

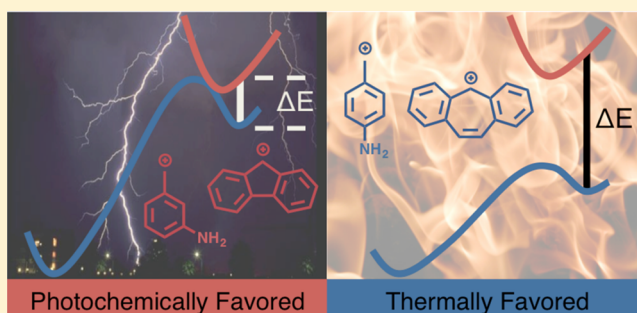
Inverted Substrate Preferences for Photochemical Heterolysis Arise from Conical Intersection Control

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S Supporting Information

ABSTRACT: Heterolytic bond scission is a staple of chemical reactions. While qualitative and quantitative models exist for understanding the thermal heterolysis of carbon–leaving group (C–LG) bonds, no general models connect structure to reactivity for heterolysis in the excited state. CASSCF conical intersection searches were performed to investigate representative systems that undergo photoheterolysis to generate carbocations. Certain classes of unstabilized cations are found to have structurally nearby, low-energy conical intersections, whereas stabilized cations are found to have high-energy, unfavorable conical intersections. The former systems are often favored from photochemical heterolysis, whereas the latter are favored from thermal heterolysis. These results suggest that the frequent inversion of the substrate preferences for nonadiabatic photoheterolysis reactions arises from switching from transition-state control in thermal heterolysis reactions to conical intersection control for photochemical heterolysis reactions. The elevated ground-state surfaces resulting from generating unstabilized or destabilized cations, in conjunction with stabilized excited-state surfaces, can lead to productive conical intersections along the heterolysis reaction coordinate.



INTRODUCTION

The structures of organic molecules that undergo photoheterolysis to generate carbenium ion pairs defy the chemical intuition developed for thermal heterolysis. Known photoheterolysis reactions frequently generate classic examples of unstable carbenium ions, such as π -donor unconjugated ions,^{1,2} antiaromatic ions,^{3–5} and dicoordinated aryl/vinyl cations.^{6–8} Few examples report efficient heterolysis to generate stabilized cations. To date, no model connects structure to reactivity for these photoreactions, and many of the known photoremovable protecting groups,⁹ or photocages, have been discovered serendipitously or through empirical investigations. The lack of a structure–reactivity relationship for photoheterolysis reactions has hindered the rational design of new structures that undergo photoheterolysis, which are reactions of applied importance in materials,¹⁰ synthetic,^{8,11} medicinal,¹² and biological chemistry.¹³

In this Article, we attempt to understand why successful photochemical heterolysis reactions of C–LG bonds frequently generate unstabilized carbocations, the opposite of structural preferences for thermal heterolysis reactions. Inspired by Zimmerman's,^{14,15} Turro's,¹⁶ and Michl's¹⁷ early investigations on the importance of conical intersections in photoreactions, Zimmerman's later investigations into the role of the conical intersection for explaining the “*meta* effect”,¹⁸ and more recent computational advances in searching for conical intersections in complex chemical systems,^{19–23} we investigated the hypothesis that these surprising photoreactivities might be linked to

conical intersection control,²³ the concept that an increasing number of photoreactions are thought to proceed via radiationless, nonadiabatic mechanisms, channeling from the excited-state surface to the ground-state surface via an intersection where the surfaces join.^{24,25} As a result, the role and importance of the conical intersection for nonadiabatic photoreactions has been likened to that of the transition state for thermal reactions in terms of governing the photoreaction.²⁶ For example, the propensity of many photoreactions to generate strained molecules has been attributed in part to conical intersection control,¹⁶ wherein highly strained photoproducts are located at energetic spikes on the ground-state surfaces leading to nearby conical intersections with the excited state, providing a productive channel for the photoreaction to proceed from the excited-state to the strained ground-state minimum.

Similarly, we hypothesized that generation of certain unstabilized carbenium ions, while disfavored thermally, might be favored photochemically by elevating the ground-state heterolysis reaction coordinate surface at the ion pair geometry. In combination with a stabilized excited-state surface at this geometry, a productive conical intersection may result that provides a channel for the photoreaction to proceed from the excited-state to the ground-state ion pair, making the photoheterolysis reaction pathway for these structures com-

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petitive with unproductive photophysical processes (internal conversion, luminescence, etc.). In contrast, heterolysis reactions that generate stable cations necessarily have lowered ground-state surfaces along the heterolysis reaction coordinate, making it less likely for these structures to have a nearby productive conical intersection near the ion pair (Figure 1).

