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The pK_a values of *N*-aryl imidazolinium salts, their higher homologues, and formamidinium salts in dimethyl sulfoxide†

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A series of imidazolinium salts, their six-, seven- and eight-membered homologues, and the related formamidinium salts were prepared, and their pK_a values were determined in DMSO at 25 °C using the bracketing indicator method. The effect of each type of structural variation on the acidity of each salt was considered, particularly noting the importance of ring size and the effect of the steric and electronic nature of the *N*-aryl substituents. The effect of a cyclic structure was also probed through comparing the cyclic systems with the corresponding formamidinium salts, noting the importance of conformational flexibility in the latter cases. Along with allowing choice of appropriate bases for deprotonation of these species, it is anticipated that the data presented will aid in the understanding of the nucleophilicity, and potentially catalytic efficacy, of the corresponding carbenes.

Introduction

Much interest has surrounded the use of *N*-heterocyclic carbenes (NHCs) as organocatalysts due to the wide range of reactions catalysed by these systems.[1–7] Within this grouping, systems with saturated backbones have been comparably less studied than their unsaturated counterparts, with the imidazolinium salts being the most common precursors.[4] These systems have the potential for incorporating chiral centres, both in the heterocyclic ring[8,9] along with on the *N*-substituents,[10] and hence the generation of enantioselective catalysts.

There is currently little understanding of the relative efficacy of, for example, imidazolinylidines and imidazolylidenes as organocatalysts (for example, it is noted for the synthesis of butenolides by She *et al.*[11] that it is unusual that the imidazolinylidine is the most effective catalyst). In contrast to the work on other NHCs, studies towards understanding the catalytic ability of these systems are more limited, with the work of Berkessel[12,13] and Mayr[14] on isolating and studying the reactivity, respectively, of the Breslow intermediate being notable.

NHCs are typically generated *in situ* by deprotonation of the parent azolium salts. As a result, the pK_a values of the corresponding azolium salts can be used to understand the extent to which the salt would be deprotonated by a given base,[15] but also the nucleophilicity of the carbene given the Brønsted relationship.[16] The latter point is particularly relevant given the predominance of carbenes acting as nucleophiles in organocatalysis and the fact that the nucleophilicity parameters of only seven NHCs, including only one imidazolinylidine, have been reported.[17,18]

The acidities of a wide range of azolium salts have been reported in the gas phase,[15,19–22] in THF,[23] in aqueous solutions[24–28] and in DMSO.[29–35] For imidazolinium salts and related species, computational studies by Yates *et al.*[19] determined the pK_a values of an imidazolinium cation, along with the related tetrahydropyrimidinium and formamidinium species, in water, acetonitrile and DMSO (using continuum solvent models) whilst Wang *et al.*[21,22] considered an extremely large range of imidazolinium, tetrahydropyrimidinium, tetrahydro-1,3-diazepinium and hexahydro-1,3-diazocinium derivatives, amongst many others, and determined pK_a values in DMSO. In the solution phase, O'Donoghue *et al.*[25] have determined the pK_a values of both imidazolinium and tetrahydropyrimidinium salts in aqueous solutions using deuterium

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†Electronic supplementary information (ESI) available: Synthesis of the fluorenes **1**, **2**, **3**, **5** and **7**, wavelengths monitored for each fluorene indicator during pK_a titrations, synthesis and pK_a data for the salts **8–15** with cyclic cations, NMR experiments to determine the relative acidity of salts **10** and **15**, identifying and quantifying conformers in NMR spectra of the formamidinium salts **19–22**, discussion of the impact of conformers on acidity measurements, synthesis and pK_a data for the formamidinium salts **19–22**, crystal structure data for compounds **21** and **22**, NMR spectra of all prepared salts. CCDC 1973198 and 1973199. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0ob00036a

exchange methodologies. However, the range of imidazolinium and related species considered in solution remains small.

As such, this work seeks to extend the available acidity data on imidazolinium salts and related species, specifically considering how changing the structure of the cation affects its acidity in DMSO. The effects of changing the electronic nature of the substituents on the nitrogen and of changing the heterocycle ring size are examined, along with the importance of the cyclic nature of the system by considering a series of formamidinium salts.

