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Intermolecular Insertion of an N,N-Heterocyclic Carbene into a Nonacidic C–H Bond: Kinetics, Mechanism and Catalysis by $(K\text{-}HMDS)_2$ (HMDS = Hexamethyldisilazide)

Guy C. Lloyd-Jones,* Roger W. Alder, and Gareth J. J. Owen-Smith[a]

Abstract: The reaction of 2-[^{13}C]-1-ethyl-3-isopropyl-3,4,5,6-tetrahydropyrimidin-1-ium hexafluorophosphate ([$^{13}C_1$]-**1**-PF_6) with a slight excess (1.03 equiv) of dimeric potassium hexamethyldisilazide ("$(K\text{-}HMDS)_2$") in toluene generates 2-[^{13}C]-3-ethyl-1-isopropyl-3,4,5,6-tetrahydropyrimid-2-ylidene ([$^{13}C_1$]-**2**). The hindered *meta*-stable N,N-heterocyclic carbene [$^{13}C_1$]-**2** thus generated undergoes a slow but quantitative reaction with toluene (the solvent) to generate the aminal 2-[^{13}C]-2-benzyl-3-ethyl-1-isopropylhexahydropyrimidine ([$^{13}C_1$]-**14**) through formal C–H insertion of C(2) (the "carbene carbon") at the toluene methyl group. Despite a significant pK_a mismatch (ΔpK_a **1**$^+$ and toluene estimated to be ca. 16 in DMSO) the reaction shows all the characteristics of a deprotonation mechanism, the reaction rate being strongly dependent on the toluene *para* substituent ($\rho = 4.8(\pm 0.3)$), and displaying substantial and rate-limiting primary ($k_H/k_D = 4.2(\pm 0.6)$) and secondary ($k_H/k_D = 1.18(\pm 0.08)$) kinetic isotope effects on the deuteration of the toluene methyl group. The reaction is catalysed by K-HMDS, but proceeds without cross over between toluene methyl protons and does not involve an HMDS anion acting as base to generate a benzyl anion. Detailed analysis of the reaction kinetics/kinetic isotope effects demonstrates that a pseudo-first-order decay in **2** arises from a first-order dependence on **2**, a first-order dependence on toluene (in large excess) and, in the catalytic manifold, a complex noninteger dependence on the K-HMDS dimer. The rate is not satisfactorily predicted by equations based on the Brønsted salt-effect catalysis law. However, the rate can be satisfactorily predicted by a mole-fraction-weighted net rate constant: $-d[\mathbf{2}]/dt = (\{x_2 k_{uncat}\} + \{(1-x_2) k_{cat}\})[\mathbf{2}]^1[\text{toluene}]^1$, in which x_2 is determined by a standard bimolecular complexation equilibrium term. The association constant (K_a) for rapid equilibrium–complexation of **2** with $(K\text{-}HMDS)_2$ to form [**2**($K\text{-}HMDS)_2$] is extracted by nonlinear regression of the ^{13}C NMR shift of C(2) in [$^{13}C_1$]-**2** versus [$(K\text{-}HMDS)_2$] yielding: $K_a = 62(\pm 7)\,M^{-1}$; $\delta_{C(2)}$ in **2** = 237.0 ppm; $\delta_{C(2)}$ in [**2**($K\text{-}HMDS)_2$] = 226.8 ppm. It is thus concluded that there is discrete, albeit inefficient, molecular catalysis through the 1:1 carbene/$(K\text{-}HMDS)_2$ complex [**2**($K\text{-}HMDS)_2$], which is found to react with toluene more rapidly than free **2** by a factor of 3.4 ($= k_{cat}/k_{uncat}$). The greater reactivity of the complex [**2**($K\text{-}HMDS)_2$] over the free carbene (**2**) may arise from local Brønsted salt-effect catalysis by the $(K\text{-}HMDS)_2$ liberated in the solvent cage upon reaction with toluene.

Keywords: carbenes · homogeneous catalysis · isotope effects · kinetics · potassium

Introduction

Since the early demonstrations of the surprising kinetic, and even thermodynamic, stability of heteroatom-stabilised carbenes towards dimerisation,[1] the area has enjoyed sustained interest and development.[2] N,N-Heterocyclic carbenes in particular have found widespread application as ligands in transition-metal catalysis,[3] as catalysts in their own right for organic transformations[4] and as chemical entities that fascinate and challenge the theoretical and practical chemist alike. As part of a research programme exploring the mechanism of dimerisation of stable N,N-heterocyclic carbenes,[5] we recently prepared the tetrahydropyrimidinium salt **1**-PF_6 as a precursor for base-mediated generation of carbene **2**, which under certain conditions dimerises to yield tetraaminoethylene derivative **3**.[6]

To aid the analysis of the kinetics of the dimerisation reaction by $^{13}C\{^1H\}$ NMR we prepared [$^{13}C_1$]-**1**, and thus

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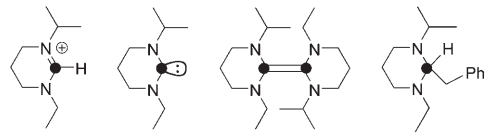
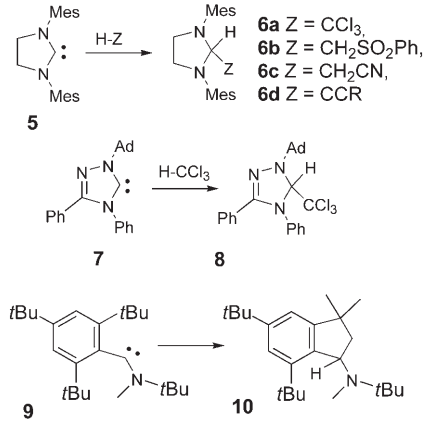


[$^{13}C_1$]-**2** and [$^{13}C_2$]-**3**, in which the carbene carbon C(2) in **2** is ^{13}C-labelled. The resulting increase in sensitivity in the $^{13}C\{^1H\}$ NMR spectrum facilitated the detection of a number of species arising as byproducts (< ca. 2.5%) from the generation of [$^{13}C_1$]-**2** in toluene. Of these species, aminal **4** was identified as a minor component, but found to increase with time to become the major product. The identification of **4** and a detailed investigation of its mechanism of generation from toluene forms the basis of the work presented herein. This is the first report of the formal intermolecular insertion of a stable carbene into a "nonacidic" ($pK_a \geq 25$) C–H bond.[7] Indeed, even the reaction of stable carbenes with "acidic" C–H bonds ($pK_a \leq 25$) is still comparatively rare, being limited to the examples shown in Scheme 1.



Scheme 1. Formal insertion of stable carbenes **5**,[7a,d] **7**[7c] and **9**[7b] into C–H bonds, the precursors for which (H–Z) all have $pK_a \leq 25$, except for **9** for which the reaction **9**→**10** is intramolecular. Mes = 2,4,6-trimethylphenyl; Ad = adamantyl. Note that for the unsaturated analogue of **5**, which is aromatic, reaction with CH_3CN fails, whilst reaction with $CHCl_3$ gives complex mixtures.[7a]

The reaction of **2** with toluene ($pK_a \approx 42$–44) is surprising: there is a significant pK_a mismatch between reactants (ΔpK_a **1** and toluene ca. 16–18) and the reaction is found to be catalysed by dimeric potassium hexamethyldisilazide ("(K-HMDS)$_2$").

Results and Discussion

The C–H deprotonation reaction of *N*,*N*,*N*′,*N*′-tetraalkylated formamidinium salts with sterically hindered strong bases has become a general procedure for the generation of N,N-heterocyclic carbenes.[8] Wanting to generate carbene **2** from salt **1**-PF_6 without competing dimerisation[5,6] to form **3**, we treated **1**-PF_6, as a vigorously agitated suspension in [D_8]toluene, under strictly anhydrous and anaerobic conditions with a small excess (1.03 equiv) of the hindered dimeric[9] base [K-N($SiMe_3$)$_2$]$_2$ ("(K-HMDS)$_2$", commercial sample, 0.43 M in toluene). This procedure exploits the extremely low solubility of the ionic precursor **1**-PF_6 and the co-product, KPF_6, in the rather apolar toluene medium, thereby avoiding extensive dimerisation of carbene **2**. Using this method, we found we could smoothly generate **2** in a sealed NMR tube, as evidenced by a low intensity singlet at $\delta = 236$ ppm arising from C(2) in the $^{13}C\{^1H\}$ NMR spectrum, which shows only small quantities of dimer **3**. The NMR tube was repeatedly agitated (sonication) and then analysed by $^{13}C\{^1H\}$ NMR spectrum until > 98% of the (K-HMDS)$_2$ (singlet at $\delta = 7.2$ ppm) had reacted, thereby generating **2** in essentially quantitative yield[10] together with HN($SiMe_3$)$_2$ ("H-HMDS"; singlet at $\delta = 2.6$ ppm).

Side products arising from generation of carbene 2 from 1 and K-HMDS: The asymmetry of **2** and the resulting complexity of the ^{1}H NMR spectrum of mixtures of **2**, (*E*)-**3** and (*Z*)-**3**, prompted us to prepare [$^{13}C_1$]-**2**, in which C(2) bears the ^{13}C-label, so that we could monitor the kinetics of the dimerisation of **2** by $^{13}C\{^1H\}$ NMR spectroscopy.[5] In doing so, the signal at $\delta = 236$ ppm arising from C(2) in **2** became approximately 99-fold stronger; we also noted a range of other minor signals at $\delta = 162.1$, 161.9, 161.7, 161.5, 106.1, 91.2 and 76.5 ppm in the $^{13}C\{^1H\}$ NMR spectrum that were not attributable to **2** (or **1** or **3**) but were clearly arising from a ^{13}C-labelled carbon, Figure 1. It should be noted that the intensity of the signal arising from C(2) in **2** is relatively weak due to poor proton-mediated nOe magnetisation and inefficient $\{^1H\}$-induced relaxation. A proton-coupled $^{13}C\{^1H$-gated$\}$ NMR spectrum revealed that the signals at $\delta = 162.1$, 161.9, 161.7, 161.5, 106.1, 91.2 and 76.5 ppm arise from C–H species and thus their relative intensity is significantly higher than C(2) in [$^{13}C_1$]-**2**. In other words, the ^{13}C-labelling had revealed the presence of some rather minor side products (< ca. 2.5%).

The signals at $\delta = 106.1$ and 91.2 ppm were found to reduce in intensity or even disappear during, or shortly-after, the reaction with an accompanying increase in the signals at $\delta = 161.5$–162.1 ppm and at $\delta = 236$ ppm ([$^{13}C_1$]-**2**). Based on the ^{13}C-chemical shifts, we speculated that the signals arose from the moieties of the type R_2N-$^{13}C(=O)H$ ($\delta =$ 162.1, 161.9, 161.7, and 161.5 ppm); $(R_2N)_2{}^{13}C(H)$-O ($\delta =$ 106.1 ppm); $(R_2N)_2{}^{13}C(H)$-N ($\delta = 91.2$ ppm) and $(R_2N)_2{}^{13}C(H)$-C ($\delta = 76.5$ ppm), in which the labelled carbon atom derives from the precursors [$^{13}C_1$]-**1** or [$^{13}C_1$]-**2**. The first two assignments were confirmed by reaction of [$^{13}C_1$]-**1** with anhydrous KOH/(K-HMDS)$_2$ in [D_6]benzene (Scheme 2); this reaction gave a mixture of alkoxide [$^{13}C_1$]-**11** and formamides [$^{13}C_1$]-**12H** and [$^{13}C_1$]-**13H** (each displaying two rotameric amide isomers in the $^{13}C\{^1H\}$ NMR spec-

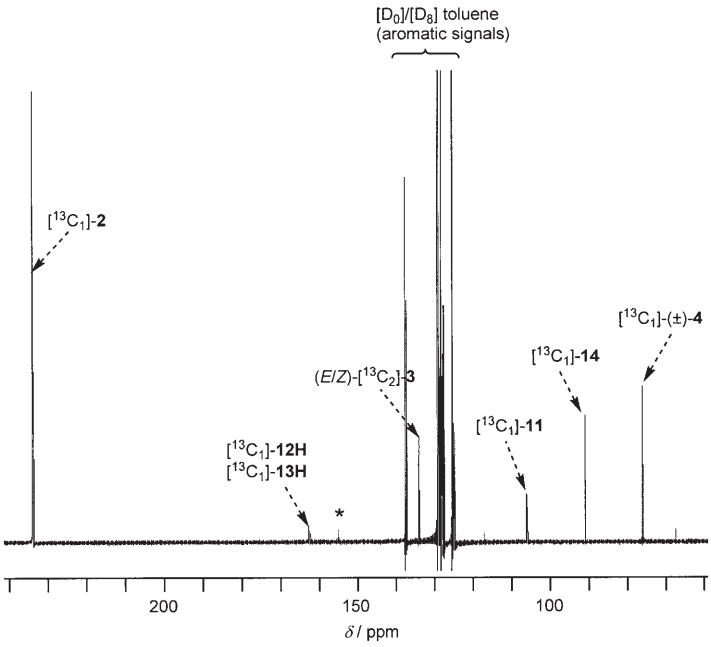
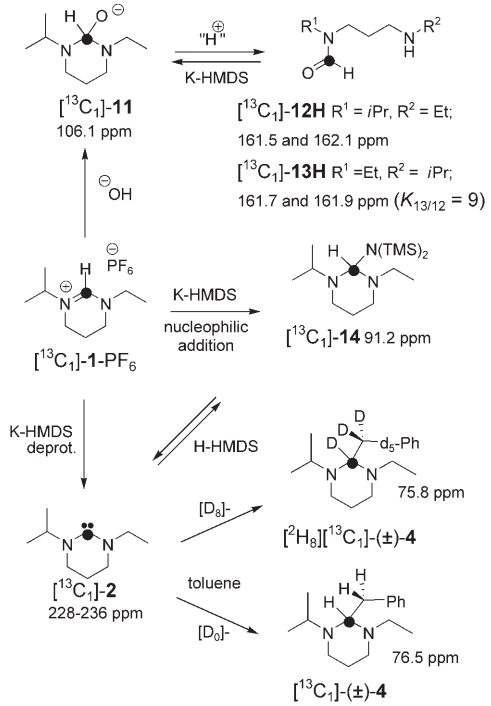


Figure 1. The $^{13}C\{^1H\}$ NMR sub-spectrum (60–240 ppm) of the product mixture obtained on sonication of a suspension of $[^{13}C_1]$-**1**-PF_6 in $[D_8]$toluene after addition of 1.03 equiv of $(K\text{-}HMDS)_2$ (0.43 M in toluene). For full assignments see text and Scheme 2. Note that **2** lacks a proton at C(2) and thus the signal intensity is about one third of that of C–H compounds **4**, **11**, **12H** and **13H**. The signal identified by "*" is unassigned, but is similar in chemical shift to C(2) of [**1**]-PF_6 ($\delta = 155$ ppm) which is only sparingly soluble in toluene.



