

Modulating Escape Channels of Cycloheptatrienyl Rhodium Carbenes To Form Semibullvalene

Croix J. Laconsay and Dean J. Tantillo*

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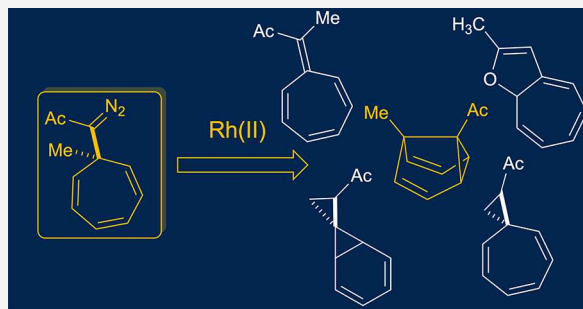


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ABSTRACT: We describe the various escape channels available to dirhodium carbene intermediates from cycloheptatrienyl diazo compounds located with density functional theory. An intramolecular cyclopropanation would, in principle, provide a new route to semibullvalenes (SBVs). A detailed exploration of the potential energy surface reveals that methylating carbon-7 suppresses a competing β -hydride migration pathway to heptafulvene products, giving SBV formation a reasonable chance. During our explorations, we additionally discovered unusual spirononatriene, spironorcaradiene, and metal-stabilized 9-barbaralyl cation structures as local minima.



INTRODUCTION

"While it is mutually advantageous to tie theory with experiment, I still feel that theory should lead, rather than follow experiment in exploring chemistry."

— Paul von Ragué Schleyer¹

"In my opinion, quantum mechanics can make two different contributions to chemistry. Firstly, it permits non-empirical comprehension of experimental results. However, we should not overlook another important aspect: the promotion of empirical chemistry from the theoretical side."

— Kenichi Fukui²

"A beautiful chemical world, of molecules waiting to be made, opens up through the ingenuity of theoretical chemists. Their predictions astound us, generate ideas, and prompt the synthesis of new structures and functions. No exaggeration, none at all, is needed to build this world."

— Roald Hoffmann, Paul von Ragué Schleyer, and Henry F. Schaefer III³

In 1966, by a fortunate stroke of serendipity, Zimmerman and Grunewald introduced semibullvalene (SBV) to the world of chemistry. Upon photolysis of barrelene, they discovered they had synthesized SBV and its C_8H_8 isomer, cyclooctatetraene (COT, Scheme 1a).⁴ In 1972, Zimmerman and Sousa then synthesized cycloheptatrienyldiazomethane and studied its thermal and photochemical rearrangement to products resulting from nitrogen loss and subsequent rearrangement of the carbene intermediate, thinking they might observe SBV among other C_8H_8 products.⁵ They did not. Instead, they isolated benzene, COT, heptafulvene, and acetylene. SBV has been observed⁶ as a side-product of

photochemical reactions leading to COT (COT on the S_1 state is notably a photostable, Baird aromatic D_{8h} energetic sink).^{7–9}

Considering advanced methods for taming carbene reactivity with transition metals (e.g., Rh),¹⁰ we wondered whether metal carbenes might, in theory, pave an alternate way to SBV. Indeed, more than 50 years after its first synthesis, SBV still remains a physical organic chemist's playground,^{11,12} and finding new synthetic routes to SBV and its derivatives would be synthetically useful. Here, we offer a theoretical prediction for a potential synthetic route to SBV via an intramolecular cyclopropanation (CP) using dirhodium carbenes derived from cycloheptatrienyl diazo compounds and describe the complex mechanistic networks surrounding such reactions.

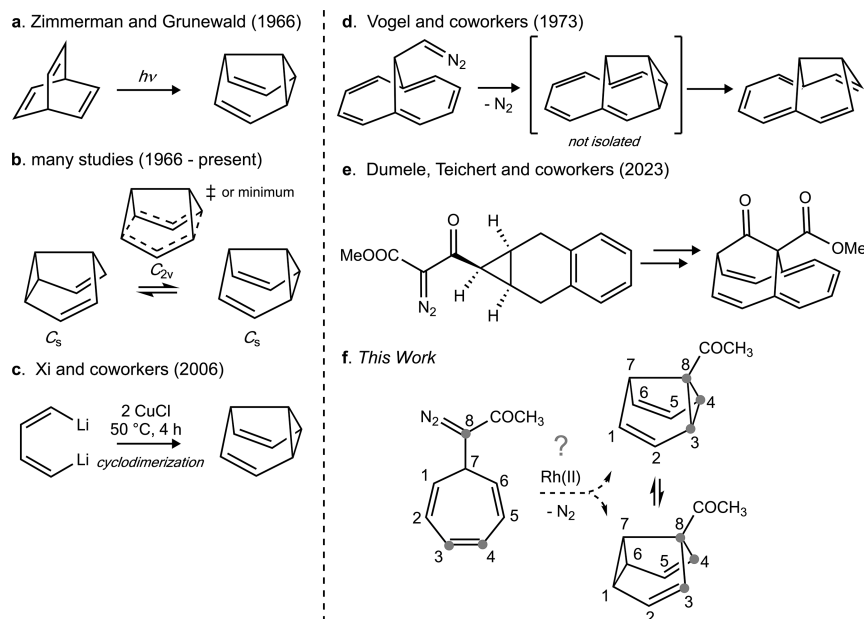
Semibullvalene in Historical Context. SBV is one of the most important molecules in the history of physical organic chemistry. Its rapid, degenerate [3,3]-sigmatropic shift (Hardy–Cope rearrangement)^{13,14} and fluxional¹⁵ (or locked¹⁶) behavior have been points of sustained interest. Other work investigated SBV's electronic structure,^{17–19} heavy-atom tunneling capabilities (a theoretical prediction²⁰ borne out by experiment),^{20–25} and [3,3] rearrangement barrier height²⁶ with quantum calculations. Some even introduced ways to reduce,²⁷ eliminate,²⁸ interrupt,²⁹ and invert the activation barrier for its rearrangement to a homoaromatic minimum (Scheme 1b).^{30–36} Its bromination mechanism³⁷ was examined in detail, as was the dynamic

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Scheme 1. Select Examples of (a–e) Semibullvalene and Related Syntheses to (f) This Work



behavior associated with its formation via a reaction with a post-transition state bifurcation (PTSB).^{38–40}

SBV is a prototypical fluxional carbon cage, a class of molecules that has gained extensive renewed interest. For instance, some have leveraged the fluxionality of related carbon cage molecules, such as bullvalene and barbaralane, for applications in materials and sensing, sparking new interest in the dynamic nature of shapeshifting molecules.^{41–49} Sanchez and Maimone recently used shapeshifting anions in a total synthesis ocellatusone C, highlighting that “the barbaralyl nucleus remains an outstanding synthetic challenge”.⁵⁰ Bullvalenes and SBV fit this mold as well.⁵¹

Efforts to synthesize SBV and SBV derivatives abound (e.g., Scheme 1c),^{52–59} and some are still seemingly stumbled upon by accident.⁶⁰ Much of the work in the late twentieth century on SBV emerged out of a strong interest in homoaromaticity (Scheme 1d),⁶¹ an interest that remains alive today (Scheme 1e).⁶² With the continuous discovery of new reactions, there remains room for breathing new life into SBV synthesis.

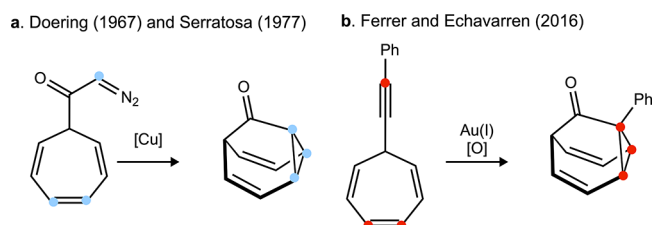
Using quantum chemical computations, we explore the viability of an approach to synthesize monosubstituted SBVs via a dirhodium(II)-catalyzed CP through a metal carbene intermediate (Scheme 1f). Sparked by our own interest in PTSBs, we additionally ask whether CP could lead directly to the [3,3] rearrangement transition structure (TS) (Scheme 1f) by a PTSB.

Targeting Semibullvalene through the Lens of Metal-Carbene Chemistry. Metal-carbene mediated chemistry has a long and winding history.¹⁰ Our group has worked independently and collaborated closely with experimental groups to understand mechanisms of Rh-carbene mediated transformations, including C–H insertion^{63,64} and ylide formation reactions,^{65–67} with the aim of developing synthetically useful models of reactivity and selectivity. This chemistry has proven to be a playground of its own—a family of synthetically relevant organometallic reactions that display behaviors considered by some to be esoteric, but which play important roles in determining product distributions. For example, our group has shown that some C–H insertion

reactions involve cryptic PTSBs that provide facile routes to unwanted side products.^{68–71} Tandem processes⁷² from Rh-carbene intermediates—such as CP/[3,3] rearrangements,^{73–76} which have been applied in total syntheses to access (otherwise difficult to synthesize) seven-membered rings, or C–H insertion/[3,3] rearrangements⁷⁷—also look to involve PTSBs.^{38,68,69,71} This line of work led us to the current Rh-catalyzed strategy to SBV, and our past experience with bifurcations led us to additionally ask whether SBV might be generated by a CP that involves a PTSB (Scheme 1f).

