Tetrahedron Vol. 41, No. 8, pp. 1555 to 1563, 1985
Printed in Great Britain.

0040-4020/85 \$3.00 + .00
Pergamon Press Ltd.

THEORETICAL STUDIES OF HALOCARBENE CYCLOADDITION SELECTIVITIES

A NEW INTERPRETATION OF NEGATIVE ACTIVATION ENERGIES AND ENTROPY CONTROL OF SELECTIVITY

K. N. HOUK,* NELSON G. RONDAN and JIRI MAREDA
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, U.S.A.

(*Received in USA* 30 *November* 1984)

Abstract—*Ab initio* RHF calculations with the 3-21G basis set have been carried out on cycloadditions of CF_2 and CCl_2 with ethylene. Although π-complex intermediates are predicted for both reactions at this level, MP2/3-21G calculations imply that there are no complexes in reactions of CCl_2 or more reactive carbenes with ethylene or substituted alkenes. Nevertheless, negative activation energies can be observed, since ΔG reaches a maximum due to the increase in $-T\Delta S$ for these bimolecular reactions. The apparent "entropy control" for reactive carbenes results from the rapid decrease in ΔH. As the reactivity of the alkene increases, the transition state shifts to an earlier point on the free energy surface, where $-T\Delta S^{\ddagger}$ is lower, but $\Delta H^{\ddagger}$ is higher than for less reactive alkenes. Model potentials are developed for ΔH and $-T\Delta S$ which reproduce experimental behavior, without the assumption of intermediates.

Carbene reactions have experienced intense scrutiny beginning even before the christening of methylenes as "carbenes" in the famous nocturnal taxi. These small, but potent, species are highly reactive electrophiles. Because they are both relatively small and interesting, carbenes have been the subject of many theoretical investigations.[1–4] The relationship between substituents, singlet–triplet gaps,[4] and singlet reactivities and selectivities[2] have been investigated in detail. The non-linear approach of singlet carbenes to alkenes has been reaffirmed numerous times.[1] Elsewhere in this Symposium-in-Print, a variety of interesting experimental phenomena recently discovered for carbene cycloadditions are described. In this article, we describe the details[3] of our most recent theoretical investigations of carbene cycloadditions, which have led us to propose new postulates about the origin of anomalous selectivities, "entropy control", and negative activation energies observed for some of these reactions.

It has long been known that most carbenes are electrophilic species which react faster with electron-rich alkenes than with electron-deficient alkenes.[5–7] Thus, halocarbenes and most substituted carbenes have negative Hammett ρs in reactions with substituted styrenes, and more highly alkylated alkenes react faster than less alkylated alkenes with most carbenes. Only potent electron-donor substituents on a carbene can render it ambiphilic or even nucleophilic.[2,8]

For dichlorocarbene, Skell showed that alkenes react in the order: tetralkyl > trialkyl > dialkyl > monoalkyl.[5,6] Moss has systematized this reactivity order for a variety of carbenes,[2,7] and has proposed a selectivity index, $m_{\rm CXY}$, which is the slope of the plot of $\log k^{\rm rel}_{\rm CXY}$ versus $\log k^{\rm rel}_{\rm CCl_2}$ towards a series of alkylethylenes.[7] We recently showed that these room temperature selectivities of carbenes toward a series of alkylethylenes (Moss' $m_{\rm CXY}$ values) are correlated with carbene stabilities.[2] Thus, whereas CH_2 is unselective, donor substituents stabilize carbenes and increase their selectivities. Presumably, the rate of reaction of the carbene is decreased, as well, although this has not been determined experimentally. This normal reactivity–selectivity relationship implies that activation enthalpy variations control selectivity.

This treatment seemed to elucidate the details of carbene selectivity satisfactorily, but in making these conclusions we had conveniently overlooked experimental data which indicated that enthalpic variations do not always control reactivity and selectivity. For example, in 1969, Skell and Cholod reported that the relative rates of CCl_2 cycloadditions to alkylethylenes were paralleled by the differences in entropies, not enthalpies, of activation.[6] Representative data are listed in Table 1. Although no regular pattern is seen in the enthalpies of activation, the entropies correlate roughly with rates. Skell proposed that more reactive alkenes have earlier transition states. The earlier transition states have lower vibrational frequencies and thus have less negative entropies than late transition states. It was assumed that all alkenes had similar small positive enthalpies of activation with CCl_2.[6]

Giese *et al.* undertook a systematic investigation of the temperature dependence of the selectivities of the halocarbenes, CF_2, CFCl, CCl_2, CClBr and CBr_2.[9–11] Figure 1 is a qualitative plot of the temperature dependence of the selectivities observed for a representative pair of alkenes. Other alkene pairs show

Table 1. Relative rates and activation parameters for reactions of CCl_2 with alkenes (Skell and Cholod)[6]

Alkene	$k_{\rm rel}$(0°C)	$\Delta\Delta H^{\ddagger}$	$\Delta\Delta S^{\ddagger}$
2-Methoxy-3-methyl-2-butene	7.8	+0.30	+5.72
2,3-Dimethyl-2-butene	4.6–5.6*	0.53–0.89*	5.97–7.95*
2-Methyl-2-butene	3.0–3.3*	0.07–0.26*	2.43–3.81*
Isobutene	[1.00]	[0.00]	[0.00]
cis-2-Butene	0.26	0.29	−1.25
Propene	0.02	1.19	−2.16

* Dependent upon the method of generation of CCl_2.

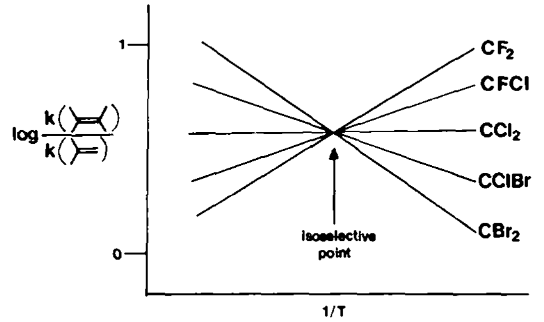

Fig. 1. Behavior observed by Giese *et al.*[9–11] for reactions of various carbenes with a pair of alkylethylenes.

very similar plots, with the more highly alkylated species always reacting faster than the less alkylated alkene. All halocarbenes are found to be equally selective at 360 K, the "isoselective temperature". Below 360 K, the "normal" selectivity is observed, but a reversal in selectivity occurs above 360 K.[9–11] The selectivity of CF_2 is "normal", controlled by enthalpies of activation. CF_2 is more selective at low temperatures than at high, and the entropy works against enthalpy, favoring the less substituted alkene (Table 2). This plot implies that the less substituted alkene would become more reactive toward CF_2 at very high temperatures, where entropy would control reactivity.