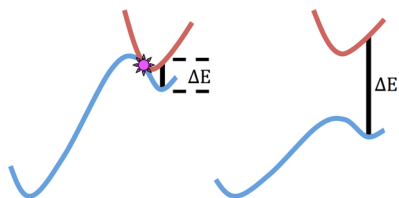


Figure 1. Schematic of hypothesis that a destabilized ground state and a stabilized excited state can lead to a favorable, nearby conical intersection. Black line indicates how S_0 – S_1 excited-state vertical energy gap for carbocation may act as a convenient, easy-to-calculate probe for a nearby conical intersection.

To test the hypothesis that these unstabilized cation structures have favorable, nearby conical intersections, we performed conical intersection searches of representative cations in combination with an excited-state energy gap probe approach that allowed us to expand our investigation to a larger number of systems. We find that stable cations, such as those with conjugated π -donors or aromatic cations, generally have higher-energy conical intersections relative to their excited-state minima. In contrast, certain unstabilized or destabilized cations (e.g., nonconjugated donor-substituted cations, antiaromatic cations, substituted aryl cations, etc.) have stabilized excited states and lower-energy, nearby conical intersections (see Figure 2). Our results suggest that the orthogonal substrate preferences between thermal and non-adiabatic photochemical heterolysis reactions may arise from conical intersection control.

COMPUTATIONAL METHODS

Conical intersections were computed using complete π active spaces for the cations in the gas phase employing the state-averaged CASSCF procedure implemented in GAMESS,^{27,28} using the 6-31G(d) basis set (giving equal weighting to ground state and excited state). Empty σ orbitals were also included in the active space (e.g., for *p*-aminophenyl cation). For the purposes of this Article, we use the term “conical intersection” to refer to the lowest energy point on the seam connecting two potential energy surfaces (sometimes called the minimum energy crossing point). Details can be found in the Supporting Information. For example, the *m*-aminobenzyl cation was computed using a (8,8) active space, consisting of eight π electrons in the eight π orbitals. To ascertain the energy gaps between the ground-state and excited-state surface, we used time-dependent density functional theory (TD-B3LYP/6-311+G(2d,p)) at the DFT-optimized geometries (RB3LYP/6-31G(d)) using Gaussian 09.²⁹ TD-DFT is known to give reasonable results for excited-state energy gaps,^{30,31} provided the ground state can be described predominantly by a single reference wave function. By computing the conical intersection and excited-state energies of the cation (and neglecting the leaving group), we assume that the photochemistry occurs to the greatest extent on the part of the molecule that becomes the cation moiety and not the leaving group. This approach was employed by Zimmerman for studying the *meta* effect^{14,15} and appears to be a reasonable assumption, because experimentally these excited-state substituent effects appear to be largely independent of the leaving group. For example, known photocage structures undergo efficient photoheterolysis with a variety of different leaving groups, suggesting that

the photochemistry is largely directed by the structure of the cation than by the leaving group. Typical leaving groups include phosphates (e.g., ATP),³² carbamates,³³ carbonates,³⁴ carboxylates,³⁵ and even “bad” leaving groups such as OH^- . We have supported this idea independently by computing the excitation energies of **12** with acetyl, chloro, and hydroxy leaving groups and found that both the nature of the absorption and the excitation energy of the highest electron are largely unperturbed (254, 287, and 271 nm, respectively). Givens has also found that the rate of release in the excited state is affected by the nature of the leaving group (with “better” leaving groups leading to faster release in the excited state), but not the photochemical preferences.⁹ Additionally, by neglecting the leaving group from our calculations, we assume that the relative cation ground-state and excited-state energies are not, to a major degree, influenced by ion pairing. However, it should be noted that a number of studies³⁶ have demonstrated the importance of the topology of the conical intersection (i.e., sloped/peaked) on the dynamics of the photo-reaction. To this end, it should be noted that a drawback of neglecting the leaving group is that it renders information about the topology of the conical intersection to be less useful, and we are limited to making conclusions of the energetic viability of the conical intersection between the closed-shell singlet and open-shell singlet of the carbocation.