We are not the first to suggest a transition metal-catalyzed synthesis of fluxional molecules from cycloheptatrienes. In 1967, the Doering group discovered a synthetic route to barbaralane from a cycloheptatriene-7-yl diazomethyl ketone,⁷⁸ and building on that work in 1977, Casas and Serratosa synthesized barbaralane with a Cu-carbene mediated CP in their synthesis of bullvalene (Scheme 2a).⁷⁹ Both methods result in products that are net CPs of the diazomethyl ketone with the central π bond of the cycloheptatriene.

Scheme 2. Select Examples of Barbaralane Syntheses by (a) Doering and Serratosa and (b) Ferrer and Echavarren



Recently, Ferrer and Echavarren synthesized barbaralones by gold(I)-catalyzed intramolecular oxidative cyclization of 7-ethynyl-1,3,5-cycloheptatrienes (Scheme 2b).⁸⁰ The same group also reported generation of closely related and highly fluxional barbaralyl cations from 7-alkynyl cycloheptatrienes by gold catalysis.⁸¹ Could Rh(II)-catalysts assist in this type of transformation? When the Echavarren group expanded on this work in 2021, they discovered that the use of Rh(II)-catalysts

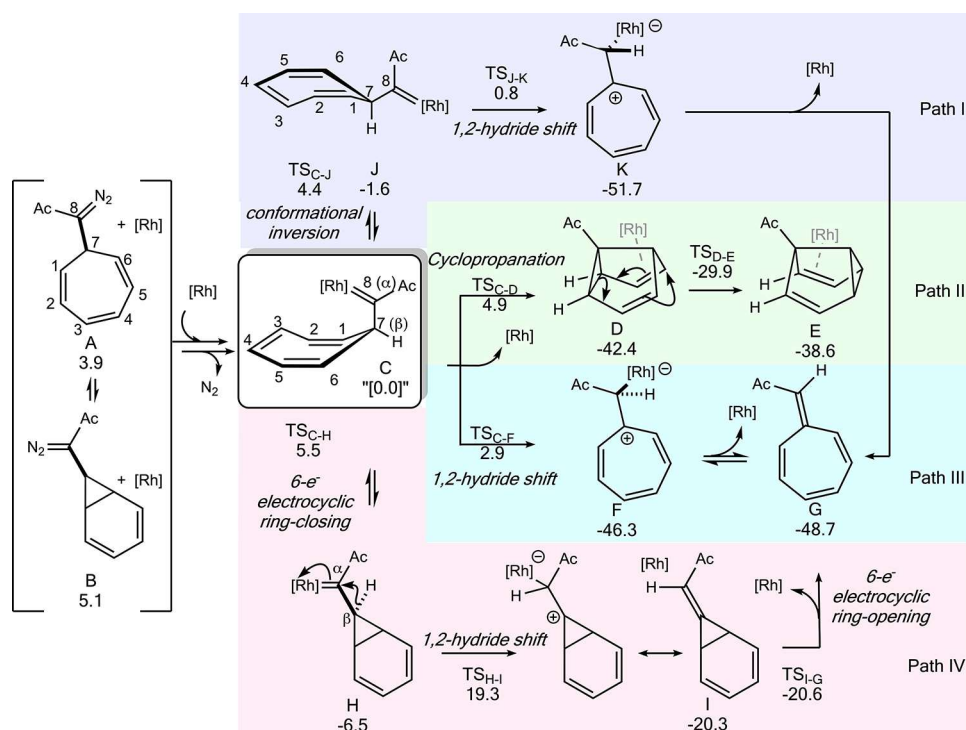


Figure 1. Possible mechanistic pathways to and from C. All relative free energies (PW6B95/def2-TZVP //PW6B95/def2-SVP) are in kcal mol⁻¹. (Path I) Top, purple: conformational inversion followed by 1,2-hydride shift; (Path II) second to top, green: SBV formation by CP and [3,3] rearrangement; (Path III) second to bottom, blue: 1,2-hydride shift; and (Path IV) bottom, red: norcaradiene formation followed by 1,2-hydride shift and electrocyclic ring-opening. [Rh] = Rh₂(OAc)₄.

led to a decarbenation to alkynylcyclopropanes from 7-alkynyl cycloheptatrienes and attributed the result to a lower barrier for decarbenation ($\Delta G^\ddagger = 21.9$ kcal mol⁻¹) than for 6-*endo*-dig cyclization ($\Delta G^\ddagger = 24.4$ kcal mol⁻¹) with the use of Rh(II) catalysts.⁸² Cu(I) catalysts similarly have been shown to work in a synthesis of barbaralyl-substituted allenyl acid esters from terminal alkynes and tropylium tetrafluoroborate.⁸³ Finally, Dumele and Teichert published an intriguing synthesis of 6 π and 10 π neutral homoaromatics during preparation of this manuscript (Scheme 1e).⁶² Their synthetic approach, inspired by the work of Vogel et al.,⁶¹ affords homoannulene esters with a barbaralane framework through an intramolecular, dearomative Buchner reaction.

May cycloheptatrienyl diazo compounds be a reasonable starting point to synthesize SBVs using Rh(II)-catalysts through an intramolecular CP? Our computational explorations allow us to predict^{1,84} that, whether this approach succeeds in the lab, unusual rearrangement chemistry of the metal carbene intermediate will likely reveal itself.

COMPUTATIONAL METHODS

Fluxional molecules are molecules that undergo rapid, degenerate rearrangements according to the International Union of Pure and Applied Chemistry (<http://goldbook.iupac.org>), and they generally have low activation barriers. The degenerate rearrangement of SBV is challenging to accurately predict computationally because it exists on a relatively flat surface—an experimental $\Delta G^\ddagger = 5.5$ kcal mol⁻¹ by ¹³C NMR.⁸⁵ Many have considered the B3LYP⁸⁶ functional reliable for obtaining reasonable geometries, and to a certain extent, reaction barriers that are consistent with the experiment.^{20,87,88} In some cases, however, spurious intermediates and/or significant deviation from experimentally derived activation barriers have clouded the consensus on the reliability of B3LYP for [3,3] rearrangements.^{89,90} Recently, Karton reported that three functionals (BMK, PW6B95, and MN12-

SX) outperformed other functionals in predicting accurate [3,3] barrier heights and reaction energies when compared to CCSD(T)/CBS benchmark calculations and experiment.⁹¹ Based on Karton's benchmark work showing that PW6B95 performs accurately for systems involving SBV and for systems including Rh,⁹² we selected PW6B95⁹³ as a functional with the def2-SVP basis set (i.e., PW6B95/def2-SVP) for geometry optimizations followed by single-point corrections to the electronic energy with a larger basis set (def2-TZVP) at those geometries.⁹⁴ We reasoned that PW6B95/def2-TZVP//PW6B95/def2-SVP is a reasonable level of theory for reactions involving dirhodium catalysts and for qualitative investigations of this kind, which have no experimental precedent against which to compare data. However, we tested PW6B95/def2-TZVP//PW6B95/def2-SVP's ability to predict the [3,3] rearrangement of SBV (experimental barrier: 5.5⁸⁵ to 6.2⁹⁵ kcal mol⁻¹) and the isomerization barrier of cycloheptatriene to norcaradiene (experimental barrier: 7.2 kcal mol⁻¹).⁹⁶ Our predicted barriers of 5.7 and 7.1 kcal mol⁻¹ for the [3,3] and isomerization barriers, respectively, are within chemical accuracy (<1 kcal mol⁻¹, see the Supporting Information for more details).

Geometry optimizations and frequency calculations were carried out with Gaussian 16.⁹⁷ Transition structures (TSs) were identified by the presence of one imaginary vibrational frequency and subsequent intrinsic reaction coordinate (IRC) calculations identified minima on the potential energy surface to which TSs are connected.^{98–100} Quasi-classical ab initio molecular dynamics simulations were run with the Prodyn script package developed by Singleton and co-workers¹⁰¹ at the PW6B95/def2-SVP level of theory. Trajectories were propagated downhill in energy from TS_{C-D} in the reactant and product directions until the C8–C3 and C8–C4 distances were greater than 2.80 Å, for which we report the trajectory as reaching the reactant well, until the C3–C4 distance is less than 1.55 Å and the C8–C3 and C8–C4 distances are less than 1.52 Å, for which we report the trajectory as reaching 'SBV product 1' (the SBV product we found from the IRC calculation), or until the C1–C6 distance is less than 1.55 Å and the C3–C4 distance is greater than 2.00 Å, for which we report the

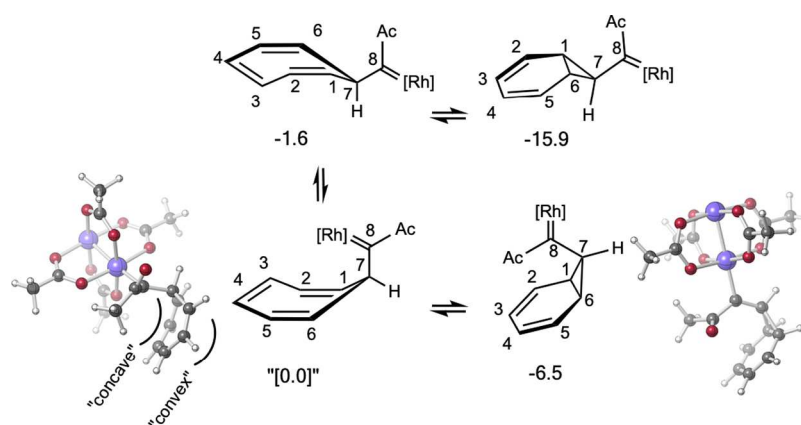


Figure 2. Cycloheptatriene–norcaradiene equilibrium. Three-dimensional depictions highlight the boat conformation of cycloheptatriene with “concave” and “convex” faces. Relative free energies (PW6B95/def2-TZVP//PW6B95/def2-SVP) are in kcal mol^{−1}. [Rh] = Rh₂(OAc)₄.

trajectory as reaching ‘SBV product 2’, the other potential product of a PTSB (Scheme 1f).

