Transition States and Selectivities of Singlet Carbene Cycloadditions

Nelson G. Rondan,[1a] **K. N. Houk,***[1a] **and Robert A. Moss***[1b]

Contribution from the Department of Chemistry, Louisiana State University, Baton Rouge, Louisiana 70803, and the Wright and Rieman Laboratories, Department of Chemistry, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903. *Received September 10, 1979*

Abstract: Transition states for the cycloadditions of the singlet carbenes CCl_2, CF_2, CFOH, and $C(OH)_2$ to ethylene have been located using ab initio calculations with the minimal STO-3G basis set. Activation energies of 5, 24, 29, and 33 kcal/mol, respectively, are predicted by STO-3G//STO-3G, and 8, 27, 37, and 45 kcal/mol are predicted by 4-31G//STO-3G calculations. The transition states range from clearly electrophilic (π approach) for CCl_2 to nucleophilic (off-center σ approach) with $C(OH)_2$. The position of the transition state is related to the substituent stabilization of the carbene and to the exothermicity of the reaction. This is also revealed in the good correlation between the empirical carbene selectivity index, m_{CXY}, for alkylethylenes and the carbene stabilization energy, determined from the isodesmic reaction: $CH_2 + CH_3X + CH_3Y \rightarrow CXY + 2CH_4$. There is a more approximate relationship between the carbene LUMO energy and the carbene electrophilic selectivity, because the carbene LUMO energy increases as the stabilization energy of the carbene increases. Finally, the 4-31G calculated stabilization of the carbene by substituents correlates very well with the empirical $\sigma_R{}^+$ constants of the substituents. Thus, relationships between heats of reaction, activation energies, empirical selectivities, and empirical substituent constants from quite a different model reaction have all been demonstrated for carbene cycloadditions.

Introduction

Nearly a quarter of a century ago, Skell and Doering and their co-workers deduced that the transition state of singlet carbene cycloadditions to alkenes involved the electrophilic approach of the carbene vacant p orbital to the π bond of alkenes.[2] Theoretical confirmation of this deduction followed over a decade later in the benchmark computations by Hoffmann on the methylene-ethylene reaction,[3a] and more recently from the studies of the CF_2-ethylene reaction.[3b] In spite of the repeated attention that singlet carbene reactions have received,[3-7] we were interested in a more refined computational study of these reactions for the following reasons.

(1) As Skell and Cholod pointed out,[2c] increasing selectivity of carbenes toward a series of alkenes should be parallel to increasing E_{act} for the carbene cycloaddition with a given substrate. However, experimentalists have only rarely measured absolute rates for a series of carbenes,[4a] so this conclusion could be made only by assuming that the usual reactivity-selectivity principle applies to carbene cycloadditions. Computations at the level we have used are capable of predicting trends in activation energies, data which are as yet unavailable from experiment. Furthermore, we hoped to be able to quantitate the concepts of electrophilicity of carbenes, and to relate this to selectivity in a theoretically viable way.

(2) Previous calculations on singlet carbene cycloadditions have either used semiempirical methods or were performed on the CH_2-ethylene reaction, which has no activation energy. In the absence of a nonzero E_{act}, no definite information can be gleaned about transition-state structure from calculations. Only preferred trajectories of approach can be deduced. That is, although there is no doubt that singlet carbenes first approach ethylene in a π fashion, there is little information available on the relative importance of electrophilic and nucleophilic interactions at the transition states of cycloadditions with nonzero E_{act}'s.

(3) No computations have been carried out on the preferred approach of nucleophilic carbenes to alkenes. We wished to quantitate the energetic and geometrical differences between "early" and "late" transition states, and between electrophilic and nucleophilic carbenes. The non-least-motion cycloadditions of carbenes are not only of inherent interest, but serve as prototypes for reactions of other species, such as SO_2, ketenes, and other molecules exhibiting electrophilic and nucleophilic character in perpendicular directions. In such molecules, the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) have mutually perpendicular extensions. The relative importance of the possible electrophilic and nucleophilic interactions is, in general, unknown.

We report here two approaches to the refinement and quantitation of our understanding of selectivities in cycloadditions of substituted carbenes.[6] The first approach involves the location, using ab initio SCF theory, of the transition states of cycloadditions of a broad spectrum of substituted carbenes to ethylene. Important differences in transition-state energies and structures are reported for cycloadditions of CCl_2, an electrophilic and relatively unselective carbene, CF_2, another electrophilic, but more selective carbene, CFOH, a model for an ambiphilic carbene, and $C(OH)_2$, a model for a nucleophilic carbene. The second approach involves a study of the relationship between the experimental or empirically based electrophilic selectivities of 12 carbenes (ClCMe, FCPh, ClCSMe, CCl_2, FCCl, CF_2, ClCOMe, FCOMe, FCOH, $C(OMe)_2$, $C(OH)_2$, and $MeOCNMe_2$) and theoretical parameters calculated for these species. The stabilization of methylene by substituents and LUMO energies of the substituted carbenes were chosen for study.

Both of these approaches show that unselective carbenes have "early" (π approach) transition states of low energy because the carbene is only slightly stabilized by the substituents, while selective carbenes have "late" (off-center σ approach) transition states of high energy because the carbene is significantly stabilized by the substituents. In both types of transition states, nucleophilic character of the carbene is more significant than previously recognized.

Transition States of Singlet Carbene Cycloadditions

The reported theoretical investigations of carbene cycloadditions have either been qualitative,[7] used semiempirical computational techniques,[3,4b] or involved the cycloaddition of methylene to ethylene,[5] a reaction which is found to have no activation barrier. Zurawski and Kutzelnigg (Z-K) recently described an ab initio surface for the cycloaddition of methylene to ethylene.[5] In order to compare directly our results to the Z-K results, we adopted the same geometrical variables in our study of the cycloadditions of substituted carbenes.

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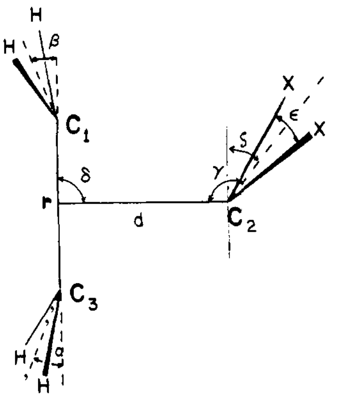


Figure 1. Variables optimized at each value of **d**.

