenes, referred to as mesionic carbenes, showed N2 to have the second highest proton affinity after the carbene itself (See ref. 34).
(48) Higgins, E. M.; Ph. D thesis; Durham University.

(49) The standard error in k_{DO} values obtained from fitting to eq 3 or 6/7 ranged from 2-8%. Any pair of k_{DO} values for two different triazolium salts in Table 1 that differ by greater than 1.1-fold may be regarded as different, when comparing values obtained by fitting to eq 3 or 6/7.
(50) DiRocco, D. A.; Oberg, K. M.; Rovis, T. *J. Am. Chem. Soc.* **2012**, *134*, 6143.
(51) Abdulsada, A. K.; Greenway, A. M.; Hitchcock, P. B.; Mohammed, T. J.; Seddon, K. R.; Zora, J. A. *J. Chem. Soc. Chem. Commun.* **1986**, 1753.
(52) Fannin, A. A.; King, L. A.; Levisky, J. A.; Wilkes, J. S. *J. Phys. Chem.* **1984**, *88*, 2609.
(53) Grasa, G. A.; Singh, R.; Scott, N. M.; Stevens, E. D.; Nolan, S. P. *Chem. Commun.* **2004**, 2890.
(54) Headley, A. D.; Jackson, N. M. *J. Phys. Org. Chem.* **2002**, *15*, 52.
(55) Holloczki, O.; Gerhard, D.; Massone, K.; Szarvas, L.; Nemeth, B.; Veszpremi, T.; Nyulaszi, L. *New J. Chem.* **2010**, *34*, 3004.
(56) Wei, S. P.; Wei, X. G.; Su, X. Y.; You, J. S.; Ren, Y. *Chem. Eur. J.* **2011**, *17*, 5965.
(57) Kaatze, U. *J. Chem. Eng. Data* **1989**, *34*, 371.
(58) Kaatze, U.; Pottel, R.; Schumacher, A. *J. Phys. Chem.* **1992**, *96*, 6017.
(59) Peon, J.; Polshakov, D.; Kohler, B. *J. Am. Chem. Soc.* **2002**, *124*, 6428.
(60) Eigen, M. *Angew. Chem. Int. Ed.* **1964**, *3*, 1.
(61) Barthel, J.; Kleebauer, M.; Buchner, R. *J. Soln. Chem.* **1995**, *24*, 1.
(62) Kresge, A. J.; More O'Ferrall, R. A.; Powell, M. F. In *Isotopes in Organic Chemistry*; Buncel, E., Lee, C. C., Eds.; Elsevier: New York, 1987; Vol. 7.
(63) Fersht, A. *Structure and Mechanism in Protein Science: Guide to Enzyme Catalysis and Protein Folding*; 3rd ed. New York, 1999.
(64) Paoletti, P.; Stern, J. H.; Vacca, A. *J. Phys. Chem.* **1965**, *69*, 3759.
(65) Curphey, T. J.; Prasad, K. S. *J. Org. Chem.* **1972**, *37*, 2259.
(66) Guerret, O.; Sole, S.; Gornitzka, H.; Trinquier, G.; Bertrand, G. *J. Organomet. Chem.* **2000**, *600*, 112.
(67) Corr, M. J.; Roydhouse, M. D.; Gibson, K. F.; Zhou, S. Z.; Kennedy, A. R.; Murphy, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 17980.
(68) Keitz, B. K.; Bouffard, J.; Bertrand, G.; Grubbs, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 8498.

Table 1 Second order rate constants for deuteroxide-catalysed exchange, k_{DO} ($M^{-1}s^{-1}$), and carbon acid pK_a values for triazolium salts **8-16-X**$^-$ in aqueous solution at 25°C and ionic strength, I = 1.0 (KCl).