RESULTS AND DISCUSSION

Acetyl-Semibullvalene. The simplest reaction that we envisioned might be achieved experimentally is the transformation of diazo compound **A** to acetyl-SBV **D/E** (Figure 1, Path II in green). We chose **R** to be a simple acetyl (Ac = COCH₃) group, given the body of the literature on acceptor and donor/acceptor carbenes.¹⁰² In addition, structures similar to (diazocarbonylmethyl)cycloheptatriene (**A**) have been described in the literature.¹⁰³

Exposure of **A** to a Rh catalyst (here, we model Rh₂(OAc)₄ for simplicity) should lead to nitrogen extrusion to form Rh-carbene species **C**. The barrier for intramolecular CP of **C** to form Ac-SBV **D** (via TS_{C–D}) is predicted to be low (4.9 kcal mol^{−1}). Formation of **D** is also predicted to be highly exergonic (−42.4 kcal mol^{−1}), and its [3,3] rearrangement is predicted to require a 12.5 kcal mol^{−1} barrier (TS_{D–E}) to form the slightly less-favorable **E** (−38.6 kcal mol^{−1}). While these results indicate that formation of Ac-SBV would not face a large barrier, possible competing reactions must be considered.³ For instance, (i) the cycloheptatriene–norcaradiene equilibrium (**C** ⇌ **H**) favors the norcaradiene **H** by 6.5 kcal mol^{−1}, (ii) conformational isomerization slightly favors the isomer wherein the hydrogen at C7, instead of the Rh-carbene, is positioned on the concave face of the cycloheptatriene (Figure 2), and (iii) once the Rh-carbene is formed, side-reactions (such as β-hydride migration to heptafulvenes, e.g., **C** → **F** → **G** or **C** → **J** → **K** → **G**)^{104,105} can occur. Thus, we are unable to ignore the kinetic instability of intermediate **C**. The variety of available escape channels is abundant, so these possibilities were investigated in detail.^{106,107}

Complications I: Electrocyclization. Cycloheptatrienes^{108–110} are generally in rapid equilibrium with norcaradienes (Figure 2).^{111–114} If our desired CP reaction is to predominate, either its barrier must be lower than that for **C** ⇌ **H** equilibration or that equilibration must not lead to an undesired reaction that serves as a kinetic trap. In our system, a π-electron acceptor—the metal carbene group¹¹⁵—exists at the 7-position (C7), and π-electron acceptors at this position tend to favor the norcaradiene isomer. We predict that **H** is lower in energy than **C** (and the **C** → **H** barrier is predicted to be 5.5 kcal mol^{−1}, comparable to the CP barrier to **D**; Figure 1). However, the subsequent 1,2-hydride migration that would

lead to catalyst dissociation is associated with a TS that is much higher in energy than that for CP (a 25.8 kcal mol^{−1} barrier out of **H**; TS_{H–I}). Therefore, the **C** → **H** → **I**... path does not appear to threaten our desired reaction.

Complications II: Conformational Bias. The π-systems of cycloheptatrienes are not flat—instead, their sp³ carbons are bent out of plane, inducing boat-like conformations (cf. Figure 2).¹¹⁶ Parent tropilidene (i.e., hydrogens at C7) has a ring-inversion barrier of ca. 6 kcal mol^{−1} by low-temperature ¹H NMR.^{117–119} As a result, the environments of the two groups on its sp³ carbon are different: one sits over the cycloheptatriene π-system, while the other points “outside”. For CP to occur, the carbene center must reside over the π-system, but the carbene center prefers to reside outside for **C** (by 1.6 kcal mol^{−1}; compare **C** vs **J**, Figure 1, Path I). When the carbene center is outside, a 1,2-hydride shift (a β-hydride migration) can occur (**J** → **K**) that is predicted to be rapid and highly exergonic.¹²⁰ In addition, our computed ring-inversion barrier (TS_{C–J}) is 4.4 kcal mol^{−1}, slightly lower than that for CP, which suggests the β-hydride migration might indeed be a dead-end kinetic trap (Path I).

Complications III: Another β-Hydride Migration. A β-hydride migration may also occur directly from conformer **C** (Figure 1, Path III). While the TS for this 1,2-hydride migration is predicted to be higher in energy than that for **J** (2.9 vs 0.8 kcal mol^{−1}), it is still lower than that for the desired CP step (4.9 kcal mol^{−1}) by 2.0 kcal mol^{−1}.

Tendency to migrate hydride is increased for α-diazo-carbonyl compounds—precursors to (donor/acceptor metal-carbenes)—due to their higher electrophilicity compared to donor and donor/donor metal-carbenes.⁶³ Indeed, in Path III, we find that the barrier for β-hydride migration directly from **C** is increased upon swapping out the carbonyl acyl group for a phenyl group, thereby making the donor/acceptor carbene into a donor/donor carbene (Path III, 2.9 vs 5.9 kcal mol^{−1}; see the SI, Figure S2 for donor/donor pathways). However, though the barrier for β-hydride migration increases upon changing the carbene from donor/acceptor to donor/donor, so does the CP barrier (Path II, 4.9 vs 8.6 kcal mol^{−1}). Swapping the acyl group for a phenyl group does not tip the selectivity in favor of CP to SBV—the data tell us (with a ΔΔG[‡] = 2.7 kcal mol^{−1}) that the reaction would still favor β-hydride migration over CP.

Thus, our metal-carbene may avoid our desired reaction through β-hydride migration escape channels to heptafulvene, **G**. Recall that heptafulvene was one product Zimmerman and

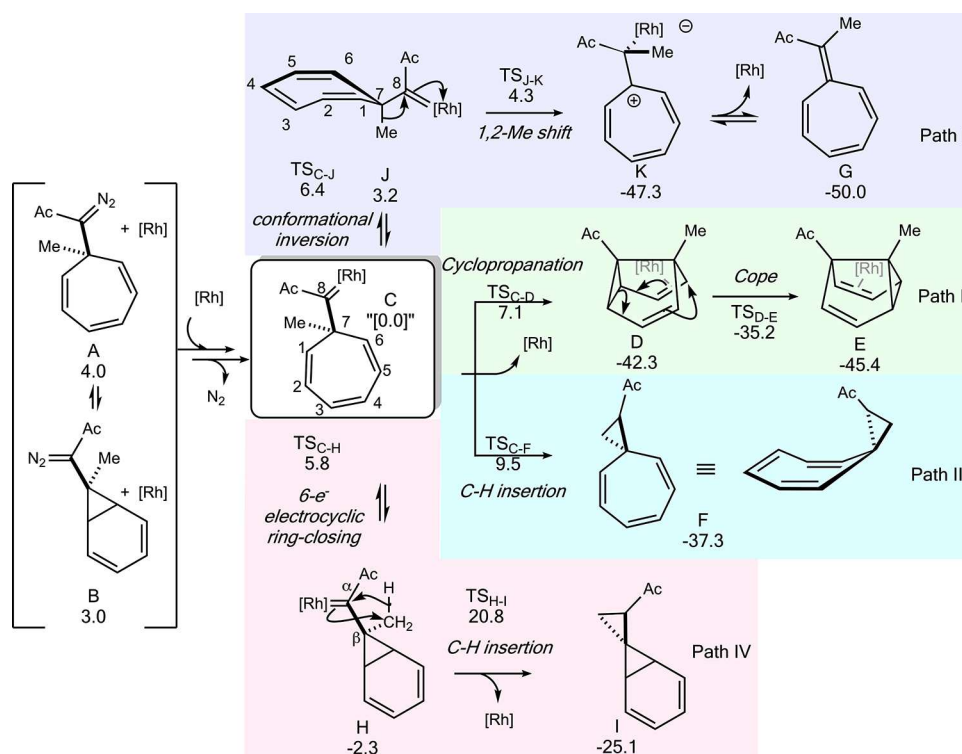


Figure 3. Possible mechanistic pathways to and from C for C7-methylated system. All relative free energies (PW6B95/def2-TZVP//PW6B95/def2-SVP) are in kcal mol^{−1}. [Rh] = Rh₂(OAc)₄.

Sousa isolated, as described in their original report.⁵ Additionally, Tomioka and Taketsuji reported heptafulvene products in the gas-phase rearrangement of phenyl carbenes, presumably through 7-membered ring intermediates.¹²¹ Heptafulvene G can additionally undergo a 10- π electrocyclic ring closure to M (not shown in Figure 1; see the SI, Figure S1) because of the acetyl group attached to C8, similar to that of the acetyl-heptafulvene reaction reported by Liu and Houk.¹²² We computed the barrier to do so and the barrier is 16.0 kcal mol^{−1} from G to M; the reaction also is downhill in energy (also see L, similar to M, in SI, Figure S3).