Table I. Calculated Energies of Activation and Reaction (kcal/mol)

	CH_2	CCl_2	CF_2	FCOH	$C(OH)_2$
		$\Delta E^{\ddagger}$			
STO-3G		5	24	29	33
4-31G	-28^{a}	8	27	37	45
4-31G + CI	-18^{a}		25	34	44
Z-K[5]	-24 to $-52^{a,b}$				
exptl			$11-12^{f}$		
		ΔE_{rxn}			
STO-3G	-138	-97	-64	-54	-47
4-31G	-96	-70	-46	-31	-18
4-31G + CI	-90		-28	-13	-1
Z-K[5]	-85 to -110^{c}				
exptl	-105^{d}	-70^{e}	-47^{g} $(-44)^{h}$		

[a] There is no activation energy for these reactions, and these are the exothermicities calculated for a point ($d = 1.8515$ Å $= 3.5a_0$) near the transition states of the other carbene reactions. [b] −24 (SCF), −22 (SCF + polarization functions on C), −24 (SCF + CI), −39 (SCF + CEPA), and −52 (SCF + IEPA).[5] [c] −85 (SCF), −95 (SCF + pol), −110 (SCF + CI), −109 (SCF + CEPA).[5] [d] From ref 5. [e] Calculated from $\Delta H_f°(CCl_2) = 53.1 \pm 2$ kcal/mol (Levi, B. A.; Taft, R. W.; Hehre, W. J. *J. Am. Chem. Soc.* **1977**, *99*, 8454. $\Delta H_f°(CH_2{=}CH_2) = 12.5$, and estimated $\Delta H_f°$(−4.3 kcal/mol) of 1,1-dichlorocyclopropane (Benson, S. W. "Thermochemical Kinetics"; Wiley-Interscience: New York, 1976) without zero-point energy corrections. [f] Estimated in Benson, S. W.; O'Neal, H. E. "Kinetic Data on Gas Phase Unimolecular Reactions", *Nat. Stand. Ref. Data Ser., Natl. Bur. Stand.* **1970**, *No. 21*, 248. [g] Calculated from $\Delta H_f°(CF_2) = -44.5$ kcal/mol (Carlson, G. A. *J. Phys. Chem.* **1971**, *75*, 1625. See: Vogt, J.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1975**, *97*, 6682, for a discussion of various values for this quantity), $\Delta H_f°(CH_2{=}CH_2) = +12.5$, and estimated $\Delta H_f°$ (−79.3 kcal/mol) of 1,1-difluorocyclopropane (Benson, S. W. "Thermochemical Kinetics"; Wiley-Interscience: New York, 1976) without zero-point energy corrections. [h] Estimate made by Benson and O'Neal in reference cited in footnote *f* of this table.

Figure 1 defines **d**, the reaction coordinate, and the other six variables optimized at each value of **d**. Computations were carried out using ab initio SCF calculations[8] with the STO-3G minimal basis set,[9] and calculations were also carried out on the transition states, reactants, and products with the split-valence 4-31G basis set.[10] Limited CI was also used in some cases.[11] Aside from the limitations in basis sets, which should influence energies but less significantly influence geometries, major assumptions are that the transition state has a plane of symmetry and that **d** is a reasonable choice of reaction coordinate.[12] Because of the size of the systems involved, relatively few points were calculated (Figure 2). The STO-3G optimized carbene geometries will be reported later in this paper.

Table I gives the activation energies and heats of reaction calculated by the various methods used here. Several points on the Z-K surface[5] were also calculated by 4-31G to verify that our results are comparable to those reported by Z-K.

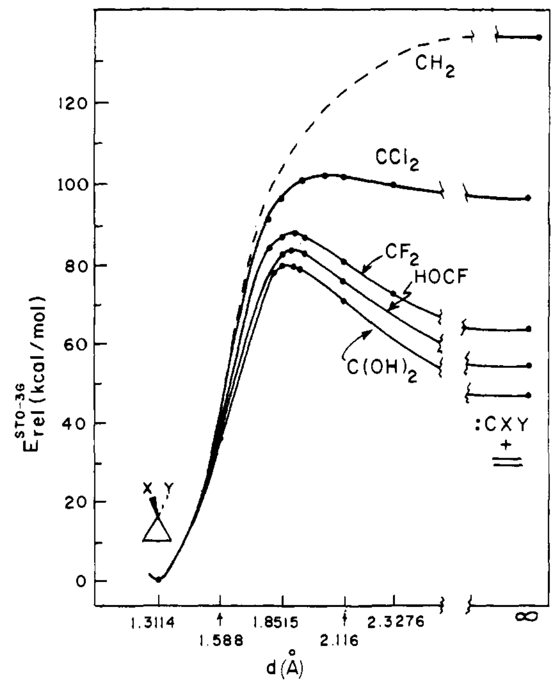


Figure 2. Energy vs. reaction coordinate diagram for reactions of CCl_2, CF_2, FCOH, and $C(OH)_2$ with ethylene.

From Table I, it appears that the calculated activation energies are probably too large,[13] whereas the experimental energies of reaction fall between the values calculated by STO-3G and 4-31G, and 4-31G calculations on difluoro- and dichlorocarbene are very close to thermochemical estimates. The 4-31G + 3 × 3 CI calculations underestimate the exothermicity of the reaction, since the carbene is stabilized unrealistically relative to the cyclopropane product. The heats of reaction and calculated activation energies are interrelated as expected according to the Evans-Polanyi[14,15] principle. A Polanyi relationship, $E_{act}{}^{4\text{-}31G} = 0.71\Delta E_{rxn}{}^{4\text{-}31G} + 58.7$, quite precisely ($r = 0.998$) fits the 4-31G calculations, and predicts $E_{act} = 0$ if $\Delta E_{rxn} < -82.7$ kcal/mol. That is, the more exothermic the reaction, the lower the activation energy, and the "earlier" the transition state. The reaction exothermicity is, in turn, related to stabilization of the carbene by substituents, and the stabilization of the singlet carbene increases along the series H < Cl < F < OH, the order of electron donation by the substituent. The relationship between carbene stabilization energy and selectivity is discussed in more detail in later sections of this paper.