Scheme 2. Side/co-products arising from generation of $[^{13}C_1]$-**2** by reaction of $[^{13}C_1]$-**1**-PF_6 with commercial solutions of $(K\text{-}HMDS)_2$ in toluene (0.43 M) as identified by $^{13}C\{^1H\}$ NMR spectroscopy in $[D_8]$toluene (see Figure 1).

trum). Addition of further $(K\text{-}HMDS)_2$ partially converted formamides $[^{13}C_1]$-**12H** and $[^{13}C_1]$-**13H** to the alkoxide $[^{13}C_1]$-**11**, whilst exposure to moisture (air) converted the alkoxide $[^{13}C_1]$-**11** to the neutral formamides $[^{13}C_1]$-**12H** and $[^{13}C_1]$-**13H**, presumably by means of an equilibrium with the ring-opened nitrogen anions $[^{13}C_1]$-**12** and $[^{13}C_1]$-**13** (not observed), which can deprotonate water. Interestingly, **12H** and **13H**, the identities of which were assigned by ^1H nOe/CH correlation, are initially generated in a 1:1 ratio, but undergo slow interconversion, presumably via **11** (or **11H**), to give an equilibrium mixture that favours **13H** ($K = 9$). It is thus concluded that **11**, **12H** and **13H** arise in the generation of carbene **2**, by reaction of salt **1** with traces of KOH in the commercial $(K\text{-}HMDS)_2$ reagent.

The signal at $\delta = 91.2$ ppm, assigned as that arising from a $(R_2N)_2{}^{13}C(H)$-N unit, was suggestive of $(K\text{-}HMDS)_2$ effecting nucleophilic attack at C(2) of $[^{13}C_1]$-**1**, in competition with deprotonation, to generate the HMDS adduct $[^{13}C_1]$-**14** (Scheme 2). A competing nucleophilic attack by Li-HMDS in the C–H deprotonation reaction of related *N*,*N*′-dialkylated tetrahydropyrimidinium salts has been reported by Alder et al.[11] The decrease in the intensity of the signal of $[^{13}C_1]$-**14** during or shortly after complete reaction suggests that the addition of the HMDS anion to **1** is reversible, as indeed is found to be the case, vide infra.

Finally, on close inspection, the signal at $\delta = 76.5$ ppm, was found to have a neighbouring multiplet ($\delta = 75.8$ ppm) of very low intensity, but with an equipollent triplet structure characteristic of a deuterium-bearing carbon atom ($^1J(C,D) = 21.5$ Hz). Since the $[D_8]$toluene, used as a co-solvent with the commercial toluene $(K\text{-}HMDS)_2$ solution, was the only source of deuterium, we repeated the procedure using freshly prepared $(K\text{-}HMDS)_2$ (prepared from KH and H-HMDS)[12] in $[D_8]$toluene: the intensity of the triplet was found to be approximately the same, but there was essentially no trace of the singlet at $\delta = 76.5$ ppm, and the amount of alkoxide/formamides (**11**/**12H** and **13H**) generated was reduced. The tentative assignment of the signal at $\delta = 76.5$ ppm as that of C(2) in the toluene adduct $[^{13}C_1]$-**4** was confirmed by independent, albeit inefficient, preparation of **4** from phenacetaldehyde.[13] When pure $[D_8]$toluene is used as solvent, the major side product from reaction of $[^{13}C_1]$-**1** with $(K\text{-}HMDS)_2$ is $[^2H_8][^{13}C_1]$-**4**, vide infra, and we initially suspected that this was generated by addition of a $[D_7]$benzyl anion to $[^{13}C_1]$-**1**-PF_6. However, it soon became evident that the concentration of $[^2H_8][^{13}C_1]$-**4** continued to increase after all of the $[^{13}C_1]$-**1**-PF_6 had been consumed, thus implicating the involvement of $[^{13}C_1]$-**2** rather than $[^{13}C_1]$-**1**.

Kinetics of reaction of carbene 2 with $[D_8]$toluene—K-HMDS catalysis: As noted above, the reaction of $[^{13}C_1]$-**1** with $(K\text{-}HMDS)_2$ in $[D_8]$toluene to generate $[^{13}C_1]$-**2**, involves alternating periods of sonication then analysis by $^{13}C\{^1H\}$ NMR until generation of $[^{13}C_1]$-**2** is complete. Although the sonication results in a stochastic profile to the evolution of $[^{13}C_1]$-**2**, the profile for the generation of $[^2H_8]$-

[$^{13}C_1$]-**4** versus time was found to be rather smooth—in other words, the rate *appeared* to be unrelated to the concentration of [$^{13}C_1$]-**2**. However, we reasoned that since the generation of [$^{13}C_1$]-**2** from [$^{13}C_1$]-**1**-PF_6 is directly coupled to the consumption of $(K\text{-}HMDS)_2$ and thus as the concentration of [$^{13}C_1$]-**2** rises, the concentration of $(K\text{-}HMDS)_2$ falls linearly,[14] a compensatory effect would arise if the K-HMDS catalysed the reaction of [$^{13}C_1$]-**2** with the toluene.

To explore this possibility, we prepared 0.08 M [D_8]toluene solutions of [$^{13}C_1$]-**2** from [$^{13}C_1$]-**1** with larger excesses of $(K\text{-}HMDS)_2$[15] (1.1, 1.5, 2.2, 3.0, 4.3 and 8.3 formal equivalents of HMDS anion). The solutions of [$^{13}C_1$]-**2** were generated very cleanly over a period of ca. 10 min, with [$^2H_8$][$^{13}C_1$]-**4** as essentially the only side product ($\leq 1\%$). Over a period of days, [$^2H_8$][$^{13}C_1$]-**4** was found to grow smoothly at the expense of [$^{13}C_1$]-**2**.

The reactions were found to evolve through a logarithmic decay in [$^{13}C_1$]-**2**, giving good linear correlations, Figure 2 (left). An additional two samples with half and double the initial concentrations of [$^{13}C_1$]-**2** behaved analogously, thus allowing determination of macroscopic first-order rate constants k_{obs} (s^{-1}) over a range of initial concentrations of [$^{13}C_1$]-**2**, $(K\text{-}HMDS)_2$ and HMDS, Table 1, entries 1–8.

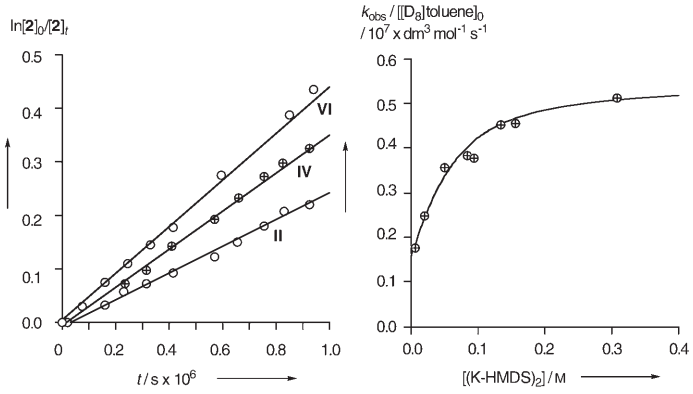


Figure 2. Left-hand graph: typical examples of the linear relationship between time and $\ln([\mathbf{2}]_0/[\mathbf{2}]_t)$ at various concentrations of $(K\text{-}HMDS)_2$ for the reaction of **2** with [D_8]toluene (solvent) to generate **4** (numbers II, IV and VI refer to entries 2, 4, and 6, respectively, in Table 1). Right-hand graph: the complex relationship between $(K\text{-}HMDS)_2$ concentration and the normalised pseudo-first-order rate constants $k_{obs}/[[D_8]\text{toluene}]_0$ (as determined by linear regression (left-hand graph) of data from Table 1, entries 1–8). The solid line passing through data points is a nonlinear regression based on a model involving catalysis by $(K\text{-}HMDS)_2$ complexation: $K_a = 62\,M^{-1}$, $k_{uncat} = 1.46\times10^{-8}\,dm^3\,mol^{-1}\,s^{-1}$, $k_{cat} = 5.11\times10^{-8}\,dm^3\,mol^{-1}\,s^{-1}$, $[\mathbf{2}] = 54.3$ mM; see text for full discussion.

Although the effect of excess [K-HMDS] on the rate results in a complex relationship (Figure 2 right), in which $-d[\mathbf{2}]/dt \propto (f[\text{K-HMDS}])$ in which f = non-linear function, vide infra, the large excess of [D_8]toluene (ca. 55–231 equiv) and constant nature of the $(K\text{-}HMDS)_2$ and H-HMDS concentrations are consistent with a simple pseudo-first-order relationship of the rate to carbene concentration, [[$^{13}C_1$]-**2**].

Table 1. Pseudo-first-order rate constants[a] (k_{obs}) for reactions of excess [D_8]toluene, toluene, substituted toluenes (4-CF_3-toluene (**15**), 4-Cl-toluene (**16**), 4-*t*Bu-toluene (**17**) and ethylbenzene (**18**); 40–118 equiv), with carbene [$^{13}C_1$]-**2** (generated in situ from [$^{13}C_1$]-**1**-PF_6) in [D_8]toluene or [D_6]benzene solvent medium, in the presence of excess $(K\text{-}HMDS)_2$ at 23 °C.

	Arene	$[\text{Arene}]_0$ [M]	$[\mathbf{2}]_0$ [mM]	$[(K\text{-}HMDS)_2]$[b] [mM]	k_{obs} [$s^{-1}\times10^7$]
1	[D_8]toluene	9.32	79	5.6	1.64(±0.05)
2	[D_8]toluene	9.29	81	20.0	2.40(±0.03)
3	[D_8]toluene	9.22	81	50.1	3.29(±0.02)
4	[D_8]toluene	9.14	82	83.3	3.49(±0.03)
5	[D_8]toluene	9.02	81	134	4.07(±0.03)
6	[D_8]toluene	8.61	85	308	4.40(±0.05)
7	[D_8]toluene	9.02	163	93.7	3.39(±0.04)
8	[D_8]toluene	9.02	39	156	4.10(±0.07)
9	[D_0]toluene	2.81	67	68	9.46(±0.31)
10	**15**	2.78	69	68	_[c]
11	**16**	2.78	68	68	67.8(±0.9)
12	**17**	2.77	68	68	2.14(±0.10)
13	**18**	2.81	69	68	1.77(±0.47)
14	[D_1]toluene[d]	2.94	68	68	6.09(±0.08)[e]
15	[D_8]toluene	9.02	24	163	4.32(±0.18)[f]

[a] Determined by linear regression of $\ln([\mathbf{2}]_0/[\mathbf{2}]_t)$ versus t, as determined by $^1H/^{13}C$ NMR analysis, see Figure 2. [b] The formal concentration of *excess* $(K\text{-}HMDS)_2$ based on consumption of 0.5 equivalents $(K\text{-}HMDS)_2$ in the deprotonation of [**1**]-PF_6. [c] Reaction complete (>95%) within 29 min. A value of $1.72\times10^{-3}\,s^{-1}$ is estimated as the lower limit for k_{obs}. [d] α-[D_1]Toluene (>98.8% $^2H_1$), contains about 1% diethyl ether. [e] The partitioning is 87.6% C–H insertion, 12.4% C–D insertion. [f] Reaction after filtration from precipitated KPF_6 (0.45 μM PTFE membrane) then 3.5-fold dilution into 0.175 M $(K\text{-}HMDS)_2$ in [D_8]toluene.

Kinetics of reaction of carbene 2 with substituted toluenes in [D_6]benzene—linear free energy relationship and kinetic isotope effects: During the reaction that generates **4**, the C–H bond of the toluene methyl group is cleaved, allowing formal insertion of C(2) of **2**, see scheme in Figure 3. To probe the polarity of the C–H cleavage, we determined the pseudo-first-order rate constants for reaction of [$^{13}C_1$]-**2**, generated in C_6D_6 from $(K\text{-}HMDS)_2$ (2.0 equiv HMDS anion) with separate samples of excess (ca. 40 equiv) toluene, 4-CF_3-toluene (**15**), 4-Cl-toluene (**16**), 4-*tert*-butyltoluene (**17**) and α-methyltoluene (ethylbenzene, **18**). All five substrates cleanly gave carbene ([$^{13}C_1$]-**2**) aryl C–H insertion products, ([$^{13}C_1$]-**4**, [$^{13}C_1$]-**19**, [$^{13}C_1$]-**20**, [$^{13}C_1$]-**21** and [$^{13}C_1$]-**22** (0% *de*), Figure 3) as evidenced by intense signals in the $\delta = 76.1$–81.9 ppm region.

The rates of reaction of [D_0]toluene, **15**, **16** and **17** (Table 1, entries 9, 10, 11 and 12) yielded a relatively large and positive ρ value ($\rho^- = 4.8(\pm0.3)$) in a standard Hammett correlation employing σ^-. By using Swain–Lupton parameters,[16] ($\sigma_{SL} = 0.73(\pm0.03)F + R$) it was determined that the correlation has a greater dependence on the resonance term than on the field term ($R/F = 1.37$), Figure 3. Both correlations are indicative of a substantial increase in electron density at the aryl-bound carbon en route to the rate-limiting transition state. The greater dependence on the resonance term (R) in the Swain–Lupton correlation also suggests that there is significant sp^2 hybridisation at the benzylic carbon atom in the transition state to facilitate π delocalisation. Re-

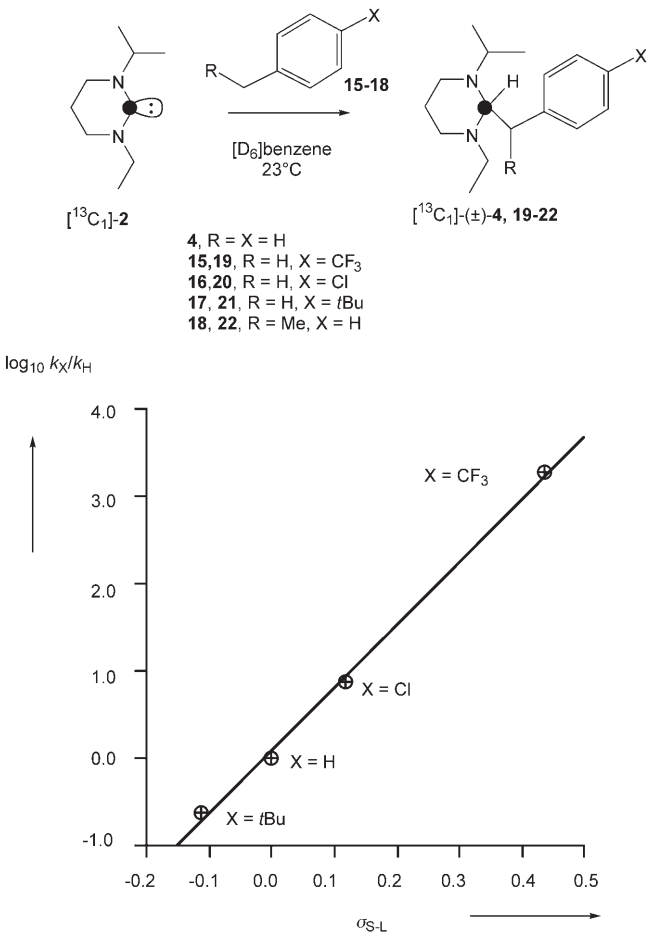


Figure 3. Linear free energy relationship of the relative rates of reaction of $[^{13}C_1]$-**2** with toluene, 4-CF_3-toluene (**15**), 4-Cl-toluene (**16**) and 4-*tert*-butyl-toluene (**17**) in $[D_6]$benzene in the presence of $(K\text{-}HMDS)_2$ (0.068 M). *y* axis: rate data from Table 1, entries 9–12; *x* axis: substituent constant σ_{SL} derived from Swain–Lupton parameters, $\sigma_{SL}=(1.0\times R)+(0.73\times F)$. A value of $\rho=4.8$ (±0.3) is obtained in a standard Hammett correlation employing σ.

action of α-$[D_1]$toluene (Ph-CH_2D) proceeded at approximately 0.64-fold the rate of $[D_0]$toluene (compare entries 9 and 14, Table 1) indicating a substantial net kinetic isotope effect, which also results in partitioning of the α-$[D_1]$toluene to give products arising from insertion into C–H (0% *de*) versus C–D in an 87.6:12.4 ratio. From these values, the primary and secondary effects are estimated as $k_H/k_D=4.2(\pm0.6)$ and $1.18(\pm0.08)$, respectively, see Experimental Section for details. The reaction of **18** (Table 1, entry 13) was found to be more than fivefold slower than that of $[D_0]$toluene.