Potential Antidote to β -Hydride Migration. One way around β -hydride migration is to introduce a different functional group at C7 in place of the hydrogen, a group with a lower migratory aptitude (e.g., CH₃ for H). Though making this substitution in a computational study is trivial, implementing it in a synthetic campaign could be challenging. Our calculations indicate, however, that swapping out the H for a CH₃ group would switch the selectivity in favor of CP over a possible concerted, intramolecular C–H insertion (TS_{C–D} vs TS_{C–F}; $\Delta\Delta G^\ddagger = 2.4$ kcal mol^{−1}; Figure 3) to a spirononatriene—a direct result of our attempts to locate a 1,2-methyl shift (not found)! Though small-ring spiro compounds have precedent in the literature,¹²³ to our knowledge, relatively few papers report structures resembling spirononatriene.^{124–127} Conformational inversion of CHT (and subsequent 1,2-methyl shift to cycloheptafulvene (G)) is again predicted to compete with CP ($\Delta\Delta G^\ddagger = 0.7$ kcal mol^{−1}; compare TS_{C–J} to TS_{C–D}). Isomerization to norcaradiene, H, is also possible. The relatively high barrier for C–H insertion of H ($\Delta G^\ddagger = 23.1$ kcal mol^{−1}) makes formation of spironorcaradiene I unlikely. Tricyclic spiro compounds like I have some literature precedent, but to our knowledge,

spironorcaradienes of the sort we describe here have not been reported.¹²⁸

In summary, although C7 methyl substitution makes CP to form SBV more likely than in the C7 hydrogen-substituted case (Figure 1), methyl migration (Path I) could still preclude the desired chemoselectivity. We also computed the donor/donor Rh-carbene system with a methyl group at C7 and predict that selectivity for heptafulvene formation is enhanced (a $\Delta\Delta G^\ddagger = 2.3$ kcal mol^{−1}; see the SI, Figure S4). Methyl substitution at C7 ameliorates the chemoselectivity troubles with the parent system in Figure 1, but simultaneously introduces the possibility of concerted, intramolecular C–H insertion to generate a spirononatriene (F).

Bifurcating Pathways. To explore whether a PTSB that leads to both D and E exists on the potential energy surface downhill in energy from TS_{C–D}, quasi-classical dynamics trajectories were run from TS_{C–D} (of Figure 3). Of trajectories that formed product (32 total), all formed D and none formed E, which suggests that a PTSB is unlikely to exist in this reaction. Rather, sequential SBV formation (D) and subsequent [3,3] rearrangement would form E.

Gold(I)-Catalyzed Synthesis of Barbaralones. How similar is our proposed reaction to published work on related fluxional molecule syntheses? For comparison, we examined Ferrer and Echavarren's gold(I)-catalyzed oxidative cyclizations^{80,129} to barbaralones (Scheme 2b). Understanding the mechanisms of these transformations could better inform a possible test of our predictions on SBV. In their 2016 study, the authors proposed two pathways to barbaralones—specifically, 6-*endo-dig*^{130,131} cyclization then oxidation or vice versa. We examined both possible pathways (Figures 4 and 5). The predicted barrier for cyclization in the unoxidized system is higher than that for the oxidized system. The oxidized system also has a significant energetic driving force

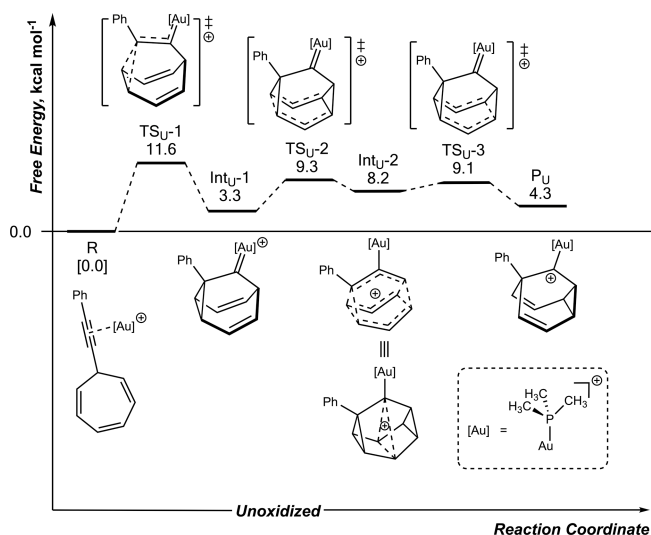


Figure 4. Potential energy surface for barbaralyl cation formation and sequential Cope rearrangements. Relative free energies (PW6B95/def2-TZVP//PW6B95/def2-SVP) shown are in kcal mol^{−1} and are relative to their respective reactants, R. [Au] = ⁺AuP(CH₃)₃.

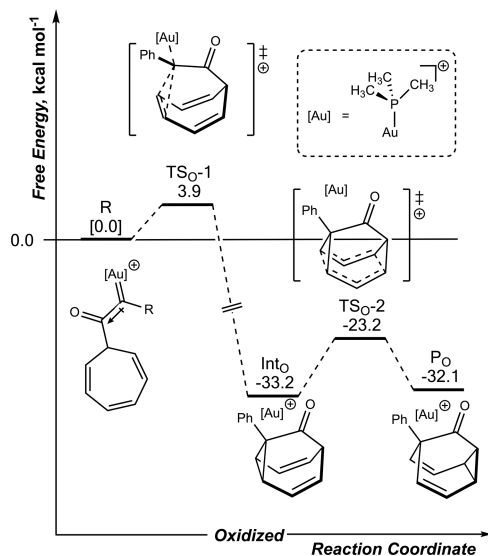


Figure 5. Potential energy surface for barbaralone cation formation and sequential [3,3] rearrangements. Relative free energies (PW6B95/def2-TZVP//PW6B95/def2-SVP) shown are in kcal mol^{−1} and are relative to their respective reactants, R. [Au] = ⁺AuP(CH₃)₃.

($\Delta G = -33.2$ kcal mol^{−1}) that the unoxidized system lacks.⁸² The results in Figure 5 resemble our computed CP path (Path II, Figure 1), but do not necessarily provide evidence for or against Ferrer and Echavarren's proposal that oxidation takes place on barbaralyl gold(I) intermediates *after* cyclization⁸⁰—further calculations would be needed. Unlike their reaction, however, questions about oxidation state are irrelevant with our [Rh₂] catalysts. The relative energies of barbaralones complexed to the gold(I)-catalyst are qualitatively consistent with experimental and theoretical work by Alonso and Echavarren on bare barbaralones: in particular, the 1-phenyl-barbaralone (Int_O in Figure 5) is the more thermodynamically stable isomer (here, by 1.1 kcal mol^{−1}).¹³²

Our results in Figure 4 suggest that the [3,3] rearrangement for the unoxidized system is stepwise (not surprising given the copious studies that have discussed interrupted and aborted pathways for metal-catalyzed pericyclic reactions).^{133–136} The intermediate that interrupts the rearrangement (Int_{U-2}) can be described as a metal-stabilized 9-barbaralyl cation.^{137,138} Free of catalyst and substituents, the 9-barbaralyl cation exhibits D_{3h} symmetry and has been the focus of several studies since its description by Schleyer and coworkers (Figure 6).¹³⁹

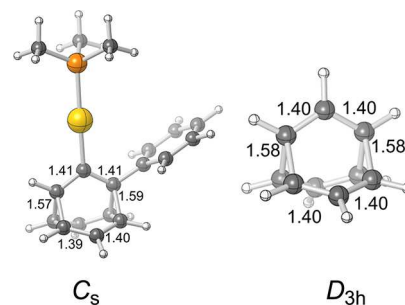


Figure 6. Comparison of C_s Int_{U-2} (Figure 4) and D_{3h} 9-barbaralyl cation. Bond lengths (C–C bonds) are in angstrom (Å). Structures shown were optimized at the PW6B95/def2-SVP level of theory.

CONCLUSIONS

We assessed the viability of a Rh(II)-catalyzed CP strategy for the synthesis of monofunctionalized SBVs from cyclohepta-

Main Takeaways

- Methylated C7 precludes β -hydride migration
- A constellation of side reactions could compete

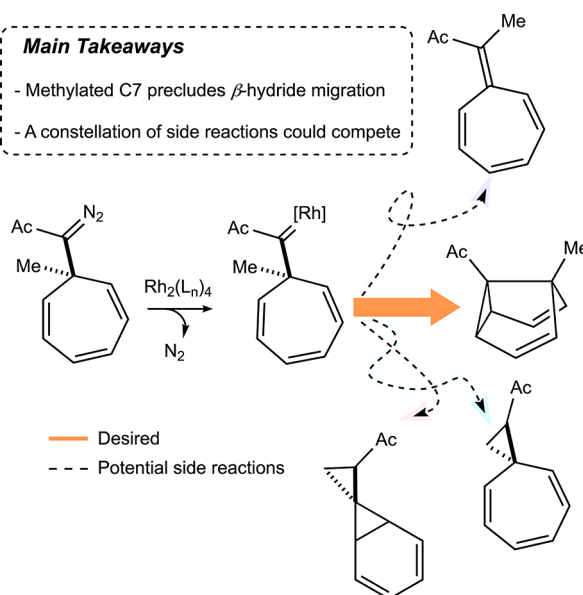


Figure 7. Main takeaways of the proposed strategy.

trienyl diazo compounds. The main takeaways (Figure 7) are as follows:

1. The potential CP step was investigated by DFT calculations, the results of which indicate that CP is energetically feasible from the Rh-carbene intermediate generated after decomposition of the diazo compound. The most promising system starts from a C7-methylated diazo compound (A in Figure 3).

