

Metal-Bound or Free Ylides as Reaction Intermediates in Metal-Catalyzed [2,3]-Sigmatropic Rearrangements? It Depends.

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KEYWORDS

Metal carbenes; onium ylides; DFT study; [2,3]-sigmatropic rearrangements; dirhodium tetracarboxylate catalyst; Doyle-Kirmse reaction; free ylide

ABSTRACT

Density functional theory calculations were applied to study four previously published metal-catalyzed [2,3]-rearrangements from onium ylide intermediates, in pursuit of generalizations about when, during these types of reactions, catalysts dissociate. Our results corroborate past studies where free ylide mechanisms were proposed to be operative. Calculations on case studies predict that the origin of metal-catalyst ‘falling off’ (dissociation) can be attributed primarily to the steric bulkiness of functional groups adjacent to the carbene carbon.

TEXT

Sigmatropic rearrangement reactions hold a privileged position in the synthetic organic chemist's toolbox for forming new carbon-carbon/carbon-heteroatom bonds. Ylide formation/[2,3]-sigmatropic rearrangement tandem reactions, or 'duets',¹ have gained attention as an important tool for synthesizing heteroatom-containing compounds with high stereochemical fidelity. Of the two main methodologies for generating ylide intermediates for these reactions, the transition-metal catalyzed variant is milder than base-promoted methodologies.^{2,98} One question that remains unanswered for many transition-metal catalyzed ylide-formation/[2,3]-sigmatropic rearrangement reactions (from here on, just 'ylide rearrangements' for simplicity) is whether the catalyst is explicitly bound to the ylide during the [2,3]-rearrangement step.²⁻⁵ Does the metal catalyst remain covalently bound (what we refer to as 'metal-bound') to the substrate or dissociate (what we refer to as a 'free-ylide' or 'metal-unbound' if the metal catalyst is nearby, but not covalently bonded to, the substrate) before the rearrangement step? This question has implications for stereoselectivity⁶ and regioselectivity,⁷ because whether the metal catalysts are able to effectively pass on chiral information depends on whether the catalyst is bound to its substrate during the stereodetermining step(s).^{6,8} For example, in a selective Au(I)-catalyzed C-H functionalization reaction of *N*-heterocycles, Jana *et al.* demonstrated using density functional theory (DFT) calculations and control experiments that the key proton shuttle step in the mechanism likely does not involve a Au-complex—the catalyst likely dissociates before the rate-determining (last) step.⁹

The combination of steps from reactant to product and concomitant regeneration of catalyst is called the catalytic cycle, and it is, often implicitly, assumed (at least in organometallic chemistry textbooks)^{10,11} that the catalyst remains bound to its substrate until the

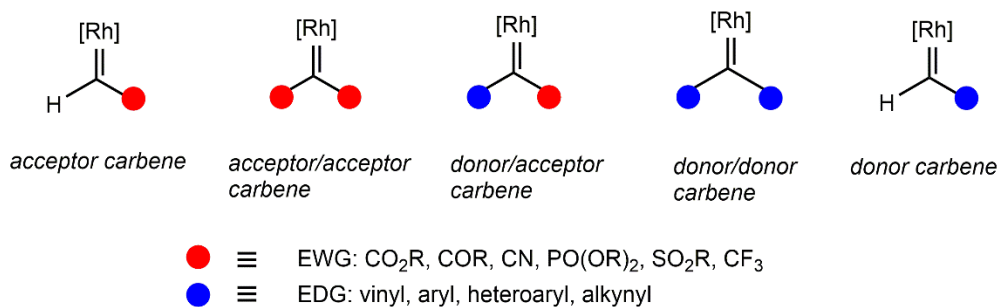
end of the cycle, when it releases the product and binds another reactant. Although this may be true for many catalytic cycles, we focus here on cases in which this assumption is not valid – specifically reactions promoted by dirhodium tetracarboxylate catalysts.

Chemists have made strides in stereoselective, ylide rearrangements with electrophilic metal carbenes: not only are these reactions highly stereoselective, but they often show excellent chemo- and regioselectivities.^{8,12–20} The focus on metal carbenes²¹ for this reaction, and in particular, rhodium (Rh) carbenes generated *in situ* from diazo compounds and metal catalyst,^{22–26} has in large part been motivated by the ability to control stereoselectivity by exploiting different chiral ligands. Rh carbenes²⁴ are now commonplace in organic synthesis and especially useful in C-H activation chemistry. They are often categorized into five main groups: i.e. acceptor,^{27,28} acceptor/acceptor,^{29,30} donor/acceptor,^{26,31,32} donor,³³ and donor/donor^{34–39} (Scheme 1a), depending on the electron withdrawing or donating ability of substituents adjacent to the carbene center. This versatility in functional group discretion enables one to fine-tune the reactivity and selectivity of the carbene intermediate, which make Rh carbenes amenable to a wide range of chemical transformations. Due to the electrophilicity of the metal-carbene intermediates bearing electron-withdrawing substituents, acceptor, acceptor/acceptor and donor/acceptor compounds are typically used in ylide rearrangements.²⁰ Presumably safety factors, including thermal stability and ease of handling under desired reaction conditions, play a significant role as well—note the recent article by Green *et al.* on the thermal stability and explosive hazards of diazo compounds.⁴⁰ To our knowledge, only one study⁴¹ has used donor *N*-tosylhydrazones as a surrogate for a donor diazo compound and donor/donor compounds have yet to be explored for this transformation. Alternatives to metal catalysts and diazo compounds involve forming the ylide by deprotonation with a strong base—for instance, Tambar's

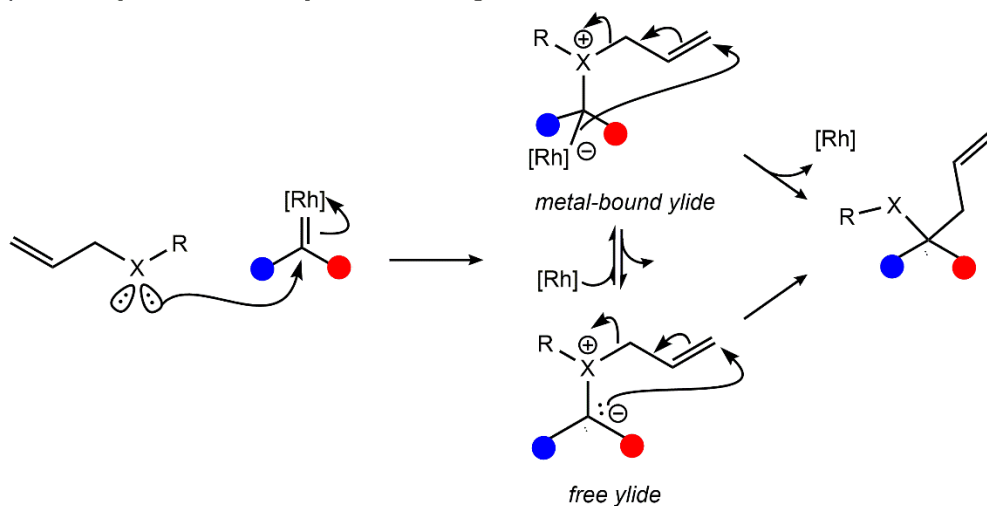
palladium-catalyzed allylic substitution chemistry,⁴² or Smith's isothiurea-catalyzed [2,3]-rearrangement.^{43,44} Low-energy light induced carbene transfer reactions have also been explored by Koenigs's group as a viable method for ylide formations posed to undergo subsequent rearrangement.^{45,46} Despite these select examples, the use of Rh carbenes from diazo precursors have generally guided much of the stereoselective ylide rearrangements—albeit, up until recently,³ with only modest enantioselectivity. We focus our efforts herein, therefore, on Rh-catalyzed ylide rearrangements.

Scheme 1.

a) The five major classes of Rh carbenes



b) Rh Catalyst: should it 'stay', or should it 'go'?



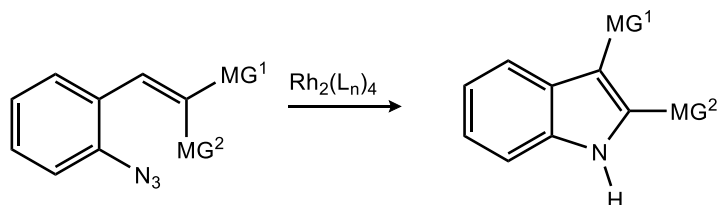
Ylide formation can occur between a metal-carbene and a Lewis-basic heteroatom such as nitrogen, oxygen, sulfur, selenium, even iodine to form ammonium,⁴⁷ oxonium,^{18,48–58} sulfonium,^{59–66} selenonium,^{67–69} and iodonium ylides,⁷⁰ respectively (Scheme 1b).⁷¹ Subsequent rearrangements (Doyle-Kirmse, Stevens, or Sommelet-Hauser) from the onium ylide can ensue thereafter (or not⁶³), and the type of rearrangement depends on the groups attached to the heteroatom. Sometimes, non-statistical dynamic effects can complicate [1,2]- and [2,3]-rearrangement product selectivity, as Singleton demonstrated for ammonium ylides.^{72,99} As Clark and Hansen discuss in their mechanistic study of metal-carbene intramolecular reactions of allylic ethers, “the intermediacy of a free oxonium ylide or a metal-bound ylide is more than just a question of semantics. If one is to engage in the rational design of new ligands and catalysts to improve ratios of diastereomeric products or to render the reaction highly enantioselective, a full understanding of the role of the metal complex in the rearrangement reaction is essential.”⁷³ This statement applies to many onium ylides, not just the ones mentioned above. For instance, the Schomaker group has reported that carbene-generated aziridinium ylides generate metal-free ylide intermediates after metal dissociation, too.⁷⁴