COMPUTATIONAL RESULTS

Carbocations that were included in this computational study are shown in Chart 1. Some of these carbocations result from photoheterolysis reactions of known substrates (structures **7–9**, **12–14**, **16**, **21**, **22**, **26–28**, **31**, **32–35**³⁷), or are simplified structures of known substrates for computational convenience (e.g., cation **15** is a chemically simplified version of the known substrate **21**, while **20** is a chemically simplified version of **26**). Other cations included in our study are those that result from substrates that are empirically known to not undergo efficient photoheterolysis (e.g., **10**, **30**). The remaining cations (**1–6**, **11**, **17–19**, **23–25**, **36–39**) were investigated to understand the effect of chemical structure on the ground-state–excited-state energy gap, which we propose may be useful as a simple computational probe for the presence of a nearby conical intersection. Photochemical substrates that do not involve direct heterolytic scission from the excited state, such as the *o*-nitroaromatic caging systems, are not relevant to the present discussion and were omitted from this study.

Many of the known successful photoheterolysis reactions that generate carbenium ions have cation structures that fall into three main classes: (1) π -donor unconjugated “benzylic” cations (e.g., 3,5-dimethoxybenzyl cation³⁸ **13**, 9-aminocoumaryl cation^{9,39,40} **26**); (2) cations that are formally antiaromatic following Hückel’s rule (e.g., fluorenyl⁴¹ **28**, indenyl cation⁴² **14**); and (3) dicoordinated carbocations (e.g., donor-substituted vinyl/aryl cations **16**^{6–8}). The unusual nature of these substrates’ favor for photoheterolysis has not gone unnoticed. Pincock and Young⁴² noted that for photoheterolysis of the indenyl cation “efficient generation by this photochemical solvolysis is in sharp contrast to the very low reactivity of related ground-state substrates.” The original report of the “*meta* effect” by Havinga⁴³ noted that rapid heterolysis of *meta*-substituted systems “defies a chemical explanation”. In contrast, the paucity of reports of photoheterolysis in substrates that generate stabilized cations is intriguing. However, two notable cases have been reported as counterpoints to successful photoheterolysis reactions. The precursor to the aromatic ion **5** was reported to not undergo photoheterolysis, while the substrate leading to antiaromatic indenyl cation does undergo facile photoheterolysis;⁴² additionally, *p*-donor-substituted benzylic systems are reported to not undergo photoheterolysis, in contrast to the *meta*-substituted derivatives,¹⁸ giving rise to the so-called “*meta* effect”. However, the observation that photochemical heterolyses generally appear to favor the formation of classic examples of unstable carbocations, while few report the formation of stabilized cations, has to our knowledge not been rigorously addressed.

Conical Intersection Searches for Cations 1–3, 8–10, 14–16, 20. To test the hypothesis that photoheterolysis reactions generate