The increase in activation energy along the series is in accord with the very rapid and relatively unselective addition of CCl_2 to alkenes,[6] the relatively facile addition of CF_2 to simple alkenes,[16] the observed "ambiphilicity" of CH_3OCCl[17] (a carbene which should be electronically similar to FCOH), and the lack of reactivity of $C(OMe)_2$ toward alkylethylenes. This last carbene, which should be electronically similar to the model, $C(OH)_2$, is nucleophilic, reacting only with electron-deficient alkenes.[18]

In all four reactions, the "two-phase" approach[2,3,5] of the carbene to ethylene is found. For relatively large values of **d**, all four carbenes approach ethylene in an electrophilic fashion (π approach) maximizing overlap of the filled π orbital of ethylene with the vacant carbene p LUMO. By contrast to semiempirical trajectories,[3,4b] ab initio calculations (here and Z-K) indicate that the carbene first approaches the center of the bond, and only later veers toward one carbon. In all of the

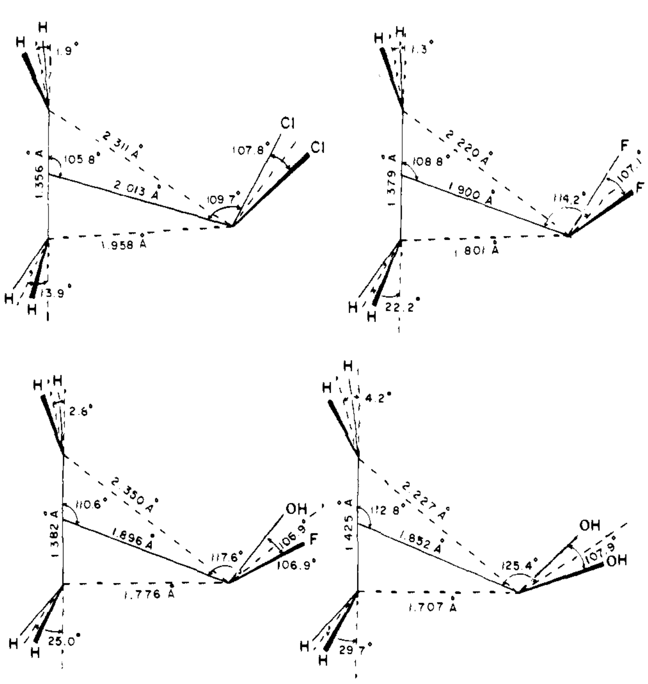


Figure 3. Scale drawings of the transition states for cycloadditions of CCl_2, CF_2, FCOH, and $C(OH)_2$ to ethylene.

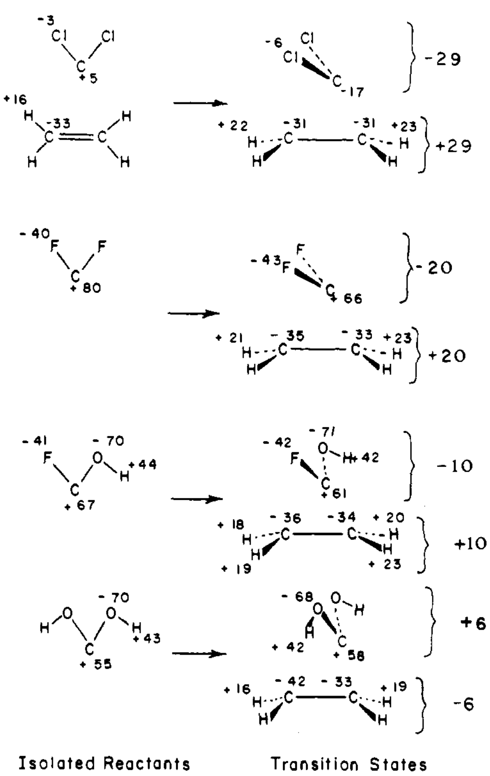


Figure 4. Mulliken 4-31G atomic charges (electrons × 10^2) in reactants and transition states.

transition states, shown in Figure 3, the carbene is off-center. At shorter distances, the carbene pivots about the carbon and moves toward one of the ethylene carbons in a so-called "nucleophilic" phase, in which the carbene lone pair becomes involved in bonding (σ approach). The substituents are pointed "inward", across the ethylene face, as shown earlier by Hoffmann,[3] but opposite to the MINDO/2 prediction.[4b] The substituent "outward" approach is higher in energy, and collapses to the "inward" approach upon optimization. This "inward" approach maximizes both the electrophilic carbene-LUMO-alkene-HOMO interaction and the nucleophilic carbene-HOMO-alkene-LUMO interaction, and incidentally appears to minimize possible steric interactions[6] between carbene and alkene substituents. Mulliken population analyses of these transition states indicate much more substantial asymmetry in bonding at the two alkene carbons (see below) than was found in the EHT calculations.[3b]

The small, but significant, activation energy calculated for the CCl_2 cycloaddition is of particular interest, since the work of Skell and Cholod suggested the possibility that singlet CCl_2 may react without activation energy at all.[2c]

There have been several suggestions that the least motion, or linear cheletropic, cycloaddition of carbenes to alkenes could occur by involvement of a carbene S_2 state which has two electrons promoted from the carbene lone pair orbital to the p orbital.[7d,19] Since S_2 is linear, such involvement would be reflected by complete or partial linearization of the carbene as it undergoes cycloaddition. However, there is little evidence for such linearization in our computed surfaces, confirming that the carbene avoids forbiddenness by the non-least-motion approach (π approach, then rotation), rather than by linearization.