Experimental groups have expressed the need for quantum chemical studies to corroborate conclusions arrived at by control experiments which support free-ylide mechanisms for onium ylide [2,3]-sigmatropic rearrangement and [1,2]-sigmatropic rearrangement reactions.^{2–4,61,68,75} Whether recently described selenonium ylide analogues are Rh-bound or ‘free’ has yet to be explored as well. In previous work, we demonstrated DFT calculations that a free ylide pathway is energetically favored over a metal-bound ylide pathway in Rh(II)-promoted indole formation of vinyl/azidoarenes.⁷⁶ We also recently reported with the Shaw group an unexpected, concerted

metal-unbound (or free-ylide), Stevens rearrangement resulting in an isoindoline product during attempts to synthesize tetrahydroisoquinolines with donor/donor Rh-carbenes.³⁴

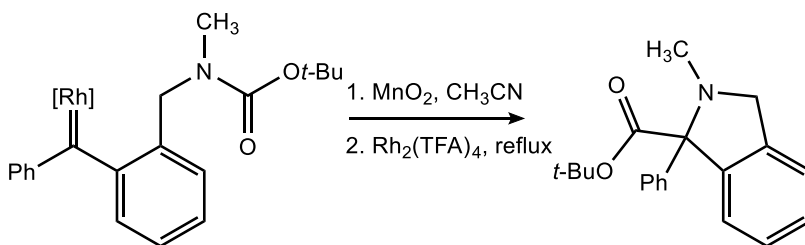
Scheme 2.

a) Rh-promoted nitrene-formation/[1s,5s]-sigmatropic shift^a



^aMG = migratory group, [1s,5s]-shift need not be Rh-promoted

b) Isoindoline synthesis via Stevens [1,2]-rearrangement by free ylide



Against this backdrop, we investigate whether Rh catalysts remain covalently bound or heterolytically dissociate before the [2,3]-sigmatropic-rearrangement step in ylide rearrangements. We report DFT calculations for three previously reported reactions as case studies. We begin with a reaction involving an oxonium ylide by Clark and Hansen⁷³ and walk down group 16 (the chalcogens) of the periodic table to a reaction involving a sulfonium ylide example by Wang and coworkers³ and, finally, end with an example of a reaction by Jana and Koenigs involving a selenonium ylide.⁶⁹ We then design a study based on Jana and Koenigs's selenonium ylide intermediate, by varying the electronic and steric nature of the ylide to find

under what conditions the Rh-catalyst remains bound. We close with a comparison to a recently reported Au-catalyzed [2,3]-rearrangement reaction.⁷⁷

Computational Methods

DFT calculations were carried out in *Gaussian 09*.⁷⁸ Transition-state structures (TSSs) were verified with frequency calculations and by identifying one imaginary frequency. Minima were verified as such by the absence of imaginary frequencies. Intrinsic Reaction Coordinate (IRC) calculations^{79,80} were used to further characterize TSSs.^{79–81} We carried out geometry optimizations at the unrestricted B3LYP level of DFT with the LANL2DZ basis set for Rh and 6-31G(d) for all other atoms—i.e., uB3LYP/LANL2DZ[6-31G(d)]. The B3LYP functional has proven to be sufficient in successfully modeling experimentally relevant geometries and energies in past studies on related chemistry.^{34,76,82,83} To ensure that relative free energies are reasonable, we conducted single-point calculations at the uB3LYP-D3(BJ) and u ω B97X-D⁸⁴ to account for dispersion.^{85,86} These calculations also made use of a larger basis set (LANL2DZ[6-31+G(d,p)]); see Supporting Information (SI) for details. A data set collection of computational results is available in the ioChem-BD repository⁸⁷ and can be accessed via <https://doi.org/10.19061/iochem-bd-6-68>.

Results and Discussion

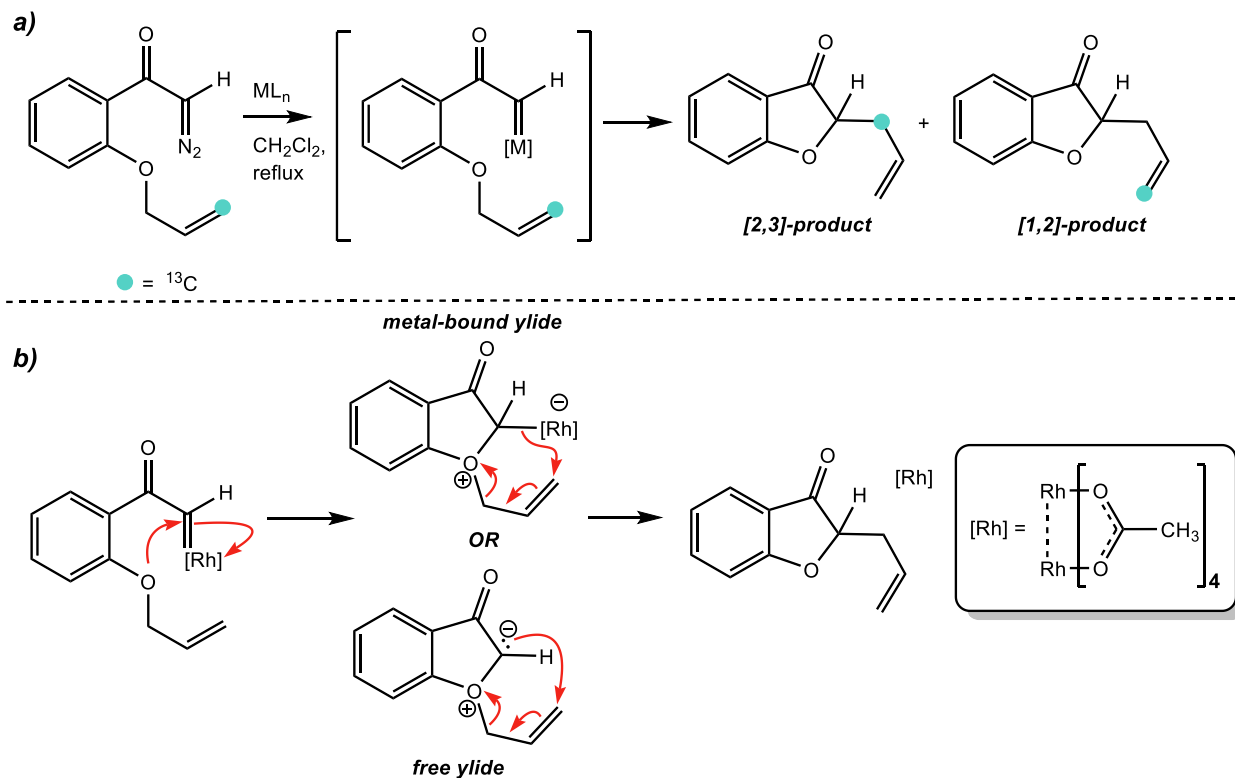


Figure 1. Metal-catalyzed oxonium-ylide rearrangement to benzofuranones by Clark and Hansen, $[\text{M}] = \text{Rh}(\text{II})$ - and $\text{Cu}(\text{II})$ -catalysts (ref. 73) a) ${}^{13}\text{C}$ -labelled experiments predict that [2,3]- to [1,2]-product ratio is dependent on nature of Rh catalyst, favoring the [2,3]-product b) system modeled here with DFT calculations, where $[\text{Rh}] = \text{Rh}_2(\text{OAc})_4$.

Oxonium ylide

Clark and Hansen performed ${}^{13}\text{C}$ -labelling studies to gain insight into the mechanism of a metal-catalyzed ylide rearrangement of diazo ketone substrates to benzofuranones, a reaction that had been studied previously by Pirrung and Werner using rhodium(II) acetate⁸⁸ and similar to a

reaction studied by Hashimoto and coworkers.⁵⁶ Expanding on this methodology, they employed Cu, Ir, and Rh complexes—[Cu(acac)₂] (acac = acetylacetonate), [$\{\text{Ir}(\text{cod})\text{Cl}\}_2$] and Rh₂(OAc)₄, among other similar catalysts (**Figure 1**).⁷³ Determining the ratio of the ¹³C-labelled [1,2]- and [2,3]-products by ¹H and ¹³C NMR spectroscopy, they observed a dependence of the ratio on the type of Rh-catalyst used. These results are inconsistent with a mechanism that forms a free oxonium ylide; either the reaction undergoes a metal-bound ylide or alternative non-ylide pathway. Is the conclusion that the rhodium-catalyzed reaction involves a metal-bound ylide supported by DFT calculations?⁴

We modeled both the free ylide mechanism and the metal-bound mechanism with DFT calculations starting from the metal-bound ylide (**Figure 2**), where the metal catalyst here, and from here on in the manuscript, is Rh₂(OAc)₄. We predict that the free ylide mechanism is kinetically unfavorable compared to the metal-bound ylide mechanism by at least 2 kcal mol⁻¹ ($\Delta\Delta G^\ddagger = 3.8 \text{ kcal mol}^{-1}$), which is consistent with the conclusions made by Clark and Hansen. IRC calculations confirm that the Rh catalyst remains bound to the substrate in the metal-bound pathway (see SI).

