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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. © 1998 Elsevier Science Ltd. All rights reserved.

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 ($k_{abs} = 1.7 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$), ethylbenzene (8.2 x 10⁴ M⁻¹ s⁻¹), and toluene (7.5 x 10³ 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 photochemically¹ from phenylchlorodiazirine.⁶ Substrates included all-*cis*-1,3,5trimethylcyclohexane (1, ChemsampCo), adamantane (2), cyclohexane (3), paraldehyde (4), and 2-methyl-1,3dioxolane (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 LFP⁷ 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



0040-4039/98/\$ - see front matter © 1998 Elsevier Science Ltd. All rights reserved. *PII*: S0040-4039(98)02196-0 (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 10⁶ M⁻¹ s⁻¹)^{1,8} or the Si-H bond of triethylsilane (2.5 x 10⁶ 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 $k = 7.5 \times 10^3$ 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 ΔS^4 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 Et₃Si-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 ΔS^4 values for C-H insertions are quite negative and similar to those for PhCCl/C=C additions, largely

substrate	$10^{-5} k_{abs}, M^{-1} s^{-1 a}$	$10^{-5} k_{calcd}, M^{-1} s^{-1} b$	$10^{-5} k_{per H}, M^{-1} s^{-1 c}$
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- <i>d</i> ₁₂		0.20 ^h	
4		0.32 ⁱ	0.11

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

^aBy LFP. ^bBy relative (competitive) kinetics. ^cCorrected for the number of reactive C-H bonds. ^dIn pentane. ^eA trace of PhCCl-pentane insertion product(s) was formed. ^fBy competition of substrates 1 and 3; $k(1)/k(3) = 3.83 \pm 0.11$. ^gCorrected 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. ^bBy competition of substrates 3 and 3- d_{12} ; $k_{rel} = 3.79 \pm 0.08$. ^bBy competition of substrates 5 and 4; $k_{rel} = 7.41 \pm 0.02$.



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 CCl₂ 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 ΔS^{\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 CCl₂, 11.2 kcal/mol, increasing with increasing carbene stability.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 CCl₂, 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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References and Notes

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- (16) With or without zero point energy corrections, insertions into the *tert*-C-H of 1 are 1-2 kcal/mol lower in E_s than the analogous reactions with the *sec*-C-H of 3 for all 3 carbenes.
- (17) Interestingly, the eq>ax kinetic advantage observed^{5d} for CCl₂ 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 CCl₂ insertions into the eq and ax *tert*-C-H bonds of methylcyclohexane are computed as 10.6 and 12.1 kcal/mol, respectively.