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Modulation of Carbenic Reactivity by π-Complexation to Aromatics

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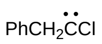
Attempts to control carbenic reactivity by intermediate carbene−substrate complex formation have a long history in which the most successful example is the control of stereoselectivity in the syn-addition of the Simmons−Smith carbenoid to cyclic allylic or homoallylic alcohols.[1] Analogous control of the reactivity of free carbenes, which lack the carbenoid's metal center carbene−substrate "link", is more problematical. Interactions of carbenes with substrate O, S, or N *n*-electrons certainly afford ylides,[2] but efforts to obtain concomitant synthetic control with (e.g.) methylene[3] or dichlorocarbene[4] have met with limited success.

Even more difficult, because the interaction energies should be smaller, is the modulation of carbenic reactivity by intermediate carbene−π electron complexation. Liu and Bonneau maintain that the transient formation of carbene−alkene π-complexes is integral to the competition between intramolecular rearrangement (Re) and intermolecular addition (Ad) when alkylhalocarbenes are generated in the presence of alkenes.[5,6] However, Houk's calculations suggest that additions of chlorocarbenes to ethylene or tetramethylethylene (TME) proceed to cyclopropanes without transiting bound carbene−alkene complexes.[7a−c] Alternatively, broad shallow wells for complexes might occur in the reaction enthalpy profile, but would not constitute minima on the free energy surface.[7d] Additionally, Platz[8] and Goodman[9] offer alternative explanations, based on the intervention of excited state carbene precursors, for the kinetic anomalies that originally triggered the suggestion of carbene−alkene complex participation.[5,6]

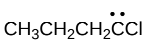
Although product-determining carbene−alkene π complexes are questionable, carbene−benzene π complexes may be more robust, if only because their direct continuation to product will be energetically less favorable than in the case of alkenes. Indeed, in a recent calorimetric study of photolytic diazomethane decomposition in benzene, Khan and Goodman invoked the formation of weak complexes between singlet CH_2 and benzene in order to explain the observation of a transient species.[10] Here, we describe Re vs Ad product distribution studies for several carbenes in isooctane, benzene, and other aromatic solvents that strongly implicate *reactivity modulation* by transient carbene−aromatic complexes; computational studies support this contention.

The carbenes include benzylchlorocarbene (**1**),[5] propylchlorocarbene (**2**),[5a] and cyclopropylchlorocarbene (**3**).[11] Each carbene was generated photochemically ($\lambda = 350$ nm, 25 °C) or thermally (78 °C) from the appropriate diazirine, prepared according to literature methods.[5,11,12] The observed Re products were those previously reported: *cis*- and *trans*-β-chloro styrenes (from **1**), cis- and *trans*-1-chloro-1-butene (from **2**), and 1-chlorocyclobutene (from **3**). In the presence of TME, each carbene also afforded the anticipated cyclopropane Ad product. All products were previously characterized,[5,11] and were identified here by capillary GC comparisons to authentic materials, GC-MS, and/or NMR spectroscopy.



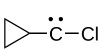
$PhCH_2\ddot{C}Cl$

1



$CH_3CH_2CH_2\ddot{C}Cl$

2



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In Table 1, we collect the Re/Ad product ratios for each carbene, determined in isooctane, benzene, or anisole solvents, in the presence of (e.g.) 0.25 M TME. Product ratios are averages of three experiments with three capillary GC analyses averaged for each experiment. Controls demonstrated that the products were stable to the thermal conditions, and that there were no products derived from reactions with the solvents (particularly benzene and anisole).

With carbenes **1** and **2**, the extent of 1,2-H rearrangement clearly increases, relative to intermolecular addition to TME, as the solvent is changed from isooctane to benzene. The enhancement of Re occurs with both thermally and photochemically generated species, and is especially pronounced with propylchlorocarbene. The behavior of carbene **3** indicates that the effect also extends to 1,2-C rearrangement. At lower [TME], the enhancement of Re/Ad is even stronger. For example, with photolytically generated carbenes and [TME] = 0.11−0.13 M, the Re/Ad distributions in isooctane vs benzene are 2.2 vs 8.3 for **1**, and 15.2 vs 109 for **2**.