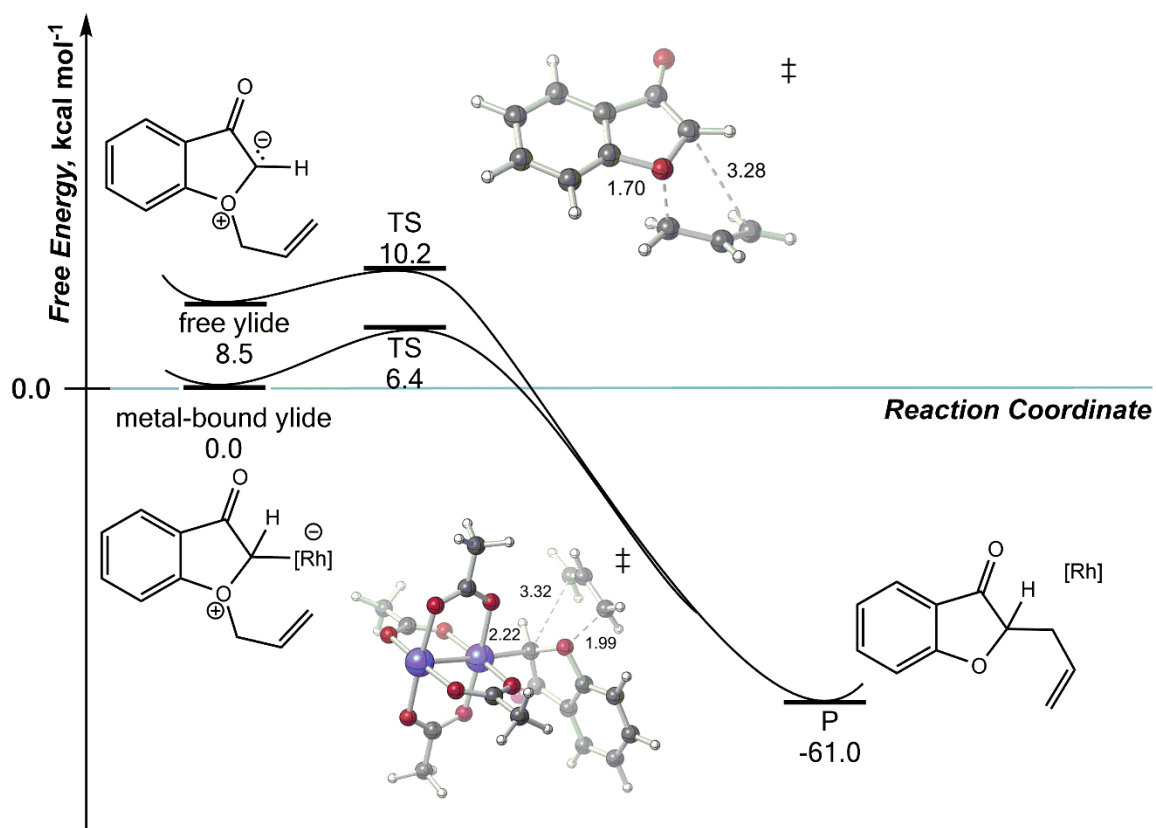


Figure 2. Energy profile for oxonium-ylide [2,3]-rearrangement step in the intramolecular cyclization to form benzofuranones (by Clark and Hansen, ref. 73). Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

Sulfonium ylide

The transition-metal catalyzed [Rh(II) or Cu(I)] reaction that generates a sulfonium ylide prior to a [2,3]-sigmatropic rearrangement is known as the Doyle-Kirmse reaction.^{2,8,41,59,89,90} Wang and co-workers³ recently reported a highly enantioselective metal carbene-catalyzed Doyle-Kirmse reaction based on previous work by Uemura and coworkers.⁹¹ Despite this method's success in forming new, chiral C(sp³)-S bonds, whether the [2,3]-sigmatropic rearrangement step in this mechanism involves the metal-catalyst bound to the substrate is still unclear. Wang and

co-workers dedicated a substantial portion of their study to control experiments to address this ambiguity. They concluded from experiments that their asymmetric trifluoromethylthiolation *via* an enantioselective Doyle-Kirmse reaction likely undergoes a free-ylide mechanism (**Figure 3**).

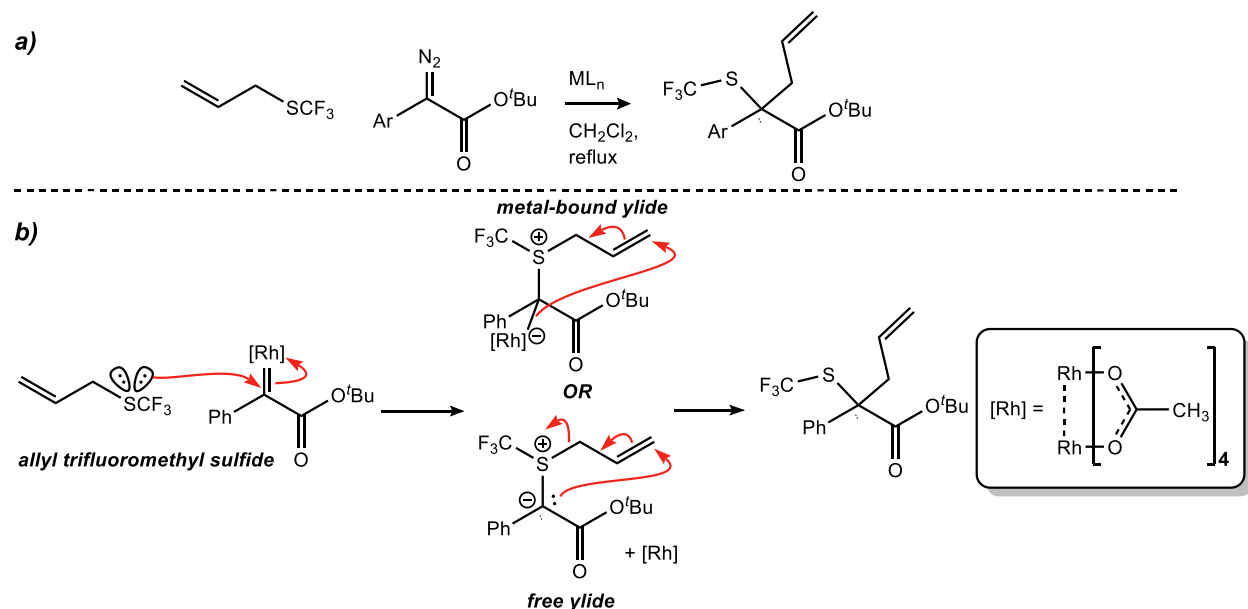


Figure 3. a) asymmetric Rh-catalyzed sulfonium-ylide rearrangement (Doyle-Kirmse reaction) by Wang and coworkers (ref. 3) where $ML_n = Rh(II)$ - and $Cu(I)$ -catalysts b) system modeled here with DFT calculations, where $[Rh] = Rh_2(OAc)_4$.

Our DFT results support the free ylide hypothesis. Every attempt to locate a TSS that corresponds to a metal-bound structure failed: specifically, potential energy scans resulted in the Rh catalyst dissociating from the ylide carbon and associating with a π -face of the aryl ring. It is unlikely that alternative Rh catalysts with bulkier ligands would diverge from this result. Attempts to find a [2,3]-rearrangement TSS with the Rh catalyst unbound resulted in the so-called “metal-unbound ylide” TSS shown in **Figure 4**. IRC calculations from this TSS led to a metal-unbound ylide (see SI).

Loss of Rh catalyst to form the free ylide is predicted to be energetically favorable by >20 kcal mol⁻¹. Activation barriers from either the free ylide or the metal-unbound ylide are comparable (~ 10 kcal mol⁻¹), which can be attributed to the fact that the metal-unbound ylide is effectively a free ylide with the metal catalyst as a nearby spectator. Unlike the oxonium ylide system discussed earlier, these results suggest that this sulfonium ylide prefers to dissociate from the metal catalyst first, and then undergoes the rearrangement step.

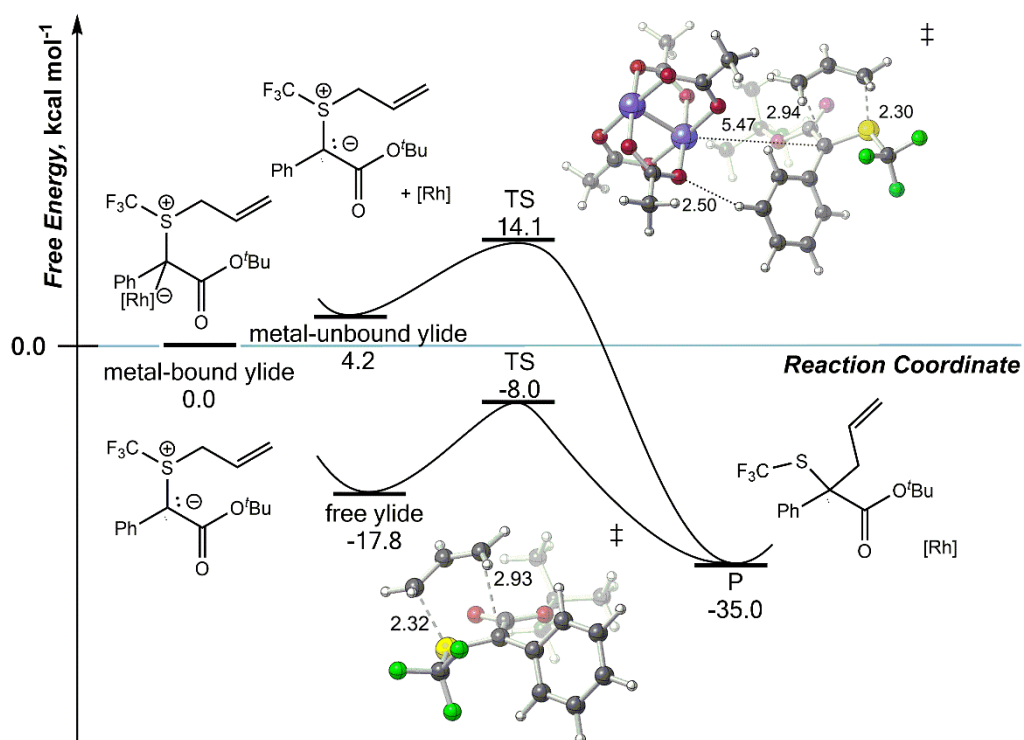


Figure 4. Energy profile for sulfonium-ylide [2,3]-rearrangement step in the Doyle-Kirmse reaction (by Wang and coworkers, ref. 3). Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