Although the differences in transition-state structures are subtle, there is a clear trend toward decreasing electrophilicity along the series CCl_2, CF_2, HOCF, $C(OH)_2$. In particular, (1) the ratio of newly forming bond lengths (r_{12}/r_{23}) increases along the series CCl_2, CF_2, CFOH, indicating greater asymmetry in bond formation until finally with $C(OH)_2$ this ratio begins to decrease as the transition state becomes rather more cyclopropane-like. The weakening of a bond is roughly proportional to the square of the stretching of the bond, Δr^2, away from its equilibrium bond length in cyclopropane. According to this measure, the ratio of bond strengths ($\Delta r_{23}^2/\Delta r_{12}^2$) in these four transition states ranges from 3.2 for the CCl_2 transition state to 12.5 for the $C(OH)_2$ transition state. The values are quite close to ratios of the STO-3G Mulliken overlap populations for the C_2C_3 and C_1C_2 bonds: 4.9, 9.8, 17.3, and 14.2 for CCl_2, CF, CFOH, and $C(OH)_2$ transition states, respectively.

(2) The angle of tilt of the CCl_2 and CF_2 planes with respect to the original ethylene plane indicates slightly greater π than σ bonding, while this angle for the $C(OH)_2$ transition state suggests a predominantly σ, or nucleophilic, interaction with ethylene in the transition state. The angle ζ (Figure 1) would be expected to be 0° for a pure electrophilic interaction and 90° for a pure nucleophilic interaction. The values of ζ are remarkably diagnostic of the type of carbene: the species which experimentally exhibit electrophilic character, CCl_2 and CF_2, have ζ's of less than 45° (36 and 43°), ClCOMe, which is experimentally found to be ambiphilic, but biased somewhat on the nucleophilic side, resembles FCOH which gives $\zeta = 48°$, and the decidedly nucleophilic $C(OMe)_2$ resembles $C(OH)_2$ which has $\zeta = 58°$. Naively, but nevertheless in good accord with the computed transition-state structures, the transition from an electrophilic to a nucleophilic carbene occurs at 45°.

(3) The increased angle of distortion away from planarity of the ethylene CH_2 groups is also indicative of increased nucleophilic character along this series. In cyclopropane, $\alpha = \beta = 30°$. The hydrogens at C_1 are very nearly in the plane of the undistorted ethylene molecule ($\beta = 1.3$-$4.2°$), while the hydrogens at C_3 are significantly bent out of this plane ($\alpha = 13.8$-$29.7°$). Whereas β remains near 0°, α varies from 46 to 99% of the value it achieves in the product. This is reminiscent of our discovery that pronounced bending of ethylene occurs in the transition states for nucleophilic attack on ethylene, whereas electrophiles cause very little ethylene bending.[20] Hoffmann's computations involved a frozen ethylene, so that this interesting point was not revealed. In other respects, the transition state for CF_2 cycloaddition by EHT is similar to

ours. In particular, Hoffmann found **d** = 1.8 Å, r_{C2C3} = 1.84 Å, and $r_{C_1C_2}$ = 2.07 Å, and an angle, ζ, of carbene tilt equal to 39°.[3b]

Contrary to EHT calculations for CH_2 and CF_2 reactions,[3b] there is more charge transfer from ethylene to CF_2 (0.20 electron) in the transition state than from ethylene to CH_2 (0.08 electron) for a comparable geometry (**d** = 1.8515 Å). This can be attributed to the lower energy LUMO of CF_2 ($\epsilon_{LUMO}{}^{4\text{-}31G}$ = 1.89 eV) than of CH_2 ($\epsilon_{LUMO}{}^{4\text{-}31G}$ = 2.04 eV). At the transition states, there is 0.29 electron transferred from ethylene to CCl_2 and 0.20 electron transferred from ethylene to CF_2. The extent of charge transfer is smaller for FCOH (0.10 electron) and reverses in direction for $C(OH)_2$: in the transition state of the $C(OH)_2$ cycloaddition, 0.06 electron is transferred from $C(OH)_2$ to ethylene. Substituent effects on carbene cycloadditions frequently have been interpreted in terms of charge separation in the transition state.[2,6] Figure 4 shows that the charge donation from ethylene to CF_2 and FCOH occurs mainly from hydrogens. The net charge on each CH_2 implies that the carbene accepts electron density more or less equally from both methylenes, whereas electron donation from carbene to ethylene occurs at the carbon overlapping better with the carbene lone pair, causing the remote methylene (left-hand CH_2 in Figure 4) to be less positive, or more negative. The carbene carbon bears most of the increased negative charge (or reduction of positive charge) in the transition states for CCl_2, CF_2, and FCOH cycloadditions, whereas the heavy atoms share more equally in electron loss in the $C(OH)_2$ transition state. For the electrophilic carbenes, electron donation is nearly equal from both ethylene termini, while, as the nucleophilic character of the carbene increases, the ethylene carbons show appreciable polarization away from the nucleophilic carbene center (see especially $C(OH)_2$ in Figure 4).

The variations in transition-state structures found here are in good accord with a frontier molecular orbital treatment of cycloadditions, in which the nature of the transition state should be determined by the relative importance of the carbene LUMO-alkene HOMO interaction—which will favor a π, or electrophilic, transition state—and the carbene HOMO-alkene LUMO interaction—which will favor an unsymmetrical σ, or nucleophilic, transition state. Figure 5 shows the frontier molecular orbital energies of ethylene and each of the four substituted carbenes. The dominant frontier orbital interaction is determined both by the energy gaps (the smaller gap leading to the larger interaction) and overlap. Using Slater orbitals for the carbene carbon and the two ethylene carbons, and the geometries and orbital coefficients obtained by the STO-3G calculations for the CF_2-ethylene transition state, the HOMO(CF_2)-LUMO(ethylene) overlap integral is 0.163 while the LUMO(CF_2)-HOMO(ethylene) overlap integral is 0.130. At this same geometry, the corresponding overlap integrals for $C(OH)_2$-ethylene reaction are 0.162 for HOMO($C(OH)_2$)-LUMO(ethylene) and 0.132 for LUMO-($C(OH)_2$)-HOMO(ethylene). At the $C(OH)_2$-ethylene transition state geometry, these overlap integrals change slightly to 0.175 and 0.138, respectively. Thus, the carbene HOMO-alkene LUMO overlap is larger than carbene LUMO-alkene HOMO overlap for reasonable CF_2, CFOH, and $C(OH)_2$ transition state geometries. However, for the much "earlier" CCl_2-ethylene transition state, the HOMO(CCl_2)-LUMO(ethylene) overlap is reduced to 0.095, while the HOMO(ethylene)-LUMO(CCl_2) overlap is 0.131. Here the overlap related to the electrophilic character of the carbene is considerably larger than that related to the nucleophilic character of the carbene. Thus, "early" transition states involve more electrophilic character than "late" transition states.

