The Nucleophilicity of a Dialkylcarbene: Unusual Activation Parameters for Additions of Adamantanylidene to Simple Alkenes

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S *Supporting Information*

ABSTRACT: Computational and experimental results demonstrate that adamantanylidene (**1**) behaves as a highly reactive nucleophile toward common alkenes. It is the only known saturated nucleophilic carbene that lacks direct or vinylogous heteroatomic substitution. The activation energy and enthalpy for addition of **1** to methyl acrylate are the most negative values yet encountered in any carbene−alkene addition.

Alkyl and dialkylcarbenes (as distinct from organometallic alkylcarbenoids) generally rearrange too rapidly to undergo efficient intermolecular additions to alkenes.[1] Exceptions occur when intramolecular processes are slowed by the formation of highly strained or energetic products such as anti-Bredt olefins, multicyclic alkanes, or allenes. Apposite carbenes include 7-norbornanylidene,[2] cyclopropylidene,[3] homocub-9-ylidene,[4] and adamantanylidene.[5,6]

Among these, adamantanylidene (**1**, Ad) exhibits a robust and well-developed intermolecular chemistry.[5−7] Long ago, we reported that photolysis of aziadamantane (**2**) afforded Ad, which added to various alkenes to give the derivative cyclopropanes (**3**).[6]

1 (Ad)   2   3   4
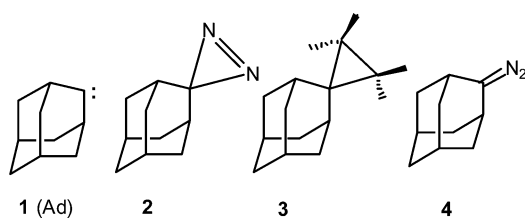
In some cases, small quantities of C−H insertion products, adamantane azine,[5a] 2,4-dehydroadamantane,[8] and adamantanone also formed.[6] Importantly, photoexcitation of diazirine **2** generated not only Ad but also diazoadamantane **4**, by isomerization of **2**.[6,9] Additions of Ad to *cis*- or *trans*-butene were stereospecific, in keeping with additions of singlet Ad, now also known to be the carbene's ground state by ~3−5 kcal/mol.[9−11]

We noted that yields of **3** were significantly greater with electron-poor rather than electron-rich alkene substrates.[6] At the time, we suggested that cyclopropanations of (e.g.) methyl acrylate (MeAcr) or acrylonitrile (AcrCN) did not occur by the addition of Ad, but by 1,3-dipolar additions of **4**, followed by the loss of nitrogen. We rejected the idea that a carbene such as

Ad, expected to be highly reactive, would manifest nucleophilic reactivity toward alkenes.[6]

Here, however, we demonstrate, by both theoretical and experimental evidence, that Ad indeed behaves as a nucleophile toward simple alkenes. Moreover, it is presently unique among the panoply of carbenes as both the least stabilized nucleophilic carbene and the only known saturated nucleophilic carbene that lacks direct or vinylogous heteroatomic substitution.[12]

Recent calculations characterize Ad as an ambiphile that exhibits both high proton and hydride affinities,[10] while in the Mieusset−Brinker scheme, based on computed C−H insertion energies, Ad would likely be classified as a "reactive-nucleophilic" carbene.[7d] In Table S-1 (Supporting Information (SI)), we present the results of our computational studies of Ad and 16 other carbenes. Collected are the HOMO and LUMO energies [HF/6-31G(d,p)//MP2/6-31G(d,p)],[10] chemical potential (μ),[13] hardness (η),[13] absolute electrophilicity (ω),[14] and stabilization energies relative to CH_2 [ΔE_{stab}, B3LYP/6-311++G(2d,p)].[15]

