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Absolute Kinetics of Phenylchlorocarbene C-H Insertion Reactions

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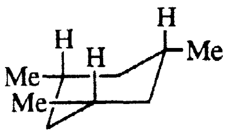
Abstract. Absolute rate constants, activation parameters, a kinetic isotope effect, and hybrid density functional theory computational results are presented for various C-H insertion reactions of PhCCl.

The absolute kinetics of singlet carbene-alkene addition reactions have been intensively studied,[1] but much less is known about the kinetics of intermolecular singlet carbene C-H insertion reactions. Laser flash photolysis (LFP) provided aggregate rate constants for the presumed insertions of ArCCl with isooctane, cyclohexane, and *n*-hexane, but products were not characterized.[2] k_{abs} values were also determined for the reactions of PhCCl with Si-H, Sn-H and C-H bonds;[3,4] the C-H substrates included cumene (k_{abs} = 1.7 x 10^5 M^{-1} s^{-1}), ethylbenzene (8.2 x 10^4 M^{-1} s^{-1}), and toluene (7.5 x 10^3 M^{-1} s^{-1}).[4]

Here we report initial results from a broad study of PhCCl absolute insertion kinetics with a variety of C-H substrates. Taken together, absolute rate constants, activation parameters, kinetic isotope effects, and computational results provide a fuller portrait of this archetypal carbene reaction.[5]

PhCCl was generated photochemically[1] from phenylchlorodiazirine.[6] Substrates included all-*cis*-1,3,5-trimethylcyclohexane (**1**, ChemsampCo), adamantane (**2**), cyclohexane (**3**), paraldehyde (**4**), and 2-methyl-1,3-dioxolane (**5**). Photolyses of concentrated solutions of the diazirine in benzene (A_{374}>3) with substrates **1**, **2** and **5** afforded >90% yields of tertiary C-H insertion products, RCPhHCl, accompanied by lesser quantities of PhCCl dimer (~3%) and azine (PhCCl=N-N=CClPh, ~2%). The insertion products were purified by chromatography, followed by recrystallization or preparative GC (SF-96, 150 °C); they were characterized by NMR, GC-MS, and elemental analysis. Insertion yields were lower with **3** and **4** (45-48%), where dimer (~8%) and azine (~46%) formation were dominant.

Absolute rate constants for the C-H insertions of PhCCl with substrates **1**, **4**, and **5** were determined by LFP[7] at 351 nm of phenylchlorodiazirine in deaerated benzene (or pentane). PhCCl decay was monitored at 310 nm as a function of added substrate, and second order rate constants were derived from the slopes of the linear



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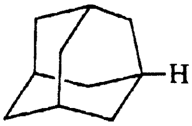

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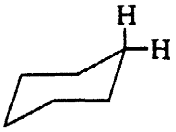

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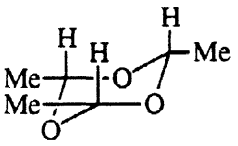

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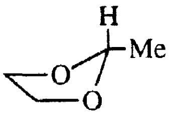

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(r>0.99) correlations of the observed pseudo-first-order rate constants for PhCCl decay with [substrate].[1] Traces of pentane insertion product(s) were detected when PhCCl was generated in a pentane solution of substrate **5**. Results appear in Table 1. For less reactive substrates **3**, **3**-d_{12}, and **4**, rate constants were determined by product-based relative reactivity experiments. These results also appear in Table 1.

