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A targeted and systematic approach to the study of pK_a values of imidazolium salts in DMSO

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KEYWORDS N-Heterocyclic carbenes, imidazolium salts, acidity, pK_a values, organocatalysis

ABSTRACT: A range of more than 25 imidazolium salts, chosen for their differing steric and electronic features, were prepared and their pK_a values were determined using the bracketing indicator method. Through systematically changing the structure of the imidazolium cation the effect of varying substituents at each position on the heterocyclic ring was determined; particularly, the transmission of electronic effects was quantified using Hammett parameters. This new data gives an indication of the strength of base required for deprotonation and the potential to correlate these data with the nucleophilicity of the corresponding carbenes.

INTRODUCTION

Over the last two decades there has been considerable development in the use of *N*-Heterocyclic Carbenes (NHCs) in organocatalysis.[1-7] They have been used to facilitate a wide range of reactions including the reaction of two aromatic aldehydes (benzoin condensations),[8-10] 1,4-additions (Stetter reactions),[11-13] reactions of α,β-unsaturated aldehydes,[14-16] and 1,2-additons.[17] In the majority of these reactions, the carbene catalyst is generated *in situ* through deprotonation of the corresponding air stable azolium salt. Given this, the pK_a value of the corresponding salt is of great interest. The pK_a allows the extent of deprotonation of the pre-catalyst in the reaction mixture (and hence the amount of catalyst present) to be determined and it gives insight into the nucleophilic nature of the carbene through the Brønsted relationship.[18,£]

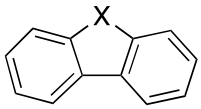
There have been few studies of the pK_a values of azolium salts. An early study by Alder[19] found the acidity of 1,3-diisopropyl-4,5-dimethylimidazolium cation to be 24.0 in DMSO using an NMR-based method. A study by Kim and Streitwieser[20] looked into the acidity of the 1,3-di-*tert*-butylimidazolium cation in THF, where it was found to be 20.0, while it was found to be in the range 22.7-23.0 in DMSO. Amyes *et al*.[21] used deuterium exchange to determine the kinetic acidities of a number of imidazolium cations in the aqueous phase. Studies by O'Donoghue[22-25] extended this to involve a large number of imidazolium and triazolium cations in aqueous solutions. Work by Yates *et al*,[26] involved the determination of gas phase acidities. The most relevant study to this work is by Chu *et al*.,[27] who investigated the pK_a values of a small number of alkyl imidazolium salts in DMSO using the bracketing indicator method, with the values obtained ranging between 19.7 and 23.4.

Despite the aforementioned literature, there has been no systematic study examining the acidity of both alkyl and aromatic imidazolium salts in DMSO. This study aims to extend the current knowledge of pK_a values of azolium cations, with particular emphasis on *N*-alkyl and *N*-aryl imidazolium cations. The study was conducted using a range of imidazolium salts in order to observe the effect of specific structural changes across the molecule and to correlate the structure of a given imidazolium salt with its pK_a value.

RESULTS AND DISCUSSION

The pK_a data presented in this paper were determined using the bracketing/overlapping indicator method,[28] in which the position of the equilibrium for the reaction of an indicator of known

pK_a value and the imidazolium salt of interest was measured. The indicators **1-6** chosen (Chart 1) were based on fluorene **5** as their deprotonated forms absorb significantly in the UV-Visible region; the change in such absorption on addition of azolium salt allowed determination of the position of equilibrium. All pK_a values discussed are determined in DMSO, with values anchored to those of indicators with known pK_a values.[28-30]



1 X = CHPh, 17.9
2 X = CH(2-MePh), 18.8
3 X = NH, 19.9
4 X = $CHCH_3$, 22.3
5 X = CH_2, 22.6
6 X = $CHC(CH_3)_3$

Chart 1. Indicators used in this study and their corresponding pK_a values in DMSO;[28-30] the value for compound **6** was determined herein.

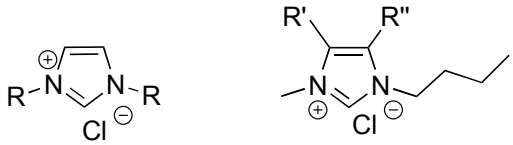
In determining the position of equilibrium, the absorption due to both the NHC and the salt are also considered, though that of the deprotonated fluorene indicator dominates. The position of equilibrium for each compound is based on all data from the titration. The uncertainties are based on replicate experiments, which are typically greater than any uncertainties from regression analysis, and hence are a truer representation of the uncertainty. Each of the pK_a values reported herein is the result of at least three measurements with an appropriate indicator and bracketed with at least one other indicator. It is important to use an appropriate fluorene indicator for each titration; that is a fluorene possessing a pK_a value that is within two pK_a of the imidazolium salt to be measured.[27] Outside of this, changes in the equilibrium for the reaction described are too difficult to follow reliably.

Several inconsistencies were noted during the application of *tert*-butylfluorene **6** as an indicator. These resulted from use of its reported pK_a value of 24.4.[29] It was initially chosen for use as a bracketing indicator for compounds with pK_a values >22.6 but in each experiment the indicator **6** gave a different pK_a value to those determined using fluorene **5** as the indicator (pK_a = 22.6). Values obtained using the *tert*-butyl fluorene **6** were routinely higher by *ca*. 1.4 which suggested that the reported value for the indicator is incorrect.

Consequently, the pK_a value of the indicator **6** was determined through titration with benzamide, which has a literature pK_a value of 23.35.[31] Using this data it was determined that the *tert*-butyl fluorene indicator **6** is more acidic than reported in the literature and has a pK_a value of 22.96 ± 0.10. There are no reports in the literature that use this indicator in the determination of pK_a values, possibly due to the error in the reported pK_a value.[31] The value of 22.96 was used throughout the calculations described herein and gave consistent data with that measured using other indicators. It should be noted that the pK_a is not unrealistic given that 9-isobutyl fluorene (pK_a = 23.2) and 9-methylfluorene **4** (pK_a = 22.3) exhibit similar pK_a values.[28]

The first series of compounds investigated was that containing *N*-alkyl chains; compounds **7-12** (Chart 2). While these aren't as common in the field of NHC organocatalysis as their *N*-aryl systems counterparts, they represent a useful starting point and are the cation of many ionic liquids.[16,32] The compounds chosen allow the effects of varying the nature of the *N*-alkyl substituents from primary through tertiary, on the pK_a value of the imidazolium salt to be determined (Table 1). Note that all the salts investigated had a common anion (chloride) to allow direct comparison. Whilst there is the potential for ion pairing even in a dissociating solvent such as DMSO[20] (and ion pairing would be expected to affect the observed pK_a value for salts containing the same cation but different anion) at the concentrations used here ion pairing would be expected to be negligible.[33] There is literature precedent supporting this argument, with demonstration that the anion has no effect (with all values within uncertainty) on the pK_a values of *N*-alkyl imidazolium salts, in particular 1-butyl-3-methylimidazolium salts in dimethyl sulfoxide under similar conditions to those used here,[27] suggesting ion pairing does not affect the pK_a values determined. This will be commented upon further below.