Most importantly, the computed E_{HO} of Ad (−8.4 eV) indicates a frontier orbital much higher-lying than those of typical electrophilic carbenes (in eV: MeCCl, −10.0; PhCCl, −9.6; CCl_2, −10.9), ambiphilic carbenes (MeOCCl, −10.5), or even known nucleophilic carbenes [$(MeO)_2C$, −10.2]. Indeed, the computed E_{HO} of Ad most resembles those of $(Me_2N)_2C$ (−8.2 eV) or *N,N'*-dimethyl-1,3-imidazolidene (−8.3 eV). The accessibility of Ad's HOMO potentiates its nucleophilic behavior toward electron-poor alkenes. Simultaneously, the electrophilicity (ω) of Ad is low (0.33 eV) relative to most of the carbenes in Table S-1 and only greater than the ω of known nucleophiles such as MeCOMe,[16] $(MeO)_2C$,[17] and amino-substituted carbenes.

The computed E_{LU} of Ad at 3.0 eV is higher than E_{LU} of the electrophilic carbenes of Table S-1, which range from 0.6 eV (CBr_2) to 2.7 eV (CF_2). However, the E_{LU} of Ad is *lower* than that of ambiphilic MeOCCl[18] (3.1 eV) and much lower than the E_{LU} of the nucleophiles MeCOMe, $(MeO)_2C$, or the amino-substituted carbenes (4.0−5.9 eV). The high-lying HOMO and relatively low-lying LUMO of Ad are consistent with accessible ambiphilicity.[10] Finally, the ΔE_{stab} of Ad (26 kcal/mol) is more than 13 kcal/mol lower than the ΔE_{stab} values of any of the 16 other carbenes in Table S-1, lower by ca. 33 kcal/mol than that of MeCOMe, and lower than those of $(MeO)_2C$ and the amino-substituted nucleophilic carbenes by

60 kcal/mol or more. Ad should therefore be much more reactive than typical ambiphilic or nucleophilic carbenes.

From the data of Table S-1, Ad appears to be a highly reactive ambiphilic/nucleophilic carbene. Its expected behavior toward alkenes can be further refined by examining the energetics of the frontier molecular orbital interactions between Ad and the alkenes. Specifically, we calculate the *differential* orbital energies $\Delta\varepsilon_E$ ($\varepsilon^{LU}_{Ad} - \varepsilon^{HO}_{C=C} = p - \pi$) and $\Delta\varepsilon_N$ ($\varepsilon^{LU}_{C=C} - \varepsilon^{HO}_{Ad} = \pi* - \sigma$), corresponding to the electrophilic and nucleophilic transition state interactions of Ad and an alkene.[19]

Neglecting orbital overlap, a smaller $\Delta\varepsilon$ results in greater TS stabilization, lower activation energy, and faster cycloaddition.[19] These "back of the envelope" calculations appear in Tables S-2 and S-3. We see that $\Delta\varepsilon_N < \Delta\varepsilon_E$ for the additions of Ad to *both* electron-rich and -poor alkenes: Ad is thus predicted to exhibit nucleophilic selectivity toward alkenes, similar to that of MeCOMe,[16] and distinct from the ambiphilicity of MeOCCl,[18,19] or the electrophilicity of CCl$_2$.[19,20] The nucleophilicity of Ad should resemble that of the stable aminocarbenes or alkylaminocarbenes.[21]

We prepared diazirine **2** by literature procedures.[6,22] Laser flash photolysis (LFP, 351 nm, 60−70 mJ) of a pentane solution of **2** ($A_{372} \approx 0.5$) containing 0.123 M pyridine afforded a strong signal for the Ad-pyridine ylide at 372 nm (reported at 390 nm in benzene[11]); cf. Figure S-1. The absolute rate constant for the addition of Ad to diethyl fumarate was determined by the ylide probe method,[23] wherein the apparent rate of ylide formation increased upon addition of an alkene at a constant concentration (0.123 M) of pyridine. Linear correlation of the observed rate constants for ylide formation vs [alkene] afforded a slope equal to k_{add} for the addition of Ad to the alkene. We thus obtained $k_{add} = 3.4 \times 10^6$ M^{-1} s^{-1} for the addition of Ad to diethyl fumarate in benzene, in reasonable agreement with the reported[11] value of 1.5×10^6 M^{-1} s^{-1}. See the SI for graphical displays of all kinetics data.