Reaction of carbene 2 with $[D_0]$toluene and $[D_8]$toluene mixtures—toluene molecularity: The large excess of $[D_8]$toluene used to explore the effect of $(K\text{-}HMDS)_2$ concentration on the rate of C–^{2}H insertion (Table 1, entries 1–8) results in a pseudo-zero-order rate dependency on the $[D_8]$toluene concentration under these conditions. To explore the toluene molecularity (under pseudo-zero-order conditions in toluene) we exploited the net kinetic isotope effects (KIEs) associated with the C–H(D) cleavage process, vide supra, by conducting a series of reactions of **2** (0.08 M) with mixtures of $[D_0]$toluene and $[D_8]$toluene (0.0, 15.0, 30.0, 45.0 and 60.0% $[D_0]$toluene; Table 2, entries 1–5).

Table 2. Pseudo-first-order rate constants (k_{obs}),[a] net primary/secondary kinetic isotope effects (k_H/k_D)[b] and partitioning ratios[c,d] for reaction of carbene $[^{13}C_1]$-**2** (82–84 mM) with $[D_0]$toluene/$[D_8]$toluene mixtures (9.13–9.15 M), in the presence of excess $(K\text{-}HMDS)_2$ (82–83 mM) at 23 °C.

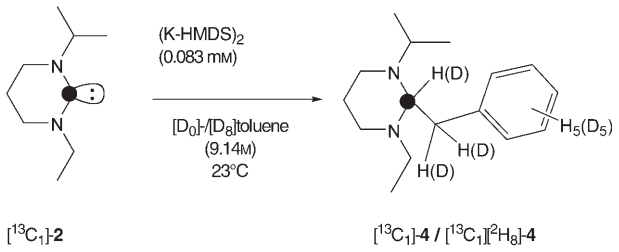
	Mol ratio $[D]_0/[D_8]$toluene	$\delta_{C(2)}$ **2** [ppm]	k_{obs} [$s^{-1}\times10^7$]	k_H/k_D	Partitioning (*P*) ($[D_0]$**4**/$[D_8]$**4**)
1	–	229.3	3.49(±0.02)	–	–[c]
2	0.176	229.4	9.26(±0.14)	10.1(±0.5)	1.78(±0.08)[d]
3	0.429	228.9	14.9(±0.3)	9.3(±0.7)	4.0(±0.3)[e]
4	0.818	229.8	21.2(±0.2)	9.5(±1.0)	7.8(±0.8)[d]
5	1.50	229.8	25.2(±0.4)	8.2(±1.4)	12.3(±2.1)[d]

[a] Determined by linear regression of $\ln([\mathbf{2}]_0/[\mathbf{2}]_t)$ versus *t*, as determined by $^1H/^{13}C$ NMR analysis. [b] Determined by the relationship $(k_{[D_0]tol}/k_{[D_8]tol})[(x_D/x_H)-\text{toluene}]=P$, errors based on ±1% error in mol fractions of $[D_8]/[D_0]$toluene and $[^2H_8][^{13}C_1]$-**4**/$[^2H_0][^{13}C_1]$-**4**. [c] Only $[^2H_8][^{13}C_1]$-**4** (+ 3.8% $[^2H_7][^{13}C_1]$-**4**) generated. [d] Determined by $^{13}C\{^1H\}$ NMR spectroscopy. [e] Determined by ^1H NMR spectroscopy.

The rate of reaction of $[^{13}C_1]$-**2** in combination with the partitioning ratio of adducts **4** derived from $[D_0]$toluene versus $[D_8]$toluene ($[^{13}C_1]$-**4**/$[^2H_8][^{13}C_1]$-**4**$=P$) can be employed to extract the net deuterium KIEs on both the partitioning[17] and the absolute rate. As with α-$[D_1]$toluene, significant partitioning (*P*) was found to occur, with the net effect determined by the mole fractions $[D_0]$toluene/$[D_8]$toluene, in conjunction with a net KIE that is essentially constant (error-weighted average $k_{[D_0]tol}/k_{[D_8]tol}=9.5\pm0.8$).[18] The mole fractions of $[D_0]$toluene/$[D_8]$toluene are also found to affect the overall reaction rate (k_{obs} in s^{-1}) in a linear manner, Figure 4.

The gradient of the correlation $k_{obs}=x_H(k_{(H)}-k_{(D)})+k_{(D)}$, in which $x_H=$mole fraction $[D_0]$toluene, yields the net KIE on the rate of reaction, $k_{(H)}/k_{(D)}=10.9\pm1.9$, which is in reasonable agreement with the isotope effect attending partitioning ($k_{[D_0]tol}/k_{[D_8]tol}=9.5\pm0.8$) and thus indicative of a unimolecular involvement of toluene in rate-limiting adduct **4** formation.[19] In all of the reactions studied, the product **4** was found to derive from a single molecule of toluene, with no evidence for cross-over. Thus, $[D_8]$toluene generates exclusively $[^2H_8][^{13}C_1]$-**4** (see Figure 5, right-hand spectrum),[20] $[D_1]$toluene generates $[^2H_1][^{13}C_1]$-**4** (as an 87.6:12.4 mixture of C(2)–H/C(2)–D) and $[D_0]$toluene generates exclusively $[^{13}C_1]$-**4**.

Mechanism of reaction of carbene 2 with toluene: The mechanism of "insertion" of singlet carbenes (R-C-R; in which one or both of "R" are "stabilising": aryl, halogen, alkoxy, amino etc.) into X–H bonds (X = O, N, C) has long been of interest. Three general classes of mechanism have been proposed,[20] which can be summarised as: 1) a pathway dominated by the electrophilic nature of the vacant p orbital on carbon ("ylidic"; pathway **I**, Scheme 3); 2) a path-



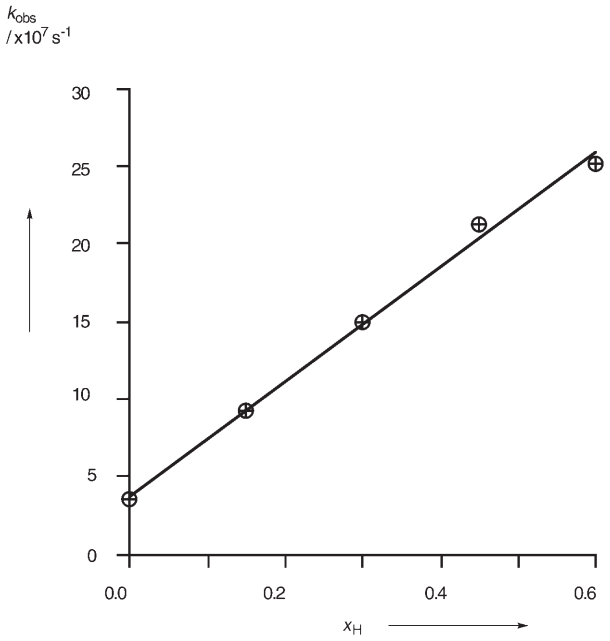
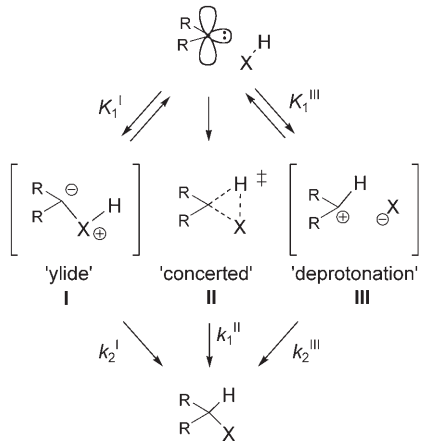


Figure 4. The linear relationship between the pseudo-first-order rate constant (k_{obs}) for reaction of [$^{13}C_1$]-**2** with [D_0]toluene/[D_8]toluene (ca. 110 equiv) and the initial mol fraction [D_0]toluene x_H. The line passing through data points is a linear regression of the equation $k_{obs} = x_H(k_{(H)} - k_{(D)}) + k_{(D)}$, in which $(k_{(H)} - k_{(D)}) = 36.9(\pm 1.4) \times 10^{-7}\ s^{-1}$ and $k_{(D)} = 3.74(\pm 0.5) \times 10^{-7}\ s^{-1}$.



Scheme 3. Three general mechanisms for the "insertion" of singlet carbenes (R-C-R; one or both R = aryl, halogen, alkoxy, amino etc.) into X–H bonds (X = O, N, C).[21] Note that the "ylide" mechanism (**I**) may involve oligomeric X–H species to facilitate proton transfer (k_2^{I}).

way in which both the vacant p orbital and filled sp^2 orbital on carbon interact simultaneously with X and H ("concerted"; pathway **II**) and 3) a pathway dominated by the nucleophilic (basic) nature of the filled sp^2 orbital on carbon ("deprotonation"; pathway **III**). Essentially all of the mechanistic investigations reported to date have centred around the insertion of singlet carbenes (generated thermally or photochemically from diazoalkanes[21a–d] or photochemically from diazirenes)[21e,f] into the O–H bond of H_2O or ROH.

Distinction between pathways **I**, **II** and **III** for the insertion of singlet carbenes into the O–H bond of H_2O or ROH has predominantly been based on the magnitude of the primary KIEs (^2H or ^3H) for the hydrogen transfer and Brønsted correlations (pK_a of RO–H versus $\log k_{obs}$). For pathway **I**, a negligible primary KIE is expected,[21d] providing that step 1 (k_1^{I}) is rate-limiting. The use of mixtures of D_2O (or T_2O) with H_2O allows the isotope effect in the second step (k_2^{I}) to be determined through partitioning.[21a] For pathway **II**, primary KIEs of an intermediate magnitude are expected due to the nonlinearity of H transfer in k_1^{II};[21f] a low degree of charge separation means that the pK_a of RO–H will be of less influence. For pathway **III**, larger primary KIEs are expected, provided that step 1 (k_1^{III}) is rate-limiting; equilibrium KIEs close to unity would be expected if step 2 (k_2^{III}) is rate-limiting. A Brønsted correlation would be expected in both cases (unless K_1^{III} is very large).[21e] The mechanism(s) involved in the C–H insertion reactions of stable carbenes (Scheme 2) have not been studied,[7] although on the basis of the

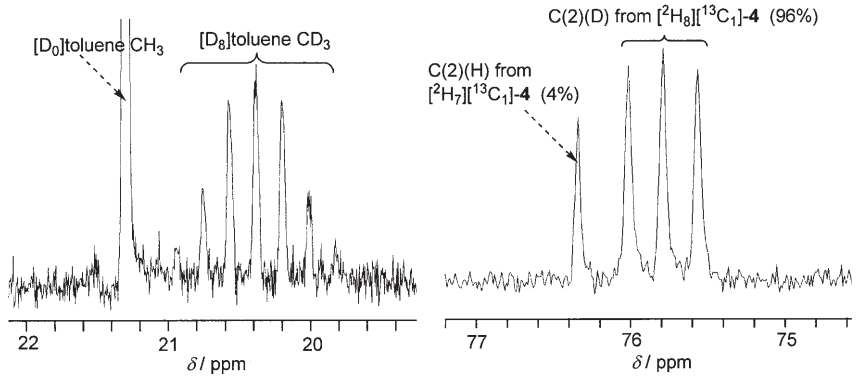


Figure 5. $^{13}C\{^1H\}$ NMR experiments probing for the involvement of the HMDS anion in the $(K\text{-}HMDS)_2$-catalysed reaction of **2** with toluene. Left-hand sub-spectrum: 50:50 v/v [D_0]toluene/[D_8]toluene containing 83 mM $(K\text{-}HMDS)_2$ + 237 mM H-HMDS, 2 weeks at 23 °C. Right-hand sub-spectrum: $(K\text{-}HMDS)_2$-catalysed reaction of [$^{13}C_1$]-**2** with [D_8]toluene (99.1% $ArCD_3$/0.9% $ArCD_2H$) in the presence of 1 equiv H-HMDS, which gives 96.2:3.8 [$^2H_8$][$^{13}C_1$]-**4**/[$^2H_7$][$^{13}C_1$]-**4** in which >98% of the benzylic carbons are dideuterated; see text for full discussion.

"acidic" nature of the C–H components, namely, CH_3CN, $CHCl_3$, $PhSO_2CH_3$ and acetylene, it has been proposed that these all involve the "deprotonation", pathway **III**.[7a,c]

The data obtained for the kinetics of the reaction of **2** with toluene, deuterated toluenes and substituted toluenes to generate the formal C–H insertion products **4** and **19**→**22** should, in principle, allow a more confident interpretation of the mechanism. The reaction has the following characteristics: 1) the rate of reaction depends on the ability of the aryl ring to support negative charge development at the toluene methyl group ($\rho = 4.8 \pm 0.3$); 2) there are substantial KIEs attending the toluene methyl C–H cleavage: namely, a net KIE, $k_H/k_D = 9.5 \pm 0.8$ for [D_8]toluene, and a primary $k_H/k_D = 4.2(\pm 0.6)$) and secondary $k_H/k_D = 1.18(\pm 0.08)$ for [D_1]toluene; 3) the reaction rate has first-order dependency on toluene, a first-order dependency on carbene (**2**), and a complex dependence in $(K\text{-HMDS})_2$; 4) there is no evidence for cross-over: each molecule of the product **4** is entirely derived from a single molecule of **2** and a single molecule of toluene and 5) the reaction is catalysed by $(K\text{-HMDS})_2$.