The p*K*a data for the six imidazolium salts measured herein is listed in Table 1. Data for compounds **9** and **10** are consistent with those reported.[20,27] On changing the substituents at the nitrogen centres of the imidazolium salts, from primary (compound **10**) to secondary (compounds **7** and **8**) and tertiary (compound **9**), an increase was observed in the pK_a values. This increase, along with the magnitude of such, is consistent with that observed previously for similar systems by Chu *et al.*[27]



7 R = ^{i}Pr
8 R = Cy
9 R = ^{t}Bu

10 R'/R" = H
11 R'/R" = Me
12 R' = Cl, R" = H

Chart 2. The alkyl imidazolium salts **7-12** investigated in this study.

Table 1. pK_a values of the *N*-alkyl imidazolium salts 7-12 in DMSO at 25°C determined using the bracketing indicator method. Uncertainties are reported as the standard deviation multiplied by the t-student value for between four and six measurements.

Compound	pK_a value
7	22.84 ± 0.09
8	22.26 ± 0.09
9	22.70 ± 0.11
10	22.00 ± 0.07
11	22.93 ± 0.13
12	20.29 ± 0.14

These results suggest that increased substitution at the α-carbon results in stabilization of the imidazolium salt relative to the conjugate carbene. However there is a negligible difference in the pK_a value between the *N*-isopropyl system **7** and the *N*-*tert*-butyl system **9**, while the pK_a value of the *N*-cyclohexylimidazolium **8** is 0.44 ± 0.14 lower than the *tert*-butyl substituted salt **9**. This suggests that pK_a value of a system relies on more than purely inductive effects (in such a case, the order of pK_a values might be expected to be **10** < **7** ≈ **8** < **9**).

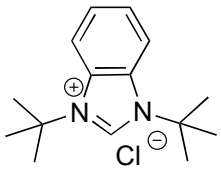
Potential contributing factors to be considered here are through space interactions, conformational differences (for example at the alpha carbon in species **7** and **8**) and solvation (larger side chains maybe harder to solvate, hence affecting the relative stability of the cationic and neutral forms). Deconvoluting each of these is not realistic with the data available.

From a comparison of the pK_a values of the 4,5-diprotioimidazolium salt **10** and the 4,5-methylated derivative **11**, incorporating methyl groups at both the 4- and 5-positions increases the pK_a value by 0.93 ± 0.15. This can be attributed to the electron donating ability of the methyl substituents, adding electron density into the imidazolium ring and stabilising the cationic form relative to the carbene. The magnitude of this change is consistent with a similar comparison between the diisopropylimidazolium salt **7** and its 4,5-dimethylated counterpart which has a reported pK_a value of 24.0.[19]

Chlorination of the 4-position on the imidazolium ring results in a substantial decrease in the pK_a value of the species; salt **12** has a pK_a value *ca*. 1.7 lower than its 4-protio counterpart, **10**. Whilst a decrease in the pK_a value on chlorination was expected, based on the electron withdrawing nature of the substituent being added, it is perhaps surprising that the magnitude of the change is greater than for the addition of two methyl groups. It may therefore be inferred that the relative effect of inductive and resonance contributions in these systems is different.

Given these substituent effects, it is also of interest to consider the impact of extending the aromatic system on the acidity of such salts by considering the benzimidazolium **13**. This salt has a pK_a value of 20.60 ± 0.13, which is markedly lower than the corresponding protiated imidazolium compound **9**, with a difference in the pK_a values of 2.1 ± 0.2. This increase in acidity is reasonable given the greater ability of salt **13** to delocalise the positive charge whilst the magnitude of the difference is consistent with the work of Amyes,[21] who noted a decrease in pK_a of 1.4 ± 0.71 for the corresponding *N*,*N*'-dimethyl species.

Given the demonstrated importance of electronic effects on azolium salt pK_a values and the ubiquity of *N*,*N*'-diarylimidazolium precatalysts in the literature, the next series considered were the compounds **14-28** (Chart 3). These permit

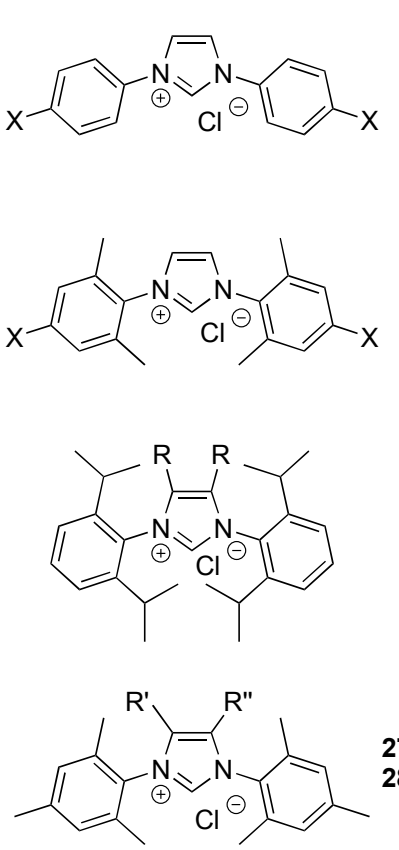


13 R = ^{t}Bu

the effects of varying the arene electronics and the imidazolium to *N*-arene conformation on the pK_a values of imidazolium salts to be discerned (Table 2). Once again all the salts investigated had a common anion (chloride) to allow direct comparison though, as discussed above, the nature of the anion would not be expected to have a significant effect in DMSO at the concentrations used. Note that in this case, in addition to salt **20**, six other 1,3-bis(2',4',6'-trimethylphenyl)imidazolium salts containing different anions (bromide, tetrafluoroborate, triflate, perchlorate, hexafluorophosphate, bis(trifluomethanesulfonyl)imide) were considered. All were found to have the same pK_a value (within uncertainty) thereby demonstrating that the pK_a value of the salt is solely dependent on the cation (see Supporting Information).

