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Estimation of activation energies for carbene/alkene additions

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ABSTRACT

Activation energies for the additions to alkenes of carbenes CXY can be estimated from the carbene selectivity indices, m_{CXY}, which are readily derived from the substituent constants (σ_I and σ_R^+) of X and Y.

Laser flash photolysis has provided activation parameters for the additions of carbenes to alkenes.[1–4] Analysis of these parameters for arylhalocarbenes[2] and dihalocarbenes[3] suggests the occurrence of 'compensation' between the energies or enthalpies of activation and the corresponding entropies of activation. That is, $\Delta H^\ddagger$ (E_a) and $\Delta S^\ddagger$ appear to increase *in tandem* for the additions of carbenes of increasing stability to a set of alkenes of decreasing degree of alkylation (decreasing reactivity).[5–7]

This behavior is at odds with expectations based on the Hammond postulate as applied to carbene/alkene additions by Skell:[8] viz. as carbenic stability increases, $\Delta H^\ddagger$ should increase; the addition transition state (TS) should occur later along the reaction coordinate; separation of reactants should decrease in the TS; steric interactions should become more important; and $\Delta S^\ddagger$ should become more negative (decrease).

We suggested that carbene/alkene additions with low activation energies ($E_a < 10$ kcal/mol) might be better analyzed by a consideration of dynamic effects and reaction trajectories, rather than classical Eyring–Hammond transition state theory.[5,9] In this regard, we might inquire how large E_a (or $\Delta H^\ddagger$) would need to be before transition state theory would be the more apposite analytical method for carbene/alkene additions. Suppose, for instance, that we take $E_a \sim 15$ kcal/mol as a threshold activation energy. Will this barrier be reached in additions of 'common' carbenes to alkylethenes? To provide a preliminary answer, it would be useful to have a 'back-of-the-envelope' method to estimate activation energies for carbene/alkene additions, a method that bypasses both arduous experimental determinations and semi-lengthy computations.

Years ago, we developed an empirically based 'carbene selectivity index,' m_{CXY}, which correlated the relative reactivities of carbenes CXY in additions to simple alkenes.[10] Moreover, m_{CXY} could be readily calculated for any CXY according to Eq. 1, where $\sum_{X,Y} \sigma_R^+$ represents the sum of the resonance substituent constants (σ_R^+) of carbene substituents X and Y, and $\sum_{X,Y} \sigma_I$ represents an analogous sum of the inductive substituent constants (σ_I).[11,12]

$$m_{CXY} = -1.10\sum_{X,Y}\sigma_R^+ + 0.53\sum_{X,Y}\sigma_I - 0.31 \tag{1}$$

Subsequently, we proposed that m_{CXY} correlated with both ε_{CXY}^{LU}, the computed LUMO energies of CXY, and ΔE_{stab}, the computed stabilization energies of CXY relative to singlet methylene.[12,13] For CXY (where X and Y are donor groups) adding to (nucleophilic) alkylethenes, the stabilization energy of the addition transition state will be largely determined by the interaction of the carbene's LUMO or p orbital with the alkene's HOMO or π orbital.[7,13,14] Given that the stabilization energy is related to the activation energy for the carbene/alkene addition, we might anticipate that E_a will also be correlated by m_{CXY}.

Here, we confirm this expectation. We then use values of m_{CXY} to estimate the activation energies of several as yet unexplored carbene/alkene addition reactions. Finally, predictions based on m_{CXY} are compared to calculated activation energies.