The large magnitude of the secondary KIEs and the dependence of reaction rate on toluene methyl C–H acidity ($\rho = 4.8 \pm 0.3$) and charge delocalisation into the aryl π system ($R/F = 1.37$ in the Swain–Lupton correlation, Figure 3) are strongly suggestive of a C–H deprotonation reaction (cf. pathway **III**, Scheme 3) with a late transition state in which substantial sp^2 character and partial negative charge has been established at the benzylic carbon.[18] However, the generation of a full benzyl anion by means of deprotonation of the toluene methyl group would require a very strong base: the pK_a of toluene is about 42 in DMSO.[22] Addition of a large excess (26 equiv) of H-HMDS to [$^{13}C_1$]-**2** in [D_8]toluene, containing less than 1% of the HMDS adduct [$^{13}C_1$]-**8**, resulted in the reasonably rapid generation of an equilibrium mixture (ca. 83% [$^{13}C_1$]-**2**/17% [$^{13}C_1$]-**8**), which on fourfold dilution into pure [D_8]toluene, underwent substantial reversion (>50%) to [$^{13}C_1$]-**2** and H-HMDS. This result ([**2**]+H-HMDS↔[**8**]; $K = 0.4 \pm 0.2\,M^{-1}$) shows that the difference in thermodynamic basicity of **2** and the HMDS anion is small. Analogously, the acidities of H-HMDS (pK_a 26 in DMSO)[22] and **1** (pK_a of **1**-Cl estimated as 26 in DMSO)[23a] are rather similar. The *quantitative* reaction of 0.5 equivalents $(K\text{-HMDS})_2$ with **1**-PF_6 in [D_8]toluene to generate **2**, H-HMDS and KPF_6, suggests that the co-generation of KPF_6 is a significant driving force; in other words, the "acidity" of **1** is counterion dependent.[23]

Mulvey et al. recently reported that $(K\text{-HMDS})_2$ cleanly deprotonates a methyl group in toluene, *m*-xylene and mesitylene, when reaction is conducted in the presence of $Zn(HMDS)_2$.[24] Such a process could conceivably proceed through $Zn(HMDS)_2$-trapping of $PhCH_2K$ generated in trace concentration by equilibrium of $PhCH_3$ with K-HMDS. However, in a control experiment involving a mixture of $(K\text{-HMDS})_2$, H-HMDS, [D_0]toluene and [D_8]toluene, we found no evidence whatsoever for cross over through reversible deprotonation of the toluene methyl group, even after 2 weeks at room temperature, Figure 5.

Although $(K\text{-HMDS})_2$ alone does not deprotonate toluene to any significant extent, the presence of **2** may increase the basicity of the HMDS anion, through complexation of **2** with $(K\text{-HMDS})_2$. The complexation of N,N-heterocyclic carbenes to Group I cations (Li^+, Na^+, K^+, etc.) was first reported by Alder et al., and has subsequently been explored in considerable detail.[25] The complexation can be readily detected in solution by an upfield shift of the signal arising from the carbene carbon in the ^{13}C NMR spectrum. Analysis of the signal arising from C(2) in [$^{13}C_1$]-**2** and the Me signals in the $(K\text{-HMDS})_2$ at the various values of excess $(K\text{-HMDS})_2$ reveals that complexation does occur and is dynamic: a single time-average chemical shift of C(2) in [$^{13}C_1$]-**2** is observed that is weakly dependent on [[$^{13}C_1$]-**2**] and strongly dependent on [$(K\text{-HMDS})_2$],[26] vide infra, Figure 6 (left). The involvement of the HMDS anion de-

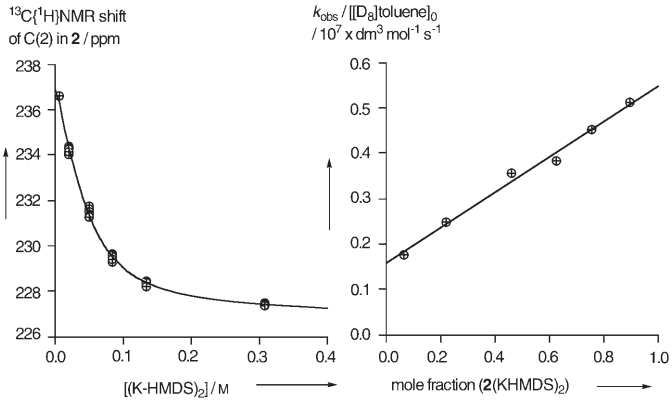


Figure 6. Left-hand graph: nonlinear regression of a 1:1 binding isotherm accounting for variation in time-average ^{13}C NMR chemical shift of C(2) in [$^{13}C_1$]-**2** with [$(K\text{-HMDS})_2$] in [D_8]toluene (data points); solid line: with freedom in all four coefficients, yielding $K_a = 62(\pm 7)\,M^{-1}$, [**2**] = 53 (± 0.5) mM, $\delta_{C(2)}$ in **2** = 237.0(± 0.2) ppm; $\delta_{C(2)}$ in [**2**(KHMDS)$_2$] = 226.8 (± 0.1) ppm) initial [**2**] = 54.3 mM; see text for full discussion. Right-hand graph: mole fraction of carbene **2** (54.3 mM) complexed to K-HMDS dimer, calculated from [$(K\text{-HMDS})_2$] and K_a, versus apparent second-order-rate constant for reaction of **2** with [D_8]toluene. $K_a = 62\,M^{-1}$ as derived from $^{13}C\{^1H\}$ NMR shifts (left-hand graph).

rived from such a complex was probed by detailed $^{13}C\{^1H\}$ NMR analysis of the C(2) signals in the product from reaction of [$^{13}C_1$]-**2**/[D_8]toluene/$(K\text{-HMDS})_2$ (4.2 equiv)/H-HMDS (1.0 equiv formed by deprotonation of salt [$^{13}C_1$]-**1** by HMDS anion); such an analysis allows the deduction of the presence of various isotopologues of **4** due to the multiplicity and isotope shifts induced by deuterium at $^{13}C(2)$. By reference to products from [D_0]toluene and [D_1]toluene, vide supra, it is evident that the process generates [^2H_n]-[$^{13}C_1$]-**4** in which 96.2% of C(2) is deuterated and >98% of the benzylic carbon dideuterated, Figure 5, right-hand section. The generation of 3.8% [$^2H_7$][$^{13}C_1$]-**4** is consistent with the isotopic purity of the [D_8]toluene solution (99.1% CD_3, 0.9% CD_2H; ^1H NMR spectroscopy).[20] The involvement of

the free HMDS anion as a base would generate D-HMDS/H-HMDS, the latter liberating [$^2H_7$][$^{13}C_1$]-**4**, in which C(2) bears a hydrogen atom. From this analysis it is evident that a free HMDS anion, derived from either K-HMDS or a complex thereof, is not acting as the base in the process generating **4**.

From the preceding analysis, it can be concluded that it is the carbene carbon C(2) of **2**, and not an HMDS anion, that acts to deprotonate the toluene. However, $(K\text{-}HMDS)_2$ whilst not actively involved as the base, demonstrably catalyses the reaction. Three limiting mechanisms can be envisaged. Firstly, in the direct reaction of carbene **2** with the toluene to generate **4** by means of pathway **III** in Scheme 3, the involvement of a benzyl/tetrahydropyrimidinium (**1**) ion-pair would cause significant charge generation from the neutral precursor pairing (**2** and toluene) on approach to the transition state. In an apolar aromatic solvent, for example, toluene or benzene, the ionogenic nature of the process (**2** + toluene $\rightarrow$ {**1**-$PhCH_2$}$^+$) would be highly susceptible to any charge-stabilising medium effect exerted by the aromatic-soluble $(K\text{-}HMDS)_2$. However, such a medium effect should obey the Brønsted salt-effect catalysis law[26] and a plot of $\log k_{obs}$ against $[(K\text{-}HMDS)_2]^{0.5}$ is nonlinear throughout the dataset ($r^2 = 0.88$).

The second and third mechanisms considered involve Brønsted salt-effect catalysis (medium effect) or discrete molecular catalysis of the reaction of **2** with toluene by its potassium complex [**2**$(K\text{-}HMDS)_2$]. The nonlinear regression of a simple 1:1 binding isotherm[28] to the ^{13}C NMR signal arising from C(2) in [$^{13}C_1$]-**2** during conversion to [$^2H_8$][$^{13}C_1$]-**4** in [D_8]toluene allows extraction of an association constant for the equilibrium of **2** and $(K\text{-}HMDS)_2$ to form [**2**$(K\text{-}HMDS)_2$]. The goodness of fit (Figure 6, left, solid line) together with low sensitivity to the concentration of [$^{13}C_1$]-**2** on the ^{13}C NMR shift of C(2),[25,27] is consistent with a low association constant for the equilibrium of [**2**$(K\text{-}HMDS)_2$] with a further molecule of **2** to form [$(\mathbf{2})_2(K\text{-}HMDS)_2$].[29]

The association constant for the 1:1 equilibrium, $K_a = 62(\pm 7)\,M^{-1}$, as determined by $^{13}C\{^1H\}$ NMR spectroscopy indicates that the proportion of **2** that is complexed under the reaction conditions at the $[(K\text{-}HMDS)_2]$ concentrations considered herein varies from about 8 to 94%. As a consequence, a mechanism involving Brønsted salt-effect catalysis by the complex [**2**$(K\text{-}HMDS)_2$] on the direct reaction of **2** with toluene can be ruled out on the basis that although the mole fraction of free **2** (x_2) relative to that which is complexed with $(K\text{-}HMDS)_2$ ($1-x_2$) is essentially *constant* through the evolution of the reaction,[28] the concentrations of both species would decrease linearly with conversion and thus the relationship: $\log k_{obs} \propto [\mathbf{2}]^1[\mathbf{2}(K\text{-}HMDS)_2]^{0.5}$ would not give rise to the simple pseudo-first-order kinetics observed under all conditions.

Considering then a mechanism involving discrete reaction of the potassium-complexed carbene [**2**$(K\text{-}HMDS)_2$] with the toluene, analysis of the second-order-rate constant (obtained by normalisation of the pseudo-first-order rate constant k_{obs} according to initial toluene concentration) with the mole fraction [**2**$(K\text{-}HMDS)_2$], $(1-x_2)$ as determined by $[(K\text{-}HMDS)_2]$ and $K_a = 62(\pm 7)\,M^{-1}$ at $[\mathbf{2}]_t = 53$ mM,[28] yields a good linear correlation, Figure 6 (right). An important ramification of such a correlation is that the observed rate is a mole-fraction-weighted average of two separate reactions of toluene: reaction with **2** (mole fraction x_2) and reaction with [**2**$(K\text{-}HMDS)_2$] (mole fraction $(1-x_2)$): $-d[\mathbf{2}]/dt = (x_2 k_{uncat} + (1-x_2)k_{cat})[\mathbf{2}]^1[\text{toluene}]^1$. Nonlinear regression thus yields second-order-rate constants for reaction proceeding via [**2**$(K\text{-}HMDS)_2$]: $k_{cat} = 5.1(\pm 0.4) \times 10^{-8}\,dm^3\,mol^{-1}\,s^{-1}$, and for the direct reaction of **2** with toluene: $k_{uncat} = 1.5(\pm 0.2) \times 10^{-8}\,dm^3\,mol^{-1}\,s^{-1}$. The latter rate constant is not easy to determine directly because the generation of **2** from **1** in the absence of a slight excess of $(K\text{-}HMDS)_2$ results in dimerisation to give **3**, at a rate that is upwards of one order of magnitude faster than toluene insertion at the concentrations considered herein.

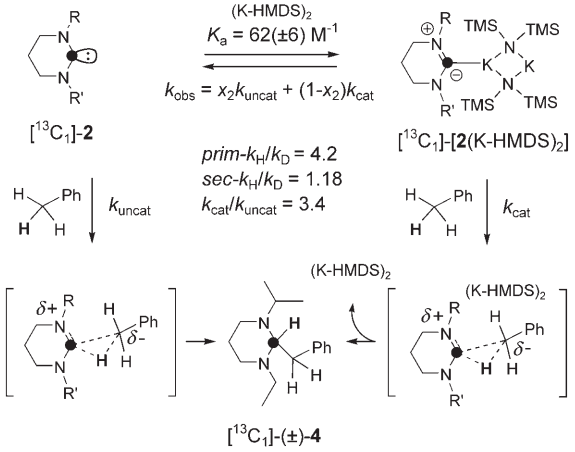
To address the possibility that the inherent rate (k_{uncat}) for direct reaction of **2** with toluene arises by catalysis from complexation of **2** with the KPF_6 (surface or solution), we conducted the following experiment. A sample of [$^{13}C_1$]-**2** in [D_8]toluene containing 0.135 M excess $(K\text{-}HMDS)_2$ was filtered (0.45 μM PTFE membrane) into 0.175 M $(K\text{-}HMDS)_2$ in [D_8]toluene, giving rise to a 0.165 M solution of $(K\text{-}HMDS)_2$ in which the KPF_6-saturated toluene has thus undergone 3.5-fold dilution and been separated from particulate KPF_6. The pseudo-first-order rate constant for the reaction of **2** to give **4** was found to be $k_{obs} = 4.32 \pm 0.18 \times 10^{-7}\,s^{-1}$ (Table 1, entry 15), which is identical to the value predicted ($4.3 \times 10^{-7}\,s^{-1}$) from the relationship $-d[\mathbf{2}]/dt = (x_2 k_{uncat} + (1-x_2)k_{cat})[\mathbf{2}]^1[\text{toluene}]^1$, using the appropriate values of $[\mathbf{2}]_0$, $[[D_8]\text{toluene}]_0$ and binding constant $K_a = 62\,M^{-1}$. It can thus be concluded that trace KPF_6 in the toluene does not catalyse reaction to any significant extent and, therefore, it appears that there is a direct reaction between the carbene **2** and the toluene to generate **4**.