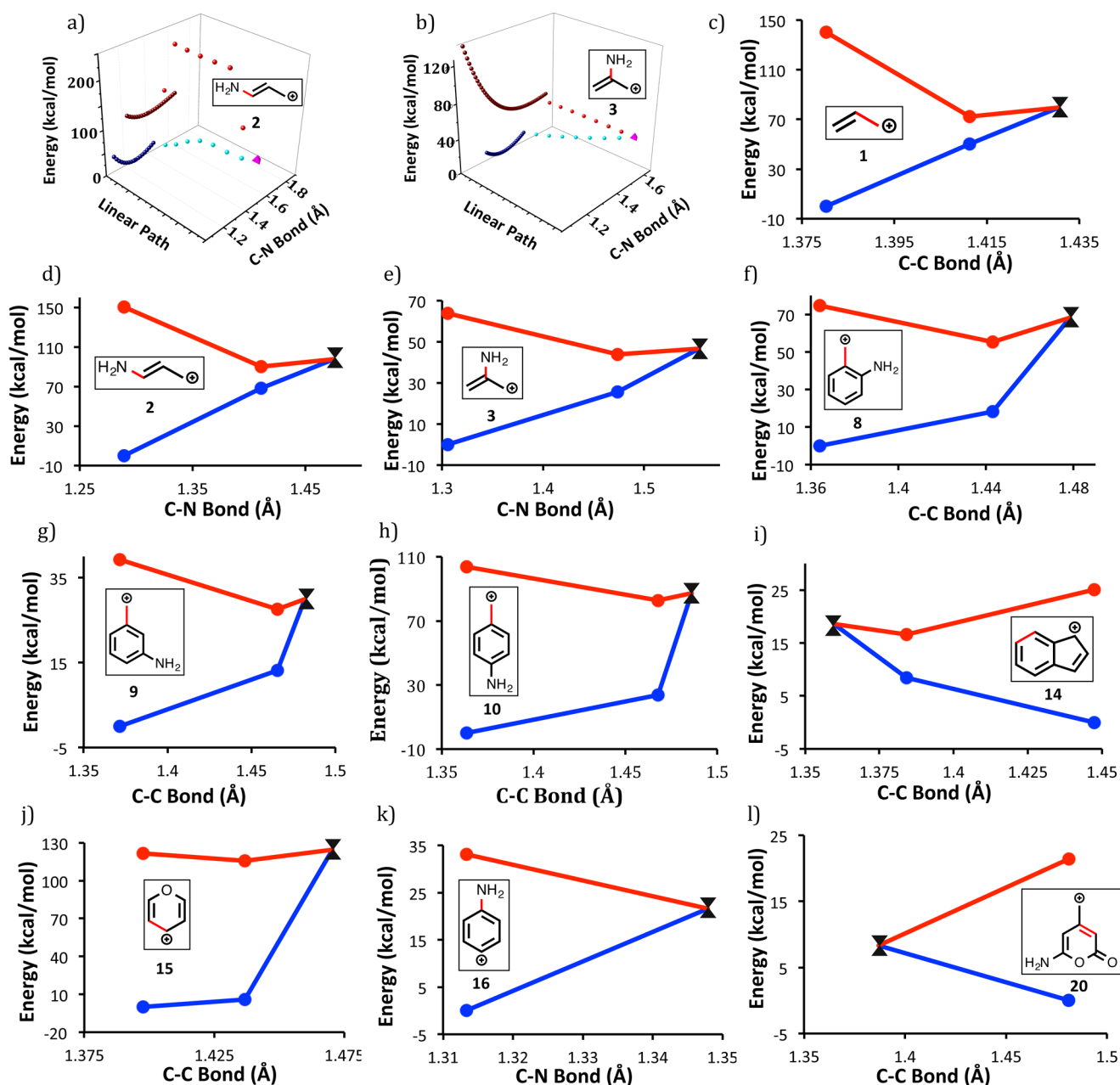
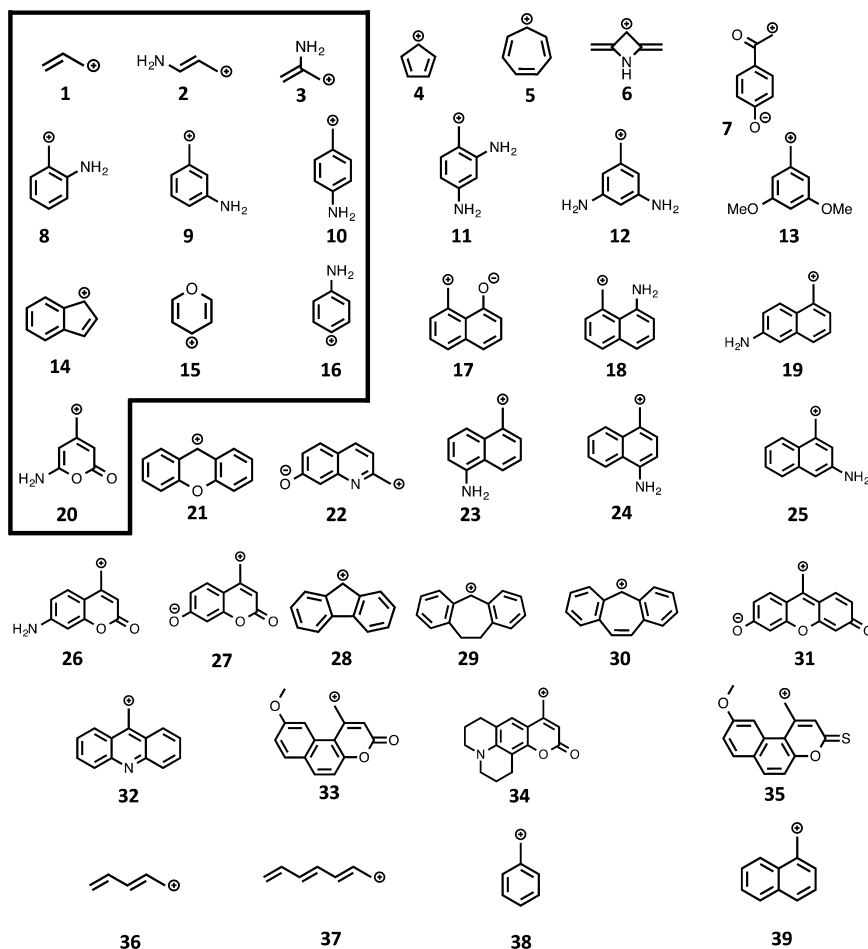