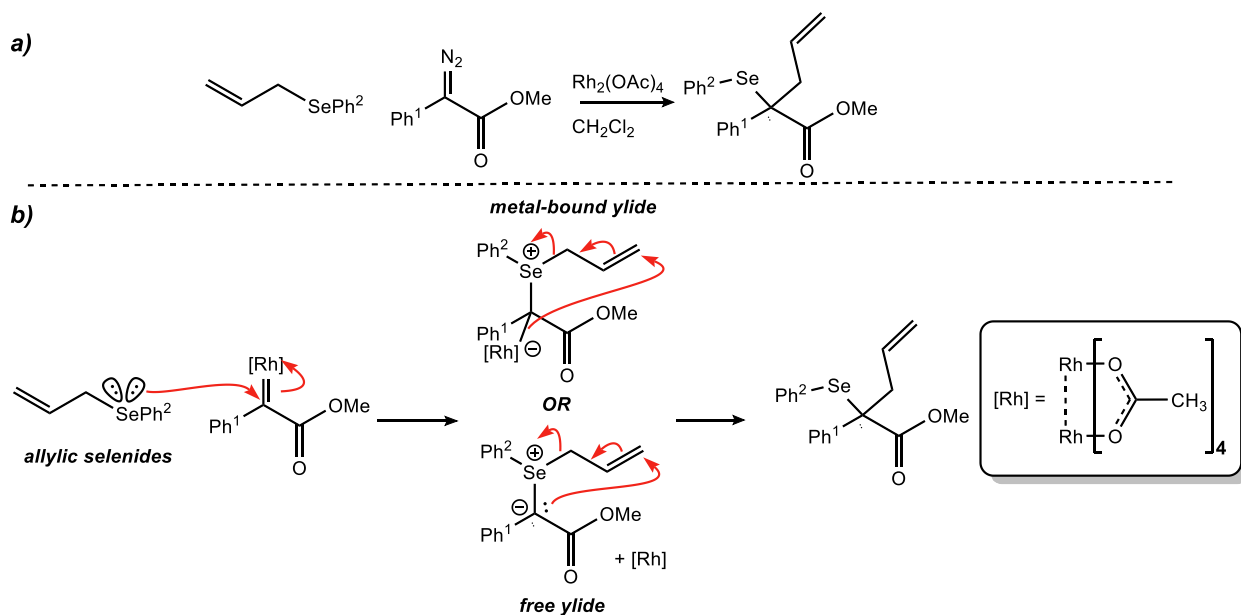


Figure 5. a) asymmetric Rh-catalyzed selenonium-ylide rearrangement (Doyle-Kirmse reaction) by Jana and Koenigs (ref. 69) where $ML_n = Rh_2(OAc)_4$ b) system modeled here with DFT calculations, where $[Rh] = Rh_2(OAc)_4$.

Selenium ylide

Although discussed less frequently in the literature, selenium ylides also can undergo rearrangements.⁹² These are effectively Doyle-Kirmse rearrangements with selenium in place of sulfur. Jana and Koenigs demonstrated this reaction recently using diazoalkanes and allyl selenides to generate homoallyl selenides (**Figure 5**).⁶⁹ They observed that the selectivity is only slightly affected by the type of catalyst, lending support to the hypothesis that this reaction undergoes a free-ylide mechanism. Is this conclusion borne out in our DFT calculations?

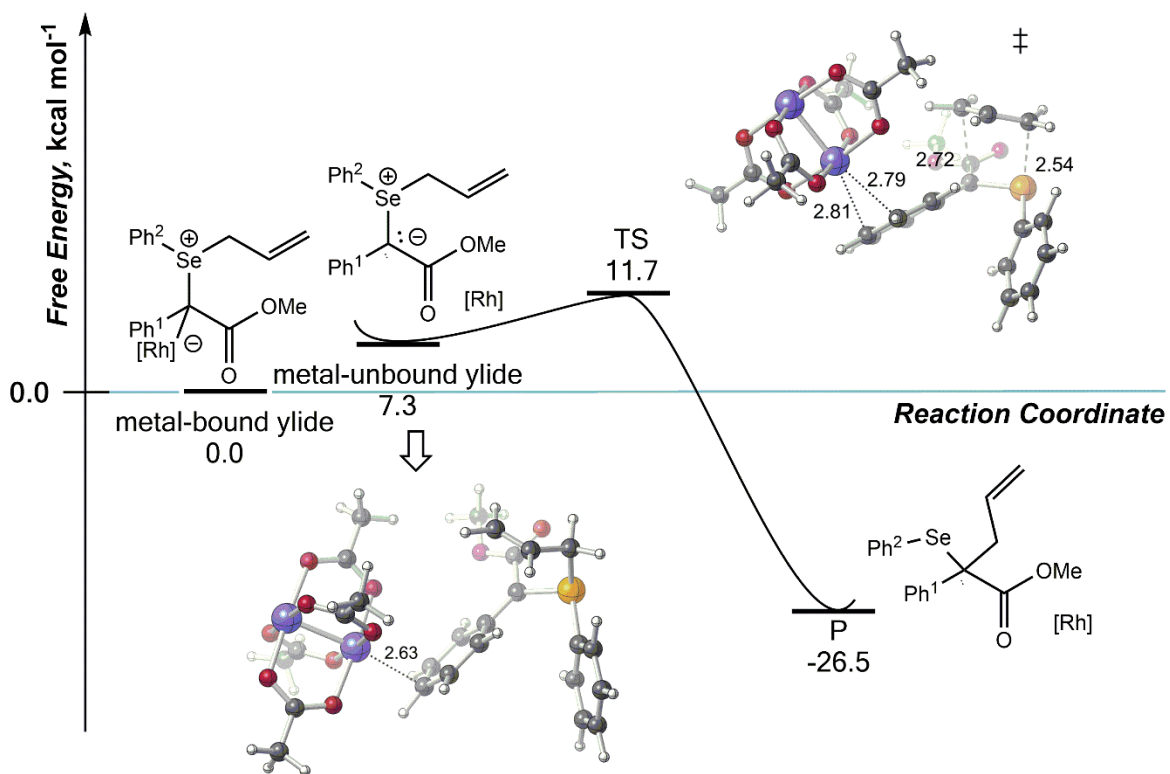


Figure 6. Energy profile for Rh-unbound selenonium-ylide [2,3]-rearrangement step in the Doyle-Kirmse reaction (by Jana and Koenigs, ref. 69). Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

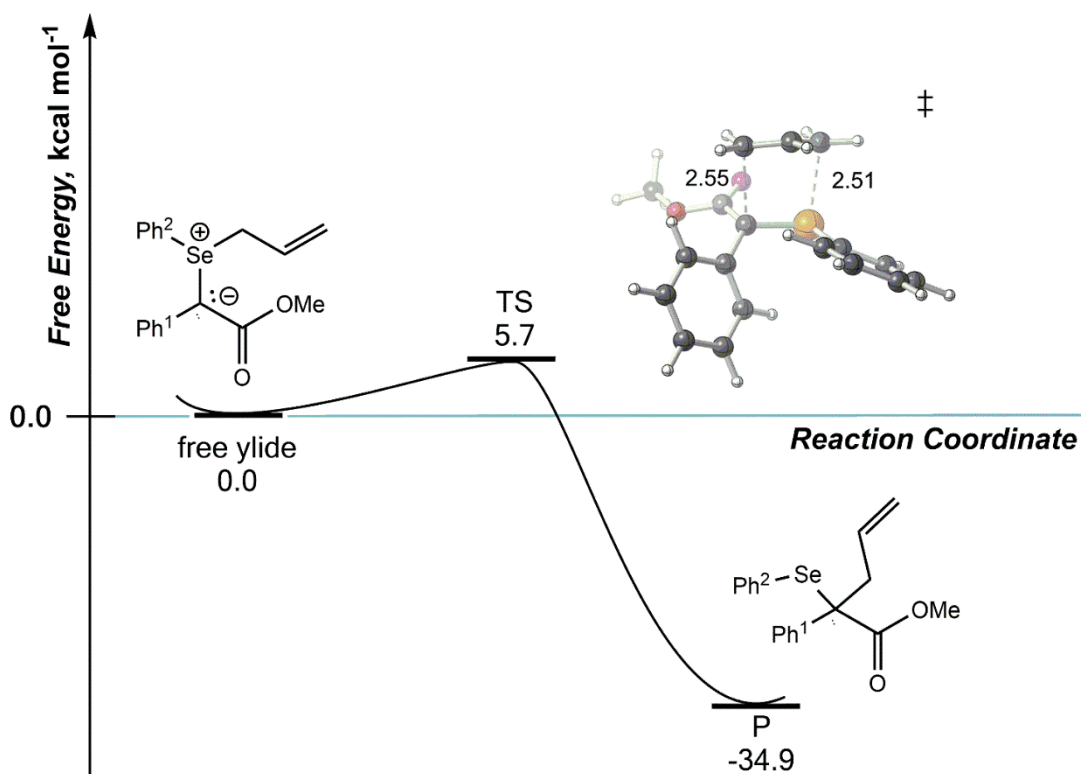


Figure 7. Energy profile for “free” selenonium ylide [2,3]-rearrangement step in the Doyle-Kirmse reaction (based on study by Jana and Koenigs, ref. 69). Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

Yes. Only a metal-dissociated TSS for the [2,3]-sigmatropic rearrangement could be located and all attempts to find a TSS with the metal bound resulted in the metal catalyst dissociating before the TSS (**Figure 6**). The free ylide pathway is energetically viable (only 5.7 kcal mol⁻¹ barrier to product), supporting the conclusion the free ylide intermediates can undergo the rearrangement step (**Figure 7**). As we observed in the sulfonium ylide system by Wang and co-workers (*vide supra*), TSS searches for a [2,3]-rearrangement TSSs with the Rh covalently bound resulted in only a catalyst-unbound TSS, with the Rh-catalyst associated to the aryl ring (Ph¹). On the surface, these results suggest that for both the sulfonium and selenonium cases,

only free ylide mechanisms are energetically viable and something about these two cases prevents the Rh catalyst from remaining bound to its substrate prior to rearrangement.