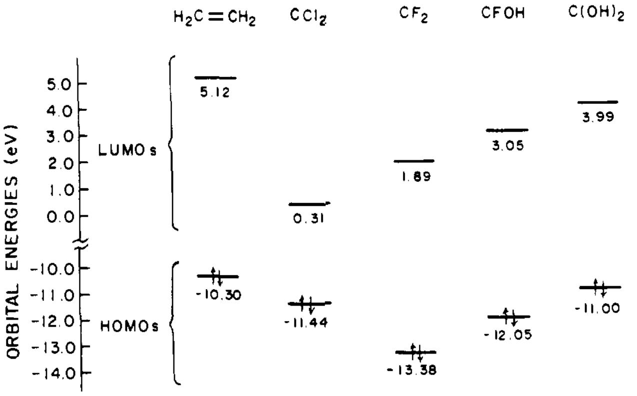


Figure 5. Frontier orbital energies for ethylene and four carbenes.

Based on these ideas, it is possible to develop a purely theoretical index to predict whether a carbene is electrophilic, ambiphilic, or nucleophilic. The squares of the ratio of nucleophilic to electrophilic overlaps, S^2(HOMO(carbene)-LUMO(ethylene))/S^2(LUMO(carbene)-HOMO(ethylene)), are 0.53, 1.59, 1.59, and 1.61 for the CCl_2, CF_2, CFOH, and $C(OH)_2$ transition states, respectively. The square of the overlap is the quantity of theoretical interest, as described below. These ratios can be fitted to a second-order polynomial in $E_{stab}{}^{4\text{-}31G}$:

$$\frac{S_n{}^2}{S_e{}^2} = 0.072E_{stab}{}^{4\text{-}31G} - 0.00048(E_{stab}{}^{4\text{-}31G})^2 - 1.03$$

That is, for a very early transition state, $S_n{}^2/S_e{}^2$ is <1, and this value increases and then levels off at ~1.6 for large values of E_{stab}. This second-order polynomial fit causes $S_n{}^2/S_e{}^2$ to begin to decrease for $E_{stab} > 73$, but this may be reasonable for very late transition state geometries. In any case, this polynomial fit allows good approximations for $S_n{}^2/S_e{}^2$, from the calculated E_{stab} for cases where the transition states are not known exactly.

According to second-order perturbation theory, the stabilization energy arising from a given frontier orbital interaction is[21]

$$\Delta E \cong \frac{S_{HOMO\text{-}LUMO}{}^2}{IP_{HOMO} - EA_{LUMO} - Q}$$

For cycloaddition transition states, Q, which represents the decrease in $IP_{HOMO} - EA_{LUMO}$ that occurs as donor and acceptor are brought into close proximity, is on the order of 3-5 eV.[21] In terms of SCF orbital energies:

$$\Delta E \simeq \frac{S_{HOMO\text{-}LUMO}{}^2}{-\epsilon_{HOMO} + \epsilon_{LUMO} - Q}$$

The ratio of stabilization caused by the nucleophilic carbene interaction, ΔE_n, to that caused by the electrophilic carbene interaction, ΔE_e, is therefore

$$\frac{\Delta E_n}{\Delta E_e} = \frac{S_n{}^2/(-\epsilon_{HOMO(carbene)} + \epsilon_{LUMO(ethylene)} - Q)}{S_e{}^2/(-\epsilon_{HOMO(ethylene)} + \epsilon_{LUMO(carbene)} - Q)}$$

This ratio predicts the relative importance of carbene electrophilicity and nucleophilicity. If the simple frontier orbital model is of predictive value, this ratio will be <1 for electrophilic carbenes, ≈1 for ambiphilic carbenes, and >1 for nucleophilic carbenes. Using the second-order polynomial to estimate $S_n{}^2/S_e{}^2$, 4-31G orbital energies given in Figure 5, and a value of 5 eV for Q, the ratio $\Delta E_n/\Delta E_e$ is calculated according to

$$PI_{CXY} = \Delta E_n/\Delta E_e = (0.072E_{stab} - 0.00048E_{stab}{}^2 - 1.03)\left[\frac{5.3 + \epsilon_{LUMO(CXY)}{}^{4\text{-}31G}}{-\epsilon_{HOMO(CXY)}{}^{4\text{-}31G} + 0.12}\right] \quad (1)$$

Although Q is not a constant, and should increase as the late-

Table II. Geometries, Orbital Energies, Stabilization Energies, and Selectivities of Disubstituted Singlet Carbenes

		geometry (STO-3G)			4-31G orbital energies, eV					
no.	carbene	∠XCY, deg	$r_{C\text{-}X}$, Å	$r_{C\text{-}Y}$, Å	LUMO	HOMO	4-31G ΔE_{stab}, kcal/mol[a]	$m_{CXY}{}^{obsd}$ [23]	$m_{CXY}{}^{calcd}$ [23] (eq 2)	PI[k] (eq 1)
1	$ClCCH_3$	105.4	1.819	1.548	1.61	−10.28	29.3	0.50	0.58	0.44
2	FCPh	106.4	1.321	1.538	1.51	−10.23[b]	45.7	0.89	0.96	0.83
3	$ClCSCH_3$	106.5	1.835	1.732	1.65	−10.23	38.7	0.91	(0.91)[c]	0.70
4	CCl_2	106.7	1.813	1.813	0.31	−11.44	26.5	1.00	0.97	0.26
5	FCCl	104.2	1.303	1.849	1.03	−11.98	42.8	1.28	1.22	0.61
6	CF_2	102.6	1.329	1.329	1.89	−13.38	62.8	1.48	1.47	0.85
7	$ClCOCH_3$	103.5[d]	1.837	1.339	2.46	−10.82	60.3		1.59	1.11
8	$FCOCH_3$	102.7[e]	1.331	1.372	3.19	−11.81	74.2		1.85	1.19
9	FCOH	102.4[f]	1.329	1.355	3.05	−12.05	74.4		2.09[g]	1.15
10	$C(OCH_3)_2$	100.7[h]	1.376	1.376	4.09	−10.81	79.8		2.22	1.43
11	$C(OH)_2$	102.0[i]	1.359	1.359	3.99	−11.00	83.0		2.71[g]	1.37
12	$CH_3OCN(CH_3)_2$	105.4[j]	1.367	1.373	5.41	−9.53	93.4		2.91	1.67