The selectivity of CCl_2 is temperature independent, indicating that the relative rates of reaction are controlled by entropies of activation, since $\Delta H^\ddagger$ is essentially identical for both alkenes. The selectivity of CBr_2 shows an inverse temperature dependence. Here, entropy favors the more alkylated alkene, while enthalpy has a small influence in the opposite direction. Thus, one would predict higher reactivity for the less alkylated alkene at sufficiently low temperature, if this plot remains linear.

CFCl and CBrCl are intermediate cases. Thus, as summarized in Table 2, enthalpic variations control selectivities of CF_2, while entropy controls the selectivities of CCl_2 and CBr_2.[12]

Table 2. Relative activation parameters for cycloadditions of carbenes with isobutene, 2-methyl-2-butene and 2,3-dimethyl-2-butene (Giese)[9–11]*

Carbene	$\Delta H^\ddagger$(DME)† $-\Delta H^\ddagger$(TriME)†	$\Delta S^\ddagger$(DME)† $-\Delta S^\ddagger$(TriME)†
CF_2	1.9	3.1
CFCl	1.2	1.2
CCl_2	−0.1	−2.6
CClBr	−0.61	−4.1
CBr_2	−1.4	−6.2
	$\Delta H^\ddagger$(DME)† $-\Delta H^\ddagger$(TME)†	$\Delta S^\ddagger$(DME)† $-\Delta S^\ddagger$(TME)†
CF_2	3.4	5.0
CCl_2	−0.3	−5.3
CBr_2	−2.4	−11.2

*W. B. Lee, Dr. rer. nat. Dissertation, Technische Hochschule Darmstadt, 1981; C. Stiehl (nee Neumann), Dr.-Ing. Dissertation, Technische Hochschule Darmstadt, 1983.

†DME = isobutene, TriME = 2-methyl-2-butene, TME = 2,3-dimethyl-2-butene. $\Delta\Delta H^\ddagger$ in kcal/mol. $\Delta\Delta S^\ddagger$ in e.u. (cal/°-mol).

Table 3. Activation parameters for phenylchlorocarbene cycloadditions to alkenes[15]

Alkene	$\Delta H^\ddagger$	$\Delta S^\ddagger$
2,3-Dimethyl-2-butene	−4.4	−23
2-Methyl-2-butene	−3.7	−22
trans-2-Pentene	−1.6	−20
1-Hexene	−1.5	−21

In the last few years, there have been experimental measurements of absolute rates of cycloadditions of some carbenes. Zero or negative activation energies were measured for processes initially believed to be cycloaddition reactions of singlet fluorenylidene, and triplet fluorenylidene,[13a] but these processes were shown by Griller *et al.* to involve the triplet carbene reactions, which may be a complicated function of intersystem crossing and reactions of both the singlet and triplet.[15] Negative activation energies have been measured for the reactions of singlet phenylchlorocarbene and various phenyl-substituted derivatives.[15] Some of these data are summarized in Table 3. It has been concluded that an intermediate (π-complex) is formed in these reactions. Conversion of this complex to products involves a second barrier which is below the energy of the reactants.[10,13–15] This postulate is represented by the energy diagram in Fig. 2. The higher reactivity at lower temperature is said to result in such a case from the fact that the dissociation of the complex to reactants is accelerated more than the formation of products as the temperature is raised. This arises because complex dissociation has a higher activation energy than cycloaddition. Giese also postulated that the reactive halocarbenes, whose reactions are entropy controlled, would have negative activation energies.[10] He proposed that the conversion of complex to products was more difficult for the more substituted alkene, since this is the nucleophilic phase of the cycloaddition.[10] This hypothesis is represented by the dashed line in Fig. 2. No explanation of the relatively favorable effect of entropy on the reaction of the more substituted alkene was offered.

Negative activation energies and entropy control of reactivity have also been observed for singlet oxygen

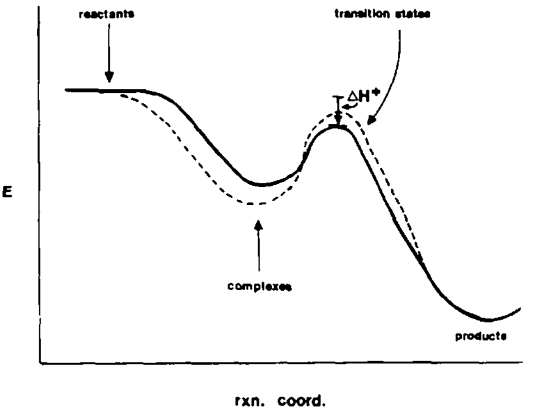

Fig. 2. Proposed energy versus reaction coordinate diagram to explain negative activation energies. For CBr_2, the full and dashed lines represent less and more substituted alkenes, respectively.

Table 4. Energies of reactants, intermediates, transition structures and products (a.u.). Relative energies (kcal/mol) are given in parentheses. All calculations were carried out at 3-21G geometries

	CF_2			CCl_2	
	3-21G	6-31G*	MP2/3-21G	3-21G	MP2/3-21G
CX_2—ethylene	−312.97580 (0)	−314.68954 (0)	−313.46901 (0)	−1029.70479 (0)	−1030.06351 (0)
Intermediate	−312.97892 (−2.0)	−314.69098 (−0.9)	−313.47207 (−1.9)	−1029.70831 (−2.2)	−1030.07033 (−4.3)
Transition structure	−312.93294 (+26.9)	−314.64033 (+30.9)	−313.44725 (+13.7)	−1029.70680 (−1.3)	−1030.07913 (−9.8)
Dihalocyclopropane*	−313.04534 (−43.6)	−314.76289 (−46.0)	−313.54232 (−46.0)	−1029.82059 (−72.7)	−1030.18324 (−75.1)

* Heats of reaction have been estimated as −46 for CF_2 and −70 for CCl_2.[2]

reactions with reactive alkenes,[16] and in the quenching of ketone triplet excited states by alkenes.[17] In both of these cases, intermediates have been postulated. In fact, it seems an inviolable tenet of organic chemistry that a negative activation energy is proof of the reversible formation of complexes and an energy profile such as those shown in Fig. 2.

In this paper, we report new theoretical investigations of dihalocarbene cycloadditions to simple alkenes.[3] Both energies and vibrational frequencies for stationary points have been calculated in order to obtain H, S and G, and to acquire some insights into the phenomena described above. Unfortunately, the systems studied have 5–7 heavy atoms, so that the calculations were carried out with rather small basis sets, and correlation energy corrections could be made in only a few cases and at a primitive level. In spite of these limitations, the calculations do lead to several reasonable conclusions about the magnitudes of enthalpic and entropic effects in these cycloadditions.