The *tert*-C-H bonds of substrates **1** and **2** react with PhCCl with $k \sim 10^5$ M^{-1} s^{-1}. They are about as reactive as the analogous cumyl C-H bond,[4] but about 20 times less reactive than either the monoalkylated C=C of 1-hexene (2.2 x 10^6 M^{-1} s^{-1})[1,8] or the Si-H bond of triethylsilane (2.5 x 10^6 M^{-1} s^{-1}).[4] However, despite the development of partial positive charge on the substrate carbon atom during C-H insertion,[9] and the expectation that α-oxygens should assist insertion by resonance delocalization of that charge,[5c,d] the *tert*-C-H of **5** is only about twice as reactive as those in **1** or **2**, while the comparable C-H bond of paraldehyde (**4**) is an order of magnitude less reactive. LFP studies reveal the development of a strong absorbance at 485 nm during the PhCCl-**4** reaction (100 times less intense in the PhCCl-**5** reaction), suggesting an incursion of an *O*-ylide in the paraldehyde case.[10] This could be responsible for the low C-H insertion efficiency. The *sec*-C-H bond of cyclohexane is about 15 times less reactive than the *tert*-C-H bond of **1**. We found no evidence (GC, GC-MS) for PhCCl insertion into the unactivated primary C-H bonds of 1,3,5-tri-*t*-butylbenzene; only dimer and azine could be detected. Note that toluene reacts with PhCCl with k = 7.5 x 10^3 M^{-1} s^{-1}.[4]

Activation parameters were determined by LFP for PhCCl insertions with substrates **1** and **2** in benzene solvent. Rate constants were measured at 6 or 7 temperatures over ranges of 296—352 K (**1**) or 280-339 K (**2**); linear correlations (r > 0.99) of ln k vs. 1/T were obtained. Values of E_a and $\Delta S^{\ddagger}$ were 2.9 kcal/mol and -25.6 eu for **1**, and 3.2 kcal/mol and -24.2 eu for **2**. These may be compared with the activation parameters for PhCCl insertion into Et_3Si-H (2.8 kcal/mol and -12.8 eu)[3] or addition to 1-hexene (1.1 kcal/mol and -27 eu).[1,11] The $\Delta S^{\ddagger}$ values for C-H insertions are quite negative and similar to those for PhCCl/C=C additions, largely

Table 1. Kinetics of PhCCl C-H Insertion Reactions in Benzene at 23 °C

substrate	$10^{-5}\,k_{\mathrm{abs}}$, M^{-1} s^{-1} [a]	$10^{-5}\,k_{\mathrm{calcd}}$, M^{-1} s^{-1} [b]	$10^{-5}\,k_{\mathrm{per\ H}}$, M^{-1} s^{-1} [c]
1	2.87		0.96
2	5.02 (11.7)[d]		1.26
5	2.38 (4.22)[d,e]		2.38
3		0.75[f]	0.062[g]
3-d_{12}		0.20[h]	
4		0.32[i]	0.11

[a] By LFP. [b] By relative (competitive) kinetics. [c] Corrected for the number of reactive C-H bonds. [d] In pentane. [e] A trace of PhCCl-pentane insertion product(s) was formed. [f] By competition of substrates **1** and **3**; k(**1**)/k(**3**) = 3.83 ± 0.11. [g] Corrected for 12 C-H bonds; ab initio calculations indicate that activation energies for axial and equatorial PhCCl insertion reactions differ by only 0.2 kcal/mol. [h] By competition of substrates **3** and **3**-d_{12}; k_{rel} = 3.79 ± 0.08. [i] By competition of substrates **5** and **4**; k_{rel} = 7.41 ± 0.02.

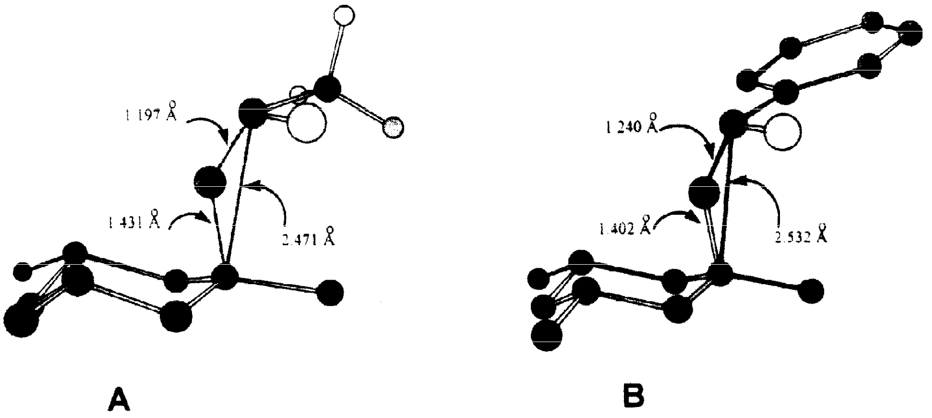

Figure 1. Calculated (B3LYP/6-31G*), fully optimized transition states for C-H insertions of (**A**) MeCCl and (**B**) PhCCl with substrate **1**. Except for the target C-H bond, substrate (and phenyl) H atoms are omitted.