We believe that these "solvent effects" on product distribution are manifestations of transient carbene−aromatic π complexes that interfere with intermolecular addition, extend the carbene lifetimes, and afford greater opportunity for intramolecular rearrangement (within the complex). It is of course known that changes in solvent *polarity* (e.g. pentane to acetonitrile) enhance the rate of 1,2-H shifts,[8b,13] but the dielectric constants, polarizabilities, and viscosities of isooctane and benzene are similar,[14] so that our observed effects are likely to have a more specific genesis. Consistent with a π complex origin for the enhancement of Re/Ad are the further increases seen in solvent anisole (Table 1), although here the polarity comes into play because the dielectric constant increases significantly between isooctane (1.94)

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Table 1. Rearrangement/Addition Product Distributions of Carbenes

			Re/Ad[a]		
carbene	conditions	*T*, °C	isooctane	benzene	anisole
1	*hν*	25	1.20 (0.05)	2.54 (0.01)	3.70 (0.08)
1	Δ	78	4.91 (0.28)	15.6 (0.5)	
2	*hν*	25	2.69 (0.08)	18.2 (0.4)	26.6 (0.1)
2	Δ	78	4.47 (0.12)	19.7 (0.4)	
3	*hν*	25	0.51 (0.02)	1.04 (0.02)	
3	Δ	78	1.61 (0.07)	2.87 (0.02)	

[a] Rearrangement to addition product distribution; average deviations of three experiments (with three capillary GC analyses each) in parentheses. The product distributions are calibrated for relative GC detector response for **1** and **2**, but not for **3**. [TME] = 0.25 M.

or benzene (2.28) and anisole (4.30). Additionally, anisole possesses oxygen *n* electrons which could also complex with the carbenes.[15]

We were concerned that the observed solvent sensitivity of Re/Ad might mainly reflect solvent-induced changes in the extent of rearrangement products derived directly from excited-state diazirines.[6,8,9] We therefore determined correlations of Ad/Re vs [TME] in isooctane or benzene for photolytically generated **1**−**3**. For carbenes **1** and **2**, these correlations were curved[5] in both solvents, consistent with intervention of a second intermediate.[5a] However, the reciprocal correlations, Re/Ad vs 1/[TME], were linear, and the extents of excited-state diazirine participation could be determined from their Y-intercepts.[6,16] These were 24% from the precursor of **1** and 51% from the precursor of **2** in isooctane, whereas in benzene, the analogous values were 20% and 30%. The correlations of Ad/Re vs [TME] for cyclopropylchlorocarbene (**3**) were linear in both solvents, suggesting minimal contributions of excited diazirine to 1,2-C shift product formation, in accord with a prior analysis.[8a]

Although there are substantial contributions of excited diazirine precursors to the rearrangement products when carbenes **1** and **2** are photolytically generated, this is *not* the origin of the benzene vs isooctane solvent effect on Re/Ad. Thus, the excited-state contribution to rearrangement is greater in *isooctane* than in benzene for both carbenes, whereas the rearrangement-enhancing solvent effect (Table 1) operates in *benzene*, not isooctane. Moreover, the latter effect is pronounced with the thermally generated carbenes, when excited-state involvement is minimal. Additionally, the benzene effect is enhanced at low [TME], where the carbenic origin of the Re products is maximal, and the effect persists with carbene **3**, where excited-state products are insignificant.

Another anticipated consequence of π complex formation is the extension of carbene lifetime in benzene vs isooctane. By laser flash photolysis, using the pyridine probe method,[2b,6,17a] we determined the rates of rearrangement of carbenes **1** and **2** in isooctane and benzene, which afforded carbene lifetimes ($\tau = 1/k_{re}$). These were the following: **1**, 23 ns (isooctane) and 285 ns (benzene) and **2**, 33 ns (isooctane) and 121 ns (benzene).[17b]