We have also developed a new hypothesis to explain the entropic control and negative activation energies described above for some halocarbene cycloadditions.[17a] In order to show that this hypothesis is capable of explaining the data quantitatively, we have devised model functions for enthalpies and entropies of halocarbene cycloadditions.

Ab initio *calculations on halocarbene cycloadditions*

In order to explore these aspects of potential energy surfaces for carbenes and related reactive species, we undertook *ab initio* calculations on the structures, energies and entropies of possible intermediates and transition structures involved in the cycloadditions of CCl_2 and CF_2 to ethylene. Structures of stationary points obtained using the 3-21G basis set[18] and gradient optimizations[19] are given in Fig. 3, while energies at 3-21G, 6-31G*,[20] and MP2/3-21G[21] levels are given in Table 4.

The 3-21G gradient optimized transition structures

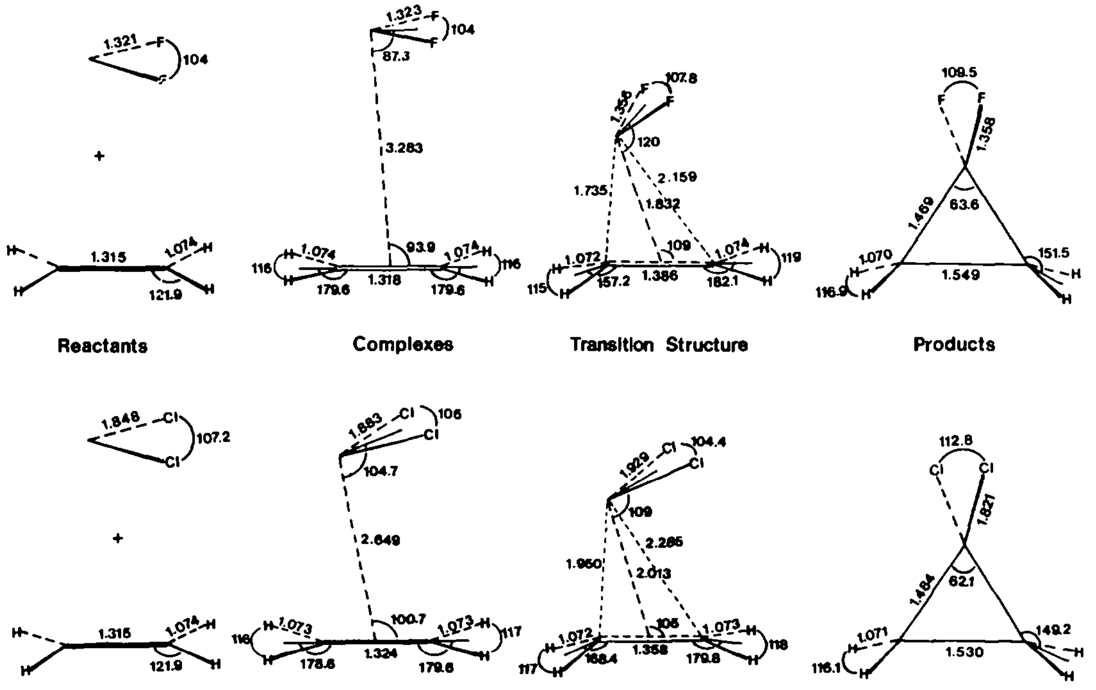

Fig. 3. 3-21G Structures of reactants, complexes, transition structures and products in CCl_2 and CF_2 cycloadditions to ethylene.

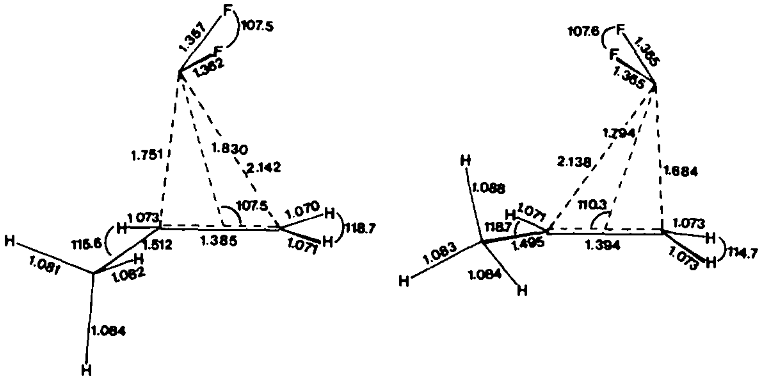

Fig. 4. 3-21G structures of transition structures for reaction of CF_2 with propene. The energies are 23.6 and 23.7 kcal/mol above the energies of isolated reactants.

are quite similar to those reported in our earlier work with the STO-3G basis set and serial optimizations.[2] Using gradient techniques, intermediates are now found for both reactions. These intermediates either do not exist at the STO-3G level, or were missed due to incomplete searching at the large values of the reaction coordinate where their minima occur.[2]

Each complex consists of an essentially undistorted ethylene arranged in a plane nearly parallel to that of the slightly distorted singlet carbene. A very small amount of charge transfer from ethylene to the carbene occurs in the complexes, but charge transfer from alkene to carbene is increased in the transition structures. Even though the carbene tilts in the transition state, the direction of charge transfer still indicates that the transition state is predominantly an electrophilic phase. The complexes are very flexible, with several vibrational frequencies near zero, so that little energy is required to move the carbene with respect to the ethylene.

We were concerned that these complexes might be artifacts of basis set superposition error. For this reason, we also carried out calculations with the 6-21G basis set, which has a more flexible inner shell, so that the superposition error should be smaller. In fact, the stability of the complexes does decrease at this level, but they still exist as energy minima (however, see below).

At the 3-21G level, the transition structure for CCl_2 cycloaddition is lower in energy than the energy of the reactants. Thus, a negative activation energy is predicted at this level, apparently in good accord with the experimental results summarized in Table 3 for related carbenes. However, with inclusion of correlation energy, even at the MP2/3-21G level, the complex disappears and no barrier at all to cycloaddition is predicted! We believe that better calculations would show that complexes are not energy minima.[22]

We also studied the reactions of CCl_2 with propene and isobutene. Even at the 3-21G level, no stable complexes and no activation barriers to cycloaddition are found. That is, attempted optimization of complexes gives the cyclopropanes. When r, the distance from the carbene carbon to the midpoint of the alkene double bond, is gradually decreased, the energy steadily decreases, and no barrier to reaction is found. When geometries were optimized at a carbene–alkene distance corresponding to that of the (artifactual) 3-21G transition state for the CCl_2–ethylene reaction ($r = 2.013$ Å), CCl_2–propene and CCl_2–isobutene supermolecules are 4.0 and 6.6 kcal/mol more stable than the isolated reactants. Thus, no stable com-

Table 5. ΔH, ΔS and ΔG from 3-21G calculations for CX_2–ethylene reactions*

	ΔE	Z.P.E.†	ΔH§	$S^{298\,K}$‖	$-T\Delta S^{298\,K}$	ΔG
CCl_2 + ethylene	0.0	36.8	0.0	116.1	0.0	0.0
π-complex¶	−2.2	38.0	−1.6	83.0	10.1	8.6
Transition state	−1.3	39.0	0.3	79.3	11.0	11.3
CF_2 + ethylene	0.0	39.2	0.0	109.6	0.0	0.0
π-complex	−2.0	39.8	−0.9	87.3	6.7	5.6
Transition state	26.9	41.4	28.2	71.7	11.4	39.6

* Energies, geometries and vibrational frequencies (ν_i) from 3-21G calculations; energies and enthalpies in kcal/mol; entropies in e.u. (Gibbs/mol).