A comparison of the pK_a values listed in Tables 1 and 2 indicates that the pK_a values of the *N*-aryl imidazolium salts are significantly lower than those determined for the *N*-alkyl imidazolium salts with equivalent 4,5-disubstitution (Table 1). This is consistent with the previous observations in deuterium oxide[22] and suggests that in DMSO the aryl groups behave as electron withdrawing groups relative to the *N*-alkyl substituents of **7**-**12**. This destabilises the parent cation relative to the carbene causing a decrease in the pK_a value.

The effect of the 4'-aryl substituents on imidazolium salt pK_a values can be quantified through considering a plot of the measured pK_a value against the Hammett sigma (σ) value of the included 4-aryl substituent in each of the salts **14**-**19** (Figure 1). A clear trend in pK_a values can be seen for compounds **14-19** with 4'-substituted aryl substituents on the nitrogen centres. As changing the substituent at this position would not be expected to have any steric effects, the differences in pK_a values in these systems derive from the electronic nature of the 4'-substituent on the aryl rings.



14 X = OMe
15 X = Me
16 X = H
17 X = F
18 X = Cl
19 X = Br

20 X = Me
21 X = H
22 X = F
23 X = Cl
24 X = Br

25 R = H
26 R = Me

27 R' = H, R'' = Me
28 R'/R'' = Me

Chart 3. The *N*-aryl imidazolium salts **14-28** investigated in this study.

Table 2. pK_a values of the *N*-aryl imidazolium salts 14-28 in DMSO at 25°C determined using the bracketing indicator method. Uncertainties reported are reported as the standard deviation multiplied by the t-student value for between four and six measurements.

Compound	pK_a value
14	18.75 ± 0.10
15	18.50 ± 0.16
16	18.33 ± 0.09
17	18.21 ± 0.16
18	18.05 ± 0.22
19	18.07 ± 0.11
20	19.40 ± 0.12
21	19.28 ± 0.14
22	19.07 ± 0.16
23	18.91 ± 0.11
24	18.95 ± 0.18
25	19.29 ± 0.07
26	23.71 ± 0.16
27	22.75 ± 0.14
28	23.79 ± 0.15

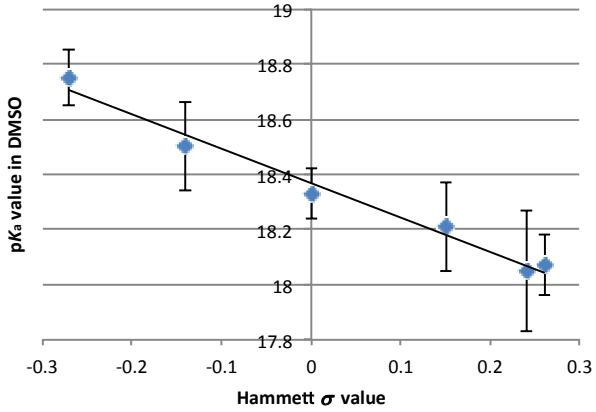


FIGURE 1. Correlation between the Hammett σ value of the 4'-aryl substituents[34] of the imidazolium salts **14-19** and their measured pK_a values in DMSO at 25°C.

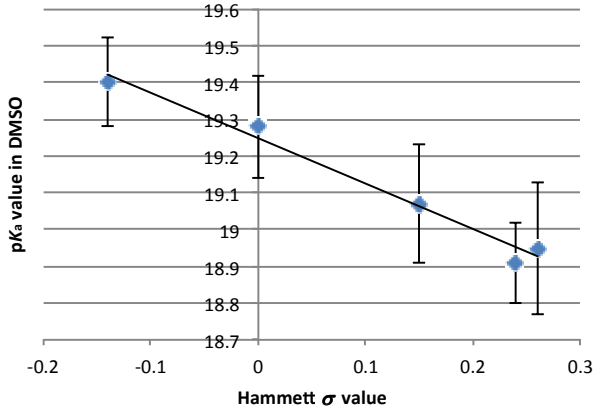


FIGURE 2. Correlation between the Hammett σ value of the 4'-aryl substituents[34] of the imidazolium salts **20-25** and their measured pK_a values in DMSO at 25°C.

The negative slope of the linear fit is consistent with the more electron withdrawing groups destabilising the cation relative to the corresponding carbene thus lowering the pK_a value. The slope corresponds to the negative of the Hammett susceptibility constant, ρ, thus allowing comparison to systems in the literature. In this case the slope is -1.25 ± 0.09 demonstrating that the substituents are having a larger effect on the acidity of the imidazolium salts **14-19** than in the acid dissociation of substituted benzoic acids. A further useful comparison is with the effect of substitution on the acid dissociation of protonated anilines, given that both reactions involve positive charges on a nitrogen centre (or centres). That process has a ρ value of *ca.* 2-4 across a range of solvents and temperatures;[35] the effect of the substituent is less in the case of the imidazolium salts **14-19**. The decrease in the magnitude of ρ is consistent with delocalisation of the positive charge on the imidazolium systems rather than on a single nitrogen centre as in the aniline case.

Further to the *N*,*N*'-diarylimidazolium salts above, the pK_a values of salts **20-24** that contain 2',6'-alkylsubsituents are also of interest. Comparison with the previous cases not only allows the effect of methylation on the pK_a values to be determined but also the investigation of the transmission of electronic effects in a system with different steric constraints, wherein the *N*,*N*'-diarylimidazolium arene to imidazolium interplanar angles could affect conjugation. The measured the pK_a values were plotted against the σ value of the 4'-substituent for each of the imidazolium salts **20-24** as before (Figure 2).

Immediately apparent is that the slope of the linear fit is once again negative, consistent with the increase of acidity of the salts with increasing electron withdrawing ability of the 4'-substituent. The slope of the linear fit is -1.23 ± 0.10; this is the same as the slope determined from the pK_a data for 2',6'-diprotioimidazolium salts **14-19** indicating that in both cases the substituents on the phenyl group affect the acidity of the salt to the same extent. That is, the methyl groups at the 2'- and 6'-positions do not change the transmission of electronic effects, irrespective of any changes to conformation that may result.

It is of interest to consider the magnitude of the difference between the parallel lines presented in Figures 1 and 2; based on the line of best fit, the difference in pK_a between the two systems is *ca.* 0.9 at the intercept. This difference can be attributed to the electronic effects of the methyl groups at the 2'- and 6'-positions; being electron donating they stabilise the cation relative to the corresponding carbene resulting in a higher pK_a value.