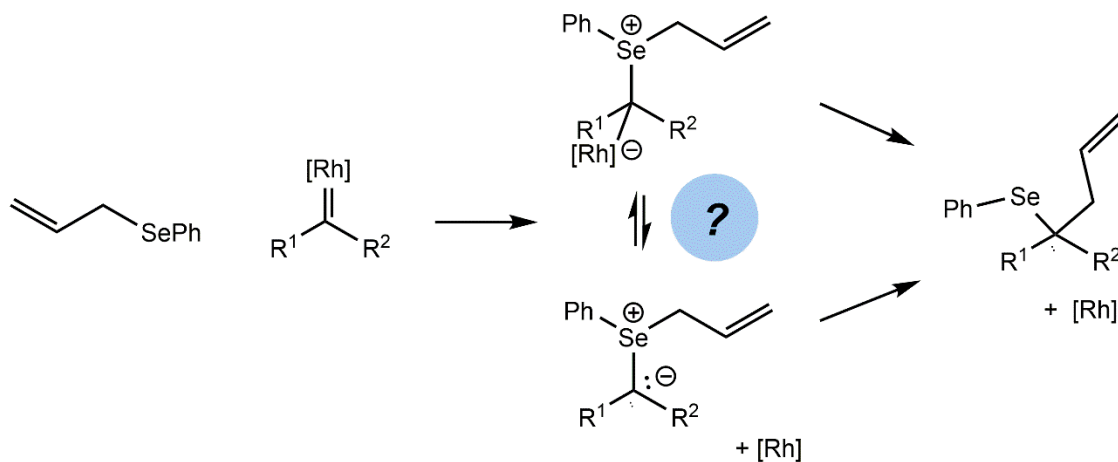
These specific examples of rearrangement for each ylide type (oxonium, sulfonium, and selenonium) should not be generalized to all similar ylides undergoing [2,3]-rearrangements. However, our results support past experimental results that proposed free-ylide mechanisms based on cross-over experiments.

Beyond donor-acceptor carbenes—studies for understanding the origin of dissociation

In an effort to understand why there is a preference for the Rh catalyst to remain covalently bound in the oxonium case, but heterolytically dissociate in the sulfonium and selenonium cases, we used the system studied by Jana and Koenigs (X = Se) as a case study. We explored how the electronic nature of the carbene center would influence the metal-bound ylide/free ylide equilibrium. In Koenigs's study,⁶⁹ an electrophilic carbene with at least one electron-withdrawing group (donor-acceptor) is used, and indeed in most [2,3]-rearrangements from diazo compound-derived ylide intermediates, this is the case.^{5,20} Although, to our knowledge, donor-donor and donor diazo compounds have not been used in these reactions, we can study the effects of such compounds computationally.

Of the five Rh carbene types (acceptor, acceptor/acceptor, donor/donor, donor/acceptor, and donor) studied here, which ones prefer to dissociate Rh catalyst prior to the [2,3]-sigmatropic shift (**Scheme 3**)? We located a metal-bound [2,3]-rearrangement with the Rh catalyst explicitly bound to the carbene carbon in the acceptor and donor carbene cases, the only carbene intermediates in which one of the substituents adjacent to the carbene carbon was hydrogen.

Scheme 3. Five types of Rh carbenes studied in [2,3]-sigmatropic rearrangement step.



Acceptor-Acceptor (AA): $R^1 = \text{CO}_2\text{Me}$, $R^2 = \text{CO}_2\text{Me}$
 Acceptor (A): $R^1 = \text{H}$, $R^2 = \text{CO}_2\text{Me}$
 Donor-Acceptor (DA): $R^1 = \text{Ph}$, $R^2 = \text{CO}_2\text{Me}$
 Donor (D): $R^1 = \text{H}$, $R^2 = \text{Ph}$
 Donor-donor (DD): $R^1 = \text{Ph}$, $R^2 = \text{Ph}$

Table 1. Selenonium-ylide [2,3]-rearrangement step in the Doyle-Kirmse reaction (based on study by Jana and Koenigs, ref. 69) for donor, donor-donor, donor-acceptor, acceptor, and acceptor-acceptor Rh carbenes. Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

Rh-Carbene	Metal-bound [2,3] TSS?	$\Delta G^\ddagger_{\text{metal-bound}}$	$\Delta G^\ddagger_{\text{free-ylide}}$
Acceptor	Yes	17.3	13.9
Donor	Yes	18.3	1.6
Acceptor-Acceptor	No	-	10.2
Donor-Acceptor	No	-	11.7
Donor-Donor	No	-	5.8

Whether the Rh catalyst dissociates is sensitive to the identity of the substituents adjacent to the carbene carbon. This begs the question whether this sensitivity is a result of steric hindrance of the adjacent substituent or the electronic nature of the carbene. To address this question, we modeled the donor variant of Koenigs's system—that is, the two adjacent groups to the carbene being H and Ph—and varied the *para* substituent on both phenyl rings (phenyl of the 'donor' group or the phenyl attached to Se atom). We reasoned that any electronic variation induced by a *para* substituent might tip the balance in favor of a fully Rh-catalyst-dissociated [2,3]-sigmatropic rearrangement as opposed to a Rh-bound one by introducing a greater build-up or reduction in electron density at the benzylic carbon.

We find, however, that varying the electronic nature of either phenyl ring does not cause catalyst dissociation. Figures **S6** and **S7** in the SI show a Hammett plot that relates the *para* substituent's Hammett constant to the free energy barrier of activation. In all cases, we found a Rh-bound [2,3]-sigmatropic rearrangement. More importantly, any change to the electronic nature of the phenyl ring has only a small effect on barriers ($< 1 \text{ kcal mol}^{-1}$). This observation led us to suspect the catalyst dissociation originates from a steric effect of substituents adjacent to the benzylic position.

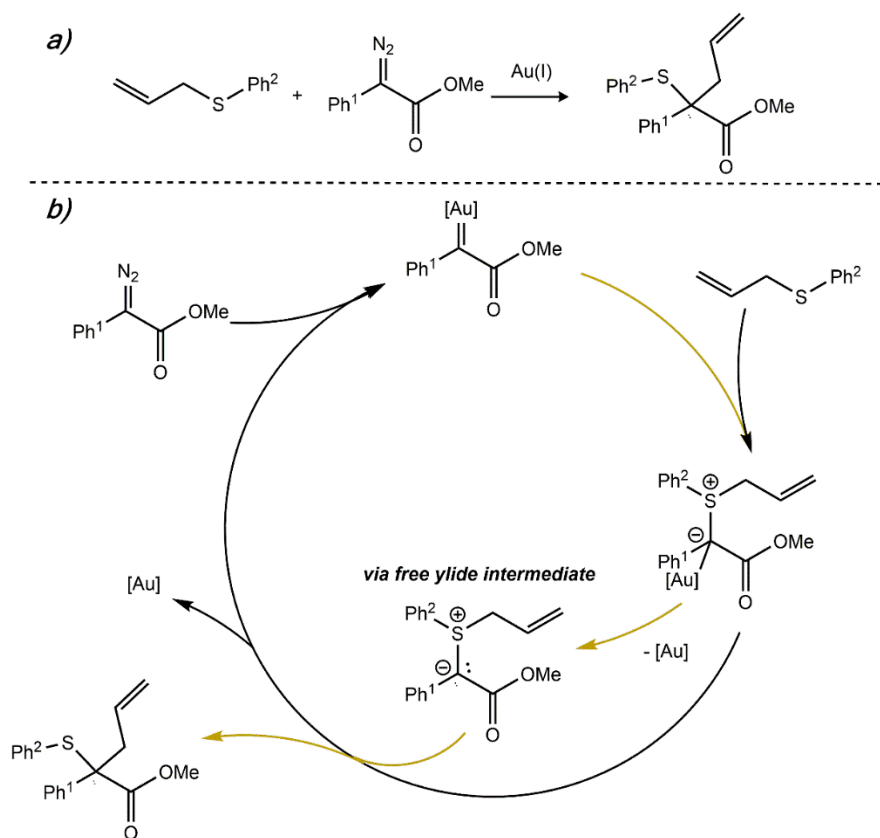
We next varied the adjacent hydrogen substituent—keeping all else the same—to substituents with increasing steric bulk. In the first variation, when changing H to Me, we could no longer optimize a [2,3]-sigmatropic shift TSS with the Rh catalyst bound to the substrate. However, we did optimize a metal-unbound [2,3] TSS with the catalyst dissociated. Failures to find metal-bound [2,3] TSSs for even more sterically bulky groups, such as ethyl and isopropyl, and phenyl (i.e., the donor/donor variation, *vide supra*) leads us to conclude that steric effects are

primarily responsible for preventing the Rh catalyst from being bound to its substrate during the [2,3]-sigmatropic shift event.

All that glitters is not gold—a comparison to a reaction with gold dissociation

During the preparation of this manuscript, Koenigs and coworkers reported a gold-catalyzed sigmatropic rearrangement from gold carbenes.⁷⁷ The authors argued for a free ylide mechanism because the diastereoselectivity of their reactions is consistent with their past reactions of similar systems.⁷⁷ We sought to find out if this conclusion is also borne out in our DFT calculations.

Scheme 4. a) Gold-catalyzed rearrangement reaction studied in ref. 77 b) proposed catalytic cycle (shown in gold color) to product.



Reported optimized conditions involved a tris-*t*-butyl phosphine gold complex (*t*Bu₃P(AuCl)), which we simplified to [CH₃P(Au)]⁺ in our modeling, given past precedent in modeling gold-catalyzed sigmatropic rearrangements.⁹³ Again, we could not successfully locate a metal-bound [2,3]-rearrangement TSS. Instead, we located a metal-unbound (or free) ylide that underwent the [2,3]-rearrangement with a barrier of ~10 kcal mol⁻¹ in free energy (**Figure 8**). This non-Rh example by Koenigs hints that this phenomenon could be more general and plague other transition-metal catalyzed rearrangements involving onium ylides.