Figure 2. Calculated points on the potential energy surfaces of the cations studied by CASSCF with full π active space. (a,b) 3D graphs of calculated points on S_0 and S_1 surface with linear path to the nearest conical intersection (pink tetrahedron). Paths connecting minimum to CI are linear least motion paths. (c–l) Graphs of the energies of the potential energy surfaces relative to respective ground states: (c) allyl **1**, (d) 1-aminoallyl **2**, (e) 2-aminoallyl **3**, (f) *o*-aminobenzyl **8**, (g) *m*-aminobenzyl **9**, (h) *p*-aminobenzyl **10**, (i) indenium **14**, (j) pyrylium **15**, (k) *p*-aminophenyl **16**, and (l) aminocoumarin analogue **20**. Red bond in the inset shows the bond chosen for the geometrical coordinate, which was chosen on the basis of the bond with the largest deformation between S_0 , S_1 , and the CI. For (a), all points at 250 kcal/mol are off scale, and the zoomed-out graph can be found in Supporting Information Figure S7.

carbocations with favorable conical intersections, we performed conical intersection searches on representative cations that fall within the three major classes of ion favored from photoheterolysis mentioned above as well as the counterpoint substrates that are known to not undergo efficient photoheterolysis. We anticipated that cations resulting from photochemically favored substrates would have low-energy nearby conical intersections, whereas cations resulting from substrates lacking a favored photoheterolysis pathway would have higher energy unfavorable conical intersections. Cations **8**–**10** were chosen for study because *ortho* and *meta* donor-substituted substrates favor photoheterolysis, whereas a *para* donor substituent does not favor photoheterolysis.^{18,44} Cation **20** was chosen as a simplified model system of the cation resulting from the popular 9-aminocoumaryl

photocage **26**, which preserves the unconjugated nature and connectivity of the amine donor substituent but eliminates the benzene ring to yield a system for which a conical intersection search is computationally tractable. Cation **14** is a representative system of the formally antiaromatic cations that are favored from photoheterolysis; pyrylium cation **15** is a simplified version of a known substrate that generates the aromatic ion **21** via an adiabatic photochemical mechanism.^{45,46} Cation **16** is chosen as representative of the dicoordinate carbocations often favored from photoheterolysis. Finally, systems **1**–**3** were investigated as possible simple new systems that may undergo photoheterolysis.

For each of the carbocations, we computed the CASSCF optimized geometries and energies for the ground-state minimum, the first singlet

Chart 1. Structure of Cations Studied^a

^aStructures studied by both TD-DFT and CASSCF conical intersection searches are shown in the box, while structures studied by TD-DFT are shown outside the box.

excited-state minimum, and the conical intersection between the ground state and the singlet excited state. These energies are plotted versus a geometrical coordinate in Figure 2. As can be seen from Figure 2, cations deriving from photochemically favored substrates (9, 14, 16, 20) are found to have low-energy conical intersections relative to the excited-state minimum. Additionally, cations resulting from photochemically favored substrates have small structural deviations between the excited-state minimum and the conical intersection structures, whereas those unfavored systems with high-energy conical intersections have large structural distortions (see Supporting Information Figure S2 for structural overlays of excited-state minimum and conical intersection geometries). Note that in two cases (16, 20) we were unable to locate an excited-state minima, suggesting that there is a direct channel from the Franck–Condon excited state to the conical intersection bypassing a minimum. These results support the idea that conical intersection control is an important feature of these photoheterolysis reactions. Those unstabilized carbocations that are favored from photoheterolysis (or their model systems) have low-energy, nearby conical intersections to the excited-state minimum. In contrast, the stabilized cations have high-energy, distant conical intersections relative to the excited-state minima.

Stabilized-Cation Excited States. Conical intersections occur at biradical geometries.^{47,48} Thus, assuming no major structural deviations in the excited state, cations having favorable nearby conical intersections should have low-energy ion diradical forms. For those species belonging to class 1 described above (donor-unconjugated cations), the excited states resemble stabilized non-Kekule diradical ions (see Figure 4). These diradical forms can be envisioned as

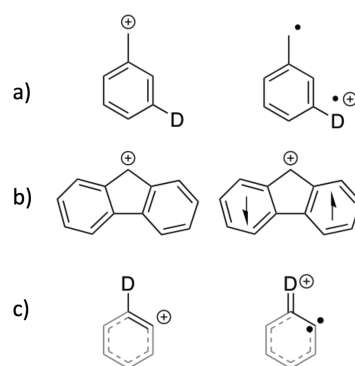


Figure 3. Representations of the different classes of excited-state cations discussed (ground-state cation shown at left, excited-state Lewis representation at right): (a) donor-unconjugated cations and stabilized non-Kekule ion diradical form (right), (b) formally antiaromatic cations, and (c) dicoordinated cations.