The effect of changing the steric nature of the substituents at the 2'- and 6'-positions on pK_a can be determined by comparing the acidities of salts **20** and **25**. The pK_a values of these two species are the same (within uncertainty) which, in combination with the very similar electronic nature of the two substituents, suggest that any steric ef-

fects of groups at these positions on pK_a value are negligible

On addition of methyl groups to the 4- and 5-positions of the *N,N*'-diarylimidazolium scaffold, the pK_a value of the salt increases by *ca.* 4.4 based comparison of salts **20** and **28**, and **25** and **26**. This is significantly larger than the effect seen in the case of *N,N*'-dialkylimidazolium salts (a change in pK_a of *ca.* 1). Including analysis of data for the salt **27**, where a single 4,5-position is methylated, these data show that the addition of the first methyl group results in an increase in the pK_a value of 3.35 ± 0.18, while the addition of the second methyl group leads to an increase in the pK_a value of 1.04 ± 0.21. The latter is comparable to the effect of *two* methyl groups at the 4- and 5-positions of *N,N*'-dialkylimidazolium systems (*viz.* salts **10** and **11**).

Crystal structures of salts **27** and **28** were determined (see Supporting Information) and compared with that reported for the 4,5-diprotio salt **20**[36] and the related 4-tolyl derivative **15**.[37] Table 3 summarises the salient information from these data; the C2'-C1'-N-C2 dihedral angle is a measure of rotational conformation of the *N*-aryl and imidazolium rings in the compound whilst the endocyclic N-C-N bond angle is a measure of π-delocalisation with a greater value indicating greater delocalization.

With the caveat that correlations between solid-state data and solution behaviour are inherently fraught, the dihedral angles presented in Table 3 allow several predictions to be made regarding the likely conformation of the *N*-aryl groups relative to the imidazolium rings of compounds **14-28**.

Table 3. Comparison of N-C-N bond angle and interplanar dihedral angles of the salts 15, 20, 27 and 28 from crystal structure data with their corresponding pK_a values.

Salt	N-C-N bond angle / °	C2'-C1'-N-C2 bond angle [a] / °	pK_a value
15[37]	109.8	12.8	18.50 ± 0.16
20[36]	108.25(9)	77.9	19.40 ± 0.12
27	108.1(2)	74.5	22.75 ± 0.14
28	107.9(2)	82.4	23.79 ± 0.15

[a]Average of the two angles; see Supporting Information for the individual values.

Firstly, the addition of methyl groups at the 2'- and 6'-positions results in substantial torsion within the resultant species (*viz.* compounds **15** and **20**). These substituents promote twisting of the *N*-aryl substituent out of the imidazolium plane (see Figure S2, Supporting Information), thereby diminishing conjugation of the π-systems. This likely contributes to the increased acidities of imidazoliums **15-19** relative to their 2',6'-dimethyl counterparts **20-24** respectively.

Secondly, while one might expect the 4-methyl and 4,5-dimethyl imidazolium salts **27** and **28** to adopt dihedral angles closer to 90° due to increased steric buttressing between the substituents, the observed dihedral angles are comparable to those in salt **20** and likewise substantially greater than those of 2',6'-diprotio analogue **15** (Table 3, Figure S3). Thus, the observed reduction in acidity from species **20** to compounds **27** and **28** results from the electronic influence of the methyl substituents rather than conformational changes.

Further to the *N*-aryl to imidazolium dihedral angles, there is no difference in the N-C-N bond angles in the species **15**, **20**, **27** and **28**. This is consistent with a similar degree of π-delocalisation across all four imidazolium systems.

Whilst these data give some insight into the structural nature of the salts **15**, **20**, **27** and **28**, they alone do not account for the differences in observed pK_a values. Factors (such as packing effects) may dominate other aspects which are important outside of the solid state.

Semi-empirical (PM3[38]) gas phase calculations were also carried out using the EMPIRE software suite[39,40] and the same information as discussed above was determined for the structure of minimum energy for the cations of salts **20**, **27** and **28** (Table 4). The data determined gave significantly different information to that from the crystal structures.

Of particular interest from the gas phase calculations is the increase in the torsion angles upon

Table 4. Comparison of N-C-N bond angle and torsion angles of the cation of salts 20, 27 and 28 determined using gas phase calculations with their corresponding pK_a values.

Cation of compound	N-C-N bond angle / °	C2'-C1'-N-C2 bond angle / °	pK_a value
20	106.5	77.4, 77.4	19.40 ± 0.12
27	106.6	85.9,[a] 75.8	22.75 ± 0.14
28	108.8	90.0, 90.0	23.79 ± 0.15

[a]For the aromatic ring nearest the 4-methyl group.

comparing the 4,5-diprotiated system to the 4-methylated system, with a further increase upon addition of the second methyl group. The increase in torsion angles is consistent with the methyl groups forcing the aryl groups to be out of the plane with the azolium ring. This change in orientation may alter the extent to which electron density is donated from the nitrogen substituents.

In order to investigate this potential electronic effect, the energies of the highest occupied molecular orbitals (HOMOs) and the lowest unoccupied molecular orbitals (LUMOs) along with their corresponding electron density maps were determined (see Figure S4 and Table S4, Supporting Information).

From the calculations, the largest HOMO–LUMO gap was observed in the 4,5-dimethyl system, with systematically smaller gaps noted for the 4-methylated and protiated systems; the predominant origin of the change is the energy of the LUMO. Consideration of the electron density in the LUMO shows that 4,5-dimethylated **28** has less electron density located on the aryl substituents than its single methylated and protiated counterparts. This highlights that the positioning of the *N*-aryl substituent compared to the heterocyclic portion can affect the extent of conjugation even at relatively high torsion angles. Therefore the increase in electron donation at the carbenic centre and subsequent increase in pK_a is likely due to a combination of the addition of methyl groups and the change in orientation (and conjugation) of the *N*-aryl substituents.

Given these data, it is important to compare them to existing measurements of pK_a values. Initially, comparison of experimental data here with values determined computationally for the cations **7**, **8**, **16** and **21** in DMSO[26] (Figure S5). Though the data set is limited, the correlation is good (R^2 = 0.987) and, interestingly, the slope is greater than one. This indicates that the theoretical calculations reported overestimate pK_a values at the upper end of the scale and underestimate them for lower values.

Comparison of the pK_a data obtained in DMSO with that in water allows an assessment of the effect of solvation. Comparison of the data for species **9**, **10**, **14**, **18**, **21** and **25** in water[22] and DMSO shows a reasonable correlation (Figure 3). While the data set is limited, as the slope of the correlation is *ca.* 1 the relative energy differences (between the protonated and deprotonated forms for two different species) are approximately the same in both solvents.