Results and discussion

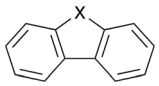
The pK_a data described herein were determined using the bracketing/overlapping indicator method,[36] in a fashion analogous to that we have reported previously,[34,35,37] in which the position of equilibrium for the reaction of an indicator of known pK_a value and the salt of interest was measured. The position of equilibrium for each compound is based on all the data from the titration. The uncertainties are based on replicate experiments; these uncertainties are typically greater than those from regression analysis, and hence are a more accurate representation of the uncertainty than any standard error from the fit. Each of the pK_a values reported herein is the result of at least four measurements involving at least two appropriate indicators.

The indicators **1–7** (Fig. 1) used were based on fluorene **6** as their deprotonated forms absorb significantly in the UV-Visible region; the decrease in such absorption on addition of the salt allowed determination of the position of equilibrium.‡ For each titration, the indicators were selected such that the pK_a value of each indicator was within two pK_a of the salt to be measured, allowing for the reliable determination of position of the equilibrium.[30]

Care must always be taken in assessing pK_a values as there is the potential for ion pairing even in a dissociating solvent such as DMSO.[23,41] At the concentrations used in this work, pK_a values in DMSO are not altered by ion pairing effects of the anion.[30,34,35] This has been examined explicitly by the Cheng[30] and the Harper[34] groups by comparing the pK_a values of azolium salts containing common cations but different anions; the pK_a values of all salts with the same cation were within uncertainty.

Imidazolinium salts and their higher homologues

Using the method discussed above, the pK_a values of a range of salts starting with the imidazolinium core were determined in order to examine the effects of altering their structure on their acidity. The salts considered (Fig. 2) allowed comparison of the effects of changing the size of the heterocylic ring (within series **8–11** and series **12–14**), the effect of changing



1 X = $CHSCH(CH_3)_2$, pK_a = 16.9 (ref. 38)
2 X = CHPh, pK_a = 17.9 (ref. 39)
3 X = CH(*o*-CH_3)Ph, pK_a = 18.8 (ref. 38)
4 X = NH, pK_a = 19.9 (ref. 40)
5 X = $CHCH_3$, pK_a = 22.3 (ref. 39)
6 X = CH_2, pK_a = 22.6 (ref. 39)
7 X = $CHC(CH_3)_3$, pK_a = 22.96 (ref. 34)

Fig. 1 Indicators used to determine the pK_a values of the salts considered and their corresponding pK_a values in DMSO.§

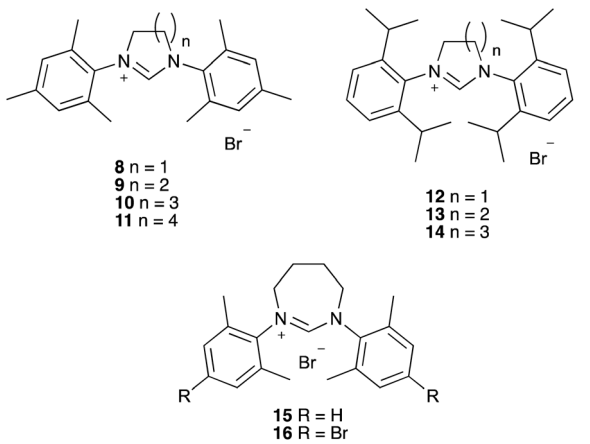


Fig. 2 The imidazolinium and related ring expanded salts considered in this work.

the steric nature of the substituents on the *N*-aryl groups (between series **8–10** and series **12–14**) and the effects of changing the electronic nature of the *N*-aryl substituents (between salts **10**, **15** and **16**). These salts were prepared through literature methods *via* the corresponding formamidines and their pK_a values are listed in Table 1, with reported computational data from literature for comparison where available.

It should be noted that care must be taken with determination of pK_a values in some of these cases (notably for salts **9–11**, **14** and **15**) as the absorbance of the mixtures decreased slightly with time. Though the reason for the decrease in absorbance is not immediately apparent, it has been noted previously by O'Donoghue *et al.*,[25] that a ring opening hydrolysis reaction was observed when determining the pK_a values of tetrahydropyrimidinium salts in water. If that process

‡The absorption due to both the carbene and the salt are also considered in determining the position of the equilibrium, though that of the deprotonated fluorene indicator dominates.

