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Activation Parameters for Additions to Alkenes of Arylchlorocarbenes with Enhanced Electrophilicity

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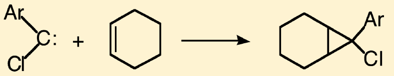
Supporting Information

ABSTRACT: Activation parameters are reported for additions of phenylchlorocarbene (PhCCl), pentafluorophenylchlorocarbene (F_5-PhCCl), and 3,5-dinitrophenyl-chlorocarbene (3,5-DN-PhCCl) to tetramethylethylene (TME), cyclohexene, and 1-hexene. The order of activation enthalpies is F_5-PhCCl > PhCCl > 3,5-DN-PhCCl. Activation enthalpies also increase as the degree of alkene alkylation decreases. In general, the entropies of activation increase in tandem with the enthalpies of activation.

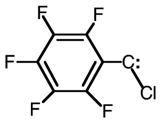


1. INTRODUCTION

Many years ago, at the dawn of absolute rate constant measurements for carbene−alkene addition reactions in solution, we reported activation parameters for the additions of phenylchlorocarbene (PhCCl) to several simple alkenes.[1] Subsequently, these studies were extended to phenylbromocarbene and phenylfluorocarbene,[2] as well as *p*-substituted phenylhalocarbenes.[3] Two important findings of these investigations were as follows: (1) negative values of activation energies and enthalpies accompanied additions of the carbenes to reactive alkenes like tetramethylethylene (TME), and (2) free energies of activation were dominated by entropic contributions, even with less reactive alkenes like 1-hexene.[1−3]

Our continuing desire to understand the relation between carbenic structure and reactivity[4] impelled us to expand the scope of our studies to include alkene additions of the dihalocarbenes (CCl_2,[5] CClF,[5] and CF_2[6]), as well as their highly electrophilic relatives trifluorochlorocarbene (CF_3CCl)[7] and *N*-methyl-3-pyridiniumchlorocarbene ($MePyr^+CCl\ BF_4^-$).[8] We may summarize the results of these more recent investigations as follows:[7] activation enthalpies decrease as the carbenes' stabilities decrease and their electrophilicities increase and also as alkene reactivities increase. Importantly, activation entropies decrease *in tandem* with activation enthalpies, suggesting the possible operation of enthalpy−entropy compensation in these carbene−alkene additions.

Here, we revisit the arylchlorocarbene systems[1−3] in light of these more recent findings.[4−7] We examine two highly electrophilic arylchlorocarbenes, pentafluorophenylchlorocarbene (**1**, F_5-PhCCl)[9,10] and 3,5-dinitrophenylchlorocarbene (**2**, 3,5-DN-PhCCl).[11] Our primary question is whether enthalpy−entropy compensation attends the alkene addition reactions of PhCCl, F_5-PhCCl, and 3,5-DN-PhCCl.



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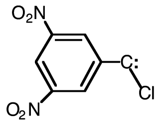

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2. RESULTS AND DISCUSSION

2.1. Computational Results. Table 1 collects computed parameters of carbene reactivity and stability for PhCCl, F_5-PhCCl, and 3,5-DN-PhCCl and (for comparison) $MePyr^+CCl$, CF_3CCl, CCl_2, and CF_2.[7,8,12−15] The electrophilicity of a singlet carbene is governed by the accessibility of the formally vacant p orbital (LUMO) at its carbenic center.[15,16] Based on orbital energy (ε_{LUMO}, Table 1), both F_5-PhCCl and 3,5-DN-PhCCl have highly accessible LUMOs, more so than parent PhCCl. The ε_{LUMO} values of 3,5-DN-PhCCl, $MePyr^+CCl$, and F_5-PhCCl are lower (more accessible) than those of the other carbenes in Table 1.

Table 1. Computed Parameters of Carbene Reactivity and Stability

carbene	ε_{LUMO}[a]	ε_{HOMO}[a]	ω[b]	ΔE_{stab}[c]
F_5-PhCCl	−0.019	−10.2	1.29	34.5
3,5-DN-PhCCl	−0.46	−10.8	1.53	37.9
PhCCl	0.94	−9.62	0.89	44.8
$MePyr^+CCl$	−0.16[d]	−10.6[d]	1.38[d]	30.2[e]
CF_3CCl	0.57	−11.3	1.21	21.3
CCl_2	1.00	−10.9	1.03	45.5
CF_2	2.74	−12.8	0.82	70.9