† Z.P.E. = $1/2\mathrm{h}\sum_i \nu_i$. The imaginary frequency is neglected in the transition state calculation.

§ $\Delta H^{298} = \Delta E + \Delta(\mathrm{Z.P.E.}) + 4RT + \sum_i \mathrm{h}\nu_i/(e^{\mathrm{h}\nu_i/kT} - 1)$. Values of the last term range from 3.4 to 4.7 kcal/mol at 298 K.

‖ Evaluated from mass, moments of inertia, and vibrational frequencies according to ref. 24. Electronic entropies were neglected. For comparison, experimental entropies are 116.1 e.u. for CCl_2 + ethylene and 109.9 e.u. for CF_2 + ethylene.[24a] Estimated entropies for difluorocyclopropane and dichlorocyclopropane are 68.7 and 73.3 e.u., respectively, using Benson's tables.[24a]

¶ ν_i were estimated for this species. ΔS for this species is not included in Fig. 5.

plexes are predicted at reasonable levels of theory, and we believe that this conclusion will survive at more respectable levels of theory.[22,23]

The relatively large activation energy for the reaction of CF_2 with ethylene, which is approximately correct[2] at the MP2/3-21G level, is a result of the large stabilization of the carbene by the fluoro substituents.[2] A very weakly bound complex is predicted for CF_2. The slight stability of this species relative to the isolated reactants may well be an artifact of the use of small basis sets and neglect of adequate correlation energy corrections.[22]

We have also located two transition states for the reaction of CF_2 with propene. These are shown in Fig. 4. The carbene shows an insignificant preference for attack in one of the regiochemically possible ways. Both of these lead to the same product. The predicted activation energies for these processes are 3.3 and 3.4 kcal/mol less than for the reaction of ethylene. The position of these transition structures along the reaction coordinate are similar for both ethylene ($r = 1.832$ Å) and propene ($r = 1.794$ or 1.839 Å).

Thus, the picture given by the calculations fits well with expectation. (1) Alkyl groups on the alkene lead to a more stabilizing alkene–carbene interaction; (2) the relatively unreactive carbene, CF_2, has a substantial barrier which is lowered by alkyl groups on the alkene; (3) there is no barrier for the reaction of CCl_2 with alkenes.

However, these calculations are for vibrationless species at 0 K. In order to make zero point energy corrections, as well as determinations of enthalpies and entropies, we carried out calculations of enthalpies and entropies of the 3-21G stationary points using standard formulae,[24] and the masses, 3-21G moments of inertia, and 3-21G vibrational frequencies. The harmonic vibrational frequencies of reactants, complexes, and transition structures were computed from analytical second derivatives and diagonalizations of the resulting force constant matrices. These quantities, and the $\Delta G°$ for each species at 298 K are listed in Table 5.

In each case, the largest portion of the negative ΔS is caused by the decrease in translational entropy (-35 e.u.), which is essentially constant for bimolecular reactions. The smaller differences in entropies for weak complexes and tighter transition states are due to increases in vibrational frequencies, which lower vibrational entropies.

We also discovered that the differences in entropies of reactants and different stationary points are remarkably independent of the carbene. For example, the experimental entropies of reaction of CH_2, CF_2 and CCl_2 with ethylene are -41.9, -41.2, and -42.8 e.u., respectively.[24a] Using these values, and our computed values for complexes and transition states, we find that $S^c = 10.35r - 56.67$, where r is the reaction coordinate, which is the distance from the carbene carbon to the midpoint of the alkene C=C bond. The straight line in Fig. 5 shows the corresponding correlation for $-T\Delta S$. This should only be an accurate linear relationship for relatively late geometries. This linear function seems a reasonable approximation for r between 4 Å and the product cyclopropanes, but $-T\Delta S$ should drop off to zero at moderate distances. We used the curved function shown to treat more reactive carbenes (see later).

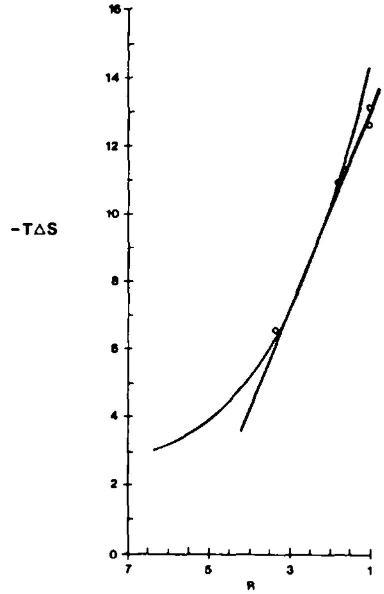

Fig. 5. Linear correlation of $-T\Delta S$ versus r, between 1.2 and 4 Å. The points used in deriving this correlation are shown. The curved line represents the function used for $-T\Delta S$ at $r > 4$ Å, assuming a smooth decrease in $-T\Delta S$ to zero at $r > 7$ Å.