§The pK_a value originally reported for fluorene 7 used was 24.35.[39] However, our previous work[34] in the area identified inconsistencies when that value was used *cf.* to the use of other indicators. Separate titration experiments with acids of known pK_a determined a pK_a value of fluorene 7 of 22.96; when this value was used, it gave consistent results to titrations with other indicators. This value has been used in this work and, again, all data from titrations using this indicator and that pK_a value gave results consistent with titrations with other indicators. Further, the arguments presented are the same, irrespective of whether data using this indicator is included or not.

Table 1 The pK_a values of the salts **8–16** in DMSO at 25 °C determined using the bracketing indicator method, with reported computational data where available

Compound	pK_a value[a]	Calculated pK_a value
8	19.52 ± 0.12	20.8 (ref. 21)
9	21.58 ± 0.17	24.2 (ref. 22)
10	20.99 ± 0.13	24.5 (ref. 22)
11	21.18 ± 0.16	27.7 (ref. 22)
12	19.33 ± 0.20	20.1 (ref. 21)
13	21.98 ± 0.13	24.5 (ref. 22)
14	21.74 ± 0.13	—
15	21.50 ± 0.15	—
16	20.69 ± 0.19	—

[a] Uncertainties are reported as the standard deviation multiplied by the Student *t*-value for at least four, and up to six, measurements.

occurred here (noting the different reaction conditions) and resulted in generation of acidic species, it might account for the observation. Irrespective, through carrying out the processes rapidly, data that fit well to the derived equation[34] was obtained.

Immediately apparent is that the experimental data agrees reasonably well the previously reported computational values.[21,22] Experimental values are generally lower than the computed pK_a data though the trends observed in each series of salts are very similar. In both the 2,4,6-trimethylphenyl-substituted series of salts (**8–11**) and the 2,6-diisopropylphenyl-substituted series (salts **12–14**), there was a marked increase in pK_a (*ca.* 2–2.5) as the ring size is increased from five to six, with little change on further increase in the ring size. The causes for the relative acidities are not immediately apparent though it should be noted that computational models have also predicted an increase (albeit much larger) for the corresponding *N*-methyl (*ca.* 5),[19] *N*-2,4,6-trimethylphenyl (3.4)[21,22] and *N*-2,6-diisopropylphenyl salts (4.4).[21,22] Data in water also showed an increase (again large, *ca.* 7) in pK_a between imidazolinium and tetrahydropyrimidinium salts, though in that case there is also likely contribution from changing the *N*-substituent.[25]

An increase in pK_a (or a decrease in acidity) often suggests an increase in the stability of the cation relative to the carbene, which would alter the position of the equilibrium of deprotonation towards the protonated form. In these cases, such an increase in stability may be a result of removing strain in the smaller ring systems; this strain is notable in crystal structures of imidazolinium salts[42] in deviation from ideal bond angles. By comparison, crystallographic studies have shown that the strain in the six-,[43] seven-,[44] and eight-membered[45] cations is alleviated by twisting. However, why these strain effects might be so much more notable in the cation than the carbene is not clear, particularly given that, upon deprotonation of 1,3-dimethyl-4,5-dihydroimidazolium chloride the NCN bond angle decreases by *ca.* 8° with only a slight increase in the carbon–nitrogen bond lengths.[46] As such, alternative explanations must be sought.

The trend in acidity might alternatively be rationalised by considering through space electronic (field) effects arising as a result of the geometries enforced by the structure of the species in question. These effects can be evaluated using the CNC bond angles in the crystal structures (noting that crystallographic constraints might result in structural effects not present in solution, so qualitative comparisons are likely most useful) and the chemical shifts of the ^{1}H NMR signal due to the nucleus at the 2-position of the salts **8–11** determined in this work (Table 2). It should be noted that the data presented are for solutions in DMSO-d_6 to match the titration studies; the equivalent data in chloroform-*d* (see ESI†) shows qualitatively the same trend, though the difference in the data between compounds **8** and **9** are larger in that case.