[a] ε_{LUMO} and ε_{HOMO} are the LUMO and HOMO energies in eV, computed at the HF/6-31G(d,p)//MP2/6-31G(d,p) level. [b] In eV; ω = global electrophilicity = $(\varepsilon_{LUMO} + \varepsilon_{HOMO})^2/8(\varepsilon_{LUMO} - \varepsilon_{HOMO})$, computed here at the HF/6-31G(d,p)//MP2/6-31G(d,p) level; see refs 7, 8, and 12−14. [c] In kcal/mol. Defined as the negative of the reaction energy for $CH_2 + CH_3X + CH_3Y \rightarrow CXY + 2CH_4$. Computed here at the B3LYP/6-311++G(2d,p) level; see refs 4, 7, 8, and 15. [d] Calculated as the BF_4^- salt. [e] Calculated as the "naked" $MePyr^+CCl$.

A comparable picture arises from consideration of the computed global electrophilicities (ω, Table 1)[7,8,12−14] of the carbenes. Here, 3,5-DN-PhCCl exhibits the highest electro-

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philicity, followed by $MePyr^+CCl$ and F_5-PhCCl. Parent PhCCl is not dominant on this scale.

ΔE_{stab} in Table 1 represents the computed carbenic stability relative to CH_2.[4,7,8,15] Here, CF_3CCl[7] and $MePyr^+CCl$[8] are the least stabilized carbenes, followed by F_5-PhCCl, 3,5-DN-PhCCl, and PhCCl. Based on the high reactivity toward alkenes of CF_3CCl and $MePyr^+CCl$, we would also expect F_5-PhCCl and 3,5-DN-PhCCl to be similarly reactive.

The expected electrophilicity of F_5-PhCCl, 3,5-DN-PhCCl, and PhCCl follows from considerations based on frontier molecular orbital theory. The differential orbital energies corresponding to either electrophilic attack on alkenes [$\Delta E_E = \varepsilon_{CXY}^{LUMO} - \varepsilon_{C=C}^{HOMO} = p - \pi$] or nucleophilic attack [$\Delta E_N = \varepsilon_{C=C}^{LUMO} - \varepsilon_{CXY}^{HOMO} = \pi^* - \sigma$] can be estimated from the computed carbene orbital energies in Table 1 and the values of ε_π and ε_{π^*} for the alkenes that we employ (TME, cyclohexene, and 1-hexene).[17] For each carbene/alkene reactant pair, we find that $\Delta E_E < \Delta E_N$, suggesting that the carbene LUMO (p)–alkene HOMO (π) electrophilic interactions will dominate the transition states of all nine carbene–alkene additions considered in this report.

The singlet ground states of CCl_2[18] and CF_2[19] are well established. CF_3CCl is predicted to be a ground state singlet by ~4.6 kcal/mol,[7] while an even greater singlet stabilization of 10.7 kcal/mol is computed for $MePyr^+CCl\ BF_4^-$ in simulated dichloroethane.[8] Of the three carbenes studied here, computed singlet ground state stabilizations of 4.2 kcal/mol for F_5-PhCCl[10] and 7.8 kcal/mol for PhCCl[20] have been reported. Our current calculations include determination of the singlet–triplet (S-T) separations in F_5-PhCCl, PhCCl, and 3,5-DN-PhCCl at the same high computational level. Thus, at the CCSD(T)/cc-pVTZ//MP2/cc-pVTZ level, we find ΔE(S-T) = 8.3, 12.3, and 9.8 kcal/mol for F_5-PhCCl, PhCCl and 3,5-DN-PhCCl, respectively. A singlet ground state is clearly preferred for all three arylchlorocarbenes. Computational details appear in the Experimental Section.

2.2. Experimental Results. Additions of PhCCl[3] and F_5-PhCCl[9] to alkenes are well studied reactions; however, analogous additions have not been described for 3,5-DN-PhCCl. Accordingly, we photolyzed 3,5-dinitrophenylchlorodiazirine[11] at 350 nm in pentane solutions of TME, cyclohexene, and 1-hexene, isolating the appropriate cyclopropanes in yields of 70%, 35%, and 15%, respectively, after chromatography on silica gel. The products were characterized by ^1H and ^{13}C NMR and by mass spectrometry. Details appear in the Experimental Section.