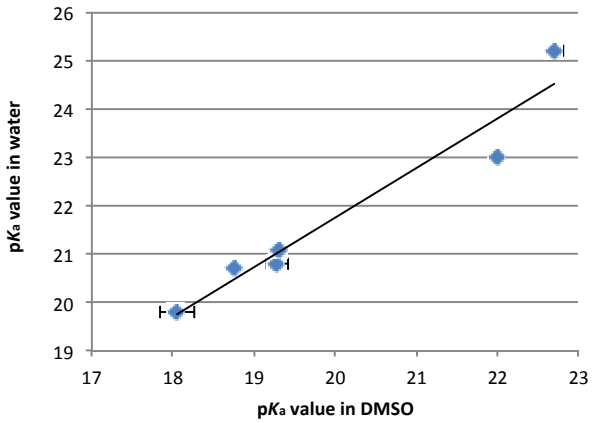


FIGURE 3. Correlation between the pK_a values of the salts **9**, **10**, **14**, **18**, **21** and **25** in DMSO at 25°C (this work) and in water at 25°C.[22]

It would be very useful to be able to make comparisons of acidity of the imidazolium salts mentioned above in other solvents such as tetrahydrofuran (particularly given its prevalence as a solvent in organocatalytic systems), however only one such pK_a value has been reported; that of the cation of salt **9**. This cation has a pK_a value of 20.0 in tetrahydrofuran,[20] which is significantly lower than the same compound in dimethyl sulfoxide (pK_a = 22.70 ± 0.11, *vida supra*) and water (pK_a = 25.2[22]). This could be due to there being a greater amount of hydrogen bonding in both dimethyl sulfoxide and water compared to tetrahydrofuran; this greater hydrogen bonding in the DMSO and water stabilises the protonated form relative to the carbene, resulting in a higher pK_a value in these solvents.

In conclusion, the pK_a values of a wide range of systematically chosen imidazolium salts have

been determined. From this work, an understanding of the effect on the acidity of an imidazolium salt on varying the structure of the cation has been gained. This has been quantified in terms of varying the electronic properties of *N*-substituents. Further the importance of conformation was probed for 4,5-substituted *N*,*N'*-diaryl imidazolium salts. These data, along with acting as a guide to the acidity of related imidazolium salts, allow determination of appropriate bases for the use of these azolium salts as precursors for organocatalysts, as well as offering the potential for their correlation with the nucleophilicity of their corresponding carbenes.

EXPERIMENTAL

Fluorene **5** and carbazole **3** were acquired from commercial sources and used without further purification. The substituted fluorenes **1**, **2**, **4** and **6** were prepared through reaction of fluorenone with the corresponding Grignard reagent, followed by reduction of the resultant alcohols (see Supporting Information).[41]

Imidazolium salts **8** and **13** were acquired from commercial sources and used without further purification. The diaryl derivatives **16** and **26** were purchased from Star Synthesis Inc. The alkyl imidazolium salts **10** and **11** were prepared according to literature methods from the corresponding imidazoles,[27] while the chloro derivative **12** was the generous gift of Rebecca Hawker.[42] The symmetrical salts **7**, **9, 15** and **17-19** were prepared from the corresponding amines in a one pot synthesis with glyoxal and paraformaldehyde.[36,43] The aryl imidazolium salts **14** and **20-25** were prepared from the corresponding anilines through the 1,4-diazabutadiene intermediates with subsequent reaction with paraformaldehyde.[44,45] The methylated imidazolium salts **27** and **28** were prepared from the corresponding anilines through the formamidine intermediates in a manner analagous to previously reported.[46,47] A range of 1,3-*bis*(trimethylphenyl)imidazolium salts with different anions were prepared through metathesis of the chloride **20**; ion chromatography was used to confirm successful transformation of the precursor (see Supporting Information). High resolution mass spectra were obtained on a Waters Q-TOF Ultima tandem mass spectrometer.

1,3-*bis*(4'-Chlorophenyl)imidazolium chloride 18. To a solution of *p*-chloroaniline (3.19 g, 25.0 mmol) in acetic acid/water (3:1 v/v, 20 cm^3), 37% aqueous formaldehyde (1.0 cm^3, 0.37 g, 12 mmol) was added dropwise over ten minutes. After a few seconds, a solid precipitated from solution. To this mixture, glyoxal (40% in water, 1.50 cm^3, 1.89 g, 13.1 mmol) was added and the mixture was stirred at 40°C for an hour. After being allowed to cool to room temperature, hydrochloric acid (6.0 cm^3, 3 M, 18 mmol) was added and the mixture was heated at reflux for 30 minutes during, which time all the solids dissolved. The solution was allowed to cool to room temperature and diluted with water (20 cm^3), whereupon a solid precipitated from solution. The solid was collected through filtration, air dried and recrystallised from dichloromethane/diethylether to give the title compound **18** as a white crystalline solid (4.95 g, 15.2 mmol, 61%). m.p. 260-262°C (lit.[22] not reported). ^{1}H NMR (300 MHz, dimethyl sulfoxide-d_6) δ 10.50 (br s, 1H, C2-H), 8.61 (s, 2H, C4,5-H), 7.99 (m, 4H, C3'-H), 7.82 (m, 4H, C2'-H). ^{13}C NMR (300 MHz, dimethyl sulfoxide-d_6) δ 135.1 (C2), 134.6 (C4'), 133.5 (C1'), 130.5 (C2'), 124.9 (C3'), 121.9 (C4,5). IR (Solid): ν_{max} 3339 (br, w), 3090 (w), 2999 (w), 1554 (sh,m), 1488 (sh, m), 1310 (w), 1257 (sh, m), 1096 (sh, s), 1008 (sh, m) 824 (sh, s) cm^{-1}. Found HRMS (ESI-TOF) *m/z*: (M^+). Calcd for $C_{15}H_{11}Cl_2N_2^+$: 289.0294; Found 289.0295. . Found: C 52.32; H 3.93; N 7.93%. $C_{15}H_{11}Cl_3N_2.H_2O$ requires C 52.43; H 3.81; N 8.15%.