Salt	k_{DO} ($M^{-1}s^{-1}$)	pK_a[d]	Salt	k_{DO} ($M^{-1}s^{-1}$)	pK_a[d]
8a-BF_4^-	$6.82 (\pm 0.25) \times 10^8$ [b] $7.95 (\pm 1.25) \times 10^8$ [b,c]	16.6 17.3 [c]	**12-BF_4^-**	$4.81 (\pm 0.22) \times 10^8$ [b,c]	17.5 [c]
8b-BF_4^-	$3.18 (\pm 0.08) \times 10^8$ [a]	16.9	**13-Cl^-**	$2.53 (\pm 0.12) \times 10^8$ [a]	17.0
8c-BF_4^-	$8.66 (\pm 0.11) \times 10^7$ [a]	17.4	**14b-Cl^-**	$1.36 (\pm 0.17) \times 10^9$ [b,c]	17.1 [c]
8d-BF_4^-	$6.82 (\pm 0.13) \times 10^7$ [a] $3.70 (\pm 0.15) \times 10^8$ [a,c]	17.6 17.6 [c]	**14c-Cl^-**	$2.17 (\pm 0.13) \times 10^8$ [a]	17.0
8d-Cl^-	$5.84 (\pm 0.20) \times 10^7$ [a]	17.6	**14d-Cl^-**	$1.59 (\pm 0.08) \times 10^8$ [a]	17.2
8e-BF_4^-	$5.29 (\pm 0.07) \times 10^7$ [a]	17.7	**14e-Cl^-**	$1.62 (\pm 0.06) \times 10^8$ [a]	17.2
8f-BF_4^-	$4.20 (\pm 0.23) \times 10^7$ [a]	17.8	**14f-Cl^-**	$1.22 (\pm 0.09) \times 10^8$ [a]	17.3
9-Cl^-	$7.05 (\pm 0.25) \times 10^7$ [a]	17.5	**15a-BF_4^-**	$1.95 (\pm 0.10) \times 10^{13}$ [e,c]	
10-Cl^-	$5.38 (\pm 0.60) \times 10^7$ [b,c]	18.5 [c]	**15d-BF_4^-**	$7.10 (\pm 0.47) \times 10^8$ [b,c]	17.4 [c]
11-BF_4^-	$7.05 (\pm 0.63) \times 10^8$ [b,c]	17.4 [c]	**16-BF_4^-**	$3.61 (\pm 0.16) \times 10^8$ [a]	16.8

[a]Values of k_{DO} ($M^{-1}s^{-1}$) obtained by fitting log k_{ex} – pD data to eq 3. [b]Values of k_{DO} ($M^{-1}s^{-1}$) obtained by fitting log k_{ex} – pD data to eq 6 or eq 7. [c]Deuterium exchange data acquired in 2:1 D_2O:CD_3CN. [d]pK_a values obtained by application of eq 8 as described in the text using k_{DO} values obtained from fitting log k_{ex} – pD data to either eq 3 or eq 6/7. [e]Value of k_{DO}* ($M^{-1}s^{-1}$) obtained as slope of second order plot of k_{ex} (s^{-1}) against deuteroxide concentration.

Table 2 Kinetic analysis of deuterium exchange data for triazolium salts showing an altered dependence on p*D* in aqueous solution at 25 °C and ionic strength, I = 1.0 (KCl).

Salt	K_a^{N1} (M)[c]	k_{D2O} (s^{-1})[d]	k_{DO}' ($M^{-1}s^{-1}$)[e]
8a-BF_4^-[a]	1.5 (± 0.4)	6.1×10^{-5} (± 3.6×10^{-6})	3.3×10^{10} (± 2.0×10^{9})
8a-BF_4^-[b]	0.5 (± 0.1)	1.4×10^{-4} (± 5.9×10^{-6})	1.1×10^{12} (± 4.5×10^{10})
10-Cl^-[b]	0.6 (± 0.3)	9.2×10^{-7} (± 1.7×10^{-7})	7.0×10^{9} (± 1.3×10^{9})
11-BF_4^-[b]	0.6 (± 0.2)	5.6×10^{-5} (± 3.4×10^{-6})	4.3×10^{11} (± 2.6×10^{10})
12-BF_4^-[b]	0.4 (± 0.1)	9.3×10^{-6} (± 6.3×10^{-7})	7.1×10^{10} (± 4.8×10^{9})
14b-Cl^-[b]	0.5 (± 0.1)	6.8×10^{-5} (± 5.0×10^{-6})	5.2×10^{11} (± 3.8×10^{10})
15d-BF_4^-[b]	0.3 (± 0.1)	2.1×10^{-5} (± 1.8×10^{-6})	1.6×10^{11} (± 1.4×10^{10})

[a]Deuterium exchange data acquired in D_2O. [b]Deuterium exchange data acquired in 2:1 D_2O:CD_3CN. [c]Values of K_a^{N1} (M) obtained by fitting log k_{ex} – p*D* data to eq 6 or eq 7. [d]Values of k_{D2O} (s^{-1}) obtained by fitting log k_{ex} – p*D* data to eq 6. [e]Values of k_{DO}' ($M^{-1}s^{-1}$) obtained by fitting log k_{ex} – p*D* data to eq 7.