[a] Defined as the negative of the energy of eq 4. [b] This is the energy of the carbene lone-pair orbital. Two higher energy occupied orbitals, at −9.56 and −9.92 eV, are the a_2 and b_1 phenyl π orbitals. [c] This value is actually the experimental value, since $m_{CXY}{}^{calcd}$ varies from 0.9 to 1.6, depending on which reported value of $\sigma_R{}^+$ is used.[23] [d] ∠COC = 113.7°. [e] ∠COC = 113.2°. [f] ∠COH = 106.6°. [g] $\sigma_R{}^+(OH) = -1.24$; $\sigma_I(OH) = 0.28$. Exner, 0. In "Advances in Linear Free Energy Relationships", Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1972. [h] ∠COC = 112.5°. [i] ∠COH = 106.2°. [j] ∠COC = 113.0°, ∠CNC = 121.6°. [k] See text for derivation; values of PI < 1 imply that the carbene is electrophilic, 1 ≤ PI ≤ 1.2 suggest ambiphilicity, and PI > 1.2 suggest nucleophilic carbene character.

ness of the transition state increases, the calculated values of PI are not very sensitive to the value of Q if it is kept between 3 and 5 eV. We have chosen the simplest expedient of holding Q constant at 5 eV.

PI_{CXY}, the "philicity" index or "PROPHETIC" index,[22] is 0.27, 0.85, 1.15, and 1.37 for CCl_2, CF_2, CFOH, and $C(OH)_2$, respectively, clearly paralleling the trends of electrophilicity for the first two carbenes, ambiphilicity for the third, and nucleophilicity for the fourth. Predictions will be made using this index in latter sections of this paper.

Correlations between Theoretical and Experimental Selectivity Parameters of Carbenes

The previous section defined the meaning of "early" and "late", and of electrophilic and nucleophilic, carbene cycloaddition transition states. We have also investigated whether there is any correlation between theoretical reactivity indexes such as substituent stabilization energy or LUMO energy and experimental selectivities of carbenes. Previously, no direct relationships have been established between the calculated electronic structures of carbenes and their observed reactivities or selectivities.

The most widely applicable quantitative empirical characterizations of carbenic reactivities are the linear free energy relationships between the olefinic selectivities of CXY and CCl_2.[2,6,23] Relative reactivities of CXY and CCl_2 are determined toward a standard set of alkenes at 25 °C,[24] and the "carbene selectivity index", m_{CXY}, is defined as the least-squares slope of the plot of $\log (k_i/k_{isobutene})_{CXY}$ vs. $\log (k_i/k_{isobutene})_{CCl_2}$. For nine singlet carbenes, the observed values of m_{CXY} have been correlated by eq 2, in which $\sum_{X,Y}$ represents the sum of the appropriate σ constants[25] for the X and Y carbenic substituents.

$$m_{CXY} = -1.10\Sigma_{X,Y}\sigma_R{}^+ + 0.53\Sigma_{X,Y}\sigma_I - 0.31 \qquad (2)$$

Equation 2 is derived from the selectivities of "electrophilic" carbenes; its parameters have been "normalized" to CCl_2, and it can be interpreted to provide quantitative support for the concept that decreasing electrophilicity of the carbene arises from "decreasing freeness of the vacant p orbital" and is accompanied by increasing selectivity.[6,23]

The interaction of the carbenic electrophile LUMO with the alkene HOMO is a critical factor influencing the reactivity[3] and, presumably, the selectivity of the carbene. According to the perturbation molecular orbital theory of reactivity,[21] the closer these orbitals are in energy, the more stabilization should be conferred on the transition state by charge-transfer interaction; lowering the carbene LUMO energy should increase both the reactivity and the selectivity of the carbene toward a series of electron-rich alkenes. This arises in the following ways: when there is a very large difference between the energy of an alkene HOMO and an electrophilic carbene LUMO, the carbene will be relatively unreactive. Furthermore, an increase in the alkene HOMO energy will cause a small decrease in the HOMO–LUMO gap, and only a small increase in reactivity. A carbene with a very low-lying LUMO will be more reactive because of the smaller carbene LUMO–alkene HOMO gap. The same increase in alkene HOMO energy will cause a larger percentage decrease in the HOMO–LUMO gap and a large increase in reactivity.[21] An alternative statement of this effect, which is exactly opposite to the usual selectivity relationship, is that, for a constant transition-state geometry, an increase in the electrophilicity of a reagent will induce greater positive charge on the alkene, making the transition-state stability more sensitive to substitution by donors on the alkene.

Although such anti-selectivity relationship behavior is observed in some cycloaddition reactions,[21] the more general relationship of reactivity to selectivity is that, when increased reactivity results from increased reaction exothermicity, the transition state of a reaction is shifted "earlier" along the reaction coordinate. This factor may override that discussed in the previous paragraph. As the transition is made "earlier", weaker interactions between reactants lead to decreased selectivity.[14,15] If the selectivity of a reaction is determined by the position of the transition state, then the exothermicity of the reaction should be related to selectivity.

A third factor also can influence selectivity in carbene cycloadditions: upon successive donor substitution, carbenes and other potentially ambiphilic species evolve from electrophiles to nucleophiles. In FMO terms, substituents can cause the carbene HOMO–alkene LUMO interaction to become more important than the carbene LUMO–alkene HOMO interaction. Toward electron-rich substrates, this effect will cause selectivity first to decrease and then to reverse sign as the nature of the carbene interaction with the alkene changes.

The computations reported in the first section of this paper imply that the usual selectivity relationship will hold for carbene cycloadditions, and that the reaction exothermicity is the quantity more directly related to selectivity. We have also tested whether there is a more general and quantitative relationship between experimental carbene selectivities and computed exothermicities or LUMO energies.