1,3-*bis*(4'-Bromophenyl)imidazolium chloride 19. To a solution of *p*-bromoaniline (4.27 g, 24.8 mmol) in acetic acid/water (3:1 v/v, 20 cm^3), aqueous formaldehyde (1.0 cm^3, 0.37 g, 12 mmol) was added dropwise over 10 minutes. After a few seconds, a solid precipitated from solution. To this mixture, glyoxal (40% in water, 1.50 cm^3, 1.89 g, 13.1 mmol) was added dropwise over 10 minutes and the mixture was stirred at 40°C for an hour. After being allowed to cool to room temperature, hydrochloric acid (6.0 cm^3, 3 M, 18 mmol) was added and the mixture was heated at reflux for 30 minutes, during which time all the solids dissolved. The solution was allowed to cool to room temperature and diluted with water (20 cm^3), whereupon a solid precipi-

tated from solution. The solid was collected through filtration, air dried and recrystallised from dichloromethane/diethylether to give the title compound **19** as a white crystalline solid (3.27 g, 7.89 mmol, 64%) m.p. >245°C (dec.). ^{1}H NMR (300 MHz, dimethyl sulfoxide-d_6) δ 10.49 (br s, 1H, C2-H), 8.60 (s, 2H, C4,5-H), 7.95 (m, 4H, Ar-H), 7.91 (m, 4H, Ar-H). ^{13}C NMR (75 MHz, dimethyl sulfoxide-d_6) δ 135.0 (C2), 133.9 (C4'), 133.1 (C1'), 124.1 (C3'), 123.0 (C4'), 121.9 (C4,5). IR (Solid): ν_{max} 3338 (br, w), 3087 (w), 3010 (w), 1665 (m), 1588 (sh, w), 1552 (m), 1484 (s), 1424 (m), 1341 (m), 1307 (m), 1255 (sh, m), 1072 (sh, s), 1005 (sh, s), 904 (w), 820 (sh, s), 768 (sh, m) cm^{-1}. Found HRMS (ESI-TOF) *m/z*: (M^+) Calcd for $C_{15}H_{11}{}^{79/81}Br_2N_2^+$ 376.9482 (50%), 378.9263 (100%), 380.9243 (50%); Found 376.9286 (50%), 378.9261 (100%). 380.9236 (50%). Found: C 41.97; H 3.09; N 6.29%. $C_{15}H_{11}Cl_1Br_2N_2.H_2O$ requires C 41.65; H 3.03; N 6.48%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium tetrafluoroborate. To a solution of the chloride salt **20** (8.69 g, 25.5 mmol) in dichloromethane (40 cm^3), sodium tetrafluoroborate (2.80 g, 25.5 mmol) was added in portions over 15 minutes. The resulting mixture was stirred for 12 hours at room temperature. To the reaction mixture after this time, water (40 cm^3) was added and the resulting mixture was washed with dichloromethane (4 x 10 cm^3), the organic layers were combined and cooled on an ice bath. The solid that formed was recrystallised from dichloromethane/hexane to give the title compound as a white crystalline solid (9.83 g, 25.1 mmol, 98%). m.p. 230-231°C (lit.[48] 240-243°C). ^{1}H NMR (300 MHz, chloroform-d_1) δ 8.92 (t, J = 1.6 Hz, 1H, C2-H), 7.55 (d, J = 1.6 Hz, 2H, C4,5-H), 7.06 (s, 4H, Ar-H), 2.36 (s, 6H, C4'-CH_3), 2.14 (s, 12H, C2'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.7 (C2), 137.6 (Ar-C), 134.0 (Ar-C), 130.3 (Ar-C), 130.0 (C3'), 124.9 (C4,5), 21.2 (C4'-CH_3), 17.2 (C2'-CH_3). ^{19}F NMR (282 MHz, chloroform-d_1) δ -152.83 (s, 4F, BF_4), -152.77 (s, 1F, BF_4).[$] Found: C 64.54; H 6.45; N 7.15%. $C_{21}H_{25}BF_4N_2$ requires C 64.30; H 6.42; N 7.14%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium perchlorate. To a suspension of the chloride salt **20** (3.37 g, 9.89 mmol) in chloroform (100 cm^3), silver(I) perchlorate (2.25 g, 10.8 mmol) was added portionwise over 5 minutes with stirring. After the reaction mixture had been stirred for an hour at room temperature, the resulting mixture was filtered through celite, the filtrate was collected and the solvent was removed under reduced pressure. The resulting white solid was dried *in vacuo* over 30 minutes and recrystallised from dichloromethane/hexane to yield the desired salt as white crystals (3.59 g, 8.87 mmol, 90%). m.p. 244-247°C (lit.[49] not reported). ^{1}H NMR (300 MHz, chloroform-d_1) δ 9.00 (m, 1H, C2-H), 7.57 (m, 2H, C4,5-H), 7.04 (s, 4H, Ar-H), 2.35 (s, 6H, C4'-CH_3), 2.12 (s, 12H, C2'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.7 (C2), 137.5 (Ar-C), 134.0 (Ar-C), 130.3 (Ar-C), 130.0 (C3'), 125.0 (C4,5), 21.2 (C4'-CH_3), 17.3 (C2'-CH_3). Found: C 62.33; H 6.28; N 6.98%. $C_{21}H_{25}ClO_4N_2$ requires C 62.30; H 6.22; N 6.92%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium trifluoromethanesulfonate. To a suspension of the chloride salt **20** (0.760 g, 2.23 mmol) in chloroform (25 cm^3), silver(I) trifluoromethanesulfonate (0.620 g, 2.41 mmol) was added portionwise over 5 minutes with stirring. After the reaction mixture had been stirred for an hour at room temperature, the resulting mixture was filtered through celite, the filtrate collected and the solvent was removed under reduced pressure. The resulting white solid was dried *in vacuo* over 30 minutes and recrystallised from dichloromethane. This gave the title compound as a white crystalline solid (0.66 g, 1.21 mmol, 54%). m.p. 203-205°C (lit.[49] not reported). ^{1}H NMR (300 MHz, chloroform-d_1) δ 9.22 (m, 1H, C2-H), 7.56 (m, 2H, C4,5-H), 7.02 (s, 4H, Ar-H), 2.35 (s, 6H, C4'-CH_3), 2.10 (s, 12H, C2'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.5 (C2), 138.0 (Ar-C), 134.0 (Ar-C), 130.4 (Ar-C), 129.9 (C3'), 124.9 (C4,5), 21.2 (C4'-CH_3), 17.3 (C2'-CH_3). ^{19}F NMR (282 MHz, chloroform-d_1) δ -78.73 (CF_3). Found: C 58.16; H 5.56; N 6.20%. $C_{22}H_{25}F_3N_2O_3S$ requires C 58.14; H 5.54; N 6.16%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium hexafluorophosphate. To a solution of the chloride salt **20** (5.34 g, 15.7 mmol) in water (50 cm^3), ammonium hexafluorophosphate (2.56 g, 15.7 mmol) was added portionwise over five minutes and the mixture was stirred at room temperature for one hour. The resulting suspension