The importance of π-complex formation was further examined by ab initio computational methods. Our findings accord with those of Houk et al.[7] that stable carbene−alkene complexes, in particular complexes between CCl_2 and ethylene or TME, do not exist; cyclopropanes form with no apparent activation energy barriers. However, with CCl_2 or MeCCl (model for **2**) as the featured carbenes and benzene (Bz) or anisole as aromatic substrates, 1:1 complexes were readily located.[18] Our minimum energy conformation located for CCl_2−Bz (Figure 1a) resembles the minimum energy structure proposed by Khan and Goodman for CH_2−Bz.[10] The CCl_2−Bz complex has the carbenic carbon positioned almost directly above a Bz carbon (~3.1 Å) but slightly "outside" the ring; the Cl atoms are pointed inward, above the Bz π-electron cloud. Weak interaction is indicated by the small computed binding energy (ΔE) and enthalpy (ΔH) values of only −3.23 and −2.56 kcal/mol, respectively; the free energy of binding (ΔG) is +2.62 kcal/mol, implying an equilibrium constant for complex formation significantly less than one ($K_{eq} \sim 10^{-2}$).

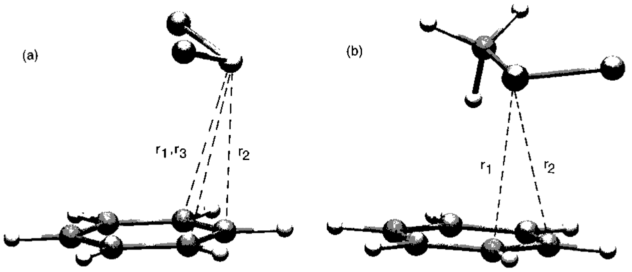

Figure 1. Geometry-optimized ab initio (MP2/6-31G*) structures for carbene-benzene π-complexes: (a) CCl_2-benzene, $r_1 = r_3 = 3.48$ Å, $r_2 = 3.14$ Å; (b) MeCCl-benzene, $r_1 = 3.15$ Å, $r_2 = 3.45$ Å. See text for details.

The minimum energy MeCCl−Bz complex (Figure 1b) also has the carbenic center positioned ~3.1 Å above a Bz carbon, "outside" of the Bz ring, but the carbene is rotated so that the Me group is directed toward the center of the Bz ring. The Cl atom in this complex is well "outside" the ring. The energetics for MeCCl−Bz complex formation are more favorable than those for CCl_2−Bz: $\Delta E = -4.81$ kcal/mol, $\Delta H = -3.54$ kcal/mol, and $\Delta G = +0.95$ kcal/mol, respectively. The alignment displayed by CCl_2 and, in particular, MeCCl with respect to an individual C−C bond maximizes the π-type interactions, as emphasized by Hoffman.[19] When the aromatic substrate is changed to the more electron-rich anisole, the interaction energies for the π complex increase further to $\Delta E = -6.96$ kcal/mol, $\Delta H = -5.65$ kcal/mol, and $\Delta G = +1.79$ kcal/mol.[20] A search for a minimum on the MeCCl−pentane potential energy surface led to a marginally stabilized complex showing interaction energies only of the order of thermal energies ($\Delta E = -2.52$ kcal/mol, $\Delta H = -1.31$ kcal/mol, and $\Delta G = +2.11$ kcal/mol). Complete details of the electronic structure calculations and results of additional studies of 1:2 carbene-aromatic and 1:1:1 aromatic−carbene−alkene "sandwich" complexes will be reported elsewhere.

Our interpretation of the computational results is that appreciable interaction energies may arise between carbenes and aromatic π-donors in solution, and that carbene−aromatic complexes can exist with sufficiently long lifetimes to affect the Re/Ad behavior of (at least) alkylhalocarbenes. In the limit of strong carbene−solvent complex formation, the complex might only be capable of rearrangement.[21]

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(15) Interestingly, there is a further increase in Re/Ad (to 8.00) for photolytically generated **1** in 1,2-dimethoxybenzene ($\epsilon = 4.45^{14}$), but a decrease (to 1.86) in trifluoromethylbenzene (under the conditions of Table 1). These results track the electron donation/withdrawal of the solvent substituents, as anticipated for carbene−π complex mediation.

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(18) Computational procedures include geometry optimization at both the HF/6-31G* and MP2/6-31G* levels of theory. Binding energies (ΔE, 0 K) are derived directly from the MP2/6-31G* calculations. Normal-mode analyses at the HF/6-31G* level provide the thermodynamic corrections needed to convert ΔE to binding enthalpy (ΔH, 298 K) and free energy (ΔG, 298 K).

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(20) An ylidic complex is comparable in energy.

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