k_{add} was similarly measured for the additions of Ad in pentane to 2-ethyl-1-butene, 1-hexene, MeAcr, and AcrCN. Only alkenes with terminal methylene groups were used so as to minimize carbene/alkene steric interactions.[6] Averaged rate constants from duplicate runs are displayed in Table 1, where they are compared to analogous data for additions of CCl$_2$.[20,24,25]

Table 1. Rate Constants (M^{-1} s^{-1}) for Additions of Adamantanylidene[a]

alkene	CCl$_2$[b]	Ad
CH$_2$=CEt$_2$	5.2×10^{8c}	1.78 ($\pm$0.04) $\times 10^5$
CH$_2$=CHBu	1.8×10^7	2.63 ($\pm$0.02) $\times 10^5$
CH$_2$=CHCO$_2$Me	5.9×10^5	4.18 ($\pm$0.03) $\times 10^7$
CH$_2$=CHCN	4.9×10^5	1.33 ($\pm$0.08) $\times 10^8$

[a]In pentane, 24−25 °C. Errors are average deviations of duplicate runs. [b]Data are from ref 20, except as noted. [c]Datum for isobutene, extrapolated from k_{add}(Me$_2$C=CMe$_2$) = 4.7×10^9 M^{-1} s^{-1} (ref 20) and k(Me$_2$C=CMe$_2$)/k(Me$_2$C=CH$_2$) = 9.0 (ref 24).

Remarkably, the reactivity pattern of Ad toward the four alkenes of Table 1 is the *inverse* of the reactivity pattern of CCl$_2$; the electrophilic selectivity of CCl$_2$ is replaced by the nucleophilic selectivity of Ad. The latter resembles the behavior of MeCOMe: the relative reactivities of Ad toward Et$_2$C=CH$_2$, CH$_2$=CHCO$_2$Me, and CH$_2$=CHCN are 1:235:747, while

those of MeCOMe[16] are 1:166:315.[26] Indeed, the nucleophilicity of Ad might have been inferred from its more rapid addition to the electron-poor diethyl fumarate ($k_{add} = 1.5 \times 10^6$ M^{-1} s^{-1}) than to the electron-rich *n*-butyl vinyl ether ($k_{add} = 3.8 \times 10^5$ M^{-1} s^{-1}),[11] and from its addition to the cyano group of fumaronitrile.[7c]

Computationally, Ad manifests an occupancy of 1.9 e in its carbenic σ lone pair[10] (HOMO) which, coupled with the energetic accessibility of this orbital ($E_{HO} = -8.4$ eV), accounts for Ad's nucleophilicity toward common alkenes. Simultaneously, hyperconjugative electron donation (amounting to 0.2 e) from vicinal C−C σ orbitals into the vacant p orbital at the carbenic center (LUMO) moderates Ad's electrophilicity.[10] We note that in reacting with the electron pairs of thiophene or pyridine to yield the appropriate ylides[11] Ad displays residual electrophilic character. Taken together with the nucleophilic behavior Ad displays toward alkenes, its intrinsic ambiphilicity[10] becomes readily apparent.

We attempted to locate TS's for additions of Ad to the alkenes of Table 1 through DFT calculations employing a number of functionals and 6-311+G(d) basis sets (see SI for details). Computed activation parameters are presented in Table 2 (MN12-SX functional).[27] Strikingly, the *computed*

Table 2. Computed Activation Parameters for Additions of Adamantanylidene (MN12-SX/6-311+G(d))[a]

alkene	$\Delta E^{\ddagger}$	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$	$\Delta G^{\ddagger b}$
CH$_2$=CEt$_2$	−2.8	−2.0[c]	−45[c]	11.5	10.3
CH$_2$=CHBu	−3.9	−3.0	−42	9.4	10.1
CH$_2$=CHCO$_2$Me	−5.3	−4.6[c]	−40[c]	7.3	7.1
CH$_2$=CHCN	−5.2	−4.6	−36	6.2	6.4