A perusal of Table 5 shows that even using the 3-21G values to obtain ΔH and ΔS, the complexes are not likely to be free energy minima at room temperature. Even if there were small depressions (and minima) in the free energy surfaces at 298 K, these would probably disappear in solution, since the solvents ordinarily used for carbene reactions (ethers or halocarbons) should be better Lewis base carbene-complexers than alkenes. For example, we optimized the structures of complexes of CCl_2 or CF_2 with H_2O. The resulting species, shown in Fig. 6, are 23.6 and 9.7 kcal/mol, respectively, more stable than the separated species at the MP2/3-21G level. These calculations probably overestimate the stabilities of these complexes, but the conclusion that the interaction of ethers with carbenes are more stabilizing than interaction of alkenes with carbenes at long distances should survive at better computational levels. Indeed, such complexes have been established experimentally.[25]

Our calculations suggest that no stable complexes, other than possible solvent "cage" complexes, are formed between alkenes and CCl_2 *or more reactive carbenes.*

If there are no complexes and no enthalpic barriers to

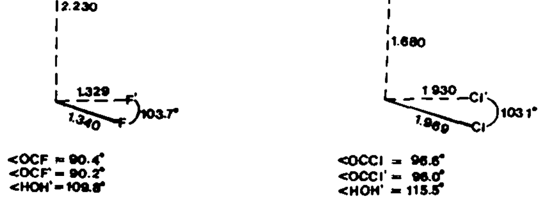

Fig. 6. 3-21G geometries of carbene–water complexes. Complexes optimized with different symmetries are very similar in energy.

reaction for the cycloadditions of CCl_2, CClBr and CBr_2 to alkenes, how can entropy control and negative activation energies be observed experimentally? We seem to have replaced a marvelous hypothesis with stupefying confusion! However, we have developed a new hypothesis to explain all of these mysteries, as well as a mathematical model which reproduces semiquantitatively the effects observed by Giese. For the moment, we offer this hypothesis couched in the familiar fabric of transition state theory,[26] but anticipate re-upholstering this argument in terms of modern dynamical theory in future publications.

A new hypothesis for negative activation energies and entropy control of reactivity

Our hypothesis is based upon several results of the calculations described earlier. First, the entropy changes in the cycloadditions of carbenes to alkenes are assumed to be a function of the reaction coordinate, r, separating the carbene carbon from the alkene midpoint, but are essentially independent of the carbene or alkene. Thus, in our model, we used the functions described earlier (Fig. 5) to approximate the entropy as a function of r.

Secondly, for ΔH, we have used information from our calculations, or judicious guesses described below, to establish potential energy surfaces. However, the remaining features of our model are not a direct result of the quantum mechanical calculations. Instead, it is a speculative proposal which we feel gives a good explanation of the data, is different from the π-complex model, and gives different, experimentally varifiable, predictions.

The key to the argument is that fast bimolecular reactions may have significant free energy barriers even in the absence of enthalpic barriers, due to the decrease in entropy occurring as two molecules unite to form one. In the absence of an enthalpic barrier, as for CCl_2 and CBr_2 reactions, the position of the transition state, and thus the rate of reaction, is determined by the point where favorable enthalpic factors overcome unfavorable entropic factors.

This idea is related to the recent suggestion, by Doubleday *et al.* that the tetramethylene diradical is an entropy-bound minimum.[28] Thus, conversion of tetramethylene to cyclobutane, or to two ethylenes occurs with no enthalpic barrier, but with an entropic barrier. Doubleday also pointed out the possible relevance of this idea to carbene reactions at the Structure-Energy Conference in Asimolar in March, 1983.

Our models for the enthalpy, entropy and free energy changes for reactions of CF_2, CCl_2 and CBr_2 with isobutene and tetramethylethylene are shown in Figs 7–9.

For each carbene, we have used an "inverted Morse function" to simulate the behavior of ΔH along the reaction coordinate:

$$\Delta H = -\Delta H_{\max}[1-e^{-\beta(r-r')}]^2.$$

Here, ΔH is the enthalpy, relative to the reactants, at 298 K. Except for the small variations in ΔH with temperature, the maxima in these functions would correspond to the position of the transition state $\Delta H^\ddagger$ at 0 K. The quantity r' is the value of the reaction coordinate at the enthalpy maximum. r' is adjusted both to be reasonable, and to make the model work. β controls the curvature of the ΔH curves, and is an adjustable parameter in our model. The various parameters used to derive the curves shown in Figs 7–9 are summarized in Table 6. The values of $\Delta H_{\max}$ for CF_2 are those estimated from the experimental value of the activation energy for the CF_2–ethylene reaction, and our calculations of the influence of methyl substituents on this activation energy. For CCl_2 and CBr_2, the values of $\Delta H_{\max}$ are chosen to be essentially zero. The small value of $\Delta H_{\max}$, and the position of the maximum, control the point from which ΔH decreases below the energy of the reactants. These "inverted Morse functions" are only good approximations to H in the region of the transition state. In order to model the full H surface, a different function would have to be used in the region of products, or a more complicated function would be necessary in order to produce a proper energy minimum at the product geometry.[29] While we anticipate the eventual development of such a model, we adopt the mathematically simpler model here.

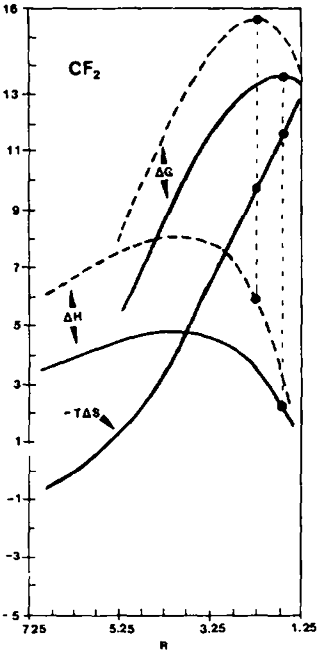

Fig. 7. ΔH, $T\Delta S$ and ΔG profiles for reaction of CF_2 with isobutene (---) and tetramethylethylene (——) at 298 K. Vertical lines represent positions of the critical points for the two reactions, and intersect the curves at values of $\Delta G^\ddagger$, $\Delta H^\ddagger$ and $-T\Delta S^\ddagger$.

For CF_2, we have performed a transition state

Table 6. Parameters derived for the "inverted Morse functions" used to model H*

Reaction*	r'	$\Delta H_{\max}$	β
CF_2+DME	4	8.0	0.25
CF_2+TME	4	4.7	0.25
CCl_2+DME	5.5	0.001	1.2
CCl_2+TME	5.5	0.001	1.4
CBr_2+DME	15	0.0001	0.432
CBr_2+TME	15	0.0001	0.451

* DME = isobutene (1,1-dimethylethylene or 2-methylpropene); TME = 2,3-dimethyl-2-butene.

Table 7. Summary of the quantities obtained from model potentials plotted in Figs 7–9

Reaction	r(Å) at G_{max}	$\Delta H^\ddagger$(298 K)*	$\Delta S^\ddagger$(298 K)†	$\Delta G^\ddagger$(298 K)†
CF_2+DME	2.35	5.91	−32.4	15.6
CF_2+TME	1.75	2.02	−38.6	13.5
CCl_2+DME	2.50	−1.27	−30.8	7.9
CCl_2+TME	3.00	−1.03	−25.6	6.6
CBr_2+DME	3.05	−3.01	−24.0	4.2
CBr_2+TME	4.28	−1.56	−15.9	3.2

* In kcal/mol.