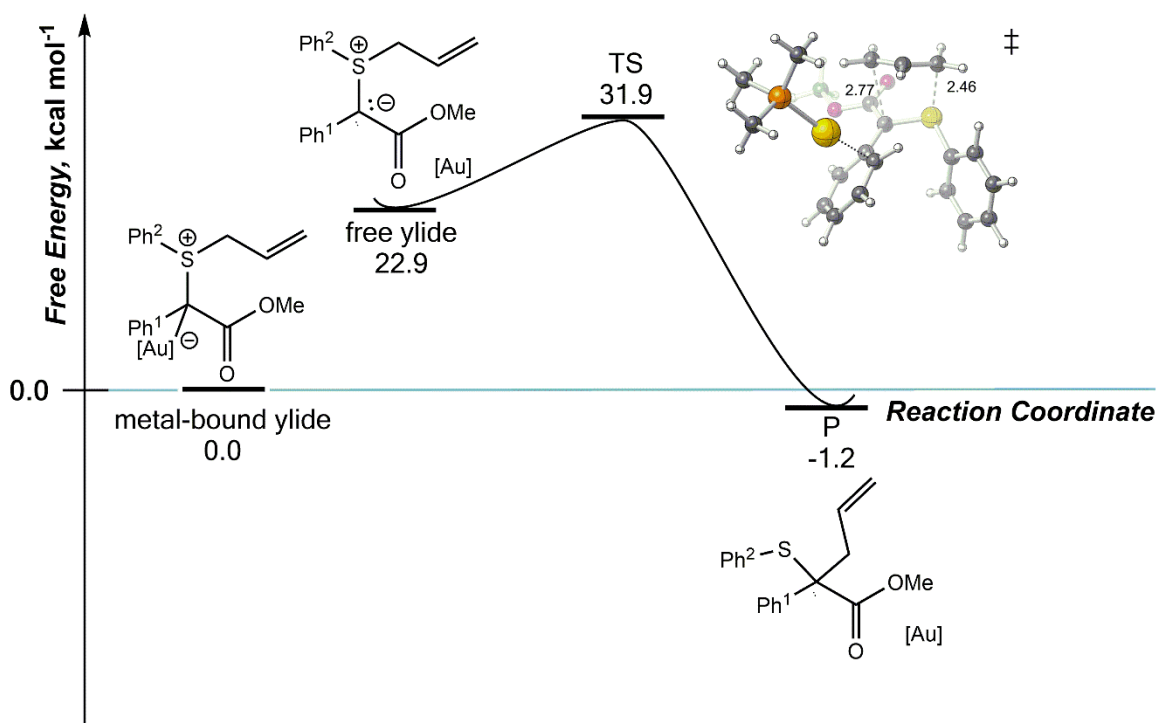


Figure 8. Energy profile for Au-catalyzed, metal-unbound sulfonium ylide [2,3]-rearrangement step (ref. 77). Free energies (in kcal mol⁻¹) are reported at the B3LYP/LANL2DZ[6-31G(d)] level.

Conclusions

Do metal-promoted [2,3]-sigmatropic rearrangements involve metal-bound or free ylide reaction intermediates?⁴ The answer is: *it depends on the system*. What metal catalyst is used? What substituents neighbor the carbene carbon? What type of onium ylide is involved? What remote functional groups can alter the electronic nature of the carbene carbon? All of these factors could have severe effects on whether the metal catalyst ‘stays’ or ‘goes’.¹⁰⁰ We sought to address these questions with DFT calculations, and from our results, the most significant factor was the steric-bulk of the neighboring functional groups at the carbene carbon. Bulkier groups favored free ylide mechanisms even when the electronic nature of the carbene carbon was changed significantly and the onium ylide (e.g., oxonium, sulfonium, and selenonium) kept the same. In sum, should the Rh catalyst ‘stay’ or ‘go’ in these reactions? *It depends on the steric clash* of substituents adjacent to the carbene carbon.¹⁰⁰

ASSOCIATED CONTENT

Supporting Information. A data set collection of computational results is available in the ioChem-BD repository and can be accessed via <https://doi.org/10.19061/iochem-bd-6-68>

The following files are available free of charge.

brief description (file type, i.e., PDF)

brief description (file type, i.e., PDF)

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Citation Diversity Statement⁹⁴

Studies in the literature find that women and other underrepresented minorities are under-cited in their respective fields.^{95,96} Herein we tried our best to accurately cite relevant studies pertinent to this study, while being mindful of the gender balance of the reference list. The references contain 69% man/man, 16% woman/man, 3% man/woman, 1% woman/woman, and 11% unknown categorization (we recognize that this list is limited to binary gender identities and we look forward to the day when this can accommodate intersex, trans-gender, and/or non-binary identities).⁹⁴ These percentages reflect the gender imbalances that persist in organic chemistry and more broadly in science, technology, engineering, and mathematics (STEM) fields.⁹⁷ Clearly, more work needs to be done to correct this imbalance for future generations of scientists.

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REFERENCES

- (1) Jones, A. C.; May, J. A.; Sarpong, R.; Stoltz, B. M. Toward a Symphony of Reactivity: Cascades Involving Catalysis and Sigmatropic Rearrangements. *Angew. Chemie - Int. Ed.* **2014**, *53* (10), 2556–2591.
- (2) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. Highly Effective Catalytic Methods for Ylide Generation from Diazo Compounds. Mechanism of the Rhodium- and Copper-Catalyzed Reactions with Allylic Compounds. *J. Org. Chem.* **1981**, *46* (25), 5094–5102.
- (3) Zhang, Z.; Sheng, Z.; Yu, W.; Wu, G.; Zhang, R.; Chu, W. D.; Zhang, Y.; Wang, J. Catalytic Asymmetric Trifluoromethylthiolation via Enantioselective [2,3]-Sigmatropic Rearrangement of Sulfonium Ylides. *Nat. Chem.* **2017**, *9*, 970–976.
- (4) Hock, K. J.; Koenigs, R. M. Metal-Bound or Free Ylides as Reaction Intermediates? *Angew. Chemie Int. Ed.* **2017**, *56*, 13566–13568.
- (5) Jana, S.; Guo, Y.; Koenigs, R. M. Recent Perspectives on Rearrangement Reactions of Ylides via Carbene Transfer Reactions. *Chem. - A Eur. J.* **2020**, *ASAP*, DOI: 10.1002/chem.202002556.
- (6) Doyle, M. P. Enantiocontrol in Catalytic Metal Carbene Reactions. *Russ. Chem. Bull.* **1999**, *48* (I), 16–20.
- (7) Demonceau, A.; Noels, A. F.; Costa, J.-L. Rhodium(II) Carboxylate-Catalyzed Reactions of Diazoesters: Evidence for an Equilibrium between Free Carbene and a Metal-Carbene Complex. *J. Mol. Catal.* **1990**, *58*, 21–26.
- (8) West, T. H.; Spoehrle, S. S. M.; Kasten, K.; Taylor, J. E.; Smith, A. D. Catalytic

- Stereoselective [2,3]-Rearrangement Reactions. *ACS Catal.* **2015**, *5* (12), 7446–7479.
- (9) Jana, S.; Empel, C.; Pei, C.; Aseeva, P.; Nguyen, T. V.; Koenigs, R. M. C-H Functionalization Reactions of Unprotected N-Heterocycles by Gold-Catalyzed Carbene Transfer. *ACS Catal.* **2020**, *10*, 9925–9931.
- (10) Hartwig, J. F. *Organotransition Metal Chemistry: From Bonding to Catalysis*; University Science Books, 2009.
- (11) Crabtree, R. *The Organometallic Chemistry of the Transition Metals*; Wiley, 2009.
- (12) Hoffmann, R. W. Stereochemistry of [2,3]-Sigmatropic Rearrangements. *Angew. Chemie Int. Ed. English* **1979**, *18* (8), 563–640.
- (13) Nakai, T.; Mikami, K. [2,3]-Wittig Sigmatropic Rearrangements in Organic Synthesis. *Chem. Rev.* **1986**, *86* (5), 885–902.
- (14) Doyle, M. P.; Forbes, D. C. Recent Advances in Asymmetric Catalytic Metal Carbene Transformations. *Chem. Rev.* **1998**, *98*, 911–935.
- (15) Mikami, K.; Nakai, T. Acyclic Stereocontrol via [2,3]-Wittig Sigmatropic Rearrangement. *Synthesis (Stuttg.)* **1991**, *1991* (8), 594–604.
- (16) Clark, J. S. *Nitrogen, Oxygen, and Sulfur Ylide Chemistry. A Practical Approach in Chemistry*; Oxford University Press: New York, 2002.
- (17) Sweeney, J. B. Sigmatropic Rearrangements of “onium” Ylids. *Chem. Soc. Rev.* **2009**, *38* (4), 1027–1038.
- (18) Murphy, G. K.; Stewart, C.; West, F. G. Intramolecular Generation and Rearrangement of

- Oxonium Ylides: Methodology Studies and Their Application in Synthesis. *Tetrahedron* **2013**, *69* (13), 2667–2686.
- (19) Bao, H.; Tambar, U. K. [2,3]-Rearrangements of Ammonium Zwitterions. In *Molecular Rearrangements in Organic Synthesis*; Rojas, C. M., Ed.; John Wiley & Sons, Inc.: New York, 2015; pp 459–496.
- (20) Sheng, Z.; Zhang, Z.; Chu, C.; Zhang, Y.; Wang, J. Transition Metal-Catalyzed [2,3]-Sigmatropic Rearrangements of Ylides: An Update of the Most Recent Advances. *Tetrahedron* **2017**, *73* (29), 4011–4022.
- (21) Caballero, A.; Pérez, P. J. Dimensioning the Term Carbenoid. *Chem. - A Eur. J.* **2017**, *23* (58), 14389–14393.
- (22) Doyle, M. P. Catalytic Methods for Metal Carbene Transformations. *Chem. Rev.* **1986**, *86* (5), 919–939.
- (23) Davies, H. M. L.; Morton, D. Guiding Principles for Site Selective and Stereoselective Intermolecular C-H Functionalization by Donor/Acceptor Rhodium Carbenes. *Chem. Soc. Rev.* **2011**, *40* (4), 1857–1869.
- (24) Davies, H. M. L.; Parr, B. T. *Rhodium Carbenes*, 1st ed.; Moss, R. A., Doyle, M. P., Eds.; John Wiley & Sons, Inc., 2014.
- (25) Adly, F. G. On the Structure of Chiral Dirhodium(II) Carboxylate Catalysts: Stereoselectivity Relevance and Insights for Improved Performance of Viable Whole-Cell Baeyer-Villiger Monooxygenase by Immobilization. *Catalysts* **2017**, *7* (11), 347.
- (26) Davies, H. M. L.; Liao, K. Dirhodium Tetracarboxylates as Catalysts for Selective