Conclusions

A study of the generation of the ^{13}C-labelled N,N-heterocyclic carbene [$^{13}C_1$]-**2** by reaction of a suspension of tetrahydropyrimidinium precursor [$^{13}C_1$]-**1**-PF_6 with excess $(K\text{-}HMDS)_2$ in toluene reveals that although carbene **2** is kinetically stable towards dimerisation, it undergoes formal insertion into the toluene methyl group to generate an aminal (**4**). The reaction is slow but quantitative and is mildly catalysed by the excess $(K\text{-}HMDS)_2$. The rate of reaction is strongly dependent on the toluene *para* substituent, yielding a Hammett ρ^- value of 4.8 ± 0.3 and, in a separate analysis, a resonance-dominated Swain–Lupton term ($\sigma_{SL} = 0.73F + R$). Deuterium labelling at the toluene methyl group ([D_8]-, [D_1]- and [D_0]toluene) results in moderate primary and large secondary KIEs for [D_1]toluene in C_6D_6 (primary (k_H/k_D) $= 4.2(\pm 0.6)$) and secondary (k_H/k_D) $= 1.18(\pm 0.08)$), and for [D_0]toluene/[D_8]toluene as reactant and solvent ($k_H/k_D =$

10.9 ± 1.9 on rate and $k_{[D_0]tol}/k_{[D_8]tol} = 9.5 \pm 0.8$ for partitioning).[30] These are consistent with rate-limiting C–H cleavage (k_1^{II} or k_1^{III} in Scheme 3) proceeding via a late transition state,[18] with an accompanying decrease in p character at the benzylic carbon and little competing internal return, which would reduce the primary KIE to an equilibrium isotope effect (K_1^{III} in Scheme 3).[31,32] Analysis of the chemical shift of the $^{13}C\{^1H\}$ NMR signal arising from C(2) in [$^{13}C_1$]-**2** indicates that there is rapid and reversible complexation of carbene **2** to the (K-HMDS)$_2$ with an association constant of $K_a = 62(\pm 6)\,M^{-1}$. Using this value to determine[28] the mole fractions of **2** that are complexed ($1-x_2$) and noncomplexed (x_2), the rate of reaction can be satisfactorily predicted by the relationship $-d[\mathbf{2}]/dt = (x_2 k_{uncat} + (1-x_2)k_{cat})[\mathbf{2}]^1[\text{toluene}]^1$ (Figure 6, right; Figure 2, right). The correlation leads to the conclusion that there are two processes for the generation of **4** from **2**: 1) direct reaction of **2** with toluene (k_{uncat}, Scheme 2) and 2) reaction of the complex [**2**(K-HMDS)$_2$] with toluene (k_{cat}, Scheme 2).[32] Careful study of the $^{13}C\{^1H\}$ NMR spectra of the products from **2** and methyl-deuterated toluenes ([D$_8$]- and [D$_1$]toluene) demonstrates that the HMDS anion is not the active base in either process as there is no evidence for cross-over exchange through bulk phase H-HMDS/D-HMDS.

The smooth generation of **2** from **1**-PF$_6$/(K-HMDS)$_2$, and the equilibrium between **2**, H-HMDS and **8**, suggests that the HMDS anion is more basic than **2**, but not exceptionally so. On the basis of lack of protium–deuterium exchange at the [D$_8$]toluene methyl group in the presence of (K-HMDS)$_2$/H-HMDS, we find no evidence for reaction **2**→**4** proceeding via toluene deprotonation by a free HMDS anion. Yet, **2** reacts smoothly with toluene by what appears to be a rate-limiting deprotonation mechanism (k_{uncat}, Scheme 4) and despite what appears to be substantial pK_a mismatch between **2** (pK_a of [**1**]≈26 in DMSO)[23] and toluene (pK_a ca. 42 in DMSO).[22] It is thus concluded that



Scheme 4. A dual-manifold mechanism ((K-HMDS)$_2$-catalysed and uncatalysed), based on observed kinetics and isotopic labelling experiments, for the reaction of **2** with [D$_8$]-, [D$_1$]- and [D$_0$]toluene, to give **4**. In [D$_8$]toluene at 23 °C, $k_{cat} = 5.1(\pm 0.4) \times 10^{-8}\,dm^{-3}mol^{-1}s^{-1}$, $k_{uncat} = 1.5(\pm 0.2) \times 10^{-8}\,dm^{-3}mol^{-1}s^{-1}$.

whilst the formal deprotonation of toluene by **2** is thermodynamically very unfavourable, the reaction between **2** and toluene may be closer to a concerted process (pathway **II**, Scheme 3) than a fully ionogenic process (pathway **III**) to facilitate a sufficiently low activation barrier (116 kJ mol^{-1}) for reaction to proceed at a reasonable rate. The magnitude of the primary and secondary deuterium isotope effects[18,31] are consistent with this in that the transition state for proton transfer would be "late". Indeed the primary KIE ($k_H/k_D = 4.2(\pm 0.6)$) is similar in magnitude to that reported by Moss et al. for the insertion of dimethoxy carbene into the O–H bond of methanol ($k_H/k_D = 3.3(\pm 0.5)$,[21e] for which a pathway of type **III** (with some characteristics of **II**) was suggested.[21f] For the generation of **4**, the lowering of both the activation barrier and the energy of the intermediate (route **III**) or transition state (route **II**), may arise from a stabilising secondary orbital interaction involving the vacant p orbital at C(2) and the *ipso*-carbon atom on toluene. Analogous interactions of aryl π systems with carbenes have been suggested on the basis of computational studies to account for rate accelerations of carbene reactions in aromatic solvents.[33] Such a process might be expected to perturb the electronic effects of the *para*-tolyl substituents and thus lead to a nonlinear Hammett correlation. However, a compensatory effect could lead to a simple attenuation, as would be consistent with the ρ value ($\rho = 4.8 \pm 0.3$, Figure 3), which is smaller than would be expected for full carbanion generation. In effect, this mechanism would have characteristics of both pathways **I** and **III** (the latter intramolecular) in Scheme 3.

The increased reactivity of the (K-HMDS)$_2$ complex [**2**-(K-HMDS)$_2$] towards toluene (ca. 3.4-fold over that of the free carbene **2**) may appear contra-intuitive: K^+ complexation by the occupied sp^2 orbital[34] should render C(2) less basic than in free **2**. However, as is evident from the single-crystal X-ray structure of [(**2′**)$_2$(K-HMDS)$_2$],[25a] in which **2′** is the *N*,*N*′-diisopropyl analogue of **2**, the carbene–potassium interaction has a predominantly electrostatic ion–dipole character. The C(2)–K bond in [(**2′**)$_2$(K-HMDS)$_2$],[25a] is long (3.00 Å) relative other N-heterocyclic-carbene–metal complexes (≤2.30 Å).[2a] A possible explanation for the increased reactivity of [**2**(K-HMDS)$_2$] towards toluene may lie in the localised polarisation and electrostriction of the nascent tight-ion pair {**1**-CH$_2$Ph}$^+$ (pathway **III**) or polarised nonsynchronous concerted process (pathway **II**) in which (K-HMDS)$_2$ is liberated from **2** (ΔG_{assoc} = ca. 10 kJ mol^{-1} at 23 °C) within the solvent shell (k_{cat}; Scheme 4). This compensatory effect of the (K-HMDS)$_2$ must just outweigh the reduced availability of the filled sp^2 orbital at C(2), resulting in a slightly increased reaction rate relative to **2** ($\Delta\Delta G^{\neq}$, based on $k_{cat}/k_{uncat} = 3$ kJ mol^{-1} at 23 °C). In effect, the reaction of the toluene with the potassium-complexed carbene experiences *localised* Brønsted salt-effect catalysis within the solvent shell surrounding the partially ionogenic process.[35]

In summary, the first "insertion" reaction of an N,N-heterocyclic carbene **2** into the "nonacidic" C–H bond of the

toluene methyl group to give aminal **4** has been investigated by kinetic and isotopic labelling strategies. The reaction appears to follow a mechanism that has characteristics of both the classic "concerted" and "deprotonation" pathways proposed for O–H insertions[20] (pathways **II** and **III**, Scheme 3) and, whilst this may be unexpected on the basis of pK_a, it is unlikely be restricted either to **2**[36] or to toluenes. The possible use of simple analogues of **2** as reagents for the preparation of aldehydes through homologation/aminal hydrolysis is of interest, particularly if more efficient catalysts can be developed, and is being actively pursued in these laboratories.

Experimental Section

General: [D_6]benzene, toluene, [D_8]toluene, [D_1]toluene, ethylbenzene and 4-*tert*-butyltoluene were distilled from sodium under a nitrogen atmosphere immediately before use. 4-Trifluoromethyltoluene and 4-chlorotoluene were distilled from P_2O_5 under a nitrogen atmosphere. HN($SiMe_3$)$_2$ ("H-HMDS") was distilled from 4 Å molecular sieves under a nitrogen atmosphere. (KN($SiMe_3$)$_2$)$_2$ ("(K-HMDS)$_2$") was prepared from H-HMDS by reaction with excess KH in [D_6]benzene or [D_8]toluene, followed by filtration and titration (diphenylacetic acid in THF). Phenacetaldehyde was obtained from Aldrich and purified by Kugelrohr distillation (125 C, 15 mmHg). *N*-Ethyl-*N*′-isopropyl-1,3-diaminopropane was prepared by adaptation[37] of the method of Yamamoto and Maruoka.[38] The salts **1**-PF_6 and [$^{13}C_1$]-**1**-PF_6 were prepared from *N*-ethyl-*N*′-isopropyl-1,3-diaminopropane and by adaptation of the method of Alder et al.[39] All manipulations were conducted under an inert (N_2) atmosphere by using Schlenk line techniques. NMR samples were prepared in 5 mm tubes, sealed by means of a Young valve. NMR spectra were acquired on JEOL instruments (ECP300, ECP400 and Alpha 500) using the ^{2}H-signal from the solvent as a frequency lock. ^{1}H and ^{13}C{^{1}H} NMR spectra were referenced internally to [D_6]benzene (^{1}H $\delta = 7.15$ ppm; ^{13}C $\delta = 128.0$ ppm) or the toluene methyl group (^{1}H $\delta = 2.09$ ppm (CD_2H); ^{13}C $\delta = 20.4$ ppm (CD_3)). Assignments are based on HH COSY, HMQC (^1J(C,H)), HMBC ($^{>1}J$(C,H)) and DEPT. Reaction kinetics were analysed by application of standard first-order (or pseudo-first-order) linear relationships, rate constants, binding constants and chemical shifts and associated errors were estimated by linear or nonlinear regression using MacCurveFit software.[40]

Preparation of 2-[^{13}C]-1-ethyl-3-isopropyl-3,4,5,6-tetrahydropyrimid-2-ylidene [$^{13}C_1$]-2 in [D_8]toluene and analysis of the kinetics of generation of [$^2H_8$][$^{13}C_1$]-4: A typical procedure was as follows: [$^{13}C_1$]-**1**-PF_6 (13.5 mg, 0.0449 mmol) was transferred into an NMR tube (with Young valve) under N_2. (K-HMDS)$_2$ (0.35 M solution (HMDS anion) in [D_8]toluene, 0.390 cm^3, 0.07 mmol (K-HMDS)$_2$) was added to the salt. Distilled [D_8]toluene (0.160 cm^3) was added to the mixture and the NMR tube was sealed. The tip of the NMR tube was submerged in an ultrasonic bath and the contents were sonicated until all of the colourless, crystalline salt [$^{13}C_1$]-**1**-PF_6 had dissolved and been replaced with a fine, white precipitate of KPF_6 (10 min). The reaction was monitored by NMR spectroscopy.

*Data for carbene [$^{13}C_1$]-**2***: ^{1}H NMR (400 MHz, [D_8]toluene, 20.8 °C): $\delta =$ 1.05 (t, ^3J(H,H) = 7.1 Hz, 3H; NCH_2CH_3), 1.07 (d, ^3J(H,H) = 6.9 Hz, 6H; $NCH(CH_3)_2$), 1.30 (quintet, ^3J(H,H) = 6.0 Hz, 2H; C(5)H_2), 2.31 (t, ^3J(H,H) = 6.0 Hz, 2H; C(4)H_2), 2.39 (t, ^3J(H,H) = 6.0 Hz, 2H; C(6)H_2), 3.23 (dq, ^3J(H,H) = 7.1 Hz, ^3J(H,C) = 5.2 Hz, 2H; NCH_2CH_3), 3.78 ppm (double septet, ^3J(H,H) = 6.9 Hz, ^3J(H,C) = 3.9 Hz, 1H; $NCH(CH_3)_2$); ^{13}C{^{1}H} NMR (100 MHz, [D_8]toluene, 22.0 °C): $\delta = 14.8$ (s; NCH_2CH_3), 21.0 (s; $NCH(CH_3)_2$), 21.7 (s; C(5)H_2), 34.7 (broad unresolved doublet; C(6)H_2), 40.4 (d, ^2J(C,C) = 5.7 Hz; C(4)H_2), 54.1 (d, ^2J(C,C) = 23.0 Hz; NCH_2CH_3), 58.6 (d, ^2J(C,C) = 24.0 Hz; $NCH(CH_3)_2$), 229.6 ppm (^{13}C(2)).

*Data for adduct [$^2H_8$]/[$^{13}C_1$]-**4***: ^{1}H NMR (500 MHz, [D_8]toluene, 24.5 °C): $\delta = 0.91$ (t, ^3J(H,H) = 7.0 Hz, 3H; NCH_2CH_3), 0.92 (d, ^3J(H,H) = 6.4 Hz, 6H; $NCH(CH_3)_2$), 1.05 (double quintet, ^2J(H,H) = 12.5 Hz, ^3J(H,H) = 3.0 Hz, 1H; C(5)H_{eq}), 1.82 (qt, ^2J(H,H) = 12.5 Hz, ^3J(H,H) = 12.5 Hz, ^3J(H,H) = 5.2 Hz, 1H; C(5)H_{ax}), 2.44 (ddq, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 7.0 Hz, ^3J(H,C) = 4.0 Hz, 1H; $NCH(CH_3)CH_3$), 2.51 (ddq, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 7.0 Hz, ^3J(H,C) = 4.0 Hz, 1H; $NCH(CH_3)CH_3$), 2.50–2.62 (m, 1H; C(4)H(H)), 2.69–2.81 (m, 3H; C(6)H_2 and C(4)H(H)), 2.83 ppm (double septet, ^3J(H,H) = 6.4 Hz, ^3J(H,C) = 3.1 Hz, 1H; $NCH(CH_3)_2$); ^{13}C{^{1}H} NMR (125 MHz, [D_8]toluene, 24.5 °C): $\delta = 13.8$ (s; NCH_2CH_3), 21.8 (s; $NCH(CH_3)CH_3$), 22.1 (s; $NCH(CH_3)CH_3$), 22.7 (s; C(5)H_2), 41.4 (s; C(6)H_2), 45.2 (s; C(4)H_2), 47.6 (s; NCH_2CH_3), 50.7 (s; $NCH(CH_3)_2$), 75.8 ppm (t, ^1J(C,D) = 21.5 Hz; ^{13}C(2)).