was filtered and the residue was washed with hexane. Ion chromatography demonstrated that the material was *ca*. 6% by mole the chloride **20**. This material was suspended in water (50 cm^3) and ammonium hexafluorophosphate (1.27 g, 7.79 mmol) was added. The resultant mixture was stirred at room temperature for one hour. The resulting suspension was filtered and the residue was washed with hexane, yielding the title compound as a white solid (6.35 g, 14.10 mmol, 90%). m.p. >300°C (lit.[50] >300°C). ^{1}H NMR (300 MHz, chloroform-d_1) δ 8.59 (t, J = 1.6 Hz, 1H, C2-H), 7.54 (d, J = 1.6 Hz, 2H, C4,5-H), 7.04 (s, 4H, Ar-H), 2.35 (s, 6H, C4'-CH_3), 2.10 (s, 12H, C2'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.8 (C2), 136.6 (Ar-C), 134.0 (Ar-C), 130.2 (Ar-C), 130.0 (C3'), 125.2 (C4,5), 21.2 (C4'-CH_3), 17.1 (C2'-CH_3). ^{19}F NMR (282 MHz, chloroform-d_1) δ -72.69 (d, $^2J_{FP}$ = 710 Hz, PF_6). Found: C 55.98; H 5.50; N 6.26%. $C_{21}H_{25}F_6N_2P$ requires C 56.00; H 5.59; N 6.22%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium *bis*(trifluoromethanesulfonyl)imide. To a solution of the chloride salt **20** (7.51 g, 22.0 mmol) in water (80 cm^3), lithium *bis*(trifluoromethanesulfonyl)imide (6.47 g, 22.5 mmol) in water (40 cm^3) was added dropwise, with stirring, over a 20 minute period. After an additional 20 minutes of stirring the bright red solution, a yellow precipitate formed. The solid was lixiviated with dichloromethane (4 x 50 cm^3), the organic layers were combined, washed with water (2 x 40 cm^3) and dried over anhydrous magnesium sulfate. The volatile components were removed under reduced pressure and the product dried *in vacuo* over 30 minutes. The compound was recrystallised from dichloromethane/hexane to give the title compound as white crystals (7.25 g, 12.4 mmol, 56%). m.p. 128-130°C. ^{1}H NMR (300 MHz, chloroform-d_1) δ 8.96 (s, 1H, C2-H), 7.50 (m, 2H, C4,5-H), 7.06 (s, 4H, Ar-H), 2.37 (s, 6H, C4'-CH_3), 2.11 (s, 12H, C4'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.8 (C2), 138.0 (Ar-C), 133.9 (Ar-C), 130.2 (Ar-C), 129.9 (C3'), 124.7 (C4,5), 119.4 (q, $^1J_{CF}$ = 321 Hz, CF_3), 21.1 (C4'-CH_3), 17.1 (C2'-CH_3). ^{19}F NMR (282 MHz, chloroform-d_1) δ -79.38 (s, C$\underline{F}_3$). Found: C 47.42; H 4.26; N 7.23%. $C_{23}H_{25}F_6N_3O_4S_2$ requires C 47.17; H 4.30; N 7.18%.

1,3-*bis*(2',4',6'-Trimethylphenyl)imidazolium bromide. To a suspension of the tetrafluoroborate salt **19** (4.96 g, 12.7 mmol) in ethyl acetate (100 cm^3), a solution of tetrapropylammonium bromide (13.37 g, 50.21 mmol) in acetone (200 cm^3) was added dropwise over ten minutes. The resulting mixture was stirred overnight at room temperature. The resulting suspension was filtered and the residue was washed with ethyl acetate and dried under vacuum. Analysis (^{19}F NMR spectroscopy) indicated the presence of tetrafluoroborate anions in this crude product. As such, the procedure was repeated with the crude product suspended in ethyl actetate (150 cm^3), with the addition of a solution of tetrabutylammonium bromide (20.03 g, 62.13 mmol) in acetone (250 cm^3). The mixture was stirred for 24 hours at room temperature. The resultant suspension was filtered and the precipitate washed with ethyl acetate and dried under reduced pressure. Analysis using ^{19}F NMR spectroscopy indicated no residual tetrafluoroborate anions. The solid was taken up into dichloromethane (100 cm^3) and washed with water (3 x 50 cm^3), the organic phase was collected, dried with magnesium sulfate and volatiles were removed under reduced pressure. This gave the title compound as a white solid (2.10 g, 5.45 mmol, 43%). m.p. 229-231°C (lit.[51] 232-234°C). ^{1}H NMR (300 MHz, chloroform-d_1) δ 8.89 (t, J = 1.6 Hz, 1H, C2-H), 7.55 (d, J = 1.6 Hz, 2H, C4,5-H), 7.04 (s, 4H, Ar-H), 2.35 (s, 6H, C4'-CH_3), 2.12 (s, 12H, C2'-CH_3). ^{13}C NMR (75.5 MHz, chloroform-d_1) δ 141.6 (C2), 137.4 (Ar-C), 134.1 (Ar-C), 130.4 (Ar-C), 130.0 (C3'), 125.0 (C4,5), 21.2 (C4'-CH_3), 17.2 (C2'-CH_3). Found: C 65.75; H 6.39; N 7.22%. $C_{21}H_{25}BrN_2$ requires C 65.46; H 6.54; N 7.27%.

General methodology for pK_a titrations. 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 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) 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 Supporting Information).

To the cell containing a solution of the deprotonated fluorene indicator, aliquots of the azolium salt solution (*ca.* 5 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 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 Supporting Information.

ASSOCIATED CONTENT

Supporting Information. Absorbance data for the deprotonated form of each of the indicators **1-6**; derivation of the fitting equation; summary tables of pK_a data for the species **6-28**; pK_a data for a range of 1,3-bis(trimethylphenyl)imidazolium salts with different anions; crystal structure data for compounds **27** and **28**; overlay of the crystal structures of compounds **15** and **20**; overlay of the crystal structures of compounds **20** and **28**; HOMO and LUMO graphical representations and their relative energies for the cations of salts **20**, **27** and **28**; correlation of pK_a data with that determined computationally; NMR spectra of new compounds; EMPIRE outputs for calculations of the cations of the salts **20**, **27** and **28**. This material is available free of charge via the Internet at http://pubs.acs.org

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Footnotes

£ It is important to acknowledge that the nucleophilic addition step is just the first in a series that form the catalytic cycle for NHC catalysed processes. To fully understand such processes the relative rates of each step must be known; the relative importance to the overall rate of the nucleophilic addition step varies with the nature of the process, the substrate and the catalyst (for example, see reference 7 and references cited therein).