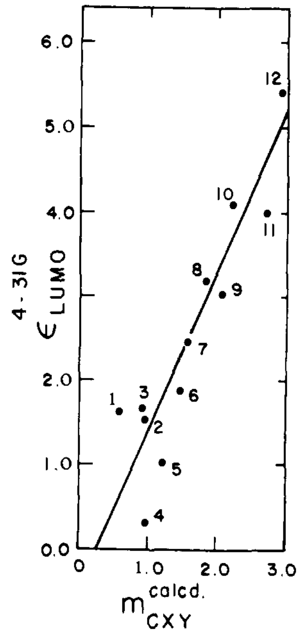


Figure 6. Calculated LUMO energies for CXY vs. $m_{\mathrm{CXY}}^{\mathrm{calcd}}$; see Table II for numbering of the carbenes.

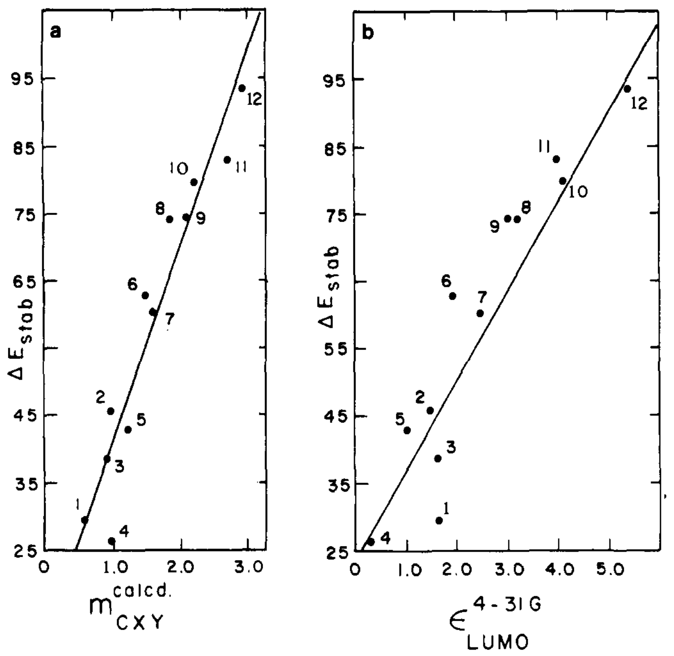
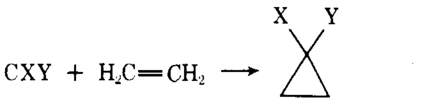


Figure 7. (a) Calculated stabilization energies for CXY vs. $m_{\mathrm{CXY}}^{\mathrm{calcd}}$. (b) Calculated stabilization energies for CXY vs. calculated LUMO energies; see Table II and text.

The geometries of a series of carbenes for which experimental or calculated (eq 2) m_{CXY} values were available were partially optimized by ab initio calculations[8] using the minimal STO-3G basis set,[9] and calculations were carried out on these geometries with the split-valence 4-31G basis set.[10,26,27] Table II includes calculational results for 12 disubstituted carbenes,[28] along with observed and calculated (from eq 2) values of m_{CXY}.[23] Figure 6 is a plot of $\epsilon_{4\text{-}31\mathrm{G}}^{\mathrm{LUMO}}$ vs. m_{CXY} calculated from eq 2.[29,30] The least-squares correlation line (slope = 1.81 eV/m unit, $r = 0.915$) is significant at the 99.9% confidence level. There is thus a reasonable linear correlation between the calculated LUMO energies of the carbenes and the empirical selectivity indexes, m_{CXY}.[31] Electron-donating substituents on the carbene raise the energy of the LUMO and increase the carbene's selectivity toward alkenes; electron-withdrawing groups lower the LUMO energy and decrease selectivity.

As noted above, a direct correlation between LUMO energies and selectivities is unexpected on the basis of perturbation theory, assuming identical transition-state geometries for all reactions. Instead, the LUMO-m_{CXY} correlation suggests that both selectivity and LUMO energy are related to a common factor, the exothermicity of the carbene reaction.

Instead of calculating the energy of each of the reactions (eq 3), the less expensive expedient was chosen of calculating the



(3)

stabilization of carbene CXY relative to the corresponding substituted methanes, according to the following isodesmic reaction:[32]

$$\mathrm{CH_2 + CH_3X + CH_3Y} \xrightarrow{-\Delta E_{\mathrm{stab}}} \mathrm{CXY + 2CH_4} \qquad (4)$$

The negatives of the 4-31G energies of the reactions are defined as the carbene stabilization energies, ΔE_{stab}, and are tabulated in Table II.

Figure 7a is a plot of these stabilization energies against $m_{\mathrm{CXY}}^{\mathrm{calcd}}$ (Table II) for 12 carbenes.[33] This correlation ($m_{\mathrm{CXY}} = 0.035\Delta E_{\mathrm{stab}} - 0.449$) indicates that the usual selectivity relationship between the heat of reaction, position of the transition state, and selectivity holds for carbenes. That is, the most stable carbenes, those which react least exothermically, exhibit the greatest selectivity, presumably due to the relative "lateness" of the transition states of their cycloaddition reactions.

Figure 7b shows a plot of the stabilization energies of the carbenes vs. their LUMO energies. A reasonable correspondence between these quantities is observed.[34] The stabilization of the carbene arises from electron donation from the π orbitals of the substituent into the vacant carbene LUMO; this also raises the energy of the carbene LUMO. However, chlorine (for example) both stabilizes the carbene and lowers the LUMO energies owing to the dual nature of the halogens: inductive electron withdrawal, which lowers the LUMO energy, has little influence on stability, whereas resonance donation, which raises the carbene LUMO energy, stabilizes the carbene.[35] Typically, as the LUMO of the carbene is raised, and the carbene becomes more stable, there is a shift to a later, more advanced bond-making transition state, leading to greater selectivity toward a series of alkenes. This, in turn, suggests that eq 2 more accurately reflects carbene stabilities rather than direct charge separation in the cycloaddition transition state.