Preparation of [$^{13}C_1$]-2 in mixed [D_0]toluene/[D_8]toluene solution and analysis of the kinetic isotope effects in generation of [$^{13}C_1$]-4 and [$^2H_8$]-[$^{13}C_1$]-4: A typical procedure was as follows: [$^{13}C_1$]-**1**-PF_6 (13.9 mg, 0.0462 mmol) was transferred into an NMR tube (with Young valve) under N_2. (K-HMDS)$_2$ (0.35 M solution (HMDS anion) in [D_8]toluene, 0.390 cm^3, 0.07 mmol (K-HMDS)$_2$) was added to the salt. The tube was sealed and the tip of the tube was submerged in liquid nitrogen until the contents were frozen. The tube was removed from the liquid nitrogen and the solvent was carefully removed under high vacuum. Under an atmosphere of nitrogen, distilled [D_0]toluene (0.330 cm^3, 3.10 mmol) and distilled [D_8]toluene (0.220 cm^3, 2.07 mmol) were then added and the NMR tube was sealed. The tip of the NMR tube was submerged in an ultrasonic bath and the contents were sonicated until all of the colourless, crystalline salt [$^{13}C_1$]-**1**-PF_6 had dissolved and been replaced with a fine, white precipitate of KPF_6 (10 min). The reaction was monitored by NMR spectroscopy. The isotopic partitioning in the products was calculated by comparison of the intensity of the double triplet signal at $\delta = 3.74$ ppm (arising from the nondeuterated product only) with intensities of signals arising from a combination of both nondeuterated and fully deuterated products.

*Data for adduct [$^{13}C_1$]-**4***: ^{1}H NMR (400 MHz, [D_8]toluene, 22.2 °C): $\delta =$ 0.91 (t, ^3J(H,H) = 7.0 Hz, 3H; NCH_2CH_3), 0.92 (d, ^3J(H,H) = 6.4 Hz, 6H; $NCH(CH_3)_2$), 1.05 (double quintet, ^2J(H,H) = 12.5 Hz, ^3J(H,H) = 3.0 Hz, 1H; C(5)H_{eq}), 1.82 (qt, ^2J(H,H) = 12.5 Hz, ^3J(H,H) = 12.5 Hz, ^3J(H,H) = 5.2 Hz, 1H; C(5)H_{ax}), 2.44 (ddq, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 7.0 Hz, ^3J(H,C) = 4.0 Hz, 1H; $NCH(CH_3)CH_3$), 2.51 (ddq, ^2J(H,H) = 12.6 Hz, ^3J(H,H) = 7.0 Hz, ^3J(H,C) = 4.0 Hz, 1H; $NCH(CH_3)CH_3$), 2.50–2.62 (m, 1H; C(4)H(H)), 2.69–2.81 (m, 3H ([$^{13}C_1$]-**4**&[$^2H_8$][$^{13}C_1$]-**4**) + 2H ([$^{13}C_1$]-**4**); C(6)H_2, C(4)H(H), and PhCH_2^{13}C(2)H), 2.83 (double septet, ^3J(H,H) = 6.4 Hz, ^3J(H,C) = 3.1 Hz, 1H; $NCH(CH_3)_2$), 3.74 (dt, ^1J(H,C) = 145 Hz, ^3J(H,H) = 6.5 Hz, 1H ([$^{13}C_1$]-**4**); PhCH_2^{13}C(2)H), 6.92–7.19 ppm (m, 5H ([$^{13}C_1$]-**4**, obscured by toluene signals); 5 × Ar-H); ^{13}C{^{1}H} NMR (100 MHz,[D_8]toluene, 23.2 °C): $\delta = 13.8$ (s; NCH_2CH_3), 21.8 (s; $NCH(CH_3)CH_3$), 22.1 (s; $NCH(CH_3)CH_3$), 22.7 (s; C(5)H_2), 29.4 (d, ^1J(C,C) = 37.6 Hz; PhCH_2^{13}C(2)H), 41.4 (s; C(6)H_2), 45.2 (s; C(4)H_2), 47.6 (s; NCH_2CH_3), 50.7 (s; $NCH(CH_3)_2$), 75.8 (t, ^1J(C,D) = 21.5 Hz; ^{13}C(2)D), 76.5 (s; ^{13}C(2)H), 141.7 (s; *ipso*-Ar (other aromatic signals obscured by toluene signals)).

Preparation of [$^{13}C_1$]-2 in [D_6]benzene/Ar-R solution and analysis of the kinetics of generation of [$^{13}C_1$]-4, [$^{13}C_1$]-19, [$^{13}C_1$]-20, [$^{13}C_1$]-21 and [$^{13}C_1$]-22: A typical procedure was as follows: [$^{13}C_1$]-**1**-PF_6 (13.9 mg, 0.0462 mmol) was transferred into an NMR tube (with Young valve) under N_2. (K-HMDS)$_2$ (0.26 M solution (HMDS anion) in [D_6]benzene, 0.350 cm^3, 0.091 mmol) was added to the salt. The tip of the NMR tube was submerged in an ultrasonic bath and the contents were sonicated for 5 min. Distilled [D_6]benzene (0.060 cm^3) and distilled 4-trifluoromethyltoluene (0.260 cm^3, 1.87 mmol) were added to the mixture (causing a colour-change from colourless to bright yellow initially, then to orange over 10 min) and the NMR tube was sealed. The contents were sonicated for a further 5 min until all of the colourless, crystalline salt [$^{13}C_1$]-**1**-PF_6 had dissolved and been replaced with a fine, white precipitate of KPF_6. Generation of the toluene adduct [$^{13}C_1$]-**4**, 4-CF_3-toluene adduct [$^{13}C_1$]-**19** and 4-Cl-toluene adduct [$^{13}C_1$]-**20** was monitored by ^{1}H NMR spectroscopy. The ^{13}C{H} NMR shifts for ^{13}C(2)H in [$^{13}C_1$]-**4**, [$^{13}C_1$]-**19** and [$^{13}C_1$]-**20** were $\delta = 76.4$, 76.1 and 76.2 ppm respectively. In the case of [$^{13}C_1$]-**19** and [$^{13}C_1$]-**20** a smaller signal at $\delta = 76.5$ ppm (ca. 10% of the intensity of the signals at $\delta = 76.1$ and 76.2 ppm, respectively) was also apparent. This

may indicate the presence of a product formed from reaction of a second molecule of carbene [$^{13}C_1$]-**2** with [$^{13}C_1$]-**19** and [$^{13}C_1$]-**20**. The 4-*tert*-butyltoluene adduct [$^{13}C_1$]-**21** and ethylbenzene adducts (two diastereomers) [$^{13}C_1$]-**22** were characterized by the appearance of the $^{13}C(2)H$ signal $\delta =$ 76.5 ppm for [$^{13}C_1$]-**21**, and $\delta = 80.1/81.9$ ppm for [$^{13}C_1$]-**22** in the $^{13}C\{^1H\}$ spectrum, and rates of formation were monitored by measuring the disappearance of the $^{13}C(2)$ signal of [$^{13}C_1$]-**2** at $\delta = 231$ ppm, by using the combined intensities of the (K-HMDS)$_2$ ($\delta = 7.2$ ppm) and H-HMDS ($\delta = 2.6$ ppm) signals as an internal standard.

*Data for 4-CF_3-adduct [$^{13}C_1$]-**19***: ^1H NMR (400 MHz, [D$_6$]benzene, 22.3 °C): $\delta = 0.86$ (t, $^3J(H,H) = 7.3$ Hz, 3H; NCH_2CH_3), 0.87 (d, $^3J(H,H) = 6.1$ Hz, 3H; $NCH(CH_3)CH_3$), 0.88 (d, $^3J(H,H) = 6.3$ Hz, 3H; $NCH(CH_3)CH_3$), 1.04 (double quintet, $^2J(H,H) = 12.7$ Hz, $^3J(H,H) = 2.7$ Hz, 1H; $C(5)H_{eq}$), 1.70–1.90 (m (obscured by CH_3 of **15**), 1H; $C(5)H_{ax}$), 2.38 (ddq, $^2J(H,H) = 11.6$ Hz, $^3J(H,H) = 7.4$ Hz, $^3J(H,C) = 4.2$ Hz, 1H; $NCH(H)CH_3$), 2.48 (ddq, $^2J(H,H) = 12.2$ Hz, $^3J(H,H) = 7.1$ Hz, $^3J(H,C) = 3.9$ Hz, 1H; $NCH(H)CH_3$), 2.49–2.59 (m, 1H; C(4)H(*H*)), 2.61–2.74 (m, 5H; $C(6)H_2$, C(4)H(*H*), and $PhCH_2{}^{13}C(2)H$), 2.77 (double septet, $^3J(H,H) = 6.4$ Hz, $^3J(H,C) = 2.9$ Hz, 1H; $NCH(CH_3)_2$), 3.63 (dt, $^1J(H,C) = 145$ Hz, $^3J(H,H) = 6.6$ Hz, 1H; $ArCH_2{}^{13}C(2)H$), 6.59–7.48 ppm (m, 5H (obscured by signals aryl protons of **15**); 5 × Ar-H); $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]benzene, 23.4 °C): $\delta = 13.6$ (s; NCH_2CH_3), 21.7 (s; $NCH(CH_3)CH_3$), 21.8 (s; $NCH(CH_3)CH_3$), 22.5 (s; $C(5)H_2$), 29.1 (d, $^1J(C,C) = 36.7$ Hz; $ArCH_2{}^{13}C(2)H$), 41.3 (s; $C(6)H_2$), 45.0 (s; $C(4)H_2$), 47.6 (s; NCH_2CH_3), 50.7 (s; $NCH(CH_3)_2$), 76.1 ppm (s; $^{13}C(2)H$); aromatic signals obscured by [D$_6$]benzene and 4-CF_3-toluene signals.

*Data for 4-Cl-adduct [$^{13}C_1$]-**20***: ^1H NMR (400 MHz, [D$_6$]benzene, 22.1 °C): $\delta = 0.87$ (t, $^3J(H,H) = 7.1$ Hz, 3H; NCH_2CH_3), 0.89 (d, $^3J(H,H) = 6.4$ Hz, 6H; $NCH(CH_3)_2$), 1.03 (double quintet, $^2J(H,H) = 12.7$ Hz, $^3J(H,H) = 2.7$ Hz, 1H; $C(5)H_{eq}$), 1.75–2.00 (m (obscured by CH_3 of **17**), 1H; $C(5)H_{ax}$), 2.39 (ddq, $^2J(H,H) = 11.5$ Hz, $^3J(H,H) = 7.6$ Hz, $^3J(H,C) = 3.9$ Hz, 1H; $NCH(H)CH_3$), 2.48 (ddq, $^2J(H,H) = 11.5$ Hz, $^3J(H,H) = 7.1$ Hz, $^3J(H,C) = 3.7$ Hz, 1H; $NCH(H)CH_3$), 2.45–2.60 (m, 1H; C(4)H(*H*)), 2.59–2.73 (m, 5H; $C(6)H_2$, C(4)H(*H*), and $ArCH_2{}^{13}C(2)H$), 2.78 (double septet, $^3J(H,H) = 6.4$ Hz, $^3J(H,C) = 2.4$ Hz, 1H; $NCH(CH_3)_2$), 3.61 (dt, $^1J(H,C) = 145$ Hz, $^3J(H,H) = 6.6$ Hz, 1H; $ArCH_2{}^{13}C(2)H$), 6.47–7.23 ppm (m, 5H (obscured by signals aryl carbons of **17**); 5 × Ar-H); $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]benzene, 23.2 °C): $\delta = 13.9$ (s; NCH_2CH_3), 21.8 (s; $NCH(CH_3)CH_3$), 22.0 (s; $NCH(CH_3)CH_3$), 22.5 (s; $C(5)H_2$), 29.7 (d, $^1J(C,C) = 37.0$ Hz; $ArCH_2{}^{13}C(2)H$), 41.3 (s; $C(6)H_2$), 45.1 (s; $C(4)H_2$), 47.6 (s; NCH_2CH_3), 50.6 (s; $NCH(CH_3)_2$), 76.2 ppm (s; $^{13}C(2)H$); aromatic signals obscured by [D$_6$]benzene and 4-Cl-toluene aromatic signals.

Preparation of [$^{13}C_1$]-2 in [D$_6$]benzene/α-[D$_1$]toluene and analysis of the kinetic isotope effects: [$^{13}C_1$]-**1**-PF_6 (13.7 mg, 0.0455 mmol) was transferred into an NMR tube (with Young valve) under N_2. (K-HMDS)$_2$ (0.26 M solution (HMDS anion) in [D$_6$]benzene, 0.350 cm^3, 0.091 mmol) was added to the salt. Distilled [D$_6$]benzene (0.120 cm^3) and distilled α-[D$_1$]toluene (0.200 cm^3, 1.97 mmol) were added to the mixture and the NMR tube was sealed. The tip of the NMR tube was immersed in an ultrasonic bath and the contents were sonicated until all of the colourless, crystalline salt [$^{13}C_1$]-**1**-PF_6 had dissolved and been replaced with a fine, white precipitate of KPF_6 (10 min). The reaction was monitored by NMR spectroscopy. The isotopic partitioning in the products was calculated by comparison of the intensity of the dd signal at $\delta = 3.77$ ppm (arising from the C(2)-protonated product only) with intensities of signals arising from a combination of both C(2)-protonated and C(2)-deuterated products. The major regioisomer produced in this reaction was the C(2)-protonated adduct. This consists of two diastereomers, which are just distinguishable by ^1H NMR spectroscopy (maximum $\Delta\delta$ of 0.002 ppm at 400 MHz).