2. Potential side reactions and isomerizations were explored. Specifically, we predict that β -hydride/methyl migration competes with, and quite possibly outcompetes, CP, potentially leading to substituted heptafulvenes. While heptafulvenes are themselves potentially useful products that can be transformed further, it is possible that a particular substitution pattern would allow heptafulvene formation to be suppressed in favor of CP (a task we leave for others, given the immensity of substituent space, and the goal of this work—to demonstrate the feasibility of Rh(II)-promoted CP to form SBVs).

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information. A data set collection of computational results, including geometries and structure coordinates, is available in the ioChem-BD repository¹⁴⁰ and can be accessed via <https://iochem-bd.bsc.es/browse/handle/100/216065>

SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.joc.3c00735>.

Donor/acceptor potential energy surface with formation of M/L; donor/donor potential energy surface; donor/acceptor, C7-Me potential energy surface; donor/donor, C7-Me potential energy surface; benchmark studies; experimental section; and energies and frequencies of computed structures (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Dean J. Tantillo — Department of Chemistry, University of California—Davis, Davis, California 95616, United States; orcid.org/0000-0002-2992-8844; Email: djtantillo@ucdavis.edu

Author

Croix J. Laconsay — Department of Chemistry, University of California—Davis, Davis, California 95616, United States; orcid.org/0000-0002-9244-1318

Complete contact information is available at: <https://pubs.acs.org/10.1021/acs.joc.3c00735>

Notes

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■ REFERENCES

- (1) Schleyer, P. v. R. An Appreciation. *J. Comput. Chem.* **2001**, *22*, ix–xi.
- (2) Fukui, K. The Role of Frontier Orbitals in Chemical Reactions (Nobel Lecture). *Angew. Chem., Int. Ed.* **1982**, *21*, 801–809.
- (3) Hoffmann, R.; Schleyer, P. v. R.; Schaefer, H. F. Predicting Molecules—More Realism, Please! *Angew. Chem., Int. Ed.* **2008**, *47*, 7164–7167.
- (4) Zimmerman, H. E.; Grunewald, G. L. The Chemistry of Barrelene. III. A Unique Photoisomerization to Semibullvalene. *J. Am. Chem. Soc.* **1966**, *88*, 183–184.
- (5) Zimmerman, H. E.; Sousa, L. R. Cycloheptatrienyldiazomethane. Its Synthesis and Behavior. *C₈H₈ Chemistry. X. Correlation Diagrams and Nodal Properties.* *J. Am. Chem. Soc.* **1972**, *94*, 834–842.
- (6) Meinwald, J.; Tsuruta, H. (CH)₈ Hydrocarbons. Photochemistry of Tricyclo[3.3.0.0^{2,6}]Octa-3,7-Diene. *J. Am. Chem. Soc.* **1970**, *92*, 2579–2580.
- (7) Zimmerman, H. E.; Iwamura, H. Mechanistic and Exploratory Photochemistry. XXXVII. The Photochemical Conversion of Cyclooctatetraene to Semibullvalene. *J. Am. Chem. Soc.* **1968**, *90*, 4763–4764.
- (8) Rosenberg, M.; Dahlstrand, C.; Kilså, K.; Ottosson, H. Excited State Aromaticity and Antiaromaticity: Opportunities for Photo-physical and Photochemical Rationalizations. *Chem. Rev.* **2014**, *114*, 5379–5425.
- (9) Garavelli, M.; Bernardi, F.; Cembran, A.; Castaño, O.; Frutos, L. M.; Merchán, M.; Olivucci, M. Cyclooctatetraene Computational Photo- and Thermal Chemistry: A Reactivity Model for Conjugated Hydrocarbons. *J. Am. Chem. Soc.* **2002**, *124*, 13770–13789.
- (10) Doyle, M. P. Catalytic Methods for Metal Carbene Transformations. *Chem. Rev.* **1986**, *86*, 919–939.
- (11) Laszlo, P. Playing with Molecular Models. *Hyle* **2000**, *6*, 85–97.
- (12) Parrish, S. *Learning Through Play*. Farnam Street. <https://fs.blog/2020/11/learning-through-play/> (accessed July 22, 2021).
- (13) Cope, A. C.; Hardy, E. M. The Introduction of Substituted Vinyl Groups. V. A Rearrangement Involving the Migration of an Allyl Group in a Three-Carbon System. *J. Am. Chem. Soc.* **1940**, *62*, 441–444.
- (14) Graulich, N. The Cope Rearrangement—the First Born of a Great Family. *WIREs Comput. Mol. Sci.* **2011**, *1*, 172–190.
- (15) Ma, Y.-Y.; Yan, M.; Li, H.-R.; Wu, Y.-B.; Tian, X.-X.; Lu, H.-G.; Li, S.-D. Probing the Fluxional Bonding Nature of Rapid Cope Rearrangements in Bullvalene C₁₀H₁₀ and Its Analogs C₈H₈, C₉H₁₀, and C₈BH₉. *Sci. Rep.* **2019**, *9*, 17074.
- (16) Williams, R. V.; Aring, A. J.; Bonifacio, M. C.; Blumenfeld, A. 4,6-Barbaralenedicarboxy-2,8-Dicarboxylic Anhydride and 1,5-Dimethyl-4,6-Semibullvalenedicarboxy-2,8-Dicarboxylic Anhydride: Examples of Unusual Barbaralanes and Semibullvalenes That Do Not Undergo the Cope Rearrangement. They Are Locked as the Closed Tautomers. *J. Phys. Org. Chem.* **2017**, *30*, No. e3622.
- (17) Hoffmann, R.; Stohrer, W. D. Cope Rearrangement Revisited. *J. Am. Chem. Soc.* **1971**, *93*, 6941–6948.
- (18) Iyengar, R.; Pina, R.; Grohmann, K.; Todaro, L. Semibullvalenes. IV. 2,6- and 2,8-Trapping of the Bicyclo[3.3.0]Octadienyl Diradical with Oxygen. *J. Am. Chem. Soc.* **1988**, *110*, 2643–2644.
- (19) Zilberg, S.; Haas, Y.; Danovich, D.; Shaik, S. The Twin-Excited State as a Probe for the Transition State in Concerted Unimolecular Reactions: The Semibullvalene Rearrangement. *Angew. Chem., Int. Ed.* **1998**, *37*, 1394–1397.
- (20) Zhang, X.; Hrovat, D. A.; Borden, W. T. Calculations Predict That Carbon Tunneling Allows the Degenerate Cope Rearrangement of Semibullvalene to Occur Rapidly at Cryogenic Temperatures. *Org. Lett.* **2010**, *12*, 2798–2801.
- (21) Schleif, T.; Mieres-Perez, J.; Henkel, S.; Ertelt, M.; Borden, W. T.; Sander, W. The Cope Rearrangement of 1,5-Dimethylsemibullvalene-2(4)-d₁: Experimental Evidence for Heavy-Atom Tunneling. *Angew. Chem., Int. Ed.* **2017**, *56*, 10746–10749.
- (22) Greer, E. M.; Kwon, K.; Greer, A.; Doubleday, C. Thermally Activated Tunneling in Organic Reactions. *Tetrahedron* **2016**, *72*, 7357–7373.
- (23) Schreiner, P. R. Tunneling Control of Chemical Reactions: The Third Reactivity Paradigm. *J. Am. Chem. Soc.* **2017**, *139*, 15276–15283.