[a]Energy values in kcal/mol, entropy values in e.u. (shown to 2 places); computed relative to the lowest energy conformers of the separated reactants. [b]Experimental data derived from $k_{add} = (RT/h) \exp(-\Delta G^{\ddagger}/RT)$; k_{add} data from Table 1. [c]See text for experimental values.

activation potential energies and enthalpies are appreciably negative for all four alkenes of Table 1 (e.g., values of $\Delta H^{\ddagger}$ range from −2.0 kcal/mol to −4.6 kcal/mol). Furthermore, very negative entropies of activation are computed (as is customary for carbene−alkene cycloadditions)[28−30] leading to overall positive free energies of activation. The computed and measured activation free energies trend similarly and are in remarkable numerical agreement. Calculations with several other functionals produce similar results (Table S-4); the observed experimental trend is consistently reproduced, and with generally very good numerical agreement.

Encouraged by these computational results, experimental activation parameters for additions of Ad to 2-ethyl-1-butene and MeAcr were derived from measurements of k_{add} at five temperatures between 274 and 309 K. Temperatures were precise to ±0.1 K, and the resulting Arrhenius correlations appear in the SI. Values of the activation parameters, determined from the slope and intercept of the correlations, are as follows: (2-ethyl-1-butene) $E_a = -1.2$ kcal/mol, $\Delta H^{\ddagger} = -1.8$ kcal/mol, $\Delta S^{\ddagger} = -40$ e.u., and $\Delta G^{\ddagger} = 10.3$ kcal/mol; (MeAcr) $E_a = -3.6$ kcal/mol, $\Delta H^{\ddagger} = -4.1$ kcal/mol, $\Delta S^{\ddagger} = -38$ e.u., and $\Delta G^{\ddagger} = 7.1$ kcal/mol. Note the negative activation energies and enthalpies, which are expected for additions of such a reactive carbene. The numerical agreement with computed $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values (Table 2) is very gratifying.

Negative activation energies have been previously observed for the additions of electrophilic carbenes (PhCCl,[28] CCl$_2$,[29] and CF$_3$CCl[30]) to reactive alkenes such as tetramethylethylene, but these are the first examples involving a nucleophilic carbene, albeit a very reactive nucleophilic carbene. The values obtained for the activation energy and enthalpy of Ad with MeAcr are the most negative values yet encountered in any carbene–alkene addition. As with previously studied highly reactive electrophilic carbenes,[28–30] the free energy barriers to the Ad additions arise from highly unfavorable entropic factors.

Further examination of the computed transition states for the Ad-alkene additions are revealing. All the TS's are "early" and "open," as anticipated for such a reactive species. The TS's for Ad adding to CH$_2$=CEt$_2$ and CH$_2$=CHBu, the reactions with the larger activation barriers (Table 2), are very similar in structure; the former TS is illustrated in Figure 1(left).

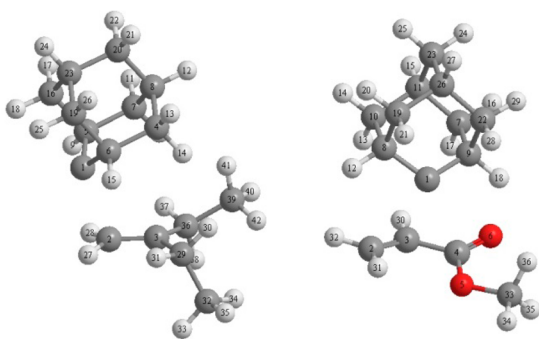**Figure 1.** Transition states for (left) Ad addition to CH$_2$=CEt$_2$ and (right) Ad addition to CH$_2$=CHCO$_2$Me.