$ The two signals are due to an isotope chemical shift and the ratio of 4:1 is consistent with the natural abundances of the two isotopes of boron – ^{11}B and ^{12}B.

REFERENCES

(1) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534.
(2) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606.
(3) Marion, N.; Díez-González, S.; Nolan, S. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2988.
(4) MacMillan, D. W. C. *Nature* **2008**, *455*, 304.
(5) Wei, S.; Wei, X.-G.; Su, X.; You, J.; Ren, Y. *Chem. Eur. J.* **2011**, *17*, 5965.
(6) Bugaut, X.; Glorius, F. *Chem. Soc. Rev.* **2012**, *41*, 3511.
(7) Flanigan, D. M.; Romanov-Michailidis, F.; White, N. A.; Rovis, T. *Chem. Rev.* **2015**, *115*, 9307.
(8) Breslow, R. *J. Am. Chem. Soc.* **1958**, *80*, 3719.
(9) Hachisu, Y.; Bode, J. W.; Suzuki, K. *J. Am. Chem. Soc.* **2003**, *125*, 8432.
(10) Li, G.-Q.; Dai, L.-X.; You, S.-L. *Chem. Commun.* **2007**, 852.
(11) Stetter, H. *Angew. Chem.* **1976**, *88*, 695.
(12) Enders, D.; Breuer, K.; Runsink, J.; Teles, J. H. *Helv. Chim. Acta* **1996**, *79*, 1899.
(13) Mattson, A. E.; Bharadwaj, A. R.; Scheidt, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 2314.
(14) Sohn, S. S.; Rosen, E. L.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 14370.
(15) Burstein, C.; Glorius, F. *Angew. Chem., Int. Ed.* **2004**, *43*, 6205.
(16) Dunn, M. H.; Cole, M. L.; Harper, J. B. *RSC Advances* **2012**, *2*, 10160.
(17) Song, J. J.; Gallou, F.; Reeves, J. T.; Tan, Z.; Yee, N. K.; Senanayake, C. H. *J. Org. Chem.* **2006**, *71*, 1273.
(18) Brønsted, J. N.; Pedersen, K. J. *Z. Phys. Chem.* **1924**, *108*, 185.
(19) Alder, R. W.; Allen, P. R.; Williams, S. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1267.
(20) Kim, Y.-J.; Streitweiser, A. *J. Am. Chem. Soc.* **2002**, *124*, 5757.
(21) Amyes, T. L.; Diver, S. T.; Richard, J. P.; Rivas, F. M.; Toth, K. *126* **2004**, 4366.
(22) 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.
(23) Massey, R. S.; Collett, C. J.; Lindsay, A. G.; Smith, A. D.; O'Donoghue, A. C. *J. Am. Chem. Soc.* **2012**, *134*, 20424.
(24) Tucker, D. E.; Quinn, P.; Massey, R. S.; Collett, C. J.; Jasiewicz, D. J.; Bramley, C. R.; Smith, A. D.; O'Donoghue, A. C. *J. Phys. Org. Chem.* **2015**, *28*, 108.

(25) Massey, R. S.; Quinn, P.; Zhou, S.; Murphy, J. A.; O'Donoghue, A. C. *J. Phys. Org. Chem.* **2016**, *29*, 735.
(26) Magill, A. M.; Cavell, K. J.; Yates, B. F. *J. Am. Chem. Soc.* **2004**, *126*, 8717.
(27) Chu, Y.; Deng, H.; Cheng, J.-P. *J. Org. Chem.* **2007**, *72*, 7790.
(28) Bordwell, F. G.; Bartmess, J. E.; Drucker, G. E.; Margolin, Z.; Matthews, W. S. *J. Am. Chem. Soc.* **1975**, *97*, 3226.
(29) Bordwell, F. G.; Drucker, G. E.; McCollum, G. J. *J. Org. Chem.* **1982**, *47*, 2504.
(30) Bordwell, F. G.; Drucker, G. E.; Fried, H. E. *J. Org. Chem.* **1981**, *46*, 632.
(31) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.
(32) Gyton, M. R.; Cole, M. L.; Harper, J. B. *Chem. Commun.* **2011**, *47*, 9200.
(33) Olmstead, W. N.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3299.
(34) Isaacs, N. S. *Physical Organic Chemistry*; Addison Wesley Longman China Limited: Singapore, 1995.
(35) Jaffé, H. H. *Chem. Rev.* **1953**, *53*, 191.
(36) Cole, M. L.; Junk, P. C. *CrystEngComm* **2004**, *6*, 173.
(37) Fuller, J.; Carlin, R. *J. Chem. Crystallogr.* **1994**, *24*, 489.
(38) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209.
(39) Hennemann, M.; Clark, T. *J. Mol. Model.* **2014**, *20*, 2331.
(40) Margraf, J. T.; Hennemann, M.; Meyer, B.; Clark, T. *J. Mol. Model.* **2015**, *21*, 144.
(41) Vougioukalakis, G. C.; Roubelakis, M. M.; Orfanopoulos, M. *J. Org. Chem.* **2010**, *75*, 4124.
(42) Hawker, R. R.; Panchompoo, J.; Aldous, L.; Harper, J. B. *ChemPlusChem* **2016**, *81*, 574.
(43) Voges, M. H.; Rømming, C.; Tilset, M. O., 18, 529. *Organometallics* **1999**, *18*, 529.
(44) Huang, J.; Nolan, S. P. *J. Am. Chem. Soc.* **1999**, *121*, 9889.
(45) Arduengo, A. J.; Krafczyk, R.; Schmutzler, R.; Craig, H. A.; Goerlich, J. R.; Marshall, W. J.; Unverzagt, M. *Tetrahedron* **1999**, *55*, 14523.
(46) Kuhn, K. M.; Grubbs, R. H. *Org. Lett.* **2008**, *10*, 2075.
(47) McGarrigle, E. M.; Fritz, S. P.; Favereau, L.; Yar, M.; Aggarwal, V. K. *Org. Lett.* **2011**, *13*, 3060.
(48) 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.
(49) Kim, J.-H. J.; Kyoung-A; Son, Y.-H.; Park, S.-R.; Ahn, K.-H.; Kang, E.-J. *Bull. Kor. Chem. Soc.* **2009**, *30*, 2464.
(50) Lindsay, D. M.; McArthur, D. *Chem. Commun.* **2010**, *46*, 2474.
(51) Li, S.; Kee, C. W.; Huang, K.-W.; Hor, T. S. A.; Zhao, J. *Organometallics* **2010**, *29*, 1924.

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