- Intermolecular C–H Functionalization. *Nat. Rev. Chem.* **2019**, *3* (6), 347–360.
- (27) Ford, A.; Miel, H.; Ring, A.; Slattery, C. N.; Maguire, A. R.; McKervey, M. A. Modern Organic Synthesis with α -Diazocarbonyl Compounds. *Chem. Rev.* **2015**, *115* (18), 9981–10080.
- (28) Doyle, M. P.; McKervey, M. A.; Ye, T. Modern Catalytic Methods for Organic Synthesis with Diazo Compounds : From Cyclopropanes to Ylides. In *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds: From Cyclopropanes to Ylides*; Wiley, 1998; pp 112–162.
- (29) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic Carbene Insertion into C-H Bonds. *Chem. Rev.* **2010**, *110*, 704–724.
- (30) Doyle, M. P.; Forbes, D. C. Recent Advances in Asymmetric Catalytic Metal Carbene Transformations. *Chem. Rev.* **1998**, *98* (2), 911–935.
- (31) Davies, H. M. L.; Beckwith, R. E. J. Catalytic Enantioselective C-H Activation by Means of Metal-Carbenoid-Induced C-H Insertion. *Chem. Rev.* **2003**, *103* (8), 2861–2903.
- (32) Davies, H. M. L.; Manning, J. R. Catalytic C-H Functionalization by Metal Carbenoid and Nitrenoid Insertion. *Nature* **2008**, *451* (7177), 417–424.
- (33) Zhu, D.; Chen, L.; Fan, H.; Yao, Q.; Zhu, S. Recent Progress on Donor and Donor–Donor Carbenes. *Chem. Soc. Rev.* **2020**, *49*, 908–950.
- (34) Nickerson, L. A.; Bergstrom, B. D.; Gao, M.; Shiue, Y.-S.; Laconsay, C. J.; Culberson, M. R.; Knauss, W. A.; Fettinger, J. C.; Tantillo, D. J.; Shaw, J. T. Enantioselective Synthesis of Isochromans and Tetrahydroisoquinolines by C–H Insertion of Donor/Donor Carbenes.

Chem. Sci. **2020**, *11*, 494–498.

- (35) Soldi, C.; Lamb, K. N.; Squitieri, R. A.; González-López, M.; Di Maso, M. J.; Shaw, J. T. Enantioselective Intramolecular C-H Insertion Reactions of Donor-Donor Metal Carbenoids. *J. Am. Chem. Soc.* **2014**, *136* (43), 15142–15145.
- (36) Shaw, J. T. C-H Insertion Reactions of Donor/Donor Carbenes: Inception, Investigation, and Insights. *Synlett* **2020**, *31* (9), 838–844.
- (37) Werlé, C.; Goddard, R.; Philipps, P.; Farès, C.; Fürstner, A. Structures of Reactive Donor/Acceptor and Donor/Donor Rhodium Carbenes in the Solid State and Their Implications for Catalysis. *J. Am. Chem. Soc.* **2016**, *138* (11), 3797–3805.
- (38) Lamb, K. N.; Squitieri, R. A.; Chintala, S. R.; Kwong, A. J.; Balmond, E. I.; Soldi, C.; Dmitrenko, O.; Castiñeira Reis, M.; Chung, R.; Addison, J. B.; et al. Synthesis of Benzodihydrofurans by Asymmetric C–H Insertion Reactions of Donor/Donor Rhodium Carbenes. *Chem. - A Eur. J.* **2017**, *23* (49), 11843–11855.
- (39) Bergstrom, B. D.; Nickerson, L. A.; Shaw, J. T.; Souza, L. W. Transition Metal Catalyzed Insertion Reactions with Donor/Donor Carbenes. *Angew. Chemie Int. Ed.* **2020**, *ASAP*, DOI: <https://doi.org/10.1002/anie.202007001>.
- (40) Green, S. P.; Wheelhouse, K. M.; Payne, A. D.; Hallett, J. P.; Miller, P. W.; Bull, J. A. Thermal Stability and Explosive Hazard Assessment of Diazo Compounds and Diazo Transfer Reagents. *Org. Process Res. Dev.* **2020**, *24* (1), 67–84.
- (41) Li, Y.; Huang, Z.; Wu, X.; Xu, P. F.; Jin, J.; Zhang, Y.; Wang, J. Rh(II)-Catalyzed [2,3]-Sigmatropic Rearrangement of Sulfur Ylides Derived from N-Tosylhydrazones and

- Sulfides. *Tetrahedron* **2012**, *68* (26), 5234–5240.
- (42) Soheili, A.; Tambar, U. K. Tandem Catalytic Allylic Amination and [2,3]-Stevens Rearrangement of Tertiary Amines. *J. Am. Chem. Soc.* **2011**, *133* (33), 12956–12959.
- (43) West, T. H.; Daniels, D. S. B.; Slawin, A. M. Z.; Smith, A. D. An Isothiourea-Catalyzed Asymmetric [2,3]-Rearrangement of Allylic Ammonium Ylides. *J. Am. Chem. Soc.* **2014**, *136* (12), 4476–4479.
- (44) West, T. H.; Walden, D. M.; Taylor, J. E.; Brueckner, A. C.; Johnston, R. C.; Cheong, P. H. Y.; Lloyd-Jones, G. C.; Smith, A. D. Catalytic Enantioselective [2,3]-Rearrangements of Allylic Ammonium Ylides: A Mechanistic and Computational Study. *J. Am. Chem. Soc.* **2017**, *139* (12), 4366–4375.
- (45) Li, F.; He, F.; Koenigs, R. M. Catalyst-Free [2,3]-Sigmatropic Rearrangement Reactions of Photochemically Generated Ammonium Ylides. *Synth.* **2019**, *51* (23), 4348–4358.
- (46) Hommelsheim, R.; Guo, Y.; Yang, Z.; Empel, C.; Koenigs, R. M. Blue-Light-Induced Carbene-Transfer Reactions of Diazoalkanes. *Angew. Chemie - Int. Ed.* **2019**, *58* (4), 1203–1207.
- (47) West, F. G. Rearrangement Processes of Oxonium and Ammonium Ylides Formed by Rhodium(II)-Catalyzed Carbene Transfer. In *Modern Rhodium-Catalyzed Organic Reactions*; Evans, P. A., Ed.; Wiley-VCH, 2005; pp 417–431.
- (48) McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. A New Rhodium(II) Phosphate Catalyst for Diazocarbonyl Reactions Including Asymmetric Synthesis. *Tetrahedron Lett.* **1992**, *33* (40), 5983–5986.

- (49) Li, Z.; Boyarskikh, V.; Hansen, J. H.; Autschbach, J.; Musaev, D. G.; Davies, H. M. L. Scope and Mechanistic Analysis of the Enantioselective Synthesis of Allenes by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Propargylic Alcohols. *J. Am. Chem. Soc.* **2012**, *134* (37), 15497–15504.
- (50) Li, Z.; Parr, B. T.; Davies, H. M. L. Highly Stereoselective C-C Bond Formation by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Chiral Allylic Alcohols. *J. Am. Chem. Soc.* **2012**, *134* (26), 10942–10946.
- (51) Ferris, L.; Haigh, D.; Moody, C. J. New Chiral Rhodium(II) Carboxylates and Their Use as Catalysts in Carbenoid Transformations. *Tetrahedron Lett.* **1996**, *37* (1), 107–110.
- (52) Doyle, M. P.; Peterson, C. S. Macrocyclic Oxonium Ylide Formation and Internal [2,3]-Sigmatropic Rearrangement. Catalyst Influence on Selectivity. *Tetrahedron Lett.* **1997**, *38* (30), 5265–5268.
- (53) Pierson, N.; Fernández-García, C.; McKervey, M. A. Catalytic Asymmetric Oxonium Ylide - [2,3] Sigmatropic Rearrangement with Diazocarbonyl Compounds : First Use of C₂-Symmetry in Rh(II) Carboxylates. *Tetrahedron Lett.* **1997**, *38* (26), 4705–4708.
- (54) Clark, J. S.; Fretwell, M.; Whitlock, G. A.; Burns, C. J.; Fox, D. N. A. Asymmetric Synthesis of Cyclic Ethers by Rearrangement of Oxonium Ylides Generated from Chiral Copper Carbenoids. *Tetrahedron Lett.* **1998**, *39* (1–2), 97–100.
- (55) Hodgson, D. M.; Petroliaigi, M. Rh(II)-Binaphthol Phosphate Catalysts in the

- Enantioselective Intramolecular Oxonium Ylide Formation-[3,2] Sigmatropic Rearrangement of α -Diazo- β -Ketoesters. *Tetrahedron Asymmetry* **2001**, *12* (6), 877–881.
- (56) Kitagaki, S.; Yanamoto, Y.; Tsutsui, H.; Anada, M.; Nakajima, M.; Hashimoto, S. Enantioselective [2,3]-Sigmatropic and [1,2]-Stevens Rearrangements via Intramolecular Formation of Allylic Oxonium Ylides Catalyzed by Chiral Dirhodium(II) Carboxylates. *Tetrahedron Lett.* **2001**, *42* (36), 6361–6364.
- (57) Shimada, N.; Nakamura, S.; Anada, M.; Shiro, M.; Hashimoto, S. Enantioselective Construction of a 2,8-Dioxabicyclo[3.2.1]Octane Ring System via [2,3]-Sigmatropic Rearrangement of Oxonium Ylide Using Chiral Dirhodium(II) Carboxylates. *Chem. Lett.* **2009**, *38* (5), 488–489.
- (58) Li, Z.; Davies, H. M. L. Enantioselective C-C Bond Formation by Rhodium-Catalyzed Tandem Ylide Formation/[2,3]-Sigmatropic Rearrangement between Donor/Acceptor Carbenoids and Allylic Alcohols. *J. Am. Chem. Soc.* **2010**, *132* (1), 396–401.
- (59) Reggelin, M. [2,3]-Sigmatropic Rearrangements of Allylic Sulfur Compounds. *Top Curr Chem* **2007**, *275*, 1–65.
- (60) Hock, K. J.; Mertens, L.; Hommelsheim, R.; Spitzner, R.; Koenigs, R. M. Enabling Iron Catalyzed Doyle-Kirmse Rearrangement Reactions with: In Situ Generated Diazo Compounds. *Chem. Commun.* **2017**, *53* (49), 6577–6580.
- (61) Yang, Z.; Guo, Y.; Koenigs, R. M. Solvent-Dependent, Rhodium Catalyzed Rearrangement Reactions of Sulfur Ylides. *Chem. Commun.* **2019**, *55* (58), 8410–8413.
- (62) Kaiser, D.; Klose, I.; Oost, R.; Neuhaus, J.; Maulide, N. Bond-Forming and -Breaking

Reactions at Sulfur(IV): Sulfoxides, Sulfonium Salts, Sulfur Ylides, and Sulfinates Salts. *Chem. Rev.* **2019**, *119* (14), 8701–8780.