deriving from promotion of a π electron on the unconjugated donor substituent to the formally empty cation π^* orbital to provide an ion diradical connected by nondisjoint singly occupied molecular orbitals (SOMOs). This view is supported by our time-dependent density functional theory (TD-DFT) computed difference density plots between the ground state and the excited state (see the Supporting Information). For example, the *meta*-donor-substituted systems have an excited singlet ion diradical form that is electronically analogous to

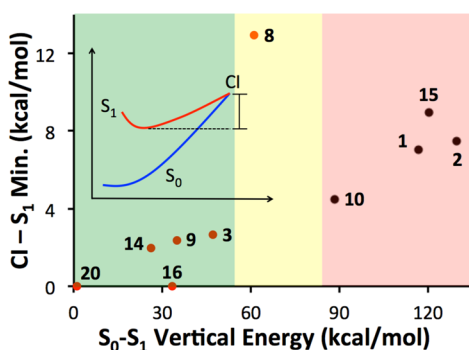


Figure 4. A plot of the difference in conical intersection energy and S_1 minimum energy vs TD-DFT computed S_0 – S_1 Franck–Condon vertical energy gap for the compounds studied. Red points show compounds that are experimentally found to be photoactive or have a nearby conical intersection. Cation 15 is a model system for cation 21 that results from photoheterolysis via an adiabatic mechanism, indicating no nearby conical intersections.

the classic *meta* xylene diradical,⁴⁹ with a radical at the “carbenium center” and a cation radical donor substituent. There are numerous examples of cations that fall within this type (9, 12, 13, 17, 18, 19, 22, 23, 24, 25, 26, 27, 31). Thus, while the donor group does not act to stabilize the ground-state cation via resonance, it leads to stabilized singlet diradical excited states. For ions belonging to class 2 (antiaromatic cations), the excited state resembles a π,π^* cation diradical. These antiaromatic cations are classic examples of cations with low-energy excited states, and Wan has suggested the excited state of these antiaromatic ions may have aromatic character.⁵ Examples falling into class 3 (dicoordinated cations, such as aryl/vinyl cations) have excited states resembling open-shell cationic carbenes. These representations can be seen from inspection of the SOMOs (see the Supporting Information) and are diagrammed in Figure 3.

Excited-State Energy Gaps As a Simple Probe for Nearby Conical Intersections. Unfortunately, the practical difficulty and computational expense associated with computing conical intersections makes a complete investigation of all systems unfeasible. Because we are interested in a broad investigation, we tested the possibility of using the ground-state–excited-state vertical energy gap of the cation to probe for a nearby conical intersection. We considered that low