Absolute rate constants for the additions of the carbenes to the alkenes were determined by laser flash photolysis (LFP) using a xenon fluoride excimer laser emitting at 351 nm.[21] The carbene precursors were diazirines: pentafluorophenylchlorodiazirine,[9] 3,5-dinitrophenylchlorodiazirine,[11] and phenylchlorodiazirine.[22] Rate constants for the alkene additions of PhCCl were determined by following the disappearance of the carbene absorption at 292 nm as a function of alkene concentration in pentane. The observed rate constants for carbene disappearance were plotted against alkene concentration, and the slope of the linear correlation thus obtained was taken as the bimolecular rate constant (M^{-1} s^{-1}) for the carbene/alkene addition. In the additions of PhCCl to TME and 1-hexene, the newly determined rate constants were in good agreement with earlier reports.[3] Rate constants for the additions of F_5-PhCCl were similarly obtained, following the disappearance of the carbene absorption at 300 nm.[9]

The absorption of 3,5-DN-PhCCl at 290 nm was weak, so the rate constants in this case were determined using Platz's pyridine ylide method.[23] Here, the apparent rate of formation of the pyridine ylide of 3,5-DN-PhCCl at 508 nm was accelerated by the addition of an alkene at a constant concentration of pyridine. Correlation of the observed rate constants for ylide formation as a function of alkene concentration gave a linear correlation whose slope was taken as the bimolecular rate constant for 3,5-DN-PhCCl/alkene addition.

Rate constants measured at 296–299 K for the nine carbene/alkene additions are collected in Table 2. Graphical representations of the rate constant determinations appear in the Supporting Information. The rate constants fall in the 10^6–10^8 M^{-1} s^{-1} regime, and as expected for electrophilic carbene additions, alkene reactivity is TME > cyclohexene >1-hexene; the more electron-rich alkene[17] reacts more rapidly. Carbene reactivity appears to fall in the order 3,5-DN-PhCCl > F_5-PhCCl > PhCCl, rather than in the inverse order of carbenic stability (F_5-PhCCl > 3,5-DNPhCCl > PhCCl). However, several rate constants are rather similar, and some differences may lie within the nominal ±10% error. A richer analysis derives from the activation parameters for these reactions.

Table 2. Absolute Rate Constants (M^{-1} s^{-1}) for Arylhalocarbene Additions[a]

alkene	F_5-PhCCl	3,5-DN-PhCCl	PhCCl
$Me_2C{=}CMe_2$	6.3×10^8	6.2×10^8	2.6×10^8
cyclohexene	2.4×10^7	5.6×10^7	4.8×10^6
n-$C_4H_9CH{=}CH_2$	1.8×10^7	3.6×10^7	2.5×10^6

[a] From diazirine photolysis in pentane at 296–299 K. Correlation coefficients are ≥0.993.

Activation parameters were obtained from measurements of the carbene/alkene addition rate constants at five temperatures (±0.1 K) between 276 and 306 K. Arrhenius correlations of ln k_{addn} vs $1/T$ were linear ($r > 0.99$), and their slopes and intercepts afforded the activation parameters compiled in Table 3. Graphical displays of carbene LFP spectra, rate constant determinations, and Arrhenius correlations appear in the Supporting Information.

As anticipated,[3] activation energies and enthalpies for the additions to TME of all three carbenes are negative. Moreover, the values for 3,5-DN-PhCCl ($E_a = -4.7$ kcal/mol, $\Delta H^\ddagger = -5.3$ kcal/mol) are the most negative yet encountered in a carbene/

Table 3. Activation Parameters for Carbene Additions[a]

carbene	alkene[b]	E_a	$\Delta H^\ddagger$	$\Delta S^\ddagger$	$-T\Delta S^\ddagger$	$\Delta G^\ddagger$
3,5-DN-PhCCl	TME	−4.70	−5.28	−36	10.8	5.52
PhCCl	TME	−1.77	−2.35	−28	8.34	5.99
F_5-PhCCl	TME	−1.78	−2.36	−26	7.75	5.39
3,5-DN-PhCCl	cyclohex	−2.23	−2.81	−33	9.71	6.90
PhCCl	cyclohex	0.80	0.22	−27	8.12	8.34
F_5-PhCCl	cyclohex	1.99	1.39	−20	5.96	7.35
3,5-DN-PhCCl	1-hex	−0.67	−1.26	−28	8.38	7.13
PhCCl	1-hex	1.25	0.68	−27	7.93	8.61
F_5-PhCCl	1-hex	2.67	2.09	−18	5.46	7.55

[a] Units are kcal/mol for E_a, $\Delta H^\ddagger$, $-T\Delta S^\ddagger$, and $\Delta G^\ddagger$; and cal·deg/mol for $\Delta S^\ddagger$. $\Delta H^\ddagger$ is calculated at 286 K; $\Delta G^\ddagger$ is calculated at 298 K. Errors are 0.2–0.3 kcal/mol or less in E_a; errors in $\Delta S^\ddagger$ are ~1 eu. [b] TME = tetramethylethylene, cyclohex = cyclohexene, 1-hex = 1-hexene.