- (24) Schleif, T.; Tatchen, J.; Rowen, J. F.; Beyer, F.; Sanchez-Garcia, E.; Sander, W. Heavy Atom Tunneling in Semibullvalenes: How Driving Force, Substituents, and Environment Influence the Tunneling Rates. *Chem. – Eur. J.* **2020**, *26*, 10452–10458.
- (25) Kirshenboim, O.; Frenklah, A.; Kozuch, S. Switch Chemistry at Cryogenic Conditions: Quantum Tunnelling under Electric Fields. *Chem. Sci.* **2021**, *12*, 3179–3187.
- (26) Karton, A. Cope Rearrangements in Shapeshifting Molecules Re-Examined by Means of High-Level CCSDT(Q) Composite Ab Initio Methods. *Chem. Phys. Lett.* **2020**, *759*, No. 138018.
- (27) Wang, S. C.; Tantillo, D. J. Selective Stabilization of Transition State Structures for Cope Rearrangements of Semibullvalene and Barbaralane through Interactions with Halogens. *J. Phys. Chem. A* **2007**, *111*, 7149–7153.
- (28) Jiao, H.; Schleyer, P. Elimination of the Barrier to Cope Rearrangement in Semibullvalene by Li⁺ Complexation. *Angew. Chem., Int. Ed.* **1993**, *32*, 1760–1763.
- (29) Laconsay, C. J.; Mallick, D.; Shaik, S. External Electric Fields Interrupt the Concerted Cope Rearrangement of Semibullvalene. *J. Org. Chem.* **2021**, *86*, 731–738.
- (30) Jiao, H.; Nagelkerke, R.; Kurtz, H. A.; Williams, R. V.; Borden, W. T.; Schleyer, P. v. R. Annulated Semibullvalenes: A Theoretical Study of How They “Cope” with Strain. *J. Am. Chem. Soc.* **1997**, *119*, 5921–5929.
- (31) Hrovat, D. A.; Williams, R. V.; Goren, A. C.; Borden, W. T. B3LYP Calculations on Bishomoaromaticity in Substituted Semibullvalenes. *J. Comput. Chem.* **2001**, *22*, 1565–1573.
- (32) Williams, R. V. Homoaromaticity. *Chem. Rev.* **2001**, *101*, 1185–1204.
- (33) Wu, H.-S.; Jiao, H.; Wang, Z.-X.; Schleyer, P. V. R. Neutral Bishomoaromatic Semibullvalenes. *J. Am. Chem. Soc.* **2003**, *125*, 10524–10525.
- (34) Seefelder, M.; Heubes, M.; Quast, H.; Edwards, W. D.; Armantrout, J. R.; Williams, R. V.; Cramer, C. J.; Goren, A. C.; Hrovat, D. A.; Borden, W. T. Experimental and Theoretical Study of Stabilization of Delocalized Forms of Semibullvalenes and Barbaralanes by Dipolar and Polarizable Solvents. Observation of a Delocalized Structure That Is Lower in Free Energy than the Localized Form. *J. Org. Chem.* **2005**, *70*, 3437–3449.
- (35) Griffiths, P. R.; Pivonka, D. E.; Williams, R. V. The Experimental Realization of a Neutral Homoaromatic Carbocycle. *Chem. – Eur. J.* **2011**, *17*, 9193–9199.
- (36) Williams, R. V.; Al-Sehemi, A. G.; Meier, A. K.; Brown, Z. Z.; Armantrout, J. R. The Role of Strain in the Homoaromatization of Semibullvalenes. *J. Org. Chem.* **2017**, *82*, 4136–4147.
- (37) Wang, S. C.; Tantillo, D. J. Selective Stabilization of Transition State Structures for Cope Rearrangements of Semibullvalene and Barbaralane through Interactions with Halogens. *J. Phys. Chem. A* **2007**, *111*, 7149–7153.
- (38) Hare, S. R.; Tantillo, D. J. Post-Transition State Bifurcations Gain Momentum-Current State of the Field. *Pure Appl. Chem.* **2017**, *89*, 679–698.
- (39) Mandal, N.; Datta, A. Dynamical Effects along the Bifurcation Pathway Control Semibullvalene Formation in Deazetization Reactions. *J. Phys. Chem. B* **2018**, *122*, 1239–1244.
- (40) Melville, J.; Hargis, C.; Davenport, M. T.; Hamilton, R. S.; Ess, D. H. Machine Learning Analysis of Dynamic-dependent Bond Formation in Trajectories with Consecutive Transition States. *J. Phys. Org. Chem.* **2022**, *35*, No. e4405.
- (41) Doering, W. v. E.; Roth, W. R. Thermal Rearrangements. *Angew. Chem., Int. Ed.* **1963**, *2*, 115–122.
- (42) Lippert, A. R.; Naganawa, A.; Keleshian, V. L.; Bode, J. W. Synthesis of Phototrappable Shape-Shifting Molecules for Adaptive Guest Binding. *J. Am. Chem. Soc.* **2010**, *132*, 15790–15799.
- (43) McKee, M. L. Fluxional Molecules. *WIREs Comput. Mol. Sci.* **2011**, *1*, 943–951.
- (44) Larson, K. K.; He, M.; Teichert, J. F.; Naganawa, A.; Bode, J. W. Chemical Sensing with Shapeshifting Organic Molecules. *Chem. Sci.* **2012**, *3*, 1825.
- (45) Teichert, J. F.; Mazunin, D.; Bode, J. W. Chemical Sensing of Polyols with Shapeshifting Boronic Acids As a Self-Contained Sensor Array. *J. Am. Chem. Soc.* **2013**, *135*, 11314–11321.
- (46) Bismillah, A. N.; Sturala, J.; Chapin, B. M.; Yufit, D. S.; Hodgkinson, P.; McGonigal, P. R. Shape-Selective Crystallisation of Fluxional Carbon Cages. *Chem. Sci.* **2018**, *9*, 8631–8636.
- (47) Bismillah, A. N.; Chapin, B. M.; Hussein, B. A.; McGonigal, P. R. Shapeshifting Molecules: The Story so Far and the Shape of Things to Come. *Chem. Sci.* **2020**, *11*, 324–332.
- (48) Pomfret, M. N.; Sun, P. B.; Huang, Z.; Freund, A. C.; Miyoshi, T.; Golder, M. R. Stochastic Bullvalene Architecture Modulates Structural Rigidity in π -Rich Macromolecules. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202301695.
- (49) Birvé, A. P.; Patel, H. D.; Price, J. R.; Bloch, W. M.; Fallon, T. Guest-Dependent Isomer Convergence of a Permanently Fluxional Coordination Cage. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202115468.
- (50) Sanchez, A.; Maimone, T. J. Taming Shapeshifting Anions: Total Synthesis of Ocellatusone C. *J. Am. Chem. Soc.* **2022**, *144*, 7594–7599.
- (51) Ferrer, S.; Echavarren, A. Synthesis of Bullvalenes: Classical Approaches and Recent Developments. *Synthesis* **2019**, *51*, 1037–1048.
- (52) Criegee, R.; Askani, R. Octamethylsemibullvalene. *Angew. Chem., Int. Ed.* **1968**, *7*, 537–537.
- (53) Paquette, L. A. Silver(I) Ion Catalyzed Rearrangements of Strained Sigma Bonds. II. Application of the Synthesis of Semibullvalene. *J. Am. Chem. Soc.* **1970**, *92*, 5765–5767.
- (54) Turro, N. J.; Liu, J.-M.; Zimmerman, H. E.; Factor, R. E. Practical Synthesis of Semibullvalene. *J. Am. Chem. Soc.* **1980**, *45*, 3511–3512.
- (55) Miller, L. S.; Grohmann, K.; Dannenberg, J. J.; Todaro, L. Semibullvalenes. I. Synthesis and Crystal Structure of 1,5-Dimethyl-2,4,6,8-Tetrakis(Carbomethoxy)Tricyclo[3.3.0.0^{2,8}]Octa-3,6-Diene a Donor-Acceptor-Substituted Semibullvalene. *J. Am. Chem. Soc.* **1981**, *103*, 6249–6251.
- (56) Mehta, G.; Ravikrishna, C. A New Synthesis of Semibullvalenes via Photodecarbonylation of Norsnoutanones. *Tetrahedron Lett.* **1998**, *39*, 4899–4900.
- (57) Sauer, J.; Bäuerlein, P.; Ebenbeck, W.; Schuster, J.; Sellner, I.; Sichert, H.; Stimmelmayer, H. An One-Pot Synthesis of Semibullvalenes and Its Mechanism. *Eur. J. Org. Chem.* **2002**, 791–801.
- (58) Zhang, S.; Zhan, M.; Wang, Q.; Wang, C.; Zhang, W.-X.; Xi, Z. Synthesis of Semibullvalene Derivatives via Co₂(CO)₈-Mediated Cyclodimerization of 1,4-Dithio-1,3-Butadienes. *Org. Chem. Front.* **2014**, *1*, 130–134.
- (59) Zhang, S.; Zhang, W.-X.; Xi, Z. Semibullvalene and Diazasemibullvalene: Recent Advances in the Synthesis, Reaction Chemistry, and Synthetic Applications. *Acc. Chem. Res.* **2015**, *48*, 1823–1831.
- (60) Berger, H.; Hopf, H.; Dix, I.; Jones, P. G. A New Route for the Thermal Isomerization of a Highly Substituted Hexadienyne Derivative. *Eur. J. Org. Chem.* **2004**, 3401–3403.
- (61) Vogel, E.; Brinker, U. H.; Nachtkamp, K.; Wassen, J.; Müllen, K. Semibullvalenes as Potential Homoaromatic Compounds. *Angew. Chem., Int. Ed.* **1973**, *12*, 758–760.
- (62) Tran Ngoc, T.; Grabicki, N.; Irran, E.; Dumele, O.; Teichert, J. F. Photoswitching Neutral Homoaromatic Hydrocarbons. *Nat. Chem.* **2023**, *15*, 377–385.
- (63) Bergstrom, B. D.; Nickerson, L. A.; Shaw, J. T.; Souza, L. W. Transition Metal Catalyzed Insertion Reactions with Donor/Donor Carbenes. *Angew. Chem., Int. Ed.* **2021**, *60*, 6864–6878.
- (64) Dishman, S. N.; Laconsay, C. J.; Fetting, J. C.; Tantillo, D. J.; Shaw, J. T. Divergent Stereochemical Outcomes in the Insertion of Donor/Donor Carbenes into the C–H Bonds of Stereogenic Centers. *Chem. Sci.* **2022**, *13*, 1030–1036.
- (65) Jana, S.; Guo, Y.; Koenigs, R. M. Recent Perspectives on Rearrangement Reactions of Ylides via Carbene Transfer Reactions. *Chem. – Eur. J.* **2021**, *27*, 1270–1281.