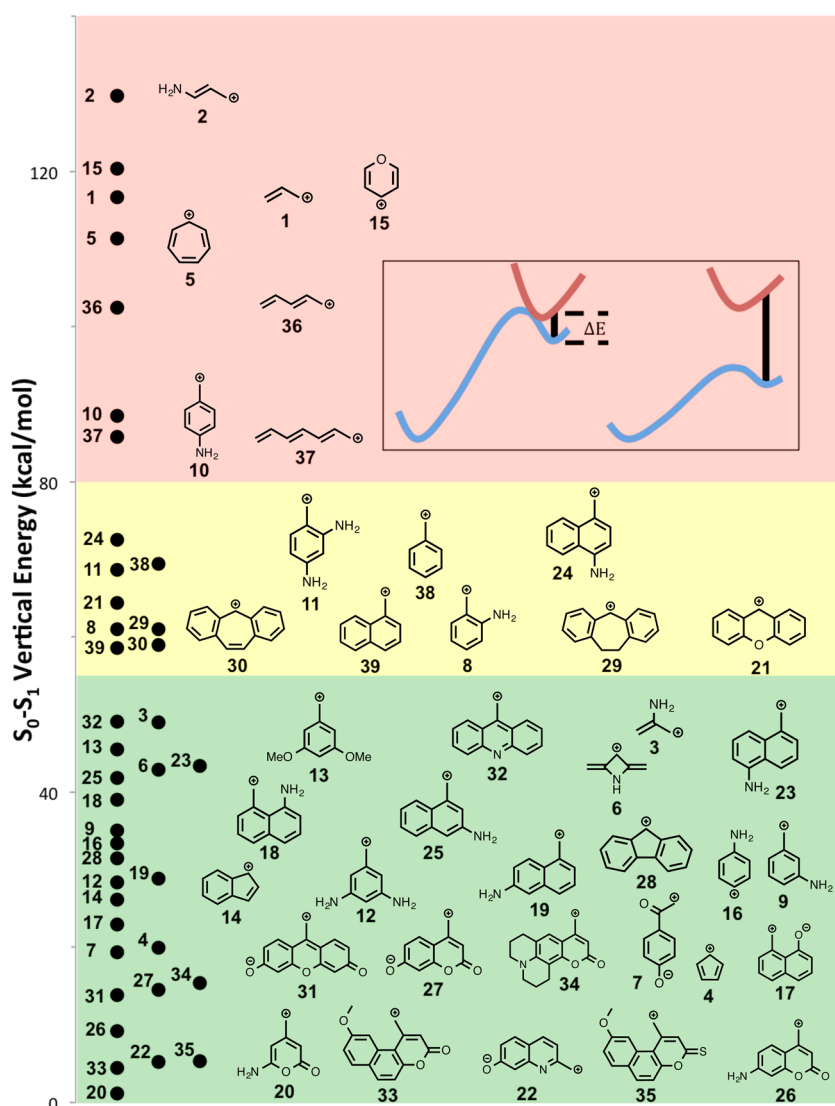


Figure 5. An energy level diagram comparing the Franck–Condon vertical energy gap (TD-B3LYP/6-311+G(2d,p)) of all of the cations studied. Compounds in the green section encompass most of the cations from the photoactive species. The maximum of the green section is where the TD-DFT gap in Figure 4 for the experimentally known cations for photoheterolysis end. Cations in the red sections would not be expected to have low-energy conical intersections. Inset: Hypothesis that a small vertical energy gap suggests a nearby conical intersection.

vertical energy gaps between the cation ground state to the first excited state, which are easily computable using TD-DFT, would implicate a nearby conical intersection, assuming that there are no major structural deformations in the cation excited-state structure. This idea is diagrammed in Figure 1.

A correlation between the energy of the conical intersections of the cations we computed and their excited-state energy gap computed by TD-DFT appears to provide some evidence to support the validity of this approach (see Figure 4), with an apparent inflection point at ca. 60 kcal/mol, where significant barriers between the ground-state minimum and the conical intersection appear. Additionally, the Franck–Condon vertical energy gaps of the unstabilized carbocations that are favored from photoheterolysis are generally lower than for stabilized carbocations (see Figure 5). Cations **1** and **36–39** are included to show the vertical gap of “normal” conjugated cations, indicating that these structures do not have a favorable conical intersection in the default case (see Figure 5).

Photoheterolysis through the π,π^* Triplet Manifold. While the discussion above focused on photoheterolysis through the singlet manifold to generate a singlet cation, some photoheterolysis reactions are reported to go through the triplet state.^{50–52} A natural question is whether the same substituent effects apply similarly to the triplet excited state, which would presumably undergo heterolysis to triplet carbocations to conserve spin. Typically one expects the triplet state to be lower in energy than the singlet excited state, given identical orbital occupation, due to the favorable exchange energy of the unpaired electrons. Thus, cations with low-energy singlet excited states should similarly have low-energy triplet excited states.

Indeed, the cations favored photochemically above generally have low-energy triplet states. In some cases, the triplet state is the ground state for the carbocation. The classic view of a carbenium ion is an approximately sp^2 -hybridized closed-shell species with an empty p orbital. However, *meta*-donor-substituted benzyl cations have very recently been found to have low-energy or ground-state, triplet-ion diradical states,¹ and antiaromatic cations,⁵³ *ortho/para* donor-substituted phenyl cations,⁵⁴ and β -donor substituted vinyl cations⁵⁵ are known to have triplet ground states. It is probably no coincidence that every known carbocation that has a low energy, or ground-state, triplet state belongs to a class of molecules that is favored from photoheterolysis.

Low-energy triplet states for the cations suggest that the π,π^* triplet surface may parallel the singlet surface. Here, the first triplet excited state T_1 would have a conical intersection with a low-energy or ground triplet T_0 surface. For instance, mechanistic studies indicate that the *p*-hydroxyphenacyl system proceeds through a π,π^* triplet surface and the intermediacy of a triplet cation,⁵² and the *p*-substituted phenyl cations are generated on the triplet surface.^{6,11,51} Thus, those photoreactions that are favored through the singlet manifold may also be favored in a π,π^* triplet manifold as well. The same substituent effects described above for the singlet excited state may similarly apply to the triplet π,π^* excited state. Additionally, the presence of low-energy triplet states for many cations resulting from photoheterolysis suggests that the singlet–triplet gap of the carbocation may also prove to be a useful probe of a nearby conical intersection, with a ground state or low-energy triplet state of the carbocation implying a low-lying singlet-diradical state and a nearby conical intersection with the closed-shell state.