- (63) Empel, C.; Hock, K. J.; Koenigs, R. M. Dealkylative Intercepted Rearrangement Reactions of Sulfur Ylides. *Chem. Commun.* **2019**, *55* (3), 338–341.
- (64) Xu, X.; Li, C.; Tao, Z.; Pan, Y. Aqueous Hemin Catalyzed Sulfonium Ylide Formation and Subsequent [2,3]-Sigmatropic Rearrangements. *Green Chem.* **2017**, *19* (5), 1245–1249.
- (65) Yan, X.; Li, C.; Xu, X.; Zhao, X.; Pan, Y.-J. Hemin Catalyzed Dealkylative Intercepted [2, 3]-Sigmatropic Rearrangement Reactions of Sulfonium Ylide with 2, 2, 2-Trifluorodiazoethane. *Adv. Synth. Catal.* **2020**, 1–8.
- (66) Qin, H.; Jia, Y.; Wang, N.; Jiang, Z.-X.; Yang, Z. Practical and Regioselective Halo-Trifluoromethylthiolation of Sulfur Ylides. *Chem. Commun.* **2020**, *56* (59), 8265–8268.
- (67) Reddy, A. C. S.; Anbarasan, P. Rhodium-Catalyzed Rearrangement of S/Se-Ylides for the Synthesis of Substituted Vinylogous Carbonates. *Org. Lett.* **2019**.
- (68) Jana, S.; Aseeva, P.; Koenigs, R. M. Rhodium Catalyzed Synthesis of Seleno-Ketals via Carbene Transfer Reactions of Diazoesters. *Chem. Commun.* **2019**, *55*, 12825–12828.
- (69) Jana, S.; Koenigs, R. M. Rhodium-Catalyzed Carbene Transfer Reactions for Sigmatropic Rearrangement Reactions of Selenium Ylides. *Org. Lett.* **2019**, *21* (10), 3653–3657.
- (70) Xu, B.; Tambar, U. K. Copper-Catalyzed Enantio-, Diastereo-, and Regioselective [2,3]-Rearrangements of Iodonium Ylides. *Angew. Chemie - Int. Ed.* **2017**, *56* (33), 9868–9871.

- (71) Padwa, A.; Hornbuckle, S. F. Ylide Formation from the Reaction of Carbenes and Carbenoids with Heteroatom Lone Pairs. *Chem. Rev.* **1991**, *91*, 263–309.
- (72) Biswas, B.; Singleton, D. A. Controlling Selectivity by Controlling the Path of Trajectories. *J. Am. Chem. Soc.* **2015**, *137* (45), 14244–14247.
- (73) Clark, J. S.; Hansen, K. E. Intramolecular Reactions of Metal Carbenoids with Allylic Ethers: Is a Free Ylide Involved in Every Case? *Chem. - A Eur. J.* **2014**, *20* (18), 5454–5459.
- (74) Dequina, H. J.; Schomaker, J. M. Aziridinium Ylides: Underused Intermediates for Complex Amine Synthesis. *Trends Chem.* **2020**, *2* (10), 874–887.
- (75) Li, S.-S.; Wang, J. Cu(I)/Chiral Bisoxazoline-Catalyzed Enantioselective Sommelet-Hauser Rearrangement of Sulfonium Ylides. *J. Org. Chem.* **2020**, *85* (19), 12343–12358.
- (76) Harrison, J. G.; Gutierrez, O.; Jana, N.; Driver, T. G.; Tantillo, D. J. Mechanism of Rh₂(II)-Catalyzed Indole Formation: The Catalyst Does Not Control Product Selectivity. *J. Am. Chem. Soc.* **2016**, *138* (2), 487–490.
- (77) He, F.; Jana, S.; Koenigs, R. M. Gold-Catalyzed Sigmatropic Rearrangement Reactions via Carbene Transfer Reactions. *J. Org. Chem.* **2020**, *85*, 11882–11891.
- (78) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E. ; Robb, G. E.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B. ; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P. ; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M. ; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T. ; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A. . P.; J. E.; Ogliaro, F.;

- Bearpark, M.; Heyd, J. J.; Brothers, E. . K.; K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J. . R.; K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J. . C.; M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B. .; et al. Gaussian 09, Revision D.01. *Gaussian Inc.* Wallingford, CT 2009.
- (79) Fukui, K. The Path of Chemical Reactions -- The IRC Approach. *Acc. Chem. Res.* **1981**, *14*, 363–368.
- (80) 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.
- (81) Maeda, S.; Harabuchi, Y.; Ono, Y.; Taketsugu, T.; Morokuma, K. Intrinsic Reaction Coordinate: Calculation, Bifurcation, and Automated Search. *Int. J. Quantum Chem.* **2015**, *115* (5), 258–269.
- (82) Schmid, S. C.; Guzei, I. A.; Fernández, I.; Schomaker, J. M. Ring Expansion of Bicyclic Methyleneaziridines via Concerted, Near-Barrierless [2,3]-Stevens Rearrangements of Aziridinium Ylides. *ACS Catal.* **2018**, *8* (9), 7907–7914.
- (83) Lee, M.; Ren, Z.; Musaev, D. G.; Davies, H. M. L. Rhodium-Stabilized Diarylcarbenes Behaving as Donor/Acceptor Carbenes. *ACS Catal.* **2020**, 6240–6247.
- (84) Chai, J. Da; Head-Gordon, M. Long-Range Corrected Hybrid Density Functionals with Damped Atom-Atom Dispersion Corrections. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615–6620.
- (85) Grimme, S.; Antony, J.; Ehrlich, S.; Krieg, H. A Consistent and Accurate Ab Initio

- Parametrization of Density Functional Dispersion Correction (DFT-D) for the 94 Elements H-Pu. *J. Chem. Phys.* **2010**, *132* (15), 154104.
- (86) Grimme, S.; Ehrlich, S.; Goerigk, L. Effect of the Damping Function in Dispersion Corrected Density Functional Theory. *J. Comput. Chem.* **2011**, *42*, 1456–1465.
- (87) 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* (1), 95–103.
- (88) Pirrung, M. C.; Werner, J. A. Intramolecular Generation and [2,3]-Sigmatropic Rearrangement of Oxonium Ylides. *J. Am. Chem. Soc.* **1986**, *108* (19), 6060–6062.
- (89) Kirmse, W.; Kapps, M. Reaktionen Des Diazomethans Mit Diallylsulfid Und Allyläthern Unter Kupfersalz-Katalyse. *Chem. Ber.* **1968**, *101* (3), 994–1003.
- (90) Zhang, Y.; Wang, J. Catalytic [2,3]-Sigmatropic Rearrangement of Sulfur Ylide Derived from Metal Carbene. *Coord. Chem. Rev.* **2010**, *254*, 941–953.
- (91) Nishibayashi, Y.; Ohe, K.; Uemura, S. The First Example of Enantioselective Carbenoid Addition to Organochalcogen Atoms: Application to [2,3]Sigmatropic Rearrangement of Allylic Chalcogen Ylides. *J. Chem. Soc. Chem. Commun.* **1995**, No. 12, 1245–1246.
- (92) Drabowicz, J.; Rzewnicka, A.; Żurawiński, R. Selenonium Ylides: Syntheses, Structural Aspects, and Synthetic Applications. *Molecules* **2020**, *25* (10), 2420.
- (93) Felix, R. J.; Weber, D.; Gutierrez, O.; Tantillo, D. J.; Gagné, M. R. A Gold-Catalysed Enantioselective Cope Rearrangement of Achiral 1,5-Dienes. *Nat. Chem.* **2012**, *4* (5), 405–409.

- (94) Dworkin, J.; Zurn, P.; Bassett, D. S. (In)Citing Action to Realize an Equitable Future. *Neuron* **2020**, *106* (6), 890–894.
- (95) Caplar, N.; Tacchella, S.; Birrer, S. Quantitative Evaluation of Gender Bias in Astronomical Publications from Citation Counts. *Nat. Astron.* **2017**, *1* (May), 0141.
- (96) Dworkin, J. D.; Linn, K. A.; Teich, E. G.; Zurn, P.; Shinohara, R. T.; Bassett, D. S. The Extent and Drivers of Gender Imbalance in Neuroscience Reference Lists. *Nat. Neurosci.* **2020**, *23* (8), 918–926.
- (97) Reisman, S. E.; Sarpong, R.; Sigman, M. S.; Yoon, T. P. Organic Chemistry: A Call to Action for Diversity and Inclusion. *J. Org. Chem.* **2020**, *22*, 6223–6228.

(98) Photolysis of diazoalkanes to generate carbene intermediates have notably gained momentum and readers are directed to Koenigs's recent minireview (ref. 5) for discussion on that topic.

(99) Non-statistical dynamic effects are increasingly being shown to be relevant for many organic reactions, including other sigmatropic rearrangement reactions (which can involve so-called bispericyclic or ambimodal TSSs), and related Rh-catalyzed reactions. For the systems described here, we leave the discussion on dynamic effects aside for now. (see Carpenter, *Angew. Chem. Int. Ed.* **1998**, *37*, 3340-3350; Tantillo, *Dynamic Effects on Organic Reactions*, 2018; Ess et al., *Angew. Chem. Int. Ed.* **2008**, *47*, 7592-7601; Hare and Tantillo, *Pure and Applied Chemistry* **2017**, *89*, 679-698; Yang and Houk, *Chem. Eur. J.*, *24*, 3916-3924; Hare and Tantillo, *Chem. Sci.* **2017**, *8*, 1442-1449)

(100) *Should I stay or should I go now / If I go there will be trouble / And if I stay it will be double / So you got to let me know / Should I stay or should I go* - The Clash