† In e.u.

calculation on the reaction with propene which indicates that the position of r' is the same for both alkenes. We estimate that ΔH_{max} for tetramethylethylene is 3.3 kcal/mol less than that for isobutene. Figure 7 shows the plot of ΔH, $-T\Delta S$ and ΔG at 298 K for the reactions of CF_2 with DME and TME. This plot is representative of expected behavior of a relatively unreactive, "enthalpy controlled", carbene. Since $-T\Delta S$ increases regularly along the reaction path, the transition state will shift to a later, tighter geometry as the alkene reactivity is increased, and the $-T\Delta S$ term will disfavor the reaction of the more substituted alkene, in opposition to ΔH. This arises due to the fact that the maximum in ΔG occurs at that value of r where the positive slope of the $-T\Delta S$ curve equals the negative slope of the ΔH curve. Table 7 summarizes the values of $\Delta H^\ddagger$, $\Delta S^\ddagger$ and $\Delta G^\ddagger$ obtained from this plot.

Of course, the position of the transition state will be temperature dependent, shifting to smaller values of r (later along the reaction coordinate) as the temperature is raised. Even if ΔH and ΔS were temperature independent, a plot of log K versus $1/T$ should give a slope and intercept indicative of some average value of $\Delta H^\ddagger$ and $\Delta S^\ddagger$, or values which deviate systematically from those obtained at a single temperature. When we plot the values of $-\Delta G^\ddagger/RT$ calculated for each temperature by finding ΔG_{max} as in Fig. 7, we find the "pseudo-experimental" values of $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$ given in Table 8. These values agree satisfactorily with Giese's experimental values.

For CCl_2, ΔH_{max} was assumed to be negligible (Table 6). The resulting ΔH, $-T\Delta S$ and ΔG functions are shown in Fig. 8. The βs for DME and TME were adjusted so that $\Delta G^\ddagger$ at 298 K was close to the experimental value of 1.3 kcal/mol. Variations of βs over a wide range give $\Delta\Delta H^\ddagger$ near zero, with the position of ΔG_{max} and the value of $\Delta G^\ddagger$, determined mainly by the $-TS$ and $-T\Delta S$ values. This agrees well with experimental results on alkylethylenes and styrenes, where $\Delta\Delta H^\ddagger$ is always near zero, and reactivity is controlled by entropy.[9–11] Numerical values obtained from Fig. 8, or the corresponding plot of $-\Delta G^\ddagger/RT$ versus $1/T$, are summarized in Tables 7 and 8. We predict small negative activation energies for these reactions, in spite of the absence of complexes in our model. Small variations in $\Delta H^\ddagger$ and entropy control are expected to be observed for reactions without barriers, and for which the position of ΔG_{max} occurs in regions where $-T\Delta S$ is increasing linear.

For a very reactive carbene like CBr_2, the relationship of ΔG, ΔH and $-T\Delta S$ is sketched in Fig. 9. Here, we assume a very small barrier of 0.0001 kcal/mol and set r' to 15 Å for both isobutene and tetramethylethylene. This corresponds to the assumption that the attractive interaction between carbene and alkene begins earlier than for CCl_2. Electron transfer may even be involved in such cases, where the electron-affinity of the electrophile is very high. Now there is a decided shift to an earlier transition state as the carbene becomes more electron-rich. Because of the relative slopes of $-T\Delta S$ and ΔH curves, the $\Delta H^\ddagger$ will be less favorable for the more electron-rich alkenes, but $-T\Delta S^\ddagger$ will be more favorable. Negative activation energies will be observed, and will increase (become less negative) as the alkene becomes more electron-rich. The $-T\Delta S$ term controls reactivity, but the origin of this behavior is the more favorable enthalpy of interaction for electron-rich alkenes at any given distance. Only when the decreasing ΔH term overcomes the $-T\Delta S$ term is the ΔG barrier reached. Such behavior should be quite general for very reactive electrophiles, when the ΔG_{max} occurs in a region where $-T\Delta S$ is increasing in a non-linear fashion with r.

Turro and Moss *et al.* found that the reactions of phenylchlorocarbene with a series of alkenes have approximately constant negative activation entropies, and activation energies ranging from small positive

Table 8. Comparisons of activation parameters obtained from model potentials and from experiment*

	Theoretical (298 K)			Theoretical Eyring plot†		Experimental		
Carbene	$\Delta\Delta H^\ddagger$	$\Delta\Delta S^\ddagger$	$\Delta\Delta G^\ddagger$	$\Delta\Delta H^\ddagger$	$\Delta\Delta S^\ddagger$	$\Delta\Delta H^\ddagger$	$\Delta\Delta S^\ddagger$	$\Delta\Delta G^\ddagger$
CF_2	3.9	6.2	2.0	3.8	6.0	3.4	5.0	1.9
CCl_2	−0.2	−5.2	1.3	−0.2	−5.0	−0.3	−5.3	1.3
CBr_2	−1.5	−8.1	0.98	−1.3	−7.7	−2.4	−11.2	0.96

* $\Delta\Delta Q^\ddagger = \Delta Q^\ddagger$ (isobutene) $-\Delta Q^\ddagger$(tetramethylethylene), where $Q = H, S$ or G.

† These plots predict isoselective temperatures of 400 K for CCl_2—CBr_2, 370 K for CBr_2—CF_2, and 364 K for CCl_2—CF_2. The experimental value is 360 K.[9–11]

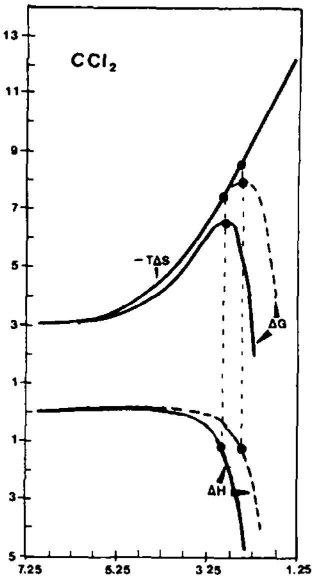

Fig. 8. ΔH, $T\Delta S$ and ΔG profiles for reaction of CCl_2 with isobutene (- - -) and tetramethylethylene (——). See caption to Fig. 7.

values with *trans*-2-pentene and 1-hexene to small negative activation energies with trimethylethylene and tetramethylethylene.[15] This is the behavior expected for a carbene intermediate in reactivity between difluorocarbene and dichlorocarbene. Phenylchlorocarbene is expected to be this type of carbene. Our model potentials, however, appear to give activation entropies which are too negative when compared to the experimental results.

Thus, we can model the experimental behavior of the different types of carbenes making reasonable assumptions about the shapes of entropy and enthalpy functions with respect to the reaction coordinate. No complexes are required to explain negative activation energies or "entropy control" of reactivity. Our model does not conclusively exclude π-complexes as intermediates, but they are not necessary to explain the data, nor do we believe that they are formed.