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alkene addition, exceeding the analogous parameters for MePyr$^+$CCl (E_a = −3.1 kcal/mol, $\Delta H^\ddagger$ = −3.7 kcal/mol)[8] or CF_3CCl (E_a = −2.1 kcal/mol, $\Delta H^\ddagger$ = −2.6 kcal/mol).[7] The normative explanation for these extraordinary effects is that the reaction enthalpy (ΔH) for such highly exothermic reactions decreases continually along the reaction coordinate, affording negative values for E_a and $\Delta H^\ddagger$.[7,8,24] At the same time, the very negative activation entropy values attending these additions ($\Delta S^\ddagger$, Table 3) generate modest barriers in free energy ($\Delta G^\ddagger$).[24]

Based upon $\varepsilon_{\text{LUMO}}$ and ω (Table 1), we expect a carbene reactivity order of 3,5-DN-PhCCl > F_5-PhCCl > PhCCl. The experimental results in Table 3 (based on $\Delta G^\ddagger$) display this ordering for carbene additions to cyclohexene and 1-hexene, but for additions to TME, the ordering is F_5-PhCCl > 3,5-DN-PhCCl > PhCCl. The contributions of $\Delta S^\ddagger$ are critical to the expressed reactivity. Thus, on the basis of E_a or $\Delta H^\ddagger$ alone, the reactivity order would be 3,5-DN-PhCCl > PhCCl > F_5-PhCCl, whereas from the $\varepsilon_{\text{LUMO}}$, ω, and ΔE_{stab} parameters of Table 1, PhCCl should be the least reactive of the three carbenes, as indeed it is (Table 3).

We set out to inquire whether enthalpy−entropy compensation attends alkene additions of these selected arylchlorocarbenes. Table 3 affords an affirmative answer. Whatever the origin of the effect, we observe a persistent increase in $\Delta S^\ddagger$ (a less negative $\Delta S^\ddagger$) that parallels an increase in $\Delta H^\ddagger$ for the additions of the three carbenes to each alkene. This tandem linkage of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ is the hallmark of compensation.[25]

Previously, we suggested that when $\Delta H^\ddagger$ is either negative or very small, simultaneous increases of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ could reflect dynamic effects, wherein the sum of successful trajectories of attack by a highly reactive carbene on an alkene might be responsive to the steric accessibility of the substrate's carbon−carbon π bond.[8] In such cases, we might anticipate parallel increases in both $\Delta H^\ddagger$ and $\Delta S^\ddagger$ as we move from more reactive but more sterically demanding alkenes (like TME) to less reactive but more accessible alkenes (like 1-hexene).[8] The current results with ArCCl fit this paradigm, as do those for alkene additions of CF_3CCl[7] and MePyr$^+$CCl.[8]

An additional facet of this "stereodynamical" analysis is that the negative activation energies observed for additions of highly reactive carbenes emerge naturally from considerations of reaction trajectories. In very exothermic reactions, where a specific mutual reactant orientation is nevertheless required (as in carbene/alkene addition[15,16,26]), successful trajectories must include appropriate molecular reorientation that will become "less pronounced as the collision energy increases and reactants have less time to rotate toward the reaction direction."[27] In such cases, the apparent activation energy will be negative.[27] We plan appropriate molecular dynamics calculations to test the ideas put forward here.

In the present study of ArCCl/alkene additions, where $\Delta H^\ddagger$ < 2.1 kcal/mol always, stereodynamic analysis might be more appropriate than classical transition state theory. However, with more stable carbenes and less reactive alkenes, $\Delta H^\ddagger$ will increase and traditional transition state theory may come to the fore.[8] Then, increasing steric interactions in tighter transition states will afford more negative values of $\Delta S^\ddagger$,[28] $\Delta H^\ddagger$ and $\Delta S^\ddagger$ will no longer increase or decrease in tandem, and compensation will be absent.

3. CONCLUSION

Activation parameters were determined for the additions of 3,5-DN-PhCCl, F_5-PhCCl, and PhCCl to tetramethylethylene, cyclohexene, and 1-hexene. Activation enthalpies increased in the order 3,5-DN-PhCCl < PhCCl < F_5-PhCCl, and in tandem with increasing entropies of activation; that is, enthalpy−entropy compensation appeared to operate. Considerations of reaction dynamics may be more appropriate than traditional transition state theory in analyzing reactions with very low or even negative values of $\Delta H^\ddagger$.