Immediately apparent is that the trend in the bond angles between the C2 carbon atom, the nitrogen atom and aromatic carbon atom qualitatively parallel the trends in pK_a of these species; there is a marked decrease between the five- and six-membered salts **8** and **9**, followed by less significant changes on subsequently changing the ring size to salts **10** and **11**. Once again, while care must be taken in inferring solution phase data from that in the solid state, these crystallographic data also indicate that the *N*-aryl rings are orientated essentially perpendicular to the plane of the NCN atoms,[42–45] so a decrease in the CNC bond angle would bring the delocalised π electrons closer to the hydrogen atom at the 2-position. Such through space effects would account for the changes in chemical shifts of the hydrogen atom in the 2-position, which again qualitatively parallel the pK_a data with the value of the chemical shift being largest in compound **8**.

Such effects could account for the changes in pK_a values seen in Table 1 with changes in ring size, as they would result in stabilisation of cations relative to their deprotonated form; this effect would be least pronounced for the five-membered case **8**, resulting in that species being most acidic. The stabilisation of the cation through these through space effects would be expected to be more significant than any equivalent effects in the corresponding NHCs. As a result, particularly in the qualitative assessment presented here, the effect on the cation would be expected to dominate the position of the protonated equilibria. Such through space effects would also account for the changes seen in the calculated data[19] for the corresponding *N*-methylated salts with five- and six-membered heterocycles.

Table 2 Selected pK_a, spectroscopic and crystallographic data for compounds **8–11**: the bond angle between the C2 carbon atom, the nitrogen atom and the aromatic carbon atom (CNC bond angle) and the ^{1}H NMR chemical shifts of the H2 proton measured in DMSO-d_6

Compound	pK_a value	CNC angle[a]	δ ^{1}H (DMSO-d_6)
8	19.52 ± 0.12	124.7°, 126.1° (ref. 42)	9.00
9	21.58 ± 0.17	120.38° (ref. 43)	8.64
10	20.99 ± 0.13	117.51°, 118.87° (ref. 44)	8.27
11	21.18 ± 0.16	116.6°, 115.8° (ref. 45)	8.46

[a] Where the reported crystal structures are not symmetric, both bond angles are reported.

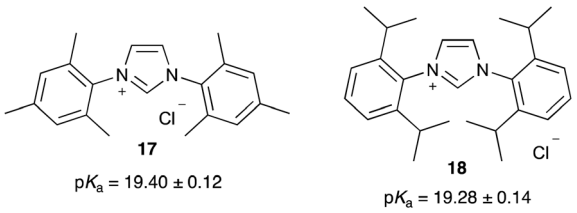


Fig. 3 The pK_a values of imidazolium salts **17** and **18** in DMSO at 25 °C reported previously.[34]

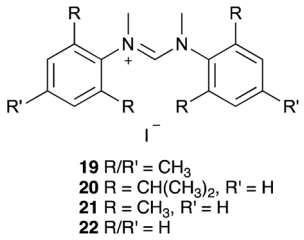


Fig. 4 The formamidinium salts **19–22** examined herein.

It is worth noting that the differences between the pK_a values of the salts containing the same size heterocyclic ring but different 2,6-substituents on the *N*-aryl group (**8** *cf.* **12**, **9** *cf.* **13**, **10** *cf.* **14**) are small, if even measurable.¶ This observation is not unreasonable given the similar electronic properties of alkyl substituents as measured using Hammett σ parameters.[47] The slightly reduced acidity of the isopropyl substituted cases relative to the methyl substituted cases for the larger rings might be explained by the same field effect argument presented above; greater field effects for the *N*-aryl groups in the isopropyl case lead to greater stabilisation of the cation relative to the corresponding deprotonated form.

It is of interest to compare the pK_a values of the imidazolinium salts **8** and **12** with the equivalent imidazolium salts **17** and **18** determined under identical conditions (Fig. 3).[34] ‖ These data demonstrate that there is no significant change in pK_a value between imidazolium salts and imidazolinium salts and are consistent with the work of O'Donoghue *et al.*[25] where the aqueous pK_a values of several imidazolium salts were found to be the same within uncertainty with the equivalent imidazolinium salts. Importantly, these data show that the presence of an aromatic π system has no impact on the acidity of the salt in these cases; it may well be that imidazolinium salts and their corresponding carbenes are higher in energy than their imidazolium counterparts, but the difference in energies of deprotonation are comparable.