reflecting the entropy decrease that occurs when 2 reactant molecules combine to form a single product molecule.[1,11,12]

We also find (Table 1) that PhCCl insertions into the *tert*-C-H bonds of **2** and **5** are about twice as fast in pentane as they are in benzene, which we attribute to selective stabilization of the carbene's ground state by π-complexation in benzene. Independent evidence for such complexation has recently appeared.[13]

From the relative reactivity of PhCCl with cyclohexane and cyclohexane-d_{12} (Table 1), the primary kinetic isotope effect (KIE) for *sec*-C-H/C-D insertion is ~3.8 at 23 °C. Literature comparisons include KIE's for CCl_2 insertions into the *tert*-C-H/C-D bonds of cumene (2.6 at 120 °C),[9] 2-phenyl-1,3-dioxolane (2.77 at 0 °C),[5c] and 2-phenylbutane (2.5 at 80 °C).[5b] Conceivably, the larger KIE observed for PhCCl/cyclohexane insertion reflects the less reactive *sec*-C-H(C-D) bond, which engenders a "later," more "bond-broken" transition state and a greater KIE. Ab initio calculations do indicate significant C-H bond stretching and charge development in these reactions.

The B3LYP hydrid density functional theory method was used as contained in the Gaussian 94 package.[14] Extensive study of the MeCCl-**1** C-H insertion afforded the B3LYP/6-31G* transition state (TS) **A** (see Figure 1), which was used as a starting point for the derivation of B3LYP/6-31G* TS **B** for PhCCl-**1** insertion. Transition states were confirmed by frequency calculations and only 1 negative frequency was obtained in each case; B3LYP/6-31G* results follow.

For **B**, the E_a (with zero point energy correction) is calculated as 7.1 kcal/mol and $\Delta S^{\ddagger}$ as -39.8 eu. These values differ significantly from the experimental data (2.9 kcal/mol and -25.6 eu), although trends within the computational results are sensible. Thus, E_a's for C-H insertions with **1** are MeCCl, 5.4; PhCCl, 7.1; and CCl_2, 11.2 kcal/mol, increasing with increasing carbene stablity.[15] Also, computed E_a's increase as anticipated for insertions into the (axial) *sec*-C-H bonds of **3**: MeCCl, 7.1; PhCCl, 10.8; and CCl_2, 14.1 kcal/mol (no zero point energy correction).[16] The (uncorrected) E_a's computed for PhCCl insertions into the axial or equatorial C-H bonds of **3** are nearly identical, 10.77 and 10.96 kcal/mol, respectively, so that we divide by 12 rather than 6 to put the aggregate cyclohexane insertion rate constant on a per-bond basis.[17]

In the computed PhCl-**1** TS (Fig. 1, **B**), the target C-H bond has been stretched from 1.10 to 1.40 Å, and bonding to the carbenic carbon is well-established at a separation of 1.24 Å. A similar situation prevails in the PhCCl-**3** TS, consistent with the substantial observed primary KIE (3.8) for C-H/C-D insertion of PhCCl.

Finally, the significant C-C separation of 2.53 Å between substrate and carbene carbons in the PhCCl-**1** insertion TS is mirrored in the respective computed charges (NBO analysis) on these atoms of +0.22 and -0.20, respectively. The partial positive charge on the substrate carbon accords with experimental observations.[5b,9]

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(17) Interestingly, the eq>ax kinetic advantage observed[5d] for CCl_2 insertions into the *tert*-C-H bonds of the 4-*t*-butyl-1-methylcyclohexane isomers is reflected in the B3LYP/6-31G* calculations, where E_a's for CCl_2 insertions into the eq and ax *tert*-C-H bonds of methylcyclohexane are computed as 10.6 and 12.1 kcal/mol, respectively.