In the Ad plus CH$_2$=CEt$_2$ TS, the carbene center is positioned on the 'outside' of the unsubstituted alkene C2-atom (angle C1–C2–C3 = 106.3°) with most of the Ad core positioned on the 'inside', above the alkene double bond. The C(carbene)–C(alkene) distances are long and significantly different (C1–C2 = 2.29 Å; C1–C3 = 2.97 Å). Bond formation is more developed at the unsubstituted alkene carbon. The lengthening of the alkene double bond is small (δ = 0.02 Å), and the puckering angle at the unsubstituted carbon is 13.5°, with the CH$_2$ group bending away from the approaching Ad; changes in Ad geometry are hardly discernible. The carbene tilt angle, ζ, defined as the angle between the carbene C5–C1–C6 bisector and the alkene C=C bond[15] is approximately 52°, indicating strong nucleophilic character for Ad. The net electron transfer in the TS is 0.08e from Ad to CH$_2$=CEt$_2$, also supporting the dominance of the nucleophilic interaction. The reaction coordinate at the Ad plus CH$_2$=CEt$_2$ TS is animated in the SI and appears to represent an unhindered nucleophilic carbene addition.

The TS for Ad plus CH$_2$=CHCO$_2$Me, Figure 1 (right), is qualitatively similar to that for Ad addition to CH$_2$=CHCN, but different from the TS illustrated in Figure 1(left). Now the Ad molecule has rotated substantially relative to its orientation in Figure 1(left), and the carbene center is positioned distinctly outside the alkene double bond in a 'pocket' formed by the linked atoms C2, C3, C4, and O5; the divalent carbon center is almost equidistant from these atoms (C1–C2 = 3.12 Å; C1–C3 = 3.26 Å; C1–C4 = 3.31 Å; C1–O5 = 3.43 Å). The changes in the central bond lengths of CH$_2$=CHCO$_2$Me in the TS are all <0.005 Å (relative to the free alkene), and the net electron transfer is only 0.02e, from Ad to CH$_2$=CHCO$_2$Me.

The reaction coordinate at the Ad plus CH$_2$=CHCO$_2$Me TS is animated in the SI and resembles a twist mode that reorients the Ad relative to the alkene π-bond. These results are consistent with an extremely early TS for the Ad plus MeAcr addition. It was verified that all the TSs connect to weakly bound Ad/alkene complexes in one direction along the reaction coordinate and to the cyclopropane products in the opposite direction. Details appear in the SI.

The peculiar orientation of Ad in the TSs for addition to MeAcr and AcrCN may result from weak long-range interactions. The molecular electrostatic potentials of these alkenes appear moderately attractive to negative charge (viz. the carbenic lone pair) in the region of the TS and the local minimum preceding the TS. For a highly reactive carbene such as Ad, long-range electrostatic interactions may conceivably provide a steering mechanism to access the best path to product.

In our previous studies of halocarbene additions to simple alkenes, the calculated $\Delta S^{\ddagger}$ values were always much more negative than the observed values.[29] We,[29] and others,[31] have attributed this at least in part to the solvent inhibiting the reacting molecules, restricting translational and rotational motions in the condensed phase. Specific interactions occurring with the solvent, e.g. van der Waals or dipolar interactions, may also be invoked as a cause of increased (less negative) entropies for bimolecular reactions in solution. In the present study, the observed $\Delta S^{\ddagger}$ is very close to the computed value and hence close to the value expected for a bimolecular reaction in the gas phase. Ad appears to react with simple alkenes in solution almost as if the reactions were occurring in the gas phase with no solvent present. A reviewer suggested that "Ad is large and rigid compared to halocarbenes and solvent molecules, so that the rotational, translational, or even vibrational motions of Ad should be less affected by solvation than those of halocarbenes."

In conclusion, the additions of adamantanylidene to simple alkenes uniquely combine high carbenic reactivity, strongly expressed nucleophilicity, and unusually negative activation energies, enthalpies, and entropies.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

Spectroscopic and kinetics data, computational details and results. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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