The series of salts **10**, **15** and **16** allow evaluation of changing the electronic nature of the substituents on the *N*-aryl groups; such analyses has been carried out by us and others for series of imidazolium[34] and triazolium salts.[26,32,35] Whilst the limited number of salts in this series precludes a detailed Hammett analysis, it is immediately apparent that the results presented are counterintuitive. One would anticipate the pK_a values to be in the order **10** > **15** > **16** due to the electronic properties of the 4′-substituents (Me, $\sigma_p = -0.14$; H, $\sigma_p = 0$; Br, $\sigma_p = 0.26$),[47] with the more electron donating substituents leading to increased stabilisation of the cation relative to the corresponding carbene, resulting in less acidic salts. However, the order of pK_a values determined is **15** > **10** ∼ **16**. Separate experiments in which the salt **15** was added to the carbene formed from the deprotonation of salt **10**, showed no proton transfer (see ESI† for details) consistent with the reported data.

The origin of these somewhat unexpected acidities is unclear, though may be at least partially attributable to differences in solvation of the differently substituted salts (and their corresponding carbenes). It should also be noted that, while fairly straightforward correlations have generally been shown between pK_a values and measures of the electronic nature of substituents, in at least one case for a series of triazolium salts evaluated in deuterium oxide (data reported by O'Donoghue *et al.*,[26] some further analysis by Konstandaras *et al.*[35]) the order of acidity did not follow the electronic nature of the substituents; this effect was argued to be at least partially due to solvation effects.

Formamidinium salts

Thus far, the investigations presented have focussed on carbon acids where the resultant carbonic centre is constrained in a heterocyclic ring. In order to compare these results to those of similar species lacking ring strain and structural constraints, the formamidinium salts **19–22** ** (Fig. 4) were considered. These species were produced through literature methods from the corresponding formamidines[45,48–50] and would be expected to behave similarly to the salts considered above. Notably, the electron donating properties of the methyl group in the formamidinium salts would be almost identical to that of the alkyl groups in the ring systems[51] and the NCN portion of the formamidinium salts would be expected to sit in a plane with the four substituent atoms on the nitrogen centres.

Importantly for the determination of the pK_a values of these systems, the untethered nature of methyl *N*-alkyl substituents allows for the possibility of different conformations of the cations of salts **19–22**.†† These different conformations have been investigated in greater detail by Bielawski *et al.*[52] and the three key conformers are shown in Fig. 5. In that work, ^{1}H NMR data suggested that salts **19** and **21** predomi-

¶A similar difference is seen in water for the pK_a values of species **8** and **12**, though the absolute values are slightly larger.[25]

‖The anion effects were examined in previous studies and shown to be negligible;[30,34] hence the effects on pK_a values of the degree of saturation of the backbone can be evaluated.

**Note that these salts are iodides compared to the bromides used previously; see footnote ‖ above regarding the fact that anion effects on acidity are negligible under the conditions used.

††Note that formamidinium salts are generally drawn in the most straightforward way, analogous to the parent formamidines.

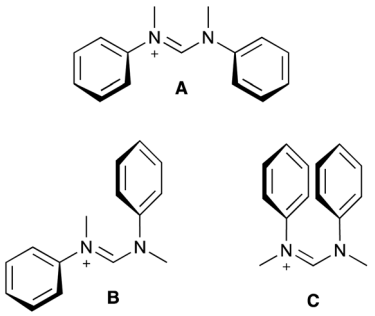


Fig. 5 The three extreme classes of conformers (**A**, **B** and **C**) of the cations of *N*,*N*′-diaryl-*N*,*N*′-dialkylformamidinium salts.[52]

nantly adopt conformation **B**, where the *N*-aryl groups are in a pseudo-*trans* orientation.