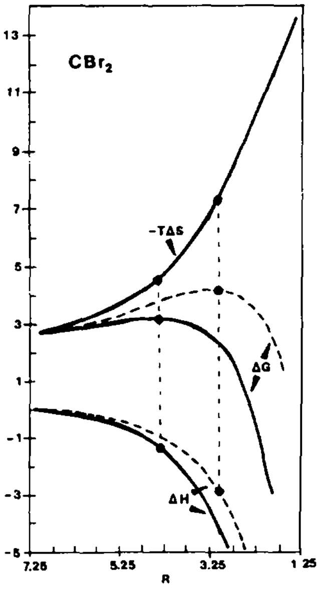

Fig. 9. ΔH, $T\Delta S$ and ΔG profiles for reaction of CBr_2 with isobutene (- - -) and tetramethylethylene (——). See caption to Fig. 7.

The Giese model implies that carbene selectivities will reverse at low temperature, and that alkyl substituents will diminish the rate of reaction of an alkene with CCl_2 and CBr_2. By contrast, we predict that reactions of CCl_2, CBrCl and CBr_2 will be unselective and diffusion controlled at low temperature, and that no complexes will be observed. These contrasting predictions are subject to experimental tests!

We offer a similar hypothesis to explain the negative activation energies and entropy control found in singlet oxygen reactions with electron-rich alkenes in solution.[16] Related descriptions have been given for the third-body mediated recombination of radicals in the gas phase.[30]

Our model can be rephrased in dynamical terminology. We have noted that the dividing surface[27] separating reactants from products in all of these reactions is different from the maximum in the potential energy surface. For the relatively unreactive CF_2, the enthalpic barriers are high, and the dividing surface occurs at similar values of r for different alkenes. However, for carbenes which react with no potential energy barrier, there is a dynamical barrier arising from the fact that the low-frequency translations and rotations of reactants are converted into relatively high-frequency vibrations of the product. This produces a dynamical bottleneck, corresponding in simple physical models to a narrowing of the pass through which the reactants must pass in order to reach the product valley. For CCl_2 and CBr_2, this dynamical bottleneck is overcome earlier for more alkylated carbenes, since the floor of the potential energy pass drops faster.

Negative activation energies are likely to be a general feature of the reactions of very energetic species. In such cases, there are no enthalpic barriers, only entropy imposed barriers. Nevertheless, selectivity can still arise, due to the substantial free energy barriers to such processes.

Why are these reactions not just diffusion controlled and unselective? When there are no enthalpic barriers to reaction, it is usually assumed that reactions are diffusion controlled, with barriers to reaction of the order of 1–2 kcal/mol, decreasing at higher temperature due to decreases in solvent viscosity. The behavior we describe will only occur when the free energy barrier to diffusion is lower than that for reaction of the molecules within the solvent cage. The entropy of diffusion at 298 K is likely to be near zero, so that the behavior we describe will occur only for reactions which have $-T\Delta S^{\ddagger}$ greater than ≈ 2 kcal/mol. At room temperature, this means that $\Delta S^{\ddagger}$ for the reaction must be greater than -6.7 e.u., in order to give a $\Delta G^{\ddagger}$ of 2 kcal/mol. Reactions which are diffusion controlled at low temperatures may become entropy-controlled at higher temperatures.

We plan to develop dynamic models of these reactions, based upon more accurate potential surfaces, in the future.

Acknowledgements—We are grateful to the National Science Foundations of the U.S.A. (research grant to K.N.H. and instrument grant to the University of Pittsburgh) and Switzerland (postdoctoral fellowship to J.M.) for financial support of this research, to Professors J. A. Pople, B. Giese, P. S. Skell and P. E. Siska for helpful comments, and to Professor M. S. Platz for comments and the invitation to take part in this Symposium-in-Print.

REFERENCES AND NOTES

[1a] R. Hoffmann, *J. Am. Chem. Soc.* **90**, 1475 (1968); [b]R. Hoffmann, D. M. Hayes and P. S. Skell, *J. Phys. Chem.* **76**, 664 (1972); [c]N. Bodor, M. J. S. Dewar and J. S. Wasson, *J. Am. Chem. Soc.* **94**, 9095 (1972); [d]B. Zurawski and W. Kutzelnigg, *Ibid.* **100**, 2654 (1978); [e]R. B. Woodward and R. Hoffmann, *Angew. Chem. Int. Ed. Engl.* **8**, 781 (1969); [f]T. Fueno, S. Nagase, K. Tatsumi and K. Yamaguchi, *Theor. Chim. Acta.* **26**, 43 (1972); [g]H. Fujimoto, S. Yamabe and K. Fukui, *Bull. Chem. Soc. Jpn.* **45**, 2424 (1972); [h]W. A. Goddard, III, *J. Am. Chem. Soc.* **94**, 793 (1972); [i]G. Klopman, *Chemical Reactivity and Reaction Paths* (Edited by G. Klopman), pp. 135–138. Wiley-Interscience, New York (1974); [j]H. E. Zimmerman, *Acc. Chem. Res.* **5**, 393 (1972), *Pericyclic Reactions* (Edited by A. P. Marchand and R. E. Lehr), Vol. 1, pp. 93–97. Academic Press, New York (1977); [k]W. W. Schoeller, *Angew. Chem. Int. Ed. Engl.* **20**, 698 (1981).

[2] N. G. Rondan, K. N. Houk and R. A. Moss, *J. Am. Chem. Soc.* **102**, 1770 (1980).

[3] Communications of this work: K. N. Houk and N. G. Rondan, *J. Am. Chem. Soc.* **106**, 4293 (1984); K. N. Houk, N. G. Rondan and J. Mareda, *Ibid.* **106**, 4291 (1984).

[4] P. H. Mueller, N. G. Rondan, K. N. Houk, J. F. Harrison, D. Hooper, B. H. Willen and J. F. Liebman, *J. Am. Chem. Soc.* **101**, 5049 (1981); P. H. Mueller, N. G. Rondan, K. N. Houk, J. E. Gano and M. S. Platz, *Tetrahedron Letters* **24**, 485 (1983) and refs therein.

[5] Reviews: W. Kirmse, *Carbene Chemistry*. Academic Press, New York (1971); R. A. Moss, *Carbenes* (Edited by M. Jones, Jr. and R. A. Moss), Vol. I, pp. 153. Wiley, New York (1973).

[6] P. S. Skell and M. S. Cholod, *J. Am. Chem. Soc.* **91**, 7131 (1969).

[7] R. A. Moss and C. B. Mallon, *J. Am. Chem. Soc.* **97**, 344 (1975); R. A. Moss, C. B. Mallon and C. T. Ho, *Ibid.* **99**, 4105 (1977); R. A. Moss, *Acc. Chem. Res.* **13**, 58 (1980).