- (66) Laconsay, C. J.; Tantillo, D. J. Metal Bound or Free Ylides as Reaction Intermediates in Metal-Catalyzed [2,3]-Sigmatropic Rearrangements? It Depends. *ACS Catal.* **2021**, *11*, 829–839.
- (67) Laconsay, C. J.; Tantillo, D. J. Melding of Experiment and Theory Illuminates Mechanisms of Metal-Catalyzed Rearrangements: Computational Approaches and Caveats. *Synthesis* **2021**, *53*, 3639–3652.
- (68) Hare, S. R.; Tantillo, D. J. Cryptic Post-Transition State Bifurcations That Reduce the Efficiency of Lactone-Forming Rh-Carbenoid C–H Insertions. *Chem. Sci.* **2017**, *8*, 1442–1449.
- (69) Hansen, J. H.; Gregg, T. M.; Ovalles, S. R.; Lian, Y.; Autschbach, J.; Davies, H. M. L. On the Mechanism and Selectivity of the Combined C–H Activation/Cope Rearrangement. *J. Am. Chem. Soc.* **2011**, *133*, 5076–5085.
- (70) Rehbein, J.; Carpenter, B. K. Do We Fully Understand What Controls Chemical Selectivity? *Phys. Chem. Chem. Phys.* **2011**, *13*, 20906.
- (71) Guo, W.; Hare, S. R.; Chen, S.-S.; Saunders, C. M.; Tantillo, D. J. C–H Insertion in Dirhodium Tetracarboxylate-Catalyzed Reactions despite Dynamical Tendencies toward Fragmentation: Implications for Reaction Efficiency and Catalyst Design. *J. Am. Chem. Soc.* **2022**, *144*, 17219–17231.
- (72) Jones, A. C.; May, J. A.; Sarpong, R.; Stoltz, B. M. Toward a Symphony of Reactivity: Cascades Involving Catalysis and Sigmatropic Rearrangements. *Angew. Chem., Int. Ed.* **2014**, *53*, 2556–2591.
- (73) Davies, H. M. L.; Smith, H. D.; Korkor, O. Tandem Cyclopropanation/Cope Rearrangement Sequence. Stereospecific [3 + 4] Cycloaddition Reaction of Vinylcarbenoids with Cyclopentadiene. *Tetrahedron Lett.* **1987**, *28*, 1853–1856.
- (74) Padwa, A.; Krumpke, K. E.; Gareau, Y.; Chiacchio, U. Rhodium(II)-Catalyzed Cyclization Reactions of Alkynyl-Substituted α -Diazo Ketones. *J. Org. Chem.* **1991**, *56*, 2523–2530.
- (75) Schwartz, B. D.; Denton, J. R.; Lian, Y.; Davies, H. M. L.; Williams, C. M. Asymmetric [4 + 3] Cycloadditions between Vinylcarbenoids and Dienes: Application to the Total Synthesis of the Natural Product (–)-5-*epi*-Vihsanin E. *J. Am. Chem. Soc.* **2009**, *131*, 8329–8332.
- (76) Miller, L. C.; Ndungu, J. M.; Sarpong, R. Parallel Kinetic Resolution Approach to the Cyathane and Cyanthiwigin Diterpenes Using a Cyclopropanation/Cope Rearrangement. *Angew. Chem., Int. Ed.* **2009**, *48*, 2398–2402.
- (77) Davies, H. M. L.; Lian, Y. The Combined C–H Functionalization/Cope Rearrangement: Discovery and Applications in Organic Synthesis. *Acc. Chem. Res.* **2012**, *45*, 923–935.
- (78) Doering, W. v. E.; Ferrier, B. M.; Fossel, E. T.; Hartenstein, J. H.; Jones, M.; Klumpp, G.; Rubin, R. M.; Saunders, M. A Rational Synthesis of Bullvalene Barbaralones and Derivatives; Bullvalone. *Tetrahedron* **1967**, *23*, 3943–3963.
- (79) Casas, J.; Serratos, F. An Alternative Synthesis of Bullvalene Through a Double Rearrangement. *An. Quim.* **1977**, *73*, 300–302.
- (80) Ferrer, S.; Echavarren, A. M. Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis. *Angew. Chem., Int. Ed.* **2016**, *55*, 11178–11182.
- (81) McGonigal, P. R.; de León, C.; Wang, Y.; Homs, A.; Solorio-Alvarado, C. R.; Echavarren, A. M. Gold for the Generation and Control of Fluxional Barbaralyl Cations. *Angew. Chem., Int. Ed.* **2012**, *51*, 13093–13096.
- (82) Mato, M.; Montesinos-Magraner, M.; Sugranyes, A. R.; Echavarren, A. M. Rh(II)-Catalyzed Alkynylcyclopropanation of Alkenes by Decarbenation of Alkynylcycloheptatrienes. *J. Am. Chem. Soc.* **2021**, *143*, 10760–10769.
- (83) Fan, Z.; Ni, S.; Pang, J.; Guo, L.; Yang, H.; Li, K.; Ma, C.; Liu, J.; Wu, B.; Yang, J. Cu(I)-Catalyzed Cross-Coupling Rearrangements of Terminal Alkynes with Tropylium Tetrafluoroborate: Facile Access to Barbaralyl-Substituted Allenyl Acid Esters and 7-Alkynyl Cycloheptatrienes. *J. Org. Chem.* **2022**, *87*, 3066–3078.
- (84) Hoffmann, R. Why Think Up New Molecules? *Am. Sci.* **2008**, *96*, 372.
- (85) Cheng, A. K.; Anet, F. A. L.; Mioduski, J.; Meinwald, J. Determination of the Fluxional Barrier in Semibullvalene by Proton and Carbon-13 Nuclear Magnetic Resonance Spectroscopy. *J. Am. Chem. Soc.* **1974**, *96*, 2887–2891.
- (86) Lee, C.; Yang, W.; Parr, R. G. Development of the Colle-Salvetti Correlation-Energy Formula into a Functional of the Electron Density. *Phys. Rev. B* **1988**, *37*, 785–789.
- (87) Guner, V.; Khuong, K. S.; Leach, A. G.; Lee, P. S.; Bartberger, M. D.; Houk, K. N. A Standard Set of Pericyclic Reactions of Hydrocarbons for the Benchmarking of Computational Methods: The Performance of ab Initio, Density Functional, CASSCF, CASPT2, and CBS-QB3 Methods for the Prediction of Activation Barriers, Reaction Energetics, and Transition State Geometries. *J. Phys. Chem. A* **2003**, *107* (51), 11445–11459.
- (88) Greer, E. M.; Hoffmann, R. Metalla-Cope Rearrangements: Bridging Organic and Inorganic Chemistry. *J. Phys. Chem. A* **2010**, *114*, 8618–8624.
- (89) Staroverov, V. N.; Davidson, E. R. Transition Regions in the Cope Rearrangement of 1,5-Hexadiene and Its Cyano Derivatives. *J. Am. Chem. Soc.* **2000**, *122*, 7377–7385.
- (90) Staroverov, V. N.; Davidson, E. R. The Cope Rearrangement in Theoretical Retrospect. *J. Mol. Struct.: THEOCHEM* **2001**, *573*, 81–89.
- (91) Karton, A. Can Density Functional Theory ‘Cope’ with Highly Fluxional Shapeshifting Molecules? *Chem. Phys.* **2021**, *540*, No. 111013.
- (92) Quintal, M. M.; Karton, A.; Iron, M. A.; Daniel Boese, A.; Martin, J. M. L. Benchmark Study of DFT Functionals for Late-Transition-Metal Reactions. *J. Phys. Chem. A* **2006**, *110*, 709–716.
- (93) Zhao, Y.; Truhlar, D. G. Design of Density Functionals That Are Broadly Accurate for Thermochemistry, Thermochemical Kinetics, and Nonbonded Interactions. *J. Phys. Chem. A* **2005**, *109*, 5656–5667.
- (94) Schäfer, A.; Horn, H.; Ahlrichs, R. Fully Optimized Contracted Gaussian Basis Sets for Atoms Li to Kr. *J. Chem. Phys.* **1992**, *97*, 2571–2577.
- (95) Moskau, D.; Aydin, R.; Leber, W.; Günther, H.; Quast, H.; Martin, H. -D.; Hassenrück, K.; Miller, L. S.; Grohmann, K. Anwendungen der ^{13}C -NMR-Spektroskopie, XXVII. Die Aktivierungsparameter der Cope-Umlagerung von 3,7-Diethoxy-1,5-dimethyl-2,4,6,8-tetraazabarbalan. *Chem. Ber.* **1989**, *122*, 925–931.
- (96) Rubin, M. B. Photolysis of Two Tricyclic Nonenediones. Direct Observation of Norcaradiene. *J. Am. Chem. Soc.* **1981**, *103*, 7791–7792.
- (97) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. *Gaussian 16, Revision A.03*; Gaussian, Inc.: Wallingford, CT, 2016.
- (98) Fukui, K. The Path of Chemical Reactions—The IRC Approach. *Acc. Chem. Res.* **1981**, *14*, 363–368.
- (99) Gonzalez, C.; Schlegel, H. B. Reaction Path Following In Mass-Weighted Internal Coordinates Cartesians and with Internal Coordinates without Mass-Weighting. *J. Phys. Chem.* **1990**, *94*, 5523–5527.
- (100) Maeda, S.; Harabuchi, Y.; Ono, Y.; Taketsugu, T.; Morokuma, K. Intrinsic Reaction Coordinate: Calculation, Bifurcation, and Automated Search. *Int. J. Quantum Chem.* **2015**, *115*, 258–269.