In this work, the cations of salts **19–21** were found to exist predominantly as conformer **B** (*ca.* 97% **B**, 2% **A**, 1% **C**) when in dimethyl sulfoxide-d_6 using ^{1}H NMR spectroscopy at 25 °C,‡‡ consistent with previous reports. The xylyl derivative **21** was also found to exist in conformer **B** in the solid state (see Fig. S5†). Under equivalent conditions, the cations of phenyl derivative **22** have conformers **A** and **B** present in the system in a 0.7 : 1 ratio.§§ It should be noted that in this case conformer **C** was only observed in the solid state (Fig. S8†), however, there is no indication of this conformer in solution for salt **22**. The relative proportions of the conformers seen for the cations of salts **19–22** correlates well with the steric bulk of the substituents on the 2,6-positions of the aryl groups. The greater the steric bulk of these substituents, the more interactions are present in conformer **A** and the greater extent to which conformer **B** is favoured. Conformer **C**, in all cases is unlikely to form due to steric interactions between aryl substituents; it has previously only been seen in high proportions in a case where the substituents on the nitrogen atoms were strategically modified to form that conformer.[52] Complete descriptions of how the conformers were determined for the cations of each salt are given in the ESI.†

The pK_a values for the salts **19–22** (Table 3) were determined using data obtained using the same methodology as for the salts **8–16**. For the salts **19–21** due to the low abundance (*ca.* 2–3%) of conformers **A** and **C** of the cation seen in ^{1}H NMR studies under the same conditions as the acidity measurements, the assumption was made that the only acidic species present in solution was the cation in conformer **B**. However, in the case of the phenyl substituted formamidinium salt **22**, significant portions of conformers **A** and **B** were shown to exist (**A** : **B**, *ca.* 0.7 : 1). The pK_a values of both conformers were considered as detailed in the ESI;† the pK_a value of conformer **B** is listed in Table 3.

Table 3 The pK_a values of the formamidinium salts **19–22** in DMSO at 25 °C determined using the bracketing indicator method

Compound	pK_a value[a]
19	19.69 ± 0.16
20	19.29 ± 0.20
21	19.19 ± 0.11
22	14.73 ± 0.10

[a] Uncertainties are reported as the standard deviation multiplied by the Student *t*-value for at least four, and up to six, measurements.

The order of pK_a values of formamidinium salts **19–21** is readily apparent. The mesityl substituted salt **19** is the least acidic due to the presence of the electron donating *para*-methyl substituents which will stabilise the cation and shift the equilibrium towards the protonated form. The pK_a values of the diisopropyl- and xylyl-substituted salts **20** and **21** are the same (given uncertainties) and more acidic than the mesityl case **19**. This similarity is consistent with the *ortho*-methyl and diisopropyl substituents donating electron density to a comparable degree.[34,51]

It is worth noting that the pK_a value of the mesityl-formamidinium salt **19** is the same as that of the mesitylimidazolinium salt **8**, and very similar to the pK_a value of the mesitylimidazolium salt **17**. This similarity indicates that the cyclic nature of the imidazolinium and imidazolium salts has little to no impact upon their acidity, at least compared to the major conformer of the acyclic form. This data is consistent with calculations on the corresponding *N*-methylated systems,[19] noting that in that case (a) no conformers were present and (b) that formamidinium salt acidity was closer to the five- than the six-membered heterocycle case.

The markedly increased acidity of the phenyl-substituted formamidinium salt **22** relative to the other formamidinium salts considered can be rationalised by noting the lack of *ortho*-substituents on the *N*-phenyl rings. Whilst the removal of such electron donating groups would be expected to increase the acidity of the species, this electronic effect can be quantified (based on previous work with imidazolium salts[34]) as *ca.* 1 and thus cannot alone account for the differences in pK_a values observed. Crystal structures of salt **21** (see Fig. S7†) (and the related cyclic species **8–11**[42–45]) indicate that the *ortho*-substituted phenyl rings lie perpendicular to the NCN plane. Such an orientation would not allow conjugation between the electron withdrawing phenyl rings and the NCN fragments, however they would stabilise the C2–H proton *via* through space effects. As no such steric restriction is present in salt **22**, the phenyl rings are free to rotate (as can be seen through the comparison of salts **21** and **22** in Fig. S9†), resulting in destabilisation of the cation through resonance electron withdrawal and through removing the stabilising through space effects around the proton, thereby destabilising the cation and markedly increasing the acidity of the salt. This

‡‡ Along with solubility reasons, use of dimethyl sulfoxide as the solvent allows the conformers present during the UV-vis titration experiments to be determined.