[8] R. A. Moss, M. Fedorynski and W.-C. Shieh, *J. Am. Chem. Soc.* **101**, 4736 (1979); R. A. Moss, C. M. Young, L. A. Perez and K. Krogh-Jespersen, *Ibid.* **103**, 2413 (1981).

[9] B. Giese and J. Meister, *Angew. Chem. Int. Ed. Engl.* **17**, 595 (1978); B. Giese and W.-B. Lee, *Ibid.* **19**, 835 (1980); B. Giese, W. B. Lee and J. Meister, *Liebigs. Ann. Chem.* 725 (1980).

[10] B. Giese and W.-B. Lee, *Chem. Ber.* **114**, 3306 (1981).

[11] B. Giese, W.-B. Lee and C. Neumann, *Angew. Chem. Int. Ed. Engl.* **21**, 310 (1982).

[12] There is always a possibility that experimental error in measurements can cause $\Delta H^{\ddagger}$ to be related to $\Delta S^{\ddagger}$ [J. E. Leffler and E. Grunwald, *Rates and Equilibria of Organic Reactions*. Wiley, New York (1963)], but the precision of Giese's data seems to be sufficiently good to exclude this trivial possibility.

[13a] J. J. Zupancic and G. B. Schuster, *J. Am. Chem. Soc.* **103**, 944 (1981); J. Zupancic, P. B. Grasse and G. B. Schuster, *Ibid.* **103**, 2423 (1981); P. C. Wong, D. Griller and J. L. Scaiano, *Chem. Phys. Lett.* **83**, 69 (1981); [b]D. Griller, C. R. Montgomery, J. C. Scaiano, M. S. Platz and L. Hadel, *J. Am. Chem. Soc.* **104**, 6813 (1982); D. Griller, L. Hadel, A. S. Nazran, M. S. Platz, P. C. Wong and J. C. Scaiano, *Ibid.*, in press.

[14] We thank Professor Platz for an extensive education on this point.

[15a] N. J. Turro, G. F. Lehr, J. A. Butcher, Jr., R. A. Moss and W. Guo, *J. Am. Chem. Soc.* **104**, 1754 (1982); [b]R. A. Moss, L. A. Perez, N. J. Turro, I. R. Gould and N. P. Hacker, *Tetrahedron Letters* **24**, 685 (1983).

[16] A. A. Gorman, I. R. Gould and I. Hamblett, *J. Am. Chem. Soc.* **104**, 7098 (1982); G. B. Schuster and J. R. Hurst, *Ibid.* **104**, 6854 (1982).

[17a] Note added in proof: Prof. John F. Garst, University of Georgia, independently pointed out that negative activation energies could arise from entropic barriers in reactions with no potential energy barriers. His conclusions are contained in a manuscript written in 1960! Related theoretical insights are contained in C. Steel and K. L. Laidler, *J. Chem. Phys.* **34**, 1827 (1961).

[18] J. S. Binkley, J. A. Pople and W. J. Hehre, *J. Am. Chem. Soc.* **102**, 939 (1980).

[19a] J. S. Binkley, R. A. Whiteside, R. Krishnan, R. Seeger, D. J. De Frees, H. B. Schlegel, S. Topiol, L. R. Kahn and J. A. Pople, GAUSSIAN 80, Carnegie-Mellon University, Pittsburgh, PA. We thank Professor Pople for the use of GAUSSIAN 82 for some of these calculations. [b]Structures of ethylene and difluorocarbene were obtained from Carnegie-Mellon Quantum Chemistry Archive, R. A. Whiteside, M. J. Frisch, J. S. Binkley, D. J. De Frees, H. B. Schlegel, K. Raghavachari and J. A. Pople, "Carnegie-Mellon Quantum Chemistry Archive", Department of Chemistry, Carnegie-Mellon University, Pittsburgh, PA.

[20] P. C. Hariharan and J. A. Pople, *Theor. Chim. Acta.* **28**, 213 (1973).

[21] C. Moller and M. S. Plesset, *Phys. Rev.* **46**, 618 (1934); J. S. Binkley and J. A. Pople, *Int. J. Quantum Chem. Symp.* **9**, 229 (1975); J. A. Pople, J. S. Binkley and R. Seeger, *Ibid.* **10**, 1 (1976); R. Krishnan and J. A. Pople, *Int. J. Quantum Chem.* **14**, 91 (1978).

[22] Higher-level calculations on the H_2O—$^1CH_2$ complex indicate that more flexible basis sets and correlation energy decreases the stability of complexes, and with zero-point corrections, the complexes are less stable than the reactants: L. B. Harding, H. B. Schlegel, R. Krishnan and J. A. Pople, *Potential Energy Surfaces and Dynamics Calculations* (Edited by D. G. Truhlar), p. 169. Plenum Press, New York (1981).

[23] The conclusion that there is no barrier and no stable complex is likely to survive at better computational levels, since it is known from studies of $CH_2 + H_2$ that the stabilizing interactions in early phases of the reaction increase when large basis sets and correlation energy are used: H. Kollmar and V. Staemmler, *Theor. Chim. Acta* **51**, 207 (1979).

[24a] S. W. Benson, *Thermochemical Kinetics* (2nd Edition). Wiley-Interscience, New York (1976); [b]G. N. Lewis and M. Randall, *Thermodynamics* (Edited by G. N. Lewis and M. Randall), pp. 419–448. McGraw-Hill, New York (1961); [c]J. H. Knox, *Molecular Thermodynamics*, pp. 95–143. Wiley, New York (1978); [d]The vibrational frequencies obtained with a split-valence basis set are usually approximately 10% too large [Y. Yamaguchi and H. F. Schaefer, III, *J. Chem. Phys.* **73**, 2310 (1980)] so that the vibrational entropies are expected to be somewhat too small.

[25] For leading refs, see J. B. Lambert, E. G. Larson and R. J. Bosch, *Tetrahedron Letters* **24**, 3799 (1983).

[26] H. Eyring, *J. Chem. Phys.* **3**, 107 (1935).

[27] D. G. Truhlar and B. C. Garrett, *Acc. Chem. Res.* **13**, 440 (1980); W. B. Hase, *Ibid.* **16** (1983) and refs therein.

[28] C. Doubleday, Jr., R. N. Camp, H. F. King, J. W. McIver, Jr., D. Mullaly and M. Page, *J. Am. Chem. Soc.* **106**, 447 (1984).

[29] We thank Professor Peter Siska for helpful suggestions and encouragement.

[30] H. Johnston and J. Birks, *Acc. Chem. Res.* **5**, 327 (1972) and refs cited.