*Data for adduct [$^2H_1$][$^{13}C_1$]-**4***: ^1H NMR (400 MHz, [D$_6$]benzene, 22.0 °C): $\delta = 0.92$ (t, $^3J(H,H) = 7.1$ Hz, 3H; NCH_2CH_3), 0.93 (d, $^3J(H,H) = 6.1$ Hz, 3H; $NCH(CH_3)CH_3$), 0.94 (d, $^3J(H,H) = 6.1$ Hz, 3H; $NCH(CH_3)CH_3$), 1.03 (double quintet, $^2J(H,H) = 12.5$ Hz, $^3J(H,H) = 2.7$ Hz, 1H; $C(5)H_{eq}$), 1.82 (qt, $^2J(H,H) = 12.4$ Hz, $^3J(H,H) = 12.4$ Hz, $^3J(H,H) = 5.1$ Hz, 1H; $C(5)H_{ax}$), 2.45 (ddq, $^2J(H,H) = 12.0$ Hz, $^3J(H,H) = 7.1$ Hz, $^3J(H,C) = 4.0$ Hz, 1H; $NCH(H)CH_3$), 2.52 (ddq, $^2J(H,H) = 12.0$ Hz, $^3J(H,H) = 7.1$ Hz, $^3J(H,C) = 4.0$ Hz, 1H; $NCH(H)CH_3$), 2.52–2.61 (m, 1H; C(4)H(H)), 2.68-2.81 (m, 3H (C(2)-protonated and C(2)-deuterated) + 2H (C(2)-deuterated) + 1H (C(2)-protonated); $C(6)H_2$, C(4)H(*H*), $PhCH_2{}^{13}C(2)D$, and $PhCH$ (D)$^{13}C(2)H$), 2.85 (double septet, $^3J(H,H) = 6.4$ Hz, $^3J(H,C) = 2.9$ Hz, 1H; $NCH(CH_3)_2$), 3.76 (dd, $^1J(H,C) = 145$ Hz, $^3J(H,H) = 6.4$ Hz, 1H (C(2)-protonated); $PhCH(D)^{13}C(2)H$), 6.95–7.22 ppm (m, 5H (Ph-) obscured by toluene signals); 5 × Ar-H); $^{13}C\{^1H\}$ NMR (100 MHz, [D$_6$]benzene, 23.2 °C): $\delta = 13.8$ (s; NCH_2CH_3), 21.7 (s; $NCH(CH_3)CH_3$ of one diastereomer), 21.8 (s; $NCH(CH_3)CH_3$ of one diastereomer), 22.1 (s; $NCH(CH_3)CH_3$), 22.6 (s; $C(5)H_2$), 29.1 (dt, $^1J(C,C) = 39.0$ Hz, $^1J(C,D) = 21$ Hz; $PhCH(D)^{13}C(2)H$), 29.7 (d, $^1J(C,C) = 38.0$ Hz; $PhCH_2{}^{13}C(2)D$), 41.5 (s; $C(6)H_2$), 45.2 (s; $C(4)H_2$), 47.6 (s; NCH_2CH_3), 50.6 (s; $NCH(CH_3)_2$), 75.9 (t, $^1J(C,D) = 22.0$ Hz; $^{13}C(2)D$), 76.4 (s; $^{13}C(2)H$), 141.7 ppm (s; *ipso*-Ar); other aromatic signals obscured by toluene signals.

Calculation of primary and secondary kinetic isotope effects: From Table 1, entry 9: $k_{obs\text{-}D0} = 3k_H = 9.46(\pm 0.31) \times 10^{-7}\ s^{-1}$. From Table 1, entry 14: $k_{obs\text{-}D1} = (2k_{H/sec}) + (1 \times k_{D/prim}) = 6.09(\pm 0.08) \times 10^{-7}\ s^{-1}$. The partitioning between C–H and C–D insertion $= P = 7.06 \pm 0.7$, thus $k_{H/sec}$ (for $PhCHD{-}H) = k_{obs\text{-}D1}/(2{+}2P^{-1})$. Secondary $KIE = k_H/k_{H/sec} = k_{obs\text{-}D0}\ (2 + 2P^{-1})/3k_{obs\text{-}D1} = 1.18(\pm 0.08)$. Primary $KIE = k_H/k_{D/prim} = k_{obs\text{-}D0}(1{+}P)/3k_{obs\text{-}D1} = 4.2(\pm 0.6)$. Errors are calculated by maximum propagation of ±1% error in C–H/C–D and the sum-squared error from linear regression of $\ln([\mathbf{2}]_0/[\mathbf{2}]_t)$ versus t.

Independent preparation of 4 from phenacetaldehyde: Phenacetaldehyde (0.020 cm^3, 0.171 mmol) was added to *N*-ethyl-*N*′-isopropyl-1,3-diaminopropane (0.0253 g, 0.176 mmol) in [D$_8$]toluene (0.500 cm^3) in an NMR tube containing two pellets of 4 Å "molecular sieves". The contents of the tube were shaken to allow proper mixing. NMR analysis showed that a mixture of products had been formed, of which adduct **4** was the major component. ^1H NMR (500 MHz, [D$_8$]toluene, 24.5 °C): $\delta = 0.91$ (t, $^3J(H,H) = 7.3$ Hz, 3H; NCH_2CH_3), 0.92 (d, $^3J(H,H) = 6.7$ Hz, 6H; $NCH(CH_3)_2$), 1.04 (double quintet, $^2J(H,H) = 12.5$ Hz, $^3J(H,H) = 2.8$ Hz, 1H; $C(5)H_{eq}$), 1.82 (qt, $^2J(H,H) = 12.5$ Hz, $^3J(H,H) = 12.5$ Hz, $^3J(H,H) = 5.2$ Hz, 1H; $C(5)H_{ax}$), 2.44 (dq, $^2J(H,H) = 12.3$ Hz, $^3J(H,H) = 7.1$ Hz, 1H; $NCH(H)CH_3$), 2.52 (dq, $^2J(H,H) = 12.5$ Hz, $^3J(H,H) = 7.0$ Hz, 1H; $NCH(H)CH_3$), 2.51–2.61 (m, 1H; C(4)H(H)), 2.70–2.81 (m, 5H; $C(6)H_2$, C(4)H(*H*), and $PhCH_2C(2)H$), 2.84 (septet, $^3J(H,H) = 6.8$ Hz, 1H; $NCH(CH_3)_2$), 3.74 (t, $^3J(H,H) = 6.6$ Hz, 1H; $PhCH_2C(2)H$), 6.92–7.14 ppm (m, 5H; 5 × Ar-H); $^{13}C\{^1H\}$ NMR (75 MHz, [D$_8$]toluene, 23.3 °C): $\delta = 13.8$ (s; NCH_2CH_3), 21.8 (s; $NCH(CH_3)CH_3$), 22.1 (s; $NCH(CH_3)CH_3$), 22.6 (s; $C(5)H_2$), 29.4 (s; $PhCH_2C(2)H$), 41.4 (s; $C(6)H_2$), 45.2 (s; $C(4)H_2$), 47.6 (s; NCH_2CH_3), 50.6 (s; $NCH(CH_3)_2$), 76.4 (s; C(2)H), 141.7 ppm (s; *ipso*-Ar); other aromatic signals obscured by [D$_8$]toluene signals.

Preparation of α-[D$_1$]toluene: Benzylmagnesium chloride (1.0 M solution in Et_2O, 100 cm^3, 100 mmol) was added by cannula to a cooled (ice bath) stirred mixture of D_2O (6 cm^3, ca. 300 mmol) and Et_2O (20 cm^3). The reaction mixture was allowed to warm slowly to room temperature over 1.5 h then filtered and the diethyl ether removed from the filtrate at 50 °C–70 °C, 760 mmHg on a rotary evaporator. The residue was distilled (15 cm Vigreux column) at 760 mmHg, then redistilled to yield the title compound (6.002 g. 64.5 mmol, 64.5%) as a colourless liquid. ^1H NMR analysis indicated that the isotopic purity was >98.8% and that ca. 1% Et_2O remained. ^1H NMR (400 MHz, α-[D$_1$]toluene, 22.5 °C): $\delta = 2.10$ (t, $^2J(H,D) = 2.6$ Hz, 2H; $PhCH_2D$), 6.97 (m, 2H; 2 × *ortho*-Ar-H), 7.01 (m, 1H; *para*-Ar-H), 7.09 (m, 2H; 2 × *meta*-Ar-H); $^{13}C\{^1H\}$ NMR (100 MHz, α-[D$_1$]toluene, 23.5 °C): $\delta = 21.1$ (t, $^1J(C,D) = 19.2$ Hz; Ph-CH_2D), 125.6 (s; *para*-Ar), 128.4 (s; *meta*-Ar), 129.3 (s; *ortho*-Ar), 137.5 ppm (s; *ipso*-Ar).

Equilibrium of H-HMDS/carbene [$^{13}C_1$]-2 with [$^{13}C_1$]-14: [$^{13}C_1$]-**1**-PF_6 (13.5 mg, 0.0449 mmol) was transferred into an NMR tube (with Young valve) under N_2. (K-HMDS)$_2$ (0.175 M solution in [D$_8$]toluene, 0.300 cm^3, 0.11 mmol) was added to the salt and the NMR tube was sealed. The tip of the NMR tube was submerged in an ultrasonic bath and the contents were sonicated until all of the colourless, crystalline salt [$^{13}C_1$]-**1**-PF_6 had dissolved and been replaced with a fine, white precipitate of KPF_6 (10 min). Distilled H-HMDS (0.150 cm^3, 1.19 mmol) was added to the mixture. The mixture was analysed by $^{13}C\{^1H\}$ NMR spectroscopy which indicated a ratio of 5.0:1.0 [$^{13}C_1$]-**2** ($\delta = 233$ ppm)/[$^{13}C_1$]-**14** ($\delta = 91.2$ ppm).

A 0.150 cm^3 portion of the solution was removed by syringe and added to distilled [D_8]toluene (0.450 cm^3) in a separate NMR tube (with Young valve) under N_2. The mixture was analysed again by $^{13}C\{^1H\}$ NMR spectroscopy which indicated a ratio of 7.2:1.0 [$^{13}C_1$]-**2**/[$^{13}C_1$]-**14**.

Lack of isotope exchange in a mixture of (K-HMDS)$_2$, H-HMDS, [D$_0$]toluene and [D$_8$]toluene: $(K\text{-HMDS})_2$ (0.175 M solution in [D_8]toluene, 0.300 cm^3, 0.11 mmol) was added to distilled H-HMDS (0.032 cm^3, 0.15 mmol) in distilled [D_0]toluene (0.300 cm^3) in an NMR tube (with Young valve) under N_2. The tube was sealed and the contents were shaken to ensure proper mixing. $^{13}C\{^1H\}$ NMR spectroscopy, immediately after reaction, and two weeks later, showed no change in the absolute or relative intensities of the Ar-CH_3 singlet and Ar-CD_3 septet, and no new signals appeared in this region of the spectrum.

Determination of the association constant K_a (M^{-1}) for the equilibrium between (K-HMDS)$_2$/2 and [2(K-HMDS)$_2$] by $^{13}C\{^1H\}$ NMR spectroscopy (Figure 6, left): The entire set of $^{13}C\{^1H\}$ chemical shift data (Table 3) for C(2) in [$^{13}C_1$]-**2** obtained from spectra acquired during determination of the kinetics of its reaction with [D_8]toluene (Table 1, entries 1–6) were plotted (*y* axis) against the $[(K\text{-HMDS})_2]$ concentration (*x* axis). A nonlinear regression based on 1:1 association of **2** with the dimer and derived from the quadratic equation for a standard A + B = C binding isotherm: $[(K_a[A]^2+((K_a[B]_0-K_a[A]_0+1)[A])-[A]_0=0]$ was applied: $y=[\{(([\{((a\times(x-b))+1)^2+(4\times a\times b)\}^{0.5}+((a\times(b-x))-1)]/(2\times a))/b)\times(c-d)\}+d]$; in which $y=\delta_{obs}$, $x=[(K\text{-HMDS})_2]$, $a=K_a$, $b=[\mathbf{2}]$, $c=\delta_{carbene}$ and $d=\delta_{complex}$. This binding isotherm requires "*b*", the concentration of **2**, to be defined. As this value varies through reaction, albeit with only a low impact on the $^{13}C\{^1H\}$ chemical shift data,[26] we included this as a fourth coefficient in the regression. The value obtained on regression of the data (53.4 mM) corresponds well with the mid-point for most runs (80→30 mM; 1.5 half-lives). The data was solved for the four unknowns: K_a, [**2**], $\delta_{carbene}$ and $\delta_{complex}$, which were found to be 62(±7) M^{-1}, 53.2(±0.5) mM, 237.0(±0.2) ppm and 226.8(±0.1) ppm) respectively. The value for $\delta_{carbene}$ (237.0(±0.2) ppm) corresponded very well with the value determined independently as 236.92 ppm from experiments in which substoichiometric quantities of $(K\text{-HMDS})_2$ were added to **1** (dimerisation of the resultant **2** proceeded rapidly and thus the $(K\text{-HMDS})_2$ concentration must be negligible or zero).

Table 3. $^{13}C\{^1H\}$-Chemical shift of C(2) in [$^{13}C_1$]-**2** at various concentrations of $(K\text{-HMDS})_2$ in [D_8]toluene at 23 °C.

	$[(K\text{-HMDS})_2]$ [M]	$\delta_{C(2)}$ **2** average [ppm]	No. of data points	SD[a]
1	0.0056	234.23	7	0.117
2	0.0515	231.45	6	0.188
3	0.0833	229.60	41	0.367
4	0.134	228.37	20	0.075
5	0.1555	228.01	1	–
6	0.3078	227.41	11	0.038

[a] Standard deviation.

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[10] The separation of the supernatent toluene solution of **2**/H-HMDS from the precipitated KPF_6 and any residual **1**, by filtration (0.45 μM PTFE filter), was found to have no effect on the chemistry described herein, other than to effect trace $<5\%$ hydrolysis of **2** to generate **5**, **6H** and **7H**.

[11] R. W. Alder, unpublished, but discussed in reference [5u].

[12] U. Wannagat, H. Niederprüim, *Chem. Ber.* **1961**, *94*, 1540–1547.

[13] Reaction of phenacetaldehyde with *N*-ethyl-*N'*-isopropyl-propane-1,3-diamine gave **4** along with a mixture of other products, including enamides and imines. Moreover, hydrolysis of a sample of [$^{13}C_1$]-**4**, generated in greater quantity by reaction of [$^{13}C_1$]-**1**/K-HMDS/toluene gave [$^{13}C_1$]-**9** (dt at $\delta=9.22$ (^{1}H) and 197.2 ppm (^{13}C), ^1J(C,H) = 175 Hz). All attempts to prepare **4** by reaction of **1** with $PhCH_2MgX$, analogous to the preparation of aminals, as reported by Perrin (C. L. Perrin, D. B. Young, *J. Am. Chem. Soc.* **2001**, *123*, 4451–4458) were unsuccessful.

[14] The slight excess (in terms of HMDS anion) of (K-HMDS)$_2$ over **2**, results in a slightly shallower gradient for $-$d[K-HMDS]/*c* than for d[**2**]/*c* (*c* = conversion in the reaction **1**-PF_6 + K-HMDS = **2** + KPF_6).

[15] K-HMDS is predominantly or exclusively dimeric in toluene see reference [9] for leading references; however, the stoichiometry of the reaction with [$^{13}C_1$]-**1** is 1:1 based on HMDS anion.

[16] C. Hansch, A. Leo, R. W. Taft, *Chem. Rev.* **1991**, *91*, 165–195, and references therein.

[17] The large excess of the toluene over carbene **2** means that the [D_0]/[D_8]toluene ratio remains essentially constant throughout reaction. Kinetic simulation, which takes the small changes in ratio into account, was also employed and gives the same values. The error in the isotope effect determination caused by the change in [D_0]/[D_8]toluene ratio is far outweighed by the error in determination of the partitioning ratios ([D_0]/[D_8] products). The molarities of [D_8]- and [D_0]toluene in the neat liquid state (9.43 and 9.40 and mol dm^{-3}, respectively) are very similar—[D_8]toluene is ca. 0.3% more concentrated.