§§ The proportions of the isomers were analysed at multiple concentrations in DMSO, ranging from *ca.* 8×10^{-2} M to *ca.* 8×10^{-4} M (that is, including the concentration range examined during a standard pK_a titration), the proportion of conformers remained consistent across this concentration range.

case is an example where change in conformation can have significant effects on the acidity of a species.

Conclusions

The work described has shown how the acidities of imidazolinium salts and related systems in DMSO are affected by common structural changes. The pK_a values of the imidazolinium salts considered were the same as equivalent imidazolium salts reported previously,[34] demonstrating negligible effects of the aromaticity of the heterocycle on the acidity of these species. Whilst conformational effects must be taken into account, the pK_a values determined for formamidinium salts generally showed negligible differences from the corresponding imidazolinium salts demonstrating that the presence of a cyclic system has little effect on the acidity of the species. The key differences in acidity were found in the ring expanded systems, where the pK_a values of the salts containing six-, seven- and eight-membered heterocycles are found to be notably higher than the five-membered case; this effect is attributed to through space effects, with the *N*-substituents stabilising the protonated forms to a greater extent in the cases of the larger rings as they are forced closer to the acidic hydrogen atom. All of the data presented allows selection of appropriate bases to allow full deprotonation these types of salts when used as precatalysts along with providing a framework for the prediction of the pK_a values of such systems.

Experimental

Fluorene **6** and carbazole **4** were acquired from commercial sources and used without further purification. The fluorenes **2**, **3**, **5** and **7** were prepared through the reaction of fluorenone with the appropriate Grignard reagent, followed by reduction.[53] The 9-isopropylsulfane-9*H*-fluorene **1** was prepared through the reaction of 9-bromofluorene with propanethiol in the presence of base.[54] Full details of these preparations are given in the ESI.†

The salts **8–15** were all prepared through literature methods *via* synthesis of the desired formamidines,[55–57] followed by reaction with the appropriate dibromoalkane to form the desired salt.[45,48–50] The salt **16** was the generous gift of Dr A. Leverett.[58] The formamidinium salts were prepared through methylation of the appropriate formamidines.[59,60]

General methodology for pK_a titrations

Determination of pK_a values was carried out as described previously.[34,35,37] Solutions were prepared containing either the appropriate indicator (*ca.* 1 mM) or the salt being analysed (*ca.* 0.2 M) in dry DMSO (distilled from calcium hydride and stored over freshly activated 3 Å molecular sieves, <50 ppm water by Karl Fischer methodology). The spectrophotometric cell was sealed, evacuated and purged three times with nitrogen before being charged with the desired indicator solution (3 mL) and the first UV spectrum of the solution was recorded to determine the baseline. Aliquots (2.5 μL each) of sodium methylsulfinylmethylide (DIMSYL, *ca.* 0.25 M) in DMSO (prepared through addition of sodium hydride to DMSO as detailed in the ESI†) were added and the UV spectrum of the solution recorded after each step, until no further increase of the absorbance value at the appropriate wavelength (dependent on indicator, see ESI†).

To the cell containing a solution of the deprotonated fluorene indicator, aliquots of the salt solution (*ca.* 2.5–10 μL each) were added and the UV spectrum of the solution recorded after each step, until either no further decrease of the absorbance was observed or 300 μL had been added. Scans were taken in at least duplicate after each injection to ensure that the system had reached equilibrium before further injections were added. With an appropriate indicator (with a pK_a value within 2 of that of the salt), an equilibrium was established resulting in a decrease in the absorbance value, indicating reprotonation of the chosen indicator.

The equilibrium constants for the titration were determined by fitting using Datafit 9 (Oakdale Engineering). Details of the fitting equation and its derivation are given in the ESI.†

Conflicts of interest

There are no conflicts to declare.

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