The carbenes we employ to test the correlation of m_{CXY} with experimentally-determined activation energies are CCl_2, CClF, CF_2, PhCCl, and C_6F_5CCl. The associated values of m_{CXY} are 0.97, 1.22, 1.47, 0.72, and 0.92, respectively.[15,16] Figures 1–3 depict the m_{CXY}/E_a correlations for additions of CXY to tetramethylethylene

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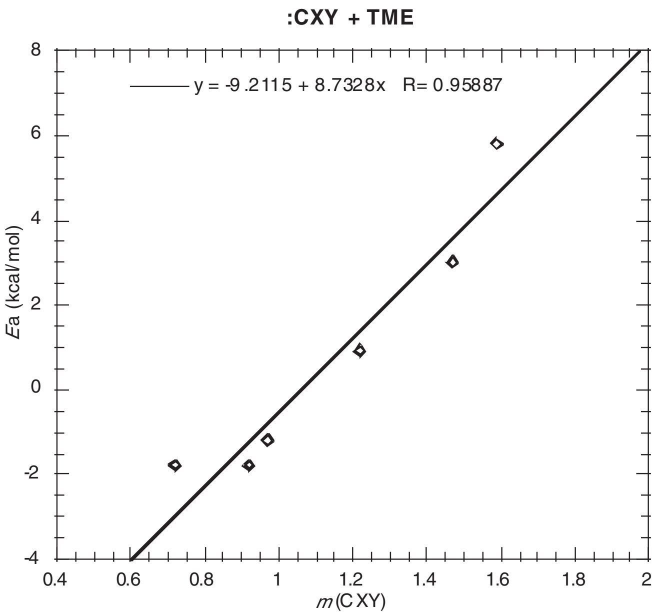

Figure 1. Experimental activation energy versus m_{CXY} for the additions of carbenes CXY to tetramethylethylene (TME).

(TME), cyclohexene, and 1-hexene. The relevant values of E_a are reported for CCl_2 and CClF in Ref. 3a, for CF_2 in Ref. 3b, and for PhCCl and C_6F_5CCl in Ref. 2.

The least-squares-determined correlation equations derived from Figures 1–3 are given in algebraic form in Eqs. 2–4.

$$\text{TME:}^{17}\ E_a = 8.73\ m_{CXY} - 9.21 (r = 0.96, \text{std.error} = 1.26\ \text{kcal/mol}) \quad (2)$$

$$\text{cyclohexene:}\ E_a = 8.40\ m_{CXY} - 5.08 (r = 0.97, \text{std.error} = 1.12\ \text{kcal/mol}) \quad (3)$$

$$\text{1-hexene:}\ E_a = 8.96\ m_{CXY} - 4.97 (r = 0.97, \text{std.error} = 1.19\ \text{kcal/mol}) \quad (4)$$

These correlations are significant at the 99% confidence level and exhibit standard errors of ~1.2 kcal/mol in E_a. We conclude that the anticipated correlation between E_a and m_{CXY} is experimentally verified for donor-substituted examples of CXY.

Using these equations, we estimated activation energies for the putative additions of MeOCF, $(MeO)_2C$, $MeOCNMe_2$, and $(Me_2N)_2C$ to TME, cyclohexene, and 1-hexene.[15] The results appear in Table 1. As we would expect, the estimated activation energies for CXY additions to alkylethenes increase as substituents *X* and *Y* become more effective (resonance) donors[18] and CXY becomes less electrophilic (more nucleophilic) and more stabilized.[15]

We note, however, that the 'training' set of carbenes used in the correlations of Figures 1–3, which generated Eqs. 2–4, are all electrophilic. Their addition transition states with TME, cyclohexene, and 1-hexene will be governed by the carbene LUMO—alkene HOMO interaction. In contrast, $(MeO)_2C$, $MeOCNMe_2$, and $(Me_2N)_2C$ are more nucleophilic;[12,14] their addition transition states with these alkenes will largely reflect the carbene HOMO—alkene LUMO interaction.[7,12–14] Therefore, we should regard the activation energies estimated for these carbenes in Table 1 as suggestive only.

If we take $E_a > 15$ kcal/mol as an arbitrary barrier value that is likely to position a carbene/alkene addition in a regime where transition state theory applies, then the estimates in Table 1 suggest that we focus on the addition reactions of $MeOCNMe_2$ and $(Me_2N)_2C$. The data also imply that additions of the well-known MeOCF[19] or $(MeO)_2C$[20] are less likely to fall in the desired regime.