4. EXPERIMENTAL SECTION

4.1. Preparative Details. *4.1.1. 1-Chloro-1-(3,5-dinitrophenyl)-2,2,3,3-tetramethylcyclopropane.* A solution of 243 mg (1 mmol) of 3,5-dinitrophenylchlorodiazirine and 420 mg (5 mmol) of tetramethylethylene in 10 mL of pentane was irradiated at room temperature in a Rayonet photoreactor at 350 nm for 3 h. Volatiles were removed by rotary evaporation, and the residue was chromatographed over silica gel, eluted with 2% ether in pentane, to afford 210 mg (70%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.97 ("s", 1H), 8.47 ("s", 2H), 1.43 (s, 6H), 1.09 (s, 6H). There is a very small (~1 Hz) long-range coupling between the aryl protons. ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.9, 144.7, 131.4, 118.06, 57.1, 27.6, 21.0, 19.65. Mass spectrum: M$^+$ at m/e 300, 298.

4.1.2. exo- or endo-7-Chloro-7-(3,5-dinitrophenyl)norcarane. In a similar manner, 243 mg (1 mmol) of 3,5-dinitrophenylchlorodiazirine and 820 mg (10 mmol) of cyclohexene in 10 mL of pentane were irradiated for 5 h. An analogous workup gave 105 mg (35%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.02 ("s", 1H), 8.63 ("s", 2H), 2.12−1.99 (m, 4H), 1.68−1.65 (m, 2H), 1.15−1.12 (m, 2H), 0.61−0.57 (m, 2H). There is a very small (~1 Hz) long-range coupling between the aryl protons. ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.17, 142.49, 131.36, 118.6, 45.71, 25.07, 20.66, 20.56. The simplicity of the spectrum suggests that only one stereoisomer may have been isolated. TLC shows only one spot. Mass spectrum: M$^+$ at m/e 298, 296.

4.1.3. cis- or trans-1-Chloro-1-(3,5-dinitrophenyl)-2-butylcyclopropane. In a similar manner, 243 mg (1 mmol) of 3,5-dinitrophenylchlorodiazirine and 1.26 g (0.15 mol) of cyclohexene in 10 mL of pentane were irradiated for 15 h. An analogous workup gave 46 mg (15%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.00 ("s", 1H), 8.62 ("s", 2H), 1.37−1.22 (m, 9H), 0.84−0.81 (m, 3H). There is a very small (~1 Hz) long-range coupling between the aryl protons. ^{13}C NMR (125 MHz, $CDCl_3$): δ 148.8, 144.22, 129.66, 118.54, 44.8, 31.0, 30.45, 30.3, 22.41, 21.34, 14.09. The simplicity of the spectrum suggests that only one stereoisomer may have been isolated. TLC shows only one spot. Mass spectrum: M$^+$ at m/e 300, 298.

Note that from the mass spectrometric parent ions (and the presence of chlorine isotopomers), we know that the foregoing compounds are composites of 3,5-DN-PhCCl and the substrate alkene. Based on general knowledge of the reactions of carbenes with alkenes, the products must therefore be either cyclopropane adducts or C−H insertion products. The absence of vinyl proton or vinyl carbon signals in their ^{1}H or ^{13}C NMR spectra eliminates insertion products. The compatibility of the NMR spectra with the cyclopropane structures then completes their identification.

4.2. LFP Experiments. A complete description of our LFP installation appears in ref 7. Graphical presentations of the kinetics results and Arrhenius correlations are included in the Supporting Information.

4.3. Computational Details. Electronic structure calculations, based on wave function (HF, MP2, CCSD(T)) or density functional theory (DFT), were carried out with the Gaussian 09 suite of programs.[29]

To generate the carbene reactivity data in Table 1, geometry optimizations were specifically executed at the MP2/6-31G(d,p)[30,31] or B3LYP/6-311++G(2d,p)[32,33] levels to conform with prior practice.[4,14]

We employed MP2[30] theory and cc-pVTZ basis sets[34] in geometry optimizations of the lowest singlet and triplet states of the three arylchlorocarbenes, PhCCl, F_5-PhCCl, and 3,5-DN-PhCCl. The stationary points located on the potential energy surfaces were characterized further by normal-mode analysis, and the (unscaled) vibrational frequencies formed the basis for the calculation of vibrational zero-point energy (ZPE) corrections. Improved electronic energies were obtained from single-point calculations at the CCSD(T)/cc-pVTZ level.[35] Singlet−triplet separations quoted in the text are derived from these CCSD(T)/cc-pVTZ energies and corrected for differential zero-point energies (MP2/cc-pVTZ level).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Spectra, kinetics, and activation parameter data, optimized geometries, and absolute energies. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01210.

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Notes

The authors declare no competing financial interest.

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