Since the 4-31G carbene stabilization energy correlates with m_{CXY}, and m_{CXY} correlates with $\sigma_{\mathrm{R}}{}^{+}$ and σ_{I} (indeed some of the m values used for the correlation with E_{stab} were calculated), there was no doubt that E_{stab} would correlate with $\sigma_{\mathrm{R}}{}^{+}$ or with $\sigma_{\mathrm{R}}{}^{+}$ and σ_{I}. Using $E_{\mathrm{stab}}{}^{4\text{-}31\mathrm{G}}$ from Table II and $\sigma_{\mathrm{R}}{}^{+}$ and σ_{I} values from ref 25, the following correlations are obtained:

$$E_{\mathrm{stab}}{}^{4\text{-}31\mathrm{G}} = -29.2\Sigma\sigma_{\mathrm{R}}{}^{+} + 17.7$$

$$(n = 12, r^2 = 0.89, F = 73.8, \mathrm{SD(slope)} = 3.40) \qquad (5)$$

Inclusion of σ_{I} does not increase the significance of the correlation:

$$E_{\mathrm{stab}}{}^{4\text{-}31\mathrm{G}} = -31.4\Sigma\sigma_{\mathrm{R}}{}^{+} + 14.5\Sigma\sigma_{\mathrm{I}} + 4.45$$

$$(n = 12, r^2 = 0.91, F = 29.0, \mathrm{SD(slope)} = 3.83)$$

We can conclude on this basis that the stabilization energy of the carbene is, in classical terms, due to resonance electron donation from the substituent to the vacant p orbital of the carbene. In turn, this suggests that the carbene selectivities are determined by carbene stabilities, rather than by charge separation in the transition state.

Finally, we note that the reactivity index, PI, described earlier to assess the nucleophilic, ambiphilic, or electrophilic character of carbenes can be applied to predict the reactivity characteristics of the carbenes in Table II for which experimental reactivity data are not available. The last column of Table II lists the values of PI calculated from 4-31G orbital energies and stabilization energies. Carbenes 8 and 9 are predicted to be ambiphilic, carbenes 4-6 are known electrophiles and 1-3 are predicted to be electrophiles, carbene 7 is a known ambiphile and 10 a nucleophile, and 11 and 12 are predicted to be nucleophiles. If only orbital energies are used, without considerations of overlaps (i.e., if S_n^2/S_e^2 is omitted from the PI calculation), carbenes 1-3 are predicted to be ambiphilic. However, in a very early transition state, the electrophilicity of the carbene is exaggerated owing to the transition-state geometry. This overrides the fact that both frontier orbital energy gaps are of comparable magnitude for the first three carbenes in Table II.

Conclusion

We have reported, for the first time, ab initio transition states for substituted carbene cycloadditions, as well as a simple relationship between the selectivities of carbene cycloadditions and the stabilization of the carbene substituents. The transition of carbenes from electrophilic to nucleophilic is a smooth one, and all of these reactions have characteristics related to those possessed by "pseudopericyclic reactions",[36] namely, the transition states resemble linear conjugated systems, originating in the carbene lone pair and terminating in the vacant p orbital, more than they resemble cyclic delocalized systems. Both nucleophilic and electrophilic interactions are significant in both early and late transition states.[37] There remain a number of important questions such as what is the relative importance of changes in $\Delta S^{\ddagger}$ and $\Delta H^{\ddagger}$ upon substituent effects.[3] This question can only be answered by a more thorough exploration of the reaction potential surface in the transition-state region.

Acknowledgments. Financial support of this research at Louisiana State University by the National Science Foundation (CHE 76-11839) and, at Rutgers University, by the National Science Foundation and the Public Health Service (Research Grant CA-14912 from the National Cancer Institute) is gratefully acknowledged. Statistical analyses and computer graphics were carried out on the PROPHET system, a national computer resource for the study of chemical-biological interactions sponsored by the Division of Research Resources of the National Institutes of Health.

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(28) Only disubstituted carbenes are included, since eq 2 has not been applied to reactions of monosubstituted carbenes, CHX.[6]

(29) The values of m_{CXY}^{calcd} were used throughout for consistency; very little difference was observed if experimental *m*'s were included for PhCF, CCl_2, CFCl, and CF_2. The coefficients of eq 2 were derived by multiple least-squares fitting of nine experimental *m* values,[23] so that any m_{CXY} calculated from eq 1 has an experimental heritage, and represents only the *electrophilic* behavior of carbenes.

(30) The experimental electron affinity of singlet methylene (1.06 ± 0.03 eV: Zittel, P. F.; Ellison, G. B.; O'Neil, S. V.; Herbst, E.; Lineberger, W. C.; Reinhardt, W. P. *J. Am. Chem. Soc.* **1976**, *98*, 3731) as compared to $\epsilon_{LUMO}^{4\text{-}31G} = +2.04$ eV suggests that the calculated LUMO energies are about 3 eV too high.

(31) Kostikov and co-workers previously suggested that m_{CXY} values for CFCl and CF_2 are related to the LUMO energies of these species: Kostikov, R. R.; Malchanov, A. P.; Golovanova, G. V.; Zenkevich, I. G. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 1846. However, the increasing selectivity with LUMO lowering predicted by perturbation theory was overwhelmed in their treatment by the empirical constants for halogens.

(32) Although calculations using CH_2XY would be more appropriate, energies of all these optimized species were not available. However, the calculated energies of five of the reactions, $CXY + H_2C{=}CH_2 \rightarrow (CH_2)_2CXY$ (Table I), are in the same order as the carbene stabilization energies, i.e., $E_{rxn} = -96 + 0.88\Delta E_{stab}$, which suggests that the cyclopropanes are also stabilized to some extent by substituents.

(33) The slope of the least-squares correlation line is 28.6 kcal·mol^{-1}/m unit, and the correlation coefficient ($r = 0.956$) indicates significance at the 99.9% confidence level.

(34) The slope of the least-squares correlation line is 12.9 kcal mol^{-1} eV^{-1}, and the correlation coefficient ($r = 0.935$) is significant at the 99.9% confidence level.

(35) The $\epsilon_{4\text{-}31G}^{LUMO}$ correlation with ΔE_{stab} holds only for a similarly substituted series of carbenes. For example, $\epsilon_{4\text{-}31G}^{LUMO}$ of $^1CH_2$ is 1.89 eV, whereas $\Delta E_{stab} = 0$, by definition.

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