- (101) Ussing, B. R.; Hang, C.; Singleton, D. A. Dynamic Effects on the Periselectivity, Rate, Isotope Effects, and Mechanism of Cycloadditions of Ketenes with Cyclopentadiene. *J. Am. Chem. Soc.* **2006**, *128*, 7594–7607.
- (102) Davies, H. M. L.; Liao, K. Dirhodium Tetracarboxylates as Catalysts for Selective Intermolecular C–H Functionalization. *Nat. Rev. Chem.* **2019**, *3*, 347–360.
- (103) Bethäuser, W.; Weber, B.; Heydt, H.; Regitz, M. Untersuchungen an Diazoverbindungen Und Aziden, LV. 7- (Diazomethyl)cycloheptatriene Durch Elektrophile Diazoalkansubstitution. *Chem. Ber.* **1985**, *118*, 1315–1328.
- (104) Doering, W. V. E.; Wiley, D. W. Heptafulvene (Methylenecycloheptatriene). *Tetrahedron* **1960**, *11*, 183–198.
- (105) Stępień, B. T.; Krygowski, T. M.; Cyrański, M. K. Variation of the π -Electron Delocalization in Exocyclically Substituted Heptafulvene Derivatives. *J. Phys. Org. Chem.* **2003**, *16*, 426–430.
- (106) Rogachev, A. Y.; Wen, X.-D.; Hoffmann, R. Jailbreaking Benzene Dimers. *J. Am. Chem. Soc.* **2012**, *134*, 8062–8065.
- (107) Parambil, P. C.; Hoffmann, R. Alkyl Isosteres. *J. Am. Chem. Soc.* **2018**, *140*, 12844–12852.
- (108) Chen, Z.; Jiao, H.; Wu, J. I.; Herges, R.; Zhang, S. B.; Schleyer, P. v. R. Homobenzene: Homoaromaticity and Homoantiaromaticity in Cycloheptatrienes. *J. Phys. Chem. A* **2008**, *112*, 10586–10594.
- (109) Williams, R. V.; Edwards, W. D.; Zhang, P.; Berg, D. J.; Mitchell, R. H. Experimental Verification of the Homoaromaticity of 1,3,5-Cycloheptatriene and Evaluation of the Aromaticity of Tropone and the Tropylium Cation by Use of the Dimethyldihydropyrene Probe. *J. Am. Chem. Soc.* **2012**, *134*, 16742–16752.
- (110) Jorner, K.; Jahn, B. O.; Bultinck, P.; Ottosson, H. Triplet State Homoaromaticity: Concept, Computational Validation and Experimental Relevance. *Chem. Sci.* **2018**, *9*, 3165–3176.
- (111) Ciganek, E. The Direct Observation of a Norcaradiene-Cycloheptatriene Equilibrium. *J. Am. Chem. Soc.* **1965**, *87*, 1149–1150.
- (112) Maier, G. The Norcaradiene Problem. *Angew. Chem., Int. Ed.* **1967**, *6*, 402–413.
- (113) Hoffmann, R. The Norcaradiene - Cycloheptatriene Equilibrium. *Tetrahedron Lett.* **1970**, *11*, 2907–2909.
- (114) Ciganek, E. The Cycloheptatriene-Norcaradiene System. III. Dependence of the Ground-State Enthalpy Difference on Substituents in the 7 Position. *J. Am. Chem. Soc.* **1971**, *93*, 2207–2215.
- (115) Berry, J. F. The Role of Three-Center/Four-Electron Bonds in Superelectrophilic Dirhodium Carbene and Nitrene Catalytic Intermediates. *Dalton Trans.* **2012**, *41*, 700–713.
- (116) Berson, J. A.; Willcott, M. R., III Thermally Induced Skeletal Rearrangements of Tropilidenes. *J. Am. Chem. Soc.* **1966**, *88*, 2494–2502.
- (117) Anet, F. A. L. Ring Inversion in Cycloheptatriene. *J. Am. Chem. Soc.* **1964**, *86*, 458–460.
- (118) Jensen, F. R.; Smith, L. A. The Structure and Interconversion of Cycloheptatriene. *J. Am. Chem. Soc.* **1964**, *86*, 956–957.
- (119) Freedberg, D. I.; Kopelevich, M.; Anet, F. A. L. Deuterium Conformational Equilibrium Isotope Effects in 1,3,5-Cycloheptatriene-7-d. *J. Phys. Org. Chem.* **2001**, *14*, 625–635.
- (120) DeAngelis, A.; Panish, R.; Fox, J. M. Rh-Catalyzed Intermolecular Reactions of α -Alkyl- α -Diazo Carbonyl Compounds with Selectivity over β -Hydride Migration. *Acc. Chem. Res.* **2016**, *49*, 115–127.
- (121) Tomioka, H.; Taketsuji, K. Formation of Heptafulvene in Reactions of [(Methoxycarbonyl)methyl]Phenylcarbene in the Gas Phases. *J. Org. Chem.* **1993**, *58*, 4196–4197.
- (122) Liu, C.-Y.; Houk, K. N. Intramolecular [8+2] Cycloaddition and 10π -Electron Electrocyclization Reactions of an 8-Acylheptafulvene. *Tetrahedron Lett.* **1987**, *28*, 1367–1370.
- (123) Liebman, J. F.; Greenberg, A. A Survey of Strained Organic Molecules. *Chem. Rev.* **1976**, *76*, 311–365.
- (124) Mukai, T.; Nakazawa, T.; Isobe, T. Thermal Decomposition of Tropone-tosylhydrazones. *Tetrahedron Lett.* **1968**, *9*, 565–569.
- (125) Rostek, C. J.; Jones, W. M. Synthesis and Diels-Alder Reactions of Spiro(2.6)Nona-4,6,8-Triene. *Tetrahedron Lett.* **1969**, *10*, 3957–3960.
- (126) Jones, W. M.; Ennis, C. L. Cycloheptatrienylidene. *J. Am. Chem. Soc.* **1969**, *91*, 6391–6397.
- (127) Waali, E. E.; Jones, W. M. An Improved Synthesis of Spiro[2.6]Nonatriene. The Addition of Cycloheptatrienylidene to Ethylene. *Synth. Commun.* **1973**, *3*, 49–52.
- (128) Li, C.; Yang, Y.; Zhou, Y.; Yu, Z. A Formal [3+3+1] Reaction of Enyne-Methylenecyclopropanes through Au(I)-Catalyzed Enyne Cycloisomerization and Rh(I)-Catalyzed [6+1] Reaction of Vinyl-spiropentanes and CO. *Asian J. Org. Chem.* **2022**, *11*, No. e202100571.
- (129) Zheng, Z.; Wang, Z.; Wang, Y.; Zhang, L. Au-Catalysed Oxidative Cyclisation. *Chem. Soc. Rev.* **2016**, *45*, 4448–4458.
- (130) Gilmore, K.; Mohamed, R. K.; Alabugin, I. V. The Baldwin Rules: Revised and Extended. *WIREs Comput. Molec. Sci.* **2016**, *6*, 487–514.
- (131) Alabugin, I. V.; Gilmore, K. Finding the Right Path: Baldwin “Rules for Ring Closure” and Stereoelectronic Control of Cyclizations. *Chem. Commun.* **2013**, *49*, 11246–11250.
- (132) Sanz-Novo, M.; Mato, M.; León, Í.; Echavarren, A. M.; Alonso, J. L. Shape-Shifting Molecules: Unveiling the Valence Tautomerism Phenomena in Bare Barbaralones. *Angew. Chem., Int. Ed.* **2022**, *61*, No. e202117045.
- (133) Felix, R. J.; Weber, D.; Gutierrez, O.; Tantilillo, D. J.; Gagné, M. R. A Gold-Catalysed Enantioselective Cope Rearrangement of Achiral 1,5-Dienes. *Nat. Chem.* **2012**, *4*, 405–409.
- (134) Vidhani, D. V.; Krafft, M. E.; Alabugin, I. V. Gold(I)-Catalyzed Allenyl Cope Rearrangement: Evolution from Asynchronicity to Trappable Intermediates Assisted by Stereoelectronic Switching. *J. Am. Chem. Soc.* **2016**, *138*, 2769–2779.
- (135) dos Passos Gomes, G.; Alabugin, I. V. Drawing Catalytic Power from Charge Separation: Stereoelectronic and Zwitterionic Assistance in the Au(I)-Catalyzed Bergman Cyclization. *J. Am. Chem. Soc.* **2017**, *139*, 3406–3416.
- (136) Ahmed, Y. G.; Tantilillo, D. J. Designing an Apparently Orbital-Symmetry-Forbidden [3s,3s]-Sigmatropic Shift through Transition-State Complexation and Stereoelectronic Effects. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202300288.
- (137) Hoffmann, R.; Stohrer, W.-D.; Goldstein, M. J. The 9-Barbaralyl Cation. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2513–2514.
- (138) Cremer, D.; Svensson, P.; Kraka, E.; Ahlberg, P. Exploration of the Potential Energy Surface of $C_9H_9^+$ by *ab initio* Methods. I. The Barbaralyl Cation. *J. Am. Chem. Soc.* **1993**, *115*, 7445–7456.
- (139) Barborak, J. C.; Daub, J.; Follweiler, D. M.; Schleyer, P. v. R. Degenerate Rearrangements of the 9-Barbaralyl Cation. *J. Am. Chem. Soc.* **1969**, *91*, 7760–7761.
- (140) Álvarez-Moreno, M.; de Graaf, C.; López, N.; Maseras, F.; Poblet, J. M.; Bo, C. Managing the Computational Chemistry Big Data Problem: The ioChem-BD Platform. *J. Chem. Inf. Model.* **2015**, *55*, 95–103.