Although reactions of $MeOCNMe_2$ appear to be largely unexplored,[21] there is a significant body of work on bis(dialkylamino)-carbenes.[22,23] The alkyl groups include isopropyl,[22e] piperidyl,[22d] ethyl,[22b] and methyl.[22b] Given that we estimate $E_a \sim 22$–27 kcal/mol for additions of $(Me_2N)_2C$ to the alkenes of Table 1, we might question whether this carbene or other bis (dialkylamino)carbenes would eschew dimerization long enough to undergo alkene addition reactions. Surprisingly, in the absence of catalysts, dimerizations of bis(dialkylamino)carbenes are very slow;[22a,b] bis(diethylamino)carbene is kinetically stable to dimerization in THF at ambient temperature.[22b] It has been reported that the barrier to dimerization of bis (dimethylamino)carbene is 78 kJ/mol,[23] but this value likely reflects a catalyzed process.[22a,b] Alkene additions of bis

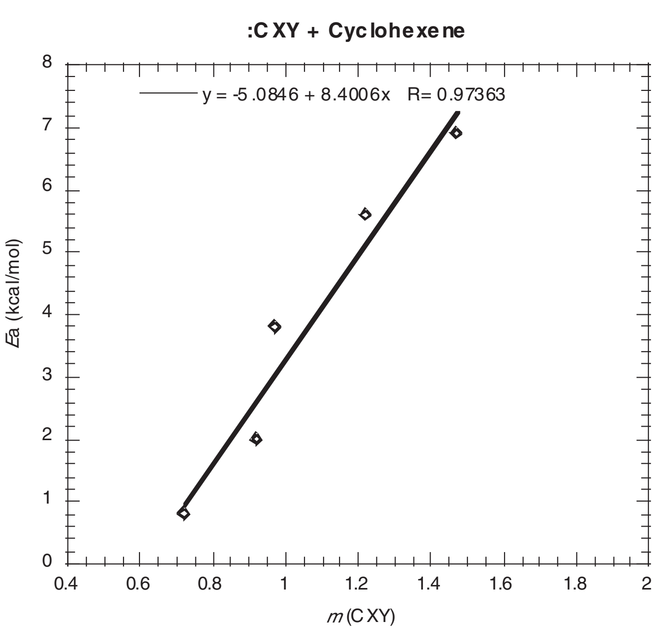

Figure 2. Experimental activation energy versus m_{CXY} for the additions of carbenes CXY to cyclohexene.

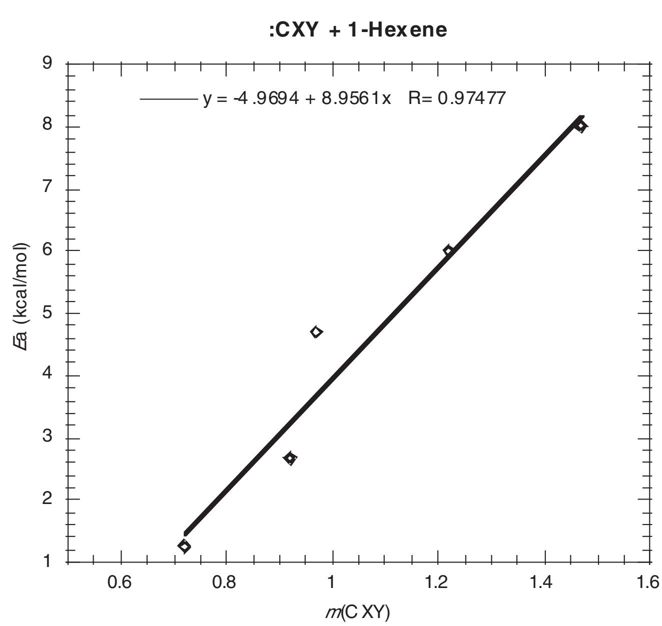

Figure 3. Experimental activation energy versus m_{CXY} for the additions of carbenes CXY to 1-hexene.