Stable Carbenes as Strong Bases

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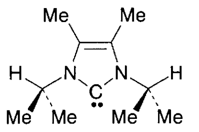
The stable carbene 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene has a $\mathrm{p}K_a$ of 24 in $(CD_3)_2SO$ and gives an elimination : substitution ratio with 2-bromopropane comparable to that of 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).

Since their first isolation in 1991,[1] stable imidazol-2-ylidene carbenes† have attracted considerable attention.[2,3] We report preliminary results which show that one of these species, 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene **1**, is a stronger base than DBN **2**, DBU **3** and the strongest proton sponge **4**, (conjugate acid $\mathrm{p}K_a$ 16.1 in 35% aqueous Me_2SO),[4] although it does not rival some of the phosphazene bases developed by Schwesinger,[5] (*e.g.* **5**, conjugate acid $\mathrm{p}K_a$ 30.25 in Me_2SO) which are the strongest known neutral bases. We have also briefly examined the nucleophilicity of **1**.

No measurements of the basicity of these carbenes have been reported,[6] but they are clearly related to the conjugate base of thiamine **6**, ($R = CH_2CH_2OH$)[7] and there has been considerable debate about the $\mathrm{p}K_a$ of this compound. Early work suggested a $\mathrm{p}K_a$ of *ca.* 13,[8] while more recent studies suggest a value of *ca.* 16.[9] The relative rates of base-catalysed deuterium exchange for the 3,4-dimethyloxazolium ion, the 3,4-dimethylthiazolium ion and the 1,3,4-trimethylimidazolium ion are reported to be in the ratio $10^{5.5} : 10^{3.5} : 1$.[10] This data suggests that imidazolium ions should have $\mathrm{p}K_a$ values for *C*-deprotonation of at least 16–20 (and much higher if the Brønsted $\alpha << 1$).

We have examined **1**, prepared from 1,3-diisopropyl-4,5-dimethylimidazole-2 (3*H*)-thione by reaction with potassium in THF, filtration under nitrogen and evaporation.[11] The ability of **1** to deprotonate typical acidic hydrocarbons was examined by NMR in $(CD_3)_2SO$. Indene ($\mathrm{p}K_a$ 20.1) was cleanly and completely converted to its anion, but 9-phenylxanthene ($\mathrm{p}K_a$ 27.7) and triphenylmethane ($\mathrm{p}K_a$ 30.6) were not measurably deprotonated.[12] The ^1H NMR spectra of 1 : 1 mixtures of **1** with fluorene ($\mathrm{p}K_a$ 22.9) and with 2,3-benzofluorene (Scheme 1; $\mathrm{p}K_a$ 23.5) showed separate absorptions for the hydrocarbons and their anions, and from the integration of these spectra an apparent $\mathrm{p}K_a$ of 24.0 for **1** can be derived.‡ When the same experiments were repeated in THF, **1** failed to deprotonate fluorene to a measurable extent but almost completely deprotonated 9-phenylfluorene ($\mathrm{p}K_a$ 18.5 in THF) and indene. This difference clearly reflects the fact that ions are created from neutral species in reactions such as that shown in Scheme 1, and this will be less favourable in the lower polarity solvent.



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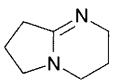

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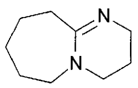

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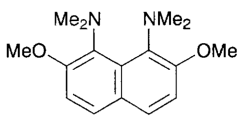

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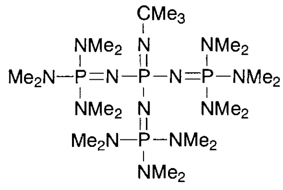

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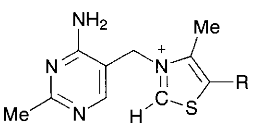

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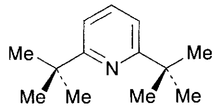

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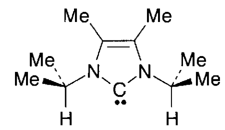
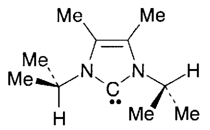


1′

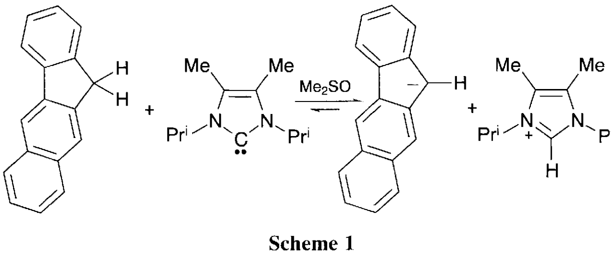


1″

An interesting feature of these NMR experiments is that, while separate spectra are seen for the hydrocarbon acids and their conjugate bases, indicative of slow proton transfer on the NMR timescale, only a (slightly broadened) averaged spectrum is seen for **1** and its conjugate acid. Clearly, proton transfer between **1** and its conjugate acid is quite fast, probably reflecting the established ability of these species to form C···H–C bonds;[13] this augurs well for the potential use of these compounds in rate-limiting proton transfer reactions.

Strong bases must meet at least two other important criteria besides high $\mathrm{p}K_a$ to be effective in synthetic applications: (*a*) they should undergo moderately fast proton-transfer reactions if they are to be used in reactions where proton transfer is rate-limiting (see above); and (*b*) they should be weakly nucleophilic. As far as factor (*b*) is concerned, **1** was chosen for initial exploration because, in its probable minimum energy conformation, it resembles 2,6-di-*tert*-butylpyridine **7**, a (weak) base known for its extreme non-nucleophilicity.[14] On the other hand, the conjugate bases of thiazolium ions like thiamine **6** are well known to be powerful nucleophiles.[7]

We have made some preliminary observations on the nucleophilicity of **1**, which reacts readily with primary and secondary haloalkanes at room temperature in $(CD_3)_2SO$. Reactions with 1-bromo-hexane or -octane give mainly the substitution product 2-hexyl (or octyl)-1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene, but small amounts of alkenes are formed (*ca.* 10%). It is noteworthy that, in the alkylation products, the first CH_2 group in the chain is completely deuteriated by exchange with the solvent, catalysed by **1**. Reaction with 2-bromopropane produces a 20 : 80 ratio of elimination and substitution products, which can be compared with the 91% alkylation reported for DBN and the 21% given by DBU.[15] It is clear that **1** itself is too nucleophilic for general use as a strong base probably because, although the preferred conformation is as shown in **1**, the unhindered conformation **1′** with C–H bonds aligned parallel to the carbene sp^2 orbital lies only 1.9 kJ mol^{-1} higher in energy, according to AM1 calculations.[16]§ We are currently examining imidazol-2-ylidenes with tertiary groups at the 1,3-positions,[1] and C_2-chiral derivatives [*e.g.* with 1,3-bis(1-phenylethyl) groups], especially with larger buttressing groups at the 4,5 positions.



Scheme 1

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Footnotes

† These species will be referred to as carbenes for simplicity; the contribution made by ylidic resonance forms has been extensively debated (see ref. 2).

‡ This value has been corrected for the statistical factor, but no correction for ionic strength and ion pairing has been attempted.

§ Surprisingly, the **1″** conformation is found to be 0.2 kJ mol^{-1} higher in energy than **1′** for the carbene, although the relative energies for the corresponding imidazolium ions are **1** (0) < **1″** (5.6) < **1′** (9.5 kJ mol^{-1}).

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