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Characterization of Tunable Radical Metal-Carbenes: Key Intermediates in Catalytic Cyclopropanation

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Abstract

A new class of radical metal-carbene complex has been characterized as having Fischer-like orbital interactions and adjacent π acceptor stabilization. Density Functional Theory (DFT) along with Natural Bond Orbital (NBO) analysis and Charge Decomposition Analysis (CDA) has given insight into the electronics of this catalytic intermediate in an open-shell cobalt-porphyrin, [Co(Por)], system. The complex has a single bond from the metal to the carbene and has radical character with localized spin density on the carbene carbon. In addition, the carbene carbon is found to be nucleophilic and “tunable” through the introduction of different α -carbon substituents. Finally, based on these findings, rational design strategies are proposed which should lead to the enhancement of catalytic activity.

Introduction

Recently, a new family of cobalt(II)-porphyrin complexes, [Co(Por)], have been introduced as effective catalysts for stereoselective cyclopropanation.^{1–10} The [Co(Por)]-catalyzed cyclopropanation has a number of distinct advantages as compared to earlier catalytic systems described below. Given this, characterizing the catalytic cycle of this new class of [Co(Por)]-complexes is imperative.¹¹ Based upon experimental results, it has been hypothesized¹ that the reaction proceeds through a stable metallocarbene intermediate with radical character on a nucleophilic α -carbon. These hypotheses are confirmed by extensive electronic structure calculations reported herein and the results explain a trend in experimental substrate reactivities.^{1–7}

Further, population and charge analyses demonstrate that the local “excess” charge density on the carbene carbon is “tunable”, as has been demonstrated for carbenes substituted with aromatic groups.¹² The magnitude of this charge can take on values from highly negative to nearly neutral (or in one unusual case, even slightly positive) values through the interchange of different carbene substituents. This suggests the ability to control reactivity *via* tuning nucleophilicity. The nature of the bonding in the [Co(Por)]-carbene complex is analyzed and found to represent a new class of metallocarbenes with demonstrated potential to serve as key intermediates for carrying out novel catalytic reactions in a controlled fashion.^{1–7}

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Supporting Information Available: Details of the electronic structure calculations, computational controls, table of properties and coordinates for several complexes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

Moreover, the present study demonstrates that these radical carbene complexes are amenable to rational design in achieving desired electronic and steric characteristics.

Cyclopropanes have found numerous synthetic, biological and practical applications. One example is the use of cyclopropyl moieties to potentiate antibiotics targeted towards both gram-negative and gram-positive bacteria.^{13–18} Given this (and other) extremely important action(s), development of efficient and controllable synthetic methods to their stereoselective formation has been pursued with zeal.¹⁹ These efforts have led to considerable success with the establishment of a number of catalytic cyclopropanation systems based on Cu-,^{20–23} Rh-,^{24–34} Fe-,³⁵ and Ru-^{36–43} complexes. Cobalt was first used as an enantioselective catalyst as a part of a chiral Co(II)-dioximato compound⁴⁴ and subsequently complexed to salen ligands in a 3+ oxidation state.^{45, 46} However, these attempts lacked either diastereomeric or enantiomeric control. Such difficulties were recently overcome by employing [Co(Por)] as catalysts that exhibit both high diastereoisomeric control and enantiomeric selectivity^{1–7} (Figure 1). In addition, the [Co(Por)]-based catalytic system can be operated in a one-pot reaction without the need for controlled diazo addition and with alkenes as the limiting reagents; this offers a significant advantage over previous metal-catalyzed procedures. Furthermore, with the support of various chiral porphyrin ligands, [Co(Por)]-catalyzed cyclopropanation reactions have been carried out for different alkenes with a wide range of diazo reagents.^{1–7} In particular, unprecedented catalytic reactivity toward electron-deficient olefins has been demonstrated with [Co(Por)] catalysts⁵ (for a highlight on the topic, please see a recent review by Doyle⁴⁷). Additionally, [Co(Por)] has exhibited other highly desirable catalytic capabilities that are fundamentally different from other metal-catalyzed reaction systems, such as the direct preparation of *N*-phosphorus-substituted aziridines from alkenes.^{48, 49}

Given the differential reactivity and stereoselectivity of [Co(Por)]-catalyzed asymmetric cyclopropanation, it is only natural that obtaining a detailed understanding of the underlying catalytic mechanism, especially the nature of the key metallocarbene intermediate, is desirable. Fortunately, the advent of efficient parallel electronic structure codes affords the opportunity to examine the complexes with sufficiently accurate quantum mechanical calculations. For example, Yamada and co-workers have carried out coordinated computational and experimental work to characterize the nature of the metal-carbene bond in a series of metallo-salen complexes, which are closely related to the metallo-porphyrin complexes. They asserted that the Co(II)-carbene interaction is best characterized as a single bond. It was also concluded that, with the carbene bonded to the metallo-salen, the lone remaining unpaired electron (*i.e.* a single radical) was delocalized along the carbonyl of the methyl diazoacetate ligand. The radical was characterized primarily by observing a 50 cm⁻¹ shift in stretching frequency of the diazoacetate carbonyl group upon binding to the metal complex.⁵⁰ In contrast, our electronic structure studies have indicated highly localized radicals on [Co(Por)]-complexes, but otherwise our conclusions are consistent with previous observations. Subsequently, they extended their work to [Co(Por)]-complexes and focused on the nature of the metal's spin state and resulting bond orders.⁵¹

Currently, there are three well-known classes of metal-carbene complexes: Fischer,⁵² Schrock^{53, 54} and Grubbs.⁵⁵ The former was first synthesized in 1964 and typically includes a low oxidation state metal whereas Schrock carbenes, first reported in 1974, are characterized by higher oxidation states. The bonding pattern in Fischer carbenes can be described as singlet carbenes bonding with singlet metals (Figure 2(a)). This is typically thought of as σ donation to the metal center and π backbonding from the metal to the carbene, as proposed in the Dewar-Chatt-Duncanson model.^{56, 57} In contrast, Schrock complexes can be depicted as an interaction between triplet carbenes and triplet metals (Figure 2(b)). Bonding in these complexes has been characterized both experimentally and

computationally with Schrock carbenes having much higher bond orders, with nearly double bonds, while Fischer complexes typically exhibit slightly less than single bond character.⁵⁸ Generally speaking, this is illustrated by both net σ and π bonding in Schrock carbenes and largely only effective σ bonding in Fischer carbenes. Detailed analysis does yield a more complicated and complete picture of the bonding in Fischer and Schrock complexes as described previously by Frenking.^{58, 59} An additional property, important in the context of the present work, is the charge environment of the carbene center: Fischer carbenes exhibit charge separation between the metal and the carbene carbon (since the magnitude of donation is larger than the backdonation) and an electrophilic carbene carbon whereas Schrock carbenes are nucleophilic. This becomes an extremely important property for cyclopropanation reactions, as electron deficient olefins are believed to react at nucleophilic carbene centers.^{1–7}

Quantum chemical methods have seen major improvements recently in both the efficient computation and analysis of transition metal complexes. For example, major strides have been made in the development of relativistic corrections⁶⁰ and effective core potentials.^{61, 62} These advances coupled with modern density functional theory (DFT), including improved functionals,^{63, 64} have made computational treatment of coordination complexes more common.^{65, 66} Additionally, powerful analysis tools like natural bond orbital analysis (NBO),^{67–69} charge decomposition analysis (CDA),^{58, 59, 70} absolutely localized molecular orbitals – energy decomposition analysis (ALMO-EDA),^{71, 72} and charge transfer based ALMO-EDA⁷³ have made possible the interpretation of calculations in chemically meaningful terms.

The two main thrusts of this work are to provide a theoretical description of the presumed carbene intermediate in [Co(Por)]-catalyzed cyclopropanation and to predict new carbene sources to “tune” the property of the carbene intermediate for desired substrate reactivity. To the point, the process of computationally designing catalytic reactions is two fold: first an in-depth understanding of the nature of the key catalytic intermediate must be achieved, and second the interaction of carbene sources (*i.e.* diazoacetate reagents) with the metallo-porphyrin must be explained. The current work explores both the fundamental nature of [Co(Por)]-carbene interactions and highlights future modifications that can be made to control reactivity of asymmetric catalytic cyclopropanation. Calculations employ a simple, unsubstituted Co(II)-porphyrin, depicted in Figure 1, to limit computational cost. However, successful controls, listed in the Supporting Information (SI), were performed to ensure that this is a reasonable approximation. This choice allowed for a more detailed and systematic examination of carbene units shown to be important experimentally^{1–7} and to explore possible carbene sources for future experimental studies.

The remainder of this manuscript is arranged as follows. The Methods section outlines the computational approaches employed and their validation as reliable indicators of [Co(Por)]-complex structure and electronics. Furthermore, the analysis tools used to draw many of the conclusions are discussed. The Results and Discussion section examines the [Co(Por)]-carbene intermediate where it becomes clear that this is a fundamentally different type of transition metal-carbene complex from known Fischer- and Schrock-types. A detailed analysis of how diazoacetate and other diazo electronic structure partially controls the cyclopropanation reactivity is presented. In particular, attention is paid to possible alternative carbene sources (and their electronic properties) that can be used to control the reaction. Finally, the last section presents our conclusions, predicts new cobalt carbenes to be catalytically generated and proposes future directions.

Methods

The ground state of [Co(Por)]-complexes has been shown to be a doublet,^{1–4, 51} which was also confirmed in this work by determining that the quartet state was higher in energy. Unrestricted Kohn-Sham DFT⁷⁴ was used in conjunction with the M06-L exchange-correlation functional⁶³ as implemented in the Q-Chem⁷⁵ and GAMESS-US⁷⁶ quantum chemistry packages. LANL2TZ basis functions and ECPs⁷⁷ were applied to the cobalt center of the metal-porphyrin with the remaining atoms being described by the 6–31G* basis set.⁷⁸ Structures were first geometry optimized on a coarse (50–194) standard grid⁷⁹ (SG-1) and then converged with a finer grid (96–302) to obtain the structures for analysis. NBO analysis yielded chemically insightful molecular orbitals for the structures, in addition to the spin density at the nucleus, partial charges and bond orders.

CDA was performed in order to gain insight into the nature of the bonding taking place between the metallo-porphyrin and carbene ligand. Previous analysis of the nature of the bonding in Fischer- and Schrock-type transition metal carbene complexes via CDA⁸⁰ is recognized. The following is a brief summary of the various terms calculated within the CDA methodology; please refer to reference⁵⁹ for details. The charge donation, d , from the ligand (L) to the metal (M) is defined as the canonical overlap of occupied (occ)/unoccupied ($unocc$) orbitals:

$$d_i = \sum_j^{occ, L} \sum_k^{unocc, M} m_i c_j c_k \langle \varphi_j | \varphi_k \rangle \quad (1)$$

where φ is the canonical molecular orbital, m is the orbital occupation and c is the orbital coefficient. Similarly, the charge back-donation, b , from the metal to the ligand is given by:

$$b_i = \sum_j^{occ, M} \sum_k^{unocc, L} m_i c_j c_k \langle \varphi_j | \varphi_k \rangle \quad (2)$$

In addition, we may consider the repulsive polarization, r , (the net flow of electron density in or out of the overlapping region) as:

$$r_i = \sum_j^{occ, M} \sum_k^{occ, L} m_i c_j c_k \langle \varphi_j | \varphi_k \rangle \quad (3)$$

And finally, the rest term, Δ , yields the measure of covalent character present in the complex:

$$\Delta_i = \sum_j^{unocc, M} \sum_k^{unocc, L} m_i c_j c_k \langle \varphi_j | \varphi_k \rangle \quad (4)$$

where the great utility of the rest term, when coupled with quantifying back donation, is to distinguish between Schrock (covalent like) or Fischer (non-covalent like) carbene bonding as has been previously reported.^{58, 59, 70} Numerous controls were conducted to validate the computational methods and are described in more detail in the SI. Briefly, the conclusions presented were not changed by use of alternative functionals, higher level basis sets,

modeling larger substituted porphyrins that were employed experimentally, or using a dielectric constant in the calculations that is characteristic of the experimental solvent environment. The substitution of the reduced complex for the parent complex was verified through several controls, and it was ultimately found that the reduced complex very accurately represented the full system. It was also checked that the methods reasonably described the individual carbene and porphyrin molecules. It was noted that the commonly used B3LYP⁸¹ functional did not properly describe the electronics of the bare cobalt-porphyrin,^{82, 83} (e.g. the HOMO was incorrect) but reasonably described the bonded [Co(Por)]-complex.

Results and Discussion

Numerous efforts have been made toward a better understanding of the nature of metal-carbene interactions. In particular, most computational efforts have focused on gaining insight into the nature of Fischer-⁵² and Schrock-type⁵³ carbene complexes.^{58, 59} It is generally accepted that Fischer complexes are electrophilic with a metal-carbene bond slightly less than unity, whereas Schrock-types are nucleophilic and possess much more double bond character.

The current work is an attempt to characterize a novel metal-carbene complex (*i.e.* [Co(Por)]-complex) that serves as an active intermediate in a highly stereoselective cyclopropanation reaction.¹⁻⁷ It is found that these carbene complexes are radical in character with bond orders similar to Fischer carbenes and nucleophilicity akin, although somewhat smaller in magnitude to Schrock-type complexes (Figure 2(c)). The nature and stability of these complexes were assessed through electronic structure analysis tools. First, NBO analysis and CDA were carried out on representative Fischer- and Schrock-type carbene complexes (**FC,SC** in Table 1). Subsequently, three [Co(Por)]-carbene complexes (**1-3** in Table 1, also see Figures 1,3) were chosen both to represent a range of experimentally observed reactivities and associated electronic properties. Three additional complexes (**4-6** in Table 1) serve to demonstrate the “tunable” nature of not-yet synthesized reactive intermediates. An additional complex, **7**, was included as a counterexample that displays distinct chemical bonding with some Fischer carbene character. Table 1 lists bond lengths, bond orders, and the cobalt and carbene α -carbon electrostatic potential (ESP) charges for all complexes examined (note that several similar complexes, including a variety of controls, were also studied with results reported in SI).

Spin densities and ESP charges reported in Table 1 clearly show significant radical character localized on nucleophilic carbene carbons, while the metal-carbene bond reveals single bond (or slightly smaller) bond orders. These results hold for all complexes except **7**, which is clearly qualitatively different (*vide infra*). The most favorable intermediate toward reaction with electron-deficient olefin substrates is formed by reacting a [Co(Por)] with ethyl diazoacetate (e.g. ethyl acrylate is a prototypical choice, see Figure 1) resulting in **1**.⁵ This complex has a metal-carbene bond order of 0.90 (1.86 Å bond distance) and displays a significant negative partial charge on the carbene carbon; -0.357 electrons (*e*). While the bond order and bond distances observed are more consistent with those of Fischer carbene complexes⁵⁸ as discussed below, it is clearly nucleophilic in nature, consistent with its high reactivity towards electron deficient species. Of the synthesized complexes, **1** has the largest negative charge while the less negatively charged **2-3** are correspondingly less reactive.

From these results it was initially hypothesized that carbene carbon charge may be correlated to both metal-carbene bond character as well as reactivity. Therefore, a series of model compounds were employed (**8-9**, Figure 4) to test this proposition. We began with **1**, which has both a large negative charge on the carbon (-0.357 *e*) and a bond distance of 1.86

Å. To selectively adjust the charge on the carbene carbon, a methyl (**8**, -CH₃) group was substituted in place of the hydrogen. As expected, this both increased the charge on the carbene carbon (now -0.027 *e*) and elongated the metal-carbene bond to 1.90 Å. The next logical step was to substitute an ethyl group (**9**, -CH₂CH₃) in place of the methyl group, which again, as suspected, caused the charge to nearly return to that of **1** (-0.349 *e*). However, interestingly the bond length remained 1.90 Å. NBO analysis revealed this was due to hyperconjugation. In fact, significant electron density was observed to be donated from the σ C-H bonding orbitals on the alkyl group into the metal-carbene σ^* orbital thus explaining the maintained elongation of the metal-carbene bond. The trend of substituent stabilization by donation into the metal-carbene σ^* orbital was consistent throughout the complexes examined and correlated perfectly with metal-carbene bond distance and order.

Complexes **1–6** all exhibit spin densities largely localized on the carbene carbon, in a nearly pure p_y orbital (where the *z* axis is defined by the metal-carbene bond), with little or no cobalt radical character; this is illustrated in Figure 5. The NBO analysis indicates that the radical is stabilized by backdonation to an adjacent π^* orbital on the carbene substituent. This π^* antibonding orbital resides on a carbonyl or sulfonyl group (**1–5**). The carbene carbon spin density varies from 0.649–0.931 (*e*) but does not obviously correlate with the other structural or electronic properties. However, coupling this property to changes in carbene carbon and cobalt philicity, *via* modification of carbene substituents, may provide a straightforward mechanism for “tuning” selectivity. For example, % yield as a function of electron deficient olefins reveals the following trend: **1** > **2** > **3**.^{4–6} This correlates well with the charge and spin density values calculated for these compounds as shown in Table 1, suggesting that the ability to control both charge and radical localization can be a powerful tool for rational catalyst/intermediate design.

Another complex, **7**, having two highly electron-withdrawing fluorine groups attached to the carbene carbon, exhibits significantly different chemical character (Table 1). This is confirmed with NBO analysis, which shows that the carbene substituent π^* orbitals, which are responsible for back-stabilization, do not exist in the -CF₂ moiety. This leads to radical “migration” from the carbene carbon to the $d_{x^2-y^2}$ orbital on the metal, making it, in a sense, more Fischer-like with an empty carbene p_y orbital and shared electrons between the metal d_{z^2} and carbene sp^2 orbitals (Figure 6). This is further confirmed by examining both partial charges and bond orders with the later indicative of single bond character as is the case in prototypical Fischer complexes. As a result of the carbene carbon’s slight electrophilic character, it is predicted that **7** should have higher reactivity toward aliphatic and other electron-rich olefins if experimentally accessible.

To further investigate the nature of the carbene complex, CDA was performed on an ambiphilic series of compounds with results reported for **1**, **7**, and representative Fischer-(**FC**), and Schrock-type (**SC**) carbenes (Table 2). CDA provides a quantitative representation of the Dewar-Chart-Duncanson model formalism. The donation and backdonation contributions to the bonding picture are calculated based upon occupied and unoccupied orbital overlap; see SI for a more complete summary of CDA methodology.

In addition to CDA donation and backdonation, the repulsive polarization of the electron density in the vicinity of the bond as well as the rest term (Δ)⁵⁹ are assessed. The rest term is indicative of the metal-carbene bond character with deviations from zero signifying the nature of covalency. For example, the metal-carbene bond in **FC**, which NBO shows to be slightly less than single, has a Δ value of 0.004 whereas the **SC** complex is essentially halfway between a single and double bond and as expected has a larger rest term (0.165). Concerning individual donation (*d*) and backdonation (*b*) values, the physically meaningful quantity, especially for Fischer carbenes, is the *d/b* ratio as it illustrates the amount of

backdonation present in the bonding of the complex. Note, attaching physical significance to the d/b ratio makes sense only with small rest term values.⁵⁸

CDA results indicate that **1** has a Fischer-like metal-carbene bond with backdonation from the metal to the carbene, stabilizing the complex, however charge and NBO analyses clearly demonstrate non-Fischer character as evident by a nucleophilic carbene carbon. Further, from the nearly zero rest term, there is little covalent character in this complex as opposed to Schrock-types. **7** is even more Fischer-like with a repulsive polarization term, r , that is negative, whereas **1** has an r value that is nearly zero with a smaller Δ rest term.

NBO analysis further reveals the nature of **1**. As noted above, it was determined that a highly localized carbon centered radical exists, which is nearly pure p_y in character (Figure 5). σ donation occurs between the sp^2 orbital of the carbene into the d_{z^2} orbital on the metal. Additionally, NBO analysis shows that the π^* orbital on the adjacent carbonyl stabilizes the radical by accepting electron density, thus facilitating favorable backdonation from the metal's d_{xz} and d_{yz} orbitals into the antibonding orbital of the metal-carbene bond. This qualitative bonding picture is illustrated in Figure 6. Again, **7** serves as a counterexample with no accessible π^* orbital acceptors.

The necessity of the π^* acceptor (*e.g.* the diazo acetate carbonyl on **1**) was examined using a [Co(Por)]-carbene substituted with an additional electron-withdrawing group (*i.e.* -NO₂, **3**). The presence of this additional group had profound effects on the structure and electronics of the complex. Surprisingly, the carbonyl group, which typically acts as a radical density acceptor, (when geometry optimized) rotated nearly perpendicular to the plane of the radical with virtually no spin density located on the oxygen ($e = 0.0369$). In contrast, the nitro group's π^* orbitals aligned well with the p_y orbital of the radical allowing the NO₂ oxygens to accept 0.269 e of spin density.

While examining the electronic and steric effects of this rearrangement it was found that at least two minima exist for this structure; the global minimum, with the carbonyl group twisted out of the radical plane (p_y orbital) as shown in Figure 7(a), and a second structure with the carbonyl in-plane, but the nitro group rotated perpendicular (Figure 7(b)). To understand the electronic and steric preferences of these two conformers, a constrained optimization was performed keeping both the carbonyl C=O and the nitro N=O in plane with the carbene p_y orbital. Examination of radical stabilization *via* NBO perturbation analysis revealed that an approximate 4 kcal/mol preference is given to the nitro group as compared to the carbonyl group. It follows that this interaction is favored and the carbonyl group rotates out-of-plane keeping the $p_y - \pi^*$ interaction intact. However, the total energy difference between these structures was found to be approximately 1 kcal/mol, again with the twisted C=O structure being more stable.

From this analysis interesting hypotheses connecting experimental reactivities can be formulated. Compound **3** has been shown to be the least reactive of the three catalytic intermediates examined (**1** > **2** > **3**) toward electron-deficient olefins. We hypothesize that the reactivity of this species is dependent upon the orientation of the carbonyl group. For example, the more reactive intermediates have their carbonyl group in the plane of the radical p_y orbital and it has been experimentally shown that **3** reacts with a yield of about 65% with appropriate substrates.⁶ We propose that the reaction proceeds by first converting from the state with the C=O out-of-plane to the slightly higher energy state where the NO₂ is out-of-plane (see Figure 7(b)). This transition serves to both position the carbonyl group correctly and simultaneously allows for the necessary electronic properties (*i.e.* radical stabilization by the π acceptor on the carbonyl group, achieving a more nucleophilic carbene carbon, *etc.*). It is not known if this transition is dominated by steric or electronic effects, but

from our analysis it seems that the electronics should be the dominant factor in controlling this transition and subsequent reactivity. Using this principle as a strategy for the rational design of selective catalytic intermediates is a logical next step.

Conclusions

The electronic structure calculations and subsequent analyses presented identify and characterize a new class of metal-carbene complexes that are key intermediates in catalytic cyclopropanation by [Co(Por)]. The bonding of these intermediates is reminiscent of Fischer carbenes, with the metal existing in a low oxidation state and metal-carbene bond order being described as slightly less than one. However, the carbene α -carbon is both “tunable” and nucleophilic which is more reminiscent of Schrock-type complexes. Additionally, it is found that significant radical character is localized on the carbene carbon.

Calculated properties correlate well with experimental observations; reactivity trends strongly suggested a localized radical intermediate that readily reacts with electrophilic substrates. The partial charge of the carbene carbon is found to take on values from slightly positive to approximately $-0.5 e$, again suggesting this can be used to “tune” reactivity toward different olefin substrates. For example, the carbene complex with an approximately neutral carbene carbon may serve as an effective reactive intermediate in catalytic cyclopropanation of less electrophilic substrates *via* this type of radical reaction mechanism. Further evidence of this tunability is demonstrated by alternating alkyl chain length of the carbene substituents which not only controls the charge of the radical carbon, but also stabilizes it *via* hyperconjugation.

The radical carbene complex is found to be critically stabilized by either backdonation into a π^* acceptor on the carbene substituents, or through hyperconjugation. Indeed, a complex such as [Co(Por)]-CF₂, which lacks available orbital acceptors, exhibits a very different bonding pattern with a radical largely localized on the cobalt metal center and Fischer-like characteristics that include an electrophilic carbene carbon and similar backdonation characteristics as judged by CDA analysis.

While the present catalytic mechanism involves a doublet [Co(Por)]-catalyst reacting with ground state triplet carbenes, the present results suggest that open-shell singlet carbenes, where the radical electrons are spin-paired but in spatially distinct locations, may also be catalytically accessible; this is hypothesized to be a fundamentally different mechanism than that of current Fischer and Schrock carbenes. Interestingly, such open-shell singlet states may be photoaccessible under certain reaction conditions. Additionally, an explanation of the experimental reactivity of intermediate **3** is offered. We hypothesize that reactivity is controlled by conformational changes associated with the adjacent carbene substituent; these conformational changes are in turn controlled by electronic stabilization of the localized carbene radical into either the carbonyl or nitro group. In fact, it is found that the in-plane nitro group (with the carbonyl rotated out-of-plane) preferentially stabilizes the radical and is therefore preferred ($\Delta E = 1.46$ kcal/mol). The reaction is thus concluded to proceed only after conformational changes align the carbonyl group back in-plane with the radical. This structural feature resembles the carbonyl and sulfonyl moieties on **1** and **2** which are known to possess larger yields and higher reactivities.

In summary, the nature of the key intermediate for [Co(Por)]-catalyzed cyclopropanation was explored *via* electronic structure calculations and subsequent analysis. The results also permit the prediction and design of novel catalytic carbene intermediates that can be “tuned” to achieve desired reactivity. Future studies will include attempts to synthesize novel [Co(Por)]-catalysts and to confirm the predicted reactivity (*e.g.* a catalytic system involving

intermediate **5** should be comparable to that of **1** in reactivity) based on the calculated properties.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Cyclopropanation reaction performed by a cobalt(II)-porphyrin catalyst. The diazoacetate reagent reacts with the porphyrin to form the carbene intermediate studied in this work.

Figure 2.

Illustration of Fischer, Schrock, and [Co(Por)] orbitals. In Fischer carbenes (a), there is σ donation from the carbene to the metal, and π backdonation from the metal to the carbene. The Schrock (b) scenario shows spin-pairing between adjacent orbitals, thus resulting in a covalent interaction. The [Co(Por)]-carbene (c), presented in this work, consists of a doublet metal into which the carbene σ donates, with π backdonation from the metal to the carbene, in the case of having a good π acceptor on the ligand (as described in the text), with the porphyrin ring also serving as an electron “buffer” to keep the π d -orbitals filled and thus leaving a radical on the carbon. Additional detail can be obtained in a related study.¹¹

Figure 3.
Perspective depiction of complexes **2** & **3**.

Figure 4.
Depiction of complexes 8 & 9.

Figure 5. Plot of the positive spin density of the [Co(Por)]-CHCO₂Et complex. As can be seen by the magnitude of the isosurface (isovalue = 0.013), the excess spin density is almost entirely localized on the carbene carbon in a nearly pure *p* atomic orbital in nature.

Figure 6.

Molecular orbital diagram of the cobalt-porphyrin in complex with the carbene ligand - CHCO_2Et (complex **1**). The complex is formed through a Fischer-like mechanism in which σ donation occurs between the sp^2 molecular orbital of the ligand and the singly-occupied dz^2 atomic orbital (where the z axis is defined perpendicular to the plane of the porphyrin ring) on the Co(II) , with stabilization taking place through a backdonation from the π -symmetry orbitals of the cobalt into the Co-C antibonding molecular orbital (and consequently yielding a bond order less than unity, as is typical in Fischer carbenes). This leaves significant excess electron density (*i.e.* the radical) on the carbene carbon, which is of nearly pure (>99 %) p_y state. Stabilization of the carbene radical occurs through partial relief of the excess electron density *via* donation from the p_y orbital into an adjacent π^* antibonding orbital on the carbonyl (other good π^* acceptors, such as sulfonyl groups, