The *trans-cis* Isomerization of $\text{Ni}(\eta^2\text{-TEMPO})_2$: Interconnections and Conformational Complexity

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ABSTRACT

Previously, reactions of the “bow-tie” $\text{Ni}(\eta^2\text{-TEMPO})_2$ complex with an assortment of donor ligands have been characterized experimentally and computationally. The X-ray crystal structures afforded $\text{Ni}(\eta^2\text{-TEMPO})_2$ with *trans*-disposed TEMPO ligands, which was validated theoretically. Surprisingly, proton transfer from the C-H bond of a variety of alkyne substrates (R) mostly produced *cis*-disposed ligands of the form $\text{Ni}(\eta^2\text{-TEMPO})(\kappa^1\text{-TEMPOH})(\kappa^1\text{-R})$. While computations validated that the experimentally observed *cis*-disposed products were thermodynamically favored, in all cases, the proposed mechanisms of alkyne addition to *cis*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ were kinetically disfavored. Therefore, a *trans-cis* isomerization must occur along the addition pathway. In order to better understand this phenomenon, an exhaustive theoretical conformational search of *cis-/trans*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ and $\text{Ni}(\eta^2\text{-TEMPO})(\eta^1\text{-TEMPO})$ structures has been performed. Our results show profound conformational and fluxional complexity for the *trans-cis* isomerization of the $\text{Ni}(\eta^2\text{-TEMPO})_2$ precursor. Surprisingly, the proposed mechanism for *trans-cis* isomerization indicates that conformational distortion of one of the TEMPO ligands of *trans*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ before ring-opening provides a transition state free energy of activation stabilization of nearly 4.0 kcal mol⁻¹ versus the most “straightforward” isomerization mechanism.

KEYWORDS

Density Functional Theory, TEMPO ligand, reaction mechanisms, conformational distortion

INTRODUCTION

The stable radical 2,2,6,6-tetramethylpiperidine-N-oxide (TEMPO),¹⁻⁴ first synthesized in 1960, has been shown to be a versatile ligand in the field of catalysis. TEMPO can participate in polymerization and polymerization initiation,⁵⁻⁹ oxidation of alcohols¹⁰⁻¹⁶ including cellulose and biomaterials,¹⁷ and the molecule possesses a host of other useful properties that make it valuable in electron transfer and spin probe studies.¹⁸⁻²⁴ The TEMPO ligand binds readily to metal centers such as nickel and copper, making it a very “green” ligand.²⁵⁻³⁰

The coordination chemistry of this paramagnetic species has also been shown to afford a variety of bonding motifs.³¹⁻⁴² For example, Evans and co-authors have characterized a samarium-centered complex that contains exclusively TEMPO ligands binding to Sm with η^1 , η^2 , and μ - η^1 binding.⁴⁰ Captain and coworkers have reported the preparation of the complex Ni(η^2 -TEMPO)₂, **1**, which is the first example of a coordinative-saturated compound with only η^2 -TEMPO ligands (with 3D representations shown in Scheme 1, and 2D representations in Scheme 2, also *vida infra*).⁴³

Scheme 1 – Hydrogen atoms omitted for clarity

Scheme 2 - 2D representation of *trans*-Ni(η²-TEMPO)₂ and *cis*-Ni(η²-TEMPO)₂ chair-chair conformations

Complex **1** also reacted via Lewis acid-base chemistry with pyridine and *tert*-butyl isocyanide, as well as alkyne donor ligands such as acetylene, phenylacetylene, trimethylsilyl acetylene, and 1,4-diethynylbenzene. These reactions are air-sensitive, but were carried out at room temperature and afforded products in high yield. Synthesis and characterization of the novel bimetallic diethynylbenzene-bridged $\text{Ni}(\eta^2\text{-TEMPO})(\kappa^1\text{-TEMPOH})[\kappa^1\text{-}\kappa^1\text{-CC(C}_6\text{H}_4\text{)CC}]\text{Ni}(\eta^2\text{-TEMPO})(\kappa^1\text{-TEMPOH})$ complex was also reported.

In collaboration with Captain, our laboratories performed a combined experimental and theoretical exploration of the properties and addition mechanisms of the aforementioned complexes.⁴⁴ Density Functional Theory (DFT) computations were used to validate many of the observed structures and properties. The possibility of easily isolating the bimetallic acetylene-bridged species was also ruled out via computations. However, apparent discrepancies between the experimental and computational results revealed an interesting interplay between kinetic and thermodynamic control of the addition mechanisms. Upon addition of *tert*-butyl isocyanide, computations showed that the experimentally observed *cis*- $\text{Ni}(\eta^2\text{-TEMPO})(\eta^1\text{-TEMPO})(\kappa^1\text{-CN}^{tBu})$ product had a nearly equivalent relative free energy to the theoretical *trans*- $\text{Ni}(\eta^2\text{-TEMPO})(\eta^1\text{-TEMPO})(\kappa^1\text{-CN}^{tBu})$ molecule. However, the one-step addition of CN^{tBu} to *cis*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ had a transition state (TS) that was 1.3 kcal mol⁻¹ higher in free energy than the *trans*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ addition TS. Six addition mechanisms were explored overall, and the case of pyridine addition was the only situation where computations and experiment agreed on the identity of both the kinetically *and* thermodynamically controlled product [*trans*- $\text{Ni}(\eta^2\text{-TEMPO})(\eta^1\text{-TEMPO})(\kappa^1\text{-py})$]. Even more worrisome was that the computed rate-limiting free energies of activation for the alkyne addition reactions of the observed products were generally

in the range of 21-24 kcal mol⁻¹, somewhat higher than those expected for reactions that occur on the minutes time scale at room temperature.

It was established that our computations were not likely to be incorrect or grossly inaccurate. Rather, our conclusions were that at some point along the addition reaction pathway, a *trans-cis* isomerization reaction must occur that circumvents the high activation energies of the simple pathways reported in Reference 44. As proposed in this earlier paper, isomerization may occur at one of the three points along the reaction coordinate. These possibilities are a) isomerization of the Ni(η^2 -TEMPO)₂ precursor, b) isomerization of the Ni(η^2 -TEMPO)(η^1 -TEMPO)(η^2 -RH) intermediate or c) isomerization of the *cis*-disposed Ni(η^2 -TEMPO)(κ^1 -TEMPOH)(κ^1 -R) product complex (Scheme 3).

Scheme 3. Isomerization possibilities of addition reactions.

This contribution represents our initial attempt to reconcile the discrepancy between theory and experiment by reporting a conformational exploration of the *trans-cis* isomerization of the initial $\text{Ni}(\eta^2\text{-TEMPO})_2$ complex **1**. The conformational landscape of this seemingly straightforward-looking molecule is surprisingly twisted (pun intended), and the role of complex pre-activation via low-energy conformational distortion will be examined with DFT. The intricacies of this computational study suggest an unknown and fascinating role of metal-

TEMPO ligand conformational distortion when the TEMPO ligand(s) is complexed in a reduced, monoanionic form.

COMPUTATIONAL METHODS

All computations were performed using the Gaussian09 software package.⁴⁵ Gas-phase energies, optimized geometries, and unscaled harmonic vibrational frequencies were obtained using Density Functional Theory (DFT).⁴⁶ The pure PBEPBE^{47,48} functional was used with default grid parameters (the PBEPBE functional will be referred to as PBE throughout the article).⁴⁹ The basis set for nickel was the Hay and Wadt basis set and effective core potential (ECP) combination (LANL2DZ)^{50,51} as modified by Couty and Hall (Ni: 341/341/41),⁵² where the two outermost p functions have been replaced by a split of the optimized Ni 4p function, respectively. All carbon, nitrogen, oxygen, and hydrogen atoms utilized the 6-31G(d') basis set.⁵³ Spherical harmonic d functions were used throughout; i.e., there are five angular basis functions per d function. The Hessian of the energy was computed at all stationary points to designate them as either minima or transition states (first-order saddle points). Zero-point energies (ZPE) and thermal enthalpy/free energy corrections were computed at 1 atm and 298.15 K. Aqueous solvation energies were computed using the SMD model with standard cavity parameters for *n*-hexane.⁵⁴ Gas-phase relative free energies throughout this investigation are generally within 0.1 to 0.5 kcal mol⁻¹ of the solution-phase values reported in the text and Figures. Though a robust comparison of methodologies is outside of the scope of this work, it should be noted that solution-phase relative free energies employing the popular B3LYP functional and basis sets described above do not differ by more than 1.5 kcal mol⁻¹.