DISCUSSION

The preponderance of successful photochemical substrates leading to cations with excited states resembling non-Kekule ion diradicals led us to consider related structures that would have lowered-energy excited states. The simplest non-Kekule diradical is the trimethylene methane diradical. The analogous cation of this structure bearing a donor substituent, 2-aminoallyl cation **3**, would be expected to have a low-energy excited state, while the conjugated 1-aminoallyl cation **2** would not be expected to have this lowered energy excited state.

Indeed, the energy from S_0 minimum to S_1 minimum for **2** is 88.2 kcal/mol, while the same gap for **3** is 43.8 kcal/mol (see Figure 2). Additionally, the energy gaps between the conical intersection and the S_1 minimum for **2** and **3** are 7.5 and 2.7 kcal/mol, respectively, supporting the idea that the 2-aminoallyl cation may have access to a productive conical intersection during photoheterolysis, in contrast to the 1-aminoallyl system. These systems would represent a simple but spectacular demonstration of the substituent orthogonality between thermal and photochemical substrate preferences for heterolysis.

It should be noted that alternative mechanisms are available for photoheterolysis other than direct nonadiabatic heterolysis via a conical intersection located on the cation. For instance, the aromatic ion **21**, for which our calculations on the model system **15** indicate has a high-energy conical intersection, is generated efficiently from photolysis, but arises via a less-common adiabatic mechanism, with formation of the singly excited carbocation that relaxes by fluorescence to yield the ground-state ion pair. Additionally, by neglecting the leaving group, we are also not considering the possibility of a conical intersection between the diradical and zwitterionic forms (e.g., $R^{\bullet}LG^{\bullet}$ and R^+LG^-), so a mechanism involving homolytic scission followed by electron transfer may be available. This mechanism may give rise to successful photoheterolysis pathways in systems yielding cations that do not have a conical intersection located on the cation moiety (e.g., possibly ortho-substituted benzylic systems). Generation of highly stabilized carbocations may also arise via hot ground-state photoreactions, although these mechanisms are thought to be rare. Thus, the cation conical intersection (or the vertical energy gap probe) may be more useful in suggesting new systems that are likely to have a productive conical intersection along the heterolysis coordinate than in suggesting systems that will be photostable.

Several other peculiar phenomena fit into place in light of viewing photoheterolysis reactions as being governed by conical intersection control, such as why substrates that undergo photoheterolysis reactions often lead to carbocations that have ground-state or low-energy triplet diradical states: A low-energy triplet diradical state implies a low-energy singlet diradical state and a nearby conical intersection between the closed-shell and diradical configurations. This idea also explains why photoheterolysis reactions to make reactive intermediates other than carbocations are largely successful independent of structure (e.g., photoheterolysis of azides to make nitrenes), because reactive intermediates like carbenes, nitrenes, and nitrenium ions inherently have low-lying diradical states (and by implication, a “built-in” nearby conical intersection), whereas carbocations in the default case do not (e.g., the singlet–triplet energy gap of CH_3^+ , NH_2^+ , NH^+ , and CH_2^+ is ca. –50, 29, 36, and 9 kcal/mol, respectively⁵⁶).¹⁵ Additionally, this hypothesis provides an explanation of why “bad” leaving groups in the ground state, such as hydroxides or alkoxides, can be “good” leaving groups in the excited state, because making a high-energy ion pair would elevate the ground-state surface.⁵⁷

In conclusion, we have shown that carbocations favored from photoheterolysis tend to have nearby, low-energy conical intersections, while stable carbocations from thermal heterolysis tend to have high-energy, distant conical intersections. These findings lend support to the idea that conical intersection control leads to the frequent inverted substrate preferences between nonadiabatic photoheterolysis and thermal heterolysis. It is clear from a great deal of work into conical intersections

that the dynamics of the surface crossings are dramatically affected by the topography of the conical intersections (peaked/sloped). There may prove to be additional insights by computing detailed surfaces and trajectory simulations for these photo reactions, with the leaving group, preferably with explicit water solvation. The idea that these photoheterolysis reactions may be governed by conical intersection control could facilitate the design of new photocages with improved light absorbing properties by searching for substrates leading to carbocations with a favorable built-in conical intersection.

■ ASSOCIATED CONTENT

● Supporting Information

Computational coordinates, absolute energies, raw figure data, orbital difference density plots, and overlaid computed ground state and conical intersection structure. 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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