[18] Based on the results from reaction of **2** with [D_0]- and [D_1]toluene (Table 1, entries 9 and 14) the net KIE arises from a medium primary KIE (k_H/k_D ca. 4.2), which is augmented by large secondary KIEs ($5\times C_{Ar}$–D: 1.62 (average 1.1 per C_{Ar}–D) and $2\times\alpha$-D (= 1.18^2): net secondary k_H/k_D: 2.26), giving a net KIE of $2.26\times4.2=9.5$. For leading references see: a) N. Isaacs in *Physical Organic Chemistry*, 2nd. ed., Longman, Harlow, England, **1995**, pp. 296–302; b) E. V. Ansyln, D. A. Dougherty in *Modern Physical Organic Chemistry*, University Science Books, Sausilito, California, USA, **2006**, pp. 428–430; c) T. H. Lowry, K. Schueller Richardson in *Mechanism and Theory in Organic Chemistry*, 3rd ed., Harper Collins, New York, **1987**, pp. 232–240.

[19] A dual toluene, six-membered-ring transition state mechanism (analogous to that proposed for RO–H insertion by carbenes, see: J. R. Pliego, Jr., W. B. DeAlmeida, *J. Phys. Chem. A* **1999**, *103*, 3904–3909) is eliminated on this basis—which would anyway be highly disfavoured on entropic grounds. The pseudo-second-order rate constant for reaction of **2** with [D_0]toluene (9.13 M) in the presence of 82 mM (K-HMDS)$_2$ is predicted to be $k_{obs}=4.4(\pm0.3)\times10^{-7}$ dm^{3}mol^{-1}s^{-1}, by extrapolation of $k_{obs}=x_H(k_{(H)}-k_{(D)})+k_{(D)}$ (Figure 4) to $x_H=1$. This is in reasonable agreement with the value of $k_{obs}=3.3(\pm0.1)\times10^{-7}$ dm^{3}mol^{-1}s^{-1} for reaction of [D_0]toluene (2.81 M) in [D_6]benzene in the presence of 68 mM (K-HMDS)$_2$.

[20] The generation of approximately 3.8% of [$^2H_7$][$^{13}C_1$]-**4**, as the C(2)–H isotopomer, is consistent with the approximate 0.9% [D_7]toluene (CHD_2 isotopomer) present in [D_1]toluene (^{1}H NMR analysis), when one takes into account the predicted primary $k_H/k_D=4.2$ (±0.6), that is, $4.2\times0.9=3.78$. The net secondary KIEs for reaction

of [D_7]- and [D_8]toluene by C–H and C–D insertion respectively being equivalent ($C_6D_5CD_2$–D vs. $C_6D_5CD_2$–H). The C–D insertion product from [D_7]toluene, whilst undoubtedly present at about a 0.2% level was not detected by $^{13}C\{^1H\}$ NMR spectroscopy due to the low nOe and slow relaxation at the C(2) carbon atom.

[21] See for example: a) D. Bethell, A. R. Newall, G. Stevens, D. Whittaker, *J. Chem. Soc. B* **1969**, 749–754; b) W. Kirmse, K. Loosen, H.-D. Sluma, *J. Am. Chem. Soc.* **1981**, *103*, 5935–5937; c) D. Bethell, R. D. Howard, *J. Chem. Soc. B* **1969**, 745–748; d) P. M. Warner, I.-S. Chu, *J. Am. Chem. Soc.* **1984**, *106*, 5366–5367; e) X.-M. Du, H. Fan, J. L. Goodman, M. A. Kesselmayer, K. Krogh-Jespersen, J. A. La-Villa, R. A. Moss, S. Shen, R. S. Sheridan, *J. Am. Chem. Soc.* **1990**, *112*, 1920–1926; f) R. A. Moss, S. Shen, M. Wlostowski, *Tetrahedron Lett.* **1988**, *29*, 6417–6420.

[22] The pK_a of toluene has been estimated as: a) 44.4±0.4 (in 70:30 THF/HMPA): B. Jaun, J. Schwarz, R. Brelow, *J. Am. Chem. Soc.* **1980**, *102*, 5741–5748; b) 40.91 (in toluene/cyclohexylamine/lithium cyclohexylamide): A. Streiweiser, Jr., M. R. Granger, F. Mares, R. A. Wolf, *J. Am. Chem. Soc.* **1973**, *102*, 4257–4261; and c) 42 (in DMSO): F. G. Bordwell, D. Algrim, N. R. Vanier, *J. Org. Chem.* **1977**, *42*, 1817–1819; d) The pK_a of H-HMDS has been determined as 26 (in DMSO): F. G. Bordwell personal communication to J. E. Bartmess, cited in D. T. Grimm, J. E. Bartmess, *J. Am. Chem. Soc.* **1992**, *114*, 1227–1231; and e) 29.5 (in THF): R. R. Fraser, T. S. Mansour, *J. Org. Chem.* **1984**, *49*, 3442–3444.

[23] a) The pK_a of the related formamidinium species 1,3-diisopropyl-3,4,5,6-tetrahydropyrimidin-1-ium hexafluorophosphate and 1,3-diethyl-3,4,5,6-tetrahydropyrimidin-1-ium in D_2O/KCl (ionic strength = 1) at 25 °C have been determined as 28.2 and 27.4, respectively, by modification of the method of Aymes et al. (ref. [23d]) to take into account background hydrolysis of the pyrimidin-1-ium cation. An analogous determination for *N*,*N*′-ditertbutylimidazolium chloride gave a pK_a value of 24.7 which can be compared to the value of 22.7 obtained for the same acid cation in DMSO (ref. [23c])—A. C. O'Donoghue, University of Durham, UK, personal communication to G. C. Lloyd-Jones. For other determinations/computed estimations of carbene pK_a values see: b) R. W. Alder, P. R. Allen, S. J. Williams, *J. Chem. Soc. Chem. Commun.* **1995**, 1267–1268; c) Y.-J. Kim, A. Streitwieser, *J. Am. Chem. Soc.* **2002** *124*, 5757–5761; d) T. L. Aymes, S. T. Diver, J. P. Richard, F. M. Rivas, K. Toth, *J. Am. Chem. Soc.* **2004**, *126*, 4366–4374; e) A. M. Magill, K. J. Cavell, B. F. Yates, *J. Am. Chem. Soc.* **2004**, *126*, 8717–8724; f) D. Martin, O. Illa, A. Baceirdo, G. Bertrand, R. M. Ortuno, V. Branchadell, *J. Org. Chem.* **2005**, *70*, 5671–5677.

[24] W. Clegg, G. C, Forbes, A. R. Kennedy, R. E. Mulvey, S. T. Liddle, *Chem. Commun.* **2003**, 406–407.

[25] a) R. W. Alder, M. E. Blake, C. Bortolotti, S. Bufali, C. P. Butts, E. Linehan, J. M. Oliva, A. G. Orpen, M. J. Quayle, *Chem. Commun.* **1999**, 241–242; b) P. L. Arnold, M. Rodden, C. Wilson, *Chem. Commun.* **2005**, 1743–1745.

[26] The chemical shift of C(2) in [$^{13}C_1$]-**2** is found to decrease fractionally with conversion on reaction with toluene. The gradient decreases with increasing concentration of excess (K-HMDS)$_2$ and most likely arises from the depletion of excess (K-HMDS)$_2$ at high [[$^{13}C_1$]-**2**] and low [(K-HMDS)$_2$]. Linear regression of plots of [[$^{13}C_1$]-**2**] (across the 0 to 80 mM range of concentrations studied) versus chemical shift of C(2) were found to have gradients orders of magnitude smaller than the $\Delta\delta$ values observed across the range of [(K-HMDS)$_2$] studied.

[27] The Brønsted salt effect catalysis rate law: $\log k_{rel} = m\{\Sigma z^2 c\}^{0.5}$; in which z = charge = 1; c = [K-HMDS]; m = a product of the Debye–Hückel parameter, as applied to the monomer or mono-ionising dimer should yield a linear correlation of $\log k_{rel}$ versus [(K-HMDS)$_2$]. See N. Isaacs in *Physical Organic Chemistry*, 2nd ed., Longman Press, Harlow, England, **1995**, pp. 213–214. It is unlikely that the dimer would undergo double ionisation.

[28] For $K_a = \{$ [**2**(K-HMDS)$_2$]/([**2**][(K-HMDS)$_2$])$\}$, an NMR-shift-detected binding isotherm was derived by solving the quadratic equation for a standard 1:1 binding isotherm: $y = [\{(([\{((a(x-b))+1)^2 + (4ab)\}^{0.5} + ((a(b-x))-1)]/(2a))/b)(c-d)\} + d]$; in which $y = \delta_{obs}$, x = [(K-HMDS)$_2$], $a = K_a$, b = [**2**], $c = \delta_{carbene}$ and $d = \delta_{complex}$ (Figure 6, left). Analogously, the equation can be applied to analyse rates in a non-linear manner (Figure 2, right) in which $y = k_{obs}$, x = [(K-HMDS)$_2$], $a = K_a$, b = [**2**], $c = k_{uncat}$ and $d = k_{cat}$. The equation $(1-x_2) = [1-\{(([\{((a(x-b))+1)^2 + (4ab)\}^{0.5} + ((a(b-x))-1)]/(2a))/b)\}]$, in which $a = K_a$, b = [**2**], c = [(K-HMDS)$_2$] can be used to calculate the mol-fraction of [**2**(K-HMDS)$_2$] and thus analyse rates in a linear correlation (Figure 6, right). These equations are used in preference to simplified equations based on the assumption that [(KHMDS)$_2$] = [(KHMDS)$_2$]$_0$ which yields a poorer correlation, K_a = 29 (±22) M^{-1}. For the quadratic equation for a standard 1:1 binding isotherm A + B = C binding isotherm: $[(K_a[A]^2 + ((K_a[B]_0 - K_a[A]_0 + 1)[A]) - [A]_0 = 0]$, the simplified binding isotherm and the associated simplified NMR-shift relationship, see: See E. V. Ansyln, D. A. Dougherty in *Modern Physical Organic Chemistry*, University Science Books, Sausilito, California, USA, **2006**, pp. 216–221.

[29] It should be noted that [(**2**′)$_2$(K-HMDS)$_2$], in which **2**′ is the *N*,*N*′-diisopropyl analogue of **2**, has been isolated and its structure determined by X-ray diffraction--see reference [25a]. This structure may of course arise through the favourable symmetry/packing/packing forces in the bis-carbene KHMDS dimer complex allowing crystallisation of the minor component of the three-stage equilibrium.

[30] a) The observation that the net KIE on the rate of reaction for [D_8]- versus [D_0]toluene as reactant and solvent, $k_{(H)}/k_{(D)} = 10.9 \pm 1.9$ is in reasonable but not complete agreement with the observed partitioning $P = k_{[D_0]tol}/k_{[D_8]tol} = 9.5 \pm 0.8$ is suggestive of a solvent KIE of about 1.2. Whilst such effects are common with protic solvents that can effect deuteration at exchangeable reaction sites, and are thus accountable by for example, proton inventory (see for example, R. L. Schowen, *Prog. Phys. Org. Chem.* **1972**, *9*, 275–332) substantial solvent KIEs in aprotic media are rather rare—see for example b) L. R. Khundkar, J. W. Perry, J. E. Hanson, P. B. Dervan, *J. Am. Chem. Soc.* **1994**, *116*, 9700–9709; c) Y. Zong, J. L. McHale, *J. Chem. Phys.* **1997**, *106*, 4963–4973; d) R. Paur-Afshari, J. Lin, R. H. Schultz, *Organometallics* **2000**, *19*, 1682–1691. Analysis of the chemical shift of the $^{13}C\{^1H\}$ NMR signal arising from C(2) in [$^{13}C_1$]-**2** in the various [D_8]/[D_0]toluene mixtures indicates that K_a for (K-HMDS)$_2$ complexation is not affected by the [D_8]/[D_0]toluene ratio.

[31] See for example, A. Streitweiser, Jr., P. H. Owens, G. Sonnichsen, W. K. Smith, G. R. Ziegler, H. M. Niemeyer, T. L. Kruger, *J. Am. Chem. Soc.* **1973**, *95*, 4254–4257.

[32] It should be noted that the KIE values calculated for (K-HMDS)$_2$-catalysed reactions of **2** with deuterated toluenes in toluene or [D_6]benzene are based on measurements in which the excess [(K-HMDS)$_2$] amounts to 60–80 mM and thus about 75% of **2** is complexed. We have not determined KIEs for the individual reactions of free **2** and complexed **2**.

[33] For example, the methylene–benzene singlet→*ipso*-π complex is computed to have a dissociation energy of 7.2 kcal mol^{-1} and experimentally (photoacoustic calorimetry) this is found to be 8.7± 3.1 kcal mol^{-1}: M. I. Khan, J. L. Goodman, *J. Am. Chem. Soc.* **1995**, *117*, 6635–6636; for a review of the area see W. Kirmse, *Eur. J. Org. Chem.* **2005**, 237–260.

[34] For an overview of heterocyclic-carbene–metal complexation and reactivity of the resulting complexes see reference [2a].

[35] Alternative explanations for the increased reactivity of the complex [**2**(K-HMDS)$_2$] towards toluene, such as toluene–K^+ π or σ complexation (pre-organisation of the toluene proximal to C(2) in the nascent carbene base generated on decomplexation) or deprotonation of toluene by the K-coordinated HMDS nitrogen to give a [**2**{K_2(HMDS)(H-HMDS)}(tetrahydropyrimidinium)][$PHCH_2$] ion pair (if collapse of the ion pair intracomplex H/K exchange are fast, then no cross over of H/D with the bulk-medium would occur) seem less likely but cannot be ruled out at this stage. For an example of π-tolyl–K^+ complexation of (K-HMDS)$_2$ detected in the solid state by X-ray crystallography, see reference [9b]. For other examples of π-aryl–K^+ and σ-aryl–K^+ complexation see, a) C. J. Schaverlen, J. B. van Mecherlen, *Organometallics* **1991**, *10*, 1704–1709; b) G. K.

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[36] The *N*,*N*′-diethyl and *N*,*N*′-diisopropyl analogues of **2** undergo analogous reaction with toluene; G. C. Lloyd-Jones, G. J. J. Owen-Smith, unpublished results.

[37] Triethyl orthoacetate was treated with *N*-isopropyl-1,3-propanediamine in the presence of catalytic *p*-TsOH.H_2O at 140 °C. The resulting tetrahydropyrimidine intermediate was reduced with DIBAL-H in toluene to afford *N*-ethyl-*N*′-isopropyl-1,3-diaminopropane.

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