RESULTS AND DISCUSSION

a) Relative free energies of Ni(η^2 -TEMPO)₂ and free TEMPO

Before undertaking an examination of the $\text{Ni}(\text{TEMPO})_2$ isomerization mechanism, the possible conformations of free TEMPO and metal-bound TEMPO ligand will be explored. Five minima on the $\text{trans-Ni}(\eta^2\text{-TEMPO})_2$ potential energy surface are shown in Scheme 3 (which details our simplified 2D representations and structure index nomenclature) and Figure 1 (which details the 3D structure of the conformations). These five representations are from the respective $\text{trans-Ni}(\eta^2\text{-TEMPO})_2$ structures optimized at the PBE 6-31G(d') level of theory. In Figure 1, all hydrogen atoms and one of the TEMPO ligands are omitted for clarity.

Figure 1. Nomenclature and 3D structures of $\text{Ni}(\eta^2\text{-TEMPO})_2$. The left cartoon is a “side” view of the *trans*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ with the hydrogen atoms and “left-side” TEMPO ligand omitted for clarity. The middle cartoon is similarly the “front” view, while the images on the right show how the *trans* and *cis* 2D structures of $\text{Ni}(\eta^2\text{-TEMPO})_2$ will be named and represented.

The visual structural parameters of these ten structures [five from $\text{trans-Ni}(\eta^2\text{-TEMPO})_2$ and five from $\text{cis-Ni}(\eta^2\text{-TEMPO})_2$] are now compared to those from free TEMPO radical and free TEMPO anion. Figure 2 shows 3D structures of the seven minima (five from TEMPO anion and two from TEMPO radical).

Figure 2. 3D structures of free anionic and radical TEMPO

Comparing Figures 1 and 2, the nomenclature of structures is as follows: **ch** signifies the TEMPO ligand on the side of the Ni-complex that is being altered is in the conventional **chair** conformation with the oxygen atom equatorially disposed, **tbt-1** signifies the typical twist-boat structure with a long N-C4 distance through the space of the TEMPO ring, **tbt-2** signifies a twist-boat structure with a short N-C4 distance through the TEMPO ring. In free anionic TEMPO, **tbt-2** resembles a conventional boat structure, but this ligand is distorted in the Ni(TEMPO)₂ complexes. The designation **ch-ax** signifies a chair form where the oxygen atom of the TEMPO moiety is axially disposed, and **tbt-3** signifies a twist-boat form with an axially disposed oxygen atom on the TEMPO ligand. The *trans* and *cis* Ni(TEMPO)₂ complexes and anionic TEMPO have five local minima corresponding to each conformer explained above. However, neutral radical TEMPO shows only two conformational minima; most of the radical twist-boat forms are transition states, and the oxygen atom is always equatorially disposed.

Figure 3. Relative solution phase free energies (in kcal mol⁻¹) of Ni(TEMPO)₂ conformers compared to free TEMPO anion and free TEMPO radical.

Solution phase relative free energies are given in Figure 3. Note that the relative energies are set to be internally consistent, meaning that the **1c-ch-ax** form is the zero reference for the **1c** relative free energies (even though **1c-ch-ax** is 4.0 kcal mol⁻¹ higher in free energy than the **1t-ch** minimum). A recent study of the gas phase TEMPO cation, neutral radical, and anion was performed by Grimme, Allan, and co-authors, combining computations and various gas phase photoelectron spectroscopy techniques.⁵⁵ Their gas-phase computed adiabatic electron affinity for free TEMPO [at the B3LYP/6-311++G(2d,p) level of theory and corrected for zero point vibrational energy] was -0.14 eV. Our computed PBE/6-31G(d') EA of +0.21 eV, on the other hand, shows an unbound anion state. This difference in sign for the adiabatic EA of TEMPO is not indicative of a failure of our methodology. In our experience, the pure PBE functional and the hybrid B3LYP functional tend to be gross estimates of relative energetic boundaries one might expect from DFT, when considering a mechanism or reaction energies for organometallic systems. Thus, when the addition of implicit *n*-hexane solvation is including in the computations,

the TEMPO electron affinity decreases to -0.63 eV, which is to be expected considering preferential solvation of a charge. Lastly, Grimme, Allan, and co-authors do not remark on the accessibility of conformationally excited TEMPO anions in their discussion of elastic and vibrational excitation cross section experiments. A more detailed comparison of TEMPO conformations, electron affinities, and activation energies using DFT and wave function-based electron correlation methods is currently in progress in our laboratories.

Figure 3 demonstrates the completely different conformational energy orderings for **1t** (**ch** < **ch-ax** < **tbt-1** < **tbt-3** < **tbt-2**), **1c** (**ch-ax** < **ch** < **tbt-3** < **tbt-1** < **tbt-2**), and free anionic TEMPO (**ch** < **tbt-2** < **ch-ax** < **tbt-1** < **tbt-3**). This difference is likely due to the different steric environments of the two TEMPO ligands in **1t** versus **1c**. It is interesting that the lowest-energy conformer of the initial *cis*-Ni(TEMPO)₂ complex is the axially-disposed chair (**ch-ax**), considering that the molecular structures from the X-ray crystal structures of the *cis*-disposed product reactions in Reference 44 all contain η^1 -TEMPO and κ^1 -TEMPOH ligands in **ch** conformations. Variation in the kinetics and thermodynamics of ring distortion arising in Ni(η^2 -TEMPO)(κ^1 -TEMPOH)(alkyne substituent) complexes will be a useful future theoretical target. Also unexpected is the relatively low energy of the **1t-ch-ax**, which is only $0.6 \text{ kcal mol}^{-1}$ higher in free energy than **1t-ch**.

b) Interconversion of Ni(η^2 -TEMPO)₂ conformers versus free TEMPO anion

Comparison of TEMPO conformational distortion in *trans*-Ni(η^2 -TEMPO)₂, *cis*-Ni(η^2 -TEMPO)₂, and free TEMPO is presented in Figures 4-6. Interestingly, the lowest-energy conformation of all three structures has only one “way out” from the respective global minimum, but these transition states lead to different conformers in each case. The **1t-ch** structure has a free energy of activation of $8.0 \text{ kcal mol}^{-1}$ to get to the **1t-tbt-1** minimum. The **1c-ch-ax** structure has

an effective free energy of activation of $7.6 \text{ kcal mol}^{-1}$ to get to the **1c-tbt-3** minimum. The **ch** conformation of free TEMPO anion must surmount a free energy of $10.0 \text{ kcal mol}^{-1}$ to get to the **tbt-2** minimum. The maximum effective free energy of activation that any one conformer must overcome in order to get to any other conformation is $8.9 \text{ kcal mol}^{-1}$ for **1t**, $8.1 \text{ kcal mol}^{-1}$ for **1c**, and $12.3 \text{ kcal mol}^{-1}$ for TEMPO anion.

Figure 4. Solution-phase free energy diagram (in kcal mol⁻¹) for the interconversion of *trans*-Ni(η^2 -TEMPO)₂ conformers.

Figure 5. Solution-phase free energy diagram (in kcal mol⁻¹) for the interconversion of *cis*-Ni(η^2 -TEMPO)₂ conformers. Free energies in parenthesis are relative to the lowest-energy *trans*-Ni(η^2 -TEMPO)₂ conformer.

Figure 6. Solution-phase free energy diagram (in kcal mol⁻¹) for the interconversion of the free TEMPO anion conformers.

c) The “shortest” paths from **1t-ch** to **1c-ch-ax**

In all, thirty-seven minima on the potential energy surface of the *trans*-Ni(η^2 -TEMPO)₂ to *cis*-Ni(η^2 -TEMPO)₂ isomerization were found. These minima were connected by fifty-seven unique first-order saddle points (transition states), giving ninety-four total unique stationary points. Clearly in order to visualize all possible proposed mechanisms and interconversions for this isomerization process, a free energy diagram, or “IRC network”⁵⁶ would be overwhelming, in both its construction and interpretation. Nonetheless, we found it easier to make a visual map of all relevant stationary points and connectivity using the *Cytoscape* software package.⁵⁷ For a visual indication of the complexity in this potential energy surface, the connectivity map is shown in the Supplementary Material (Figure S1). Progress is being made in our laboratories to generalize the organization and visualization of dense mechanistic data, and we have plans to share our products with the chemistry community.

In our comprehensive study of the conformational space of this species, a mechanism was proposed with four transition states (three intermediates) separating **1t-ch** and **1c-ch-ax**. This proposed pathway contains the least number of steps connecting the lowest-energy conformers of each Ni(η^2 -TEMPO)₂ isomer. The free energy diagram of the “shortest” mechanism is shown in Figure 7. The first transition state in this mechanism (**TS-1**) corresponds to ring opening in the *trans*-Ni(η^2 -TEMPO)₂ complex, with a $\Delta G^\ddagger$ of 23.7 kcal mol⁻¹. This leads to intermediate **2**, which has a *trans*-disposed Ni(η^2 -TEMPO)(κ^1 -TEMPO) structure at $\Delta G = 12.3$ kcal mol⁻¹ (shown in Figure 8). Intermediate **2** seems to play a central role in many of the possible isomerization pathways, as six unique transition states connect to this local minimum structure. Through a relatively low-energy TS, the three-coordinate structure undergoes a relatively low-energy conformational change to **tbt-2** in the κ^1 -TEMPO ligand to proceed to **3** at $\Delta G = 15.8$

kcal mol⁻¹. From here, **3** goes through the rate-limiting TS (**TS-3**) with a $\Delta G^\ddagger$ of 26.7 kcal mol⁻¹, where a ring closing *and* TEMPO conformational change occur in concert to form **1c-tbt-3**. Finally, a relatively low-energy TS ($\Delta G = 11.6$ kcal mol⁻¹) forms the isomerization product, **1c-ch-ax**.

Figure 7. Solution-phase free energy diagram (in kcal mol⁻¹) of the proposed mechanism for *trans-cis* isomerization of Ni(η^2 -TEMPO)₂ containing the least number of elementary steps.

Figure 8. Ball and stick representation of **2**, which is the *trans*-disposed Ni(η^2 -TEMPO)(κ^1 -TEMPO) intermediate. Hydrogen atoms are omitted for clarity.

d) Path from 1t-ch to 1c-ch-ax via 1c-ch

The high free energy transition state **TS-3** can be circumvented in the mechanism by ring closing of intermediate **2** to the **1-c-ch** conformation. This proposed mechanism contains five intermediates (Figure 9). The reaction proceeds to intermediate **2** as in Figure 7, but from there, the ring-closure transition state (**TS-5**) only has a free energy of activation of 16.4 kcal mol⁻¹. This leads to the **1c-ch** conformation, which cascades to the **1c-ch-ax** conformation via low-energy transition states, detailed in Figure 5. By avoiding **TS-3**, the ring-opening step (**TS-1**) is now the rate-limiting step of the isomerization, with a $\Delta G^\ddagger$ of 23.7 kcal mol⁻¹.

Figure 9. Solution-phase free energy diagram (in kcal mol⁻¹) showing an alternative mechanism for *trans-cis* isomerization of Ni(η^2 -TEMPO)₂ where the higher energy ring-closing transition state (TS-3) is avoided.

e) The minimum energy path from 1t-ch to 1c-ch-ax

Lastly, a “longest” minimum energy path from **1t-ch** to **1c-ch-ax** has been elucidated from the morass of local minima and transition states located for Ni(η^2 -TEMPO)₂ and Ni(η^2 -TEMPO)(κ^1 -TEMPO). This proposed mechanism has nine intermediates and the free energy diagram is shown in Figure 10. At the beginning of the mechanism, the **1t-ch** species conformationally distorts, first to the **1t-tbt-1** structure, then **1t-tbt-3**, and finally to **1t-ch-ax**.

The **1t-ch-ax** conformer then undergoes ring opening in **TS-6**, and this transition state has a free energy of activation of 19.6 kcal mol⁻¹. At this point in the mechanism, we have located a high-energy intermediate (**4**) with an agostic Ni-H interaction ($r_e = 1.786$ Å) occupying the coordination space vacated by the η^2 -TEMPO nitrogen atom. This stationary point is 17.8 kcal mol⁻¹ higher in free energy than **1t-ch**, and its 3D structure is shown in Figure 11. Intermediate **4** undergoes further ring opening and leads to the same intermediate **2** described in the previously proposed mechanisms. From here, there is relatively facile transformation to the **1c-ch-ax** isomerization product.

Figure 10. Solution-phase free energy diagram (in kcal mol⁻¹) showing an alternative mechanism for *trans-cis* isomerization of Ni(η^2 -TEMPO)₂. In this mechanism, conformational distortion of Ni(η^2 -TEMPO)₂ stabilizes the activation energy of ring-opening in **TS-6**.

Figure 11. Ball and stick representation of agostic bonding in intermediate **4**. Except for those on the methyl group involved in the agostic Ni-H bonding, all hydrogens are omitted for clarity.

f) The full conformational landscape of $\text{Ni}(\eta^2\text{-TEMPO})_2/\text{Ni}(\eta^2\text{-TEMPO})(\kappa^1\text{-TEMPO})$ and overall mechanistic context

Three other local minima have been identified with agostic Ni-CH₃ interactions similar to intermediate **4** depicted in Figure 11, and twenty-two other unique local minima with a Ni(η^2 -TEMPO)(κ^1 -TEMPO) structure besides intermediates **2** and **3** have theoretically characterized along the isomerization potential energy surface. However, any proposed mechanisms including these minima involve ring-opening or ring-closing transition states with a higher relative free energy than **TS-6** and **TS-7**. Under the assumption that all relevant transition states and local minima have been identified and mapped out, all isomerization “roads” must lead through the Ni(η^2 -TEMPO)(κ^1 -TEMPO) intermediate **2**.

What do these possible isomerization pathways mean in the context of Ni(η^2 -TEMPO)₂ reactivity? What we have shown is evidence that TEMPO ring puckering and conformational distortion can stabilize the rate-limiting transition state. There is recent computational evidence, of TS-stabilizing ring distortion occurring in the catalytic activity of glycoside hydrolases, obtained in QM/MM metadynamics investigation of an enzyme model,⁵⁸ and a coupled cluster-based study of pyranoses.⁵⁹ However, the proposed mechanism of Ni(η^2 -TEMPO)₂ isomerization does not identify the most likely route from *trans*-Ni(η^2 -TEMPO)₂ to *cis*-(η^2 -TEMPO)(κ^1 -TEMPOH)(RCCH) products, as described in reference 44! Our previous computational results (at the same level of theory used in this investigation) showed that the addition reaction mechanisms predicted the *cis*-disposed products to be thermodynamically *but not kinetically controlled* in every occurrence where an X-ray crystal structure was isolated and characterized. The computed rate-limiting free energies of alkyne addition to **1c** were in the range of 21.2 to 24.2 kcal mol⁻¹, which does not match well with experimentally observed product formation on the minutes time scale. If **1t** were to easily isomerize to **1c**, which our computations indicate is possible on a minutes time scale (rate limiting **TS-6** with a $\Delta G^\ddagger$ of 19.6 kcal mol⁻¹), it would still

need to surmount these RCCH addition barriers of 21-24 kcal mol⁻¹. We completely eliminated the first mechanism in Scheme 3, but the conformational complexity of the anionic TEMPO ligand creates another layer of possibilities shown in Scheme 4. Could a higher energy **1c** conformer have a lower rate-limiting free energy of addition? Transition state stabilization in higher energy conformers of *trans*-(η^2 -TEMPO)(κ^1 -TEMPOH)(RCCH) or *cis*-(η^2 -TEMPO)(κ^1 -TEMPOH)(RCCH) could also exist.

Scheme 4.

Conclusions

In order for isomerization of the $\text{Ni}(\eta^2\text{-TEMPO})_2$ complex to be competitive with inferred and computed kinetics of alkyne product formation on the minutes time scale, the rate-limiting step must have a free energy of activation less than 19-20 kcal mol⁻¹. A comprehensive cataloging of all intermediates and transition states along the pathway of the *trans*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ to *cis*- $\text{Ni}(\eta^2\text{-TEMPO})_2$ isomerization is reported, with 37 identified minima and 57 transition states providing a multitude of unique conceivable mechanisms. Proposed isomerization mechanisms have been discussed, many of which can be easily ruled out due to rate-limiting steps with energies of free activation beyond 23 kcal mol⁻¹. The lowest-energy mechanism leading from the experimentally characterized **1t-ch** structure to the experimentally unknown **1c-ch-ax** species was proposed. In this proposed mechanism, the $\text{Ni}(\eta^2\text{-TEMPO})_2$ complex undergoes significant conformational distortion in one of the TEMPO ligands and has a rate-limiting free energy of activation of 19.6 kcal mol⁻¹.

It is arguable that this investigation has raised many more new questions than it has provided answers. However, we highlight the following results:

- 1) free anionic TEMPO and metal-bound TEMPO ligand with anionic character possess low-energy barriers to conformational distortion,
- 2) an investigation of the $\text{Ni}(\eta^2\text{-TEMPO})_2$ isomerization has provided ideas on new methods to visualize and interpret complicated chemical mechanisms,
- 3) and transition state stabilization via conformational distortion of the TEMPO ligand has *some still unknown but crucial effect* on the kinetic control of alkynes addition reactions with $\text{Ni}(\eta^2\text{-TEMPO})_2$.

The $\text{Ni}(\eta^2\text{-TEMPO})_2$ molecule could become a fascinating target of study from both an experimental and theoretical perspective. As the complexity of the isomerization mapping was

overwhelming enough, a thorough investigation of the triplet surface of $\text{Ni}(\eta^2\text{-TEMPO})_2$ was not performed, even though we previously confirmed that the triplet states of **1t** and **1c** were significantly higher in energy than the singlet global isomeric minima. With 59 atoms in the molecule, the isomerization and conformational landscape of $\text{Ni}(\eta^2\text{-TEMPO})_2$ could be a potential test bed for more accurate computational methodologies, as well as *ab initio* molecular dynamics. An exploration of tunneling phenomenon could also be explored with more rigorous transition state theory than the typical harmonic oscillator/rigid rotor approximations used here. Lastly, the effect of conformational distortion on only one of the TEMPO ligands was characterized. In other words, we have kept one of the TEMPO ligands in its **ch** conformation in all reported computations. An investigation of the coupling of simultaneous conformational distortion on *both* TEMPO ligands of $\text{Ni}(\eta^2\text{-TEMPO})_2$ may be useful, but only perhaps as a pedagogical exercise since the amount of possible local minima on the isomerization surface would increase by at least a factor of five and may have minimal effect on the ring-opening or ring-closing free energies of activation.

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Graphical Abstract

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TOC Synopsis

The *trans-cis* isomerization of Ni(TEMPO)₂ exhibits fascinating conformational complexity and fluxionality of the coordinated TEMPO ligand. The mechanism of Ni(TEMPO)₂ isomerization has been explored with Density Functional Theory. It is observed that conformational distortion of a TEMPO ring leads to lower ring-opening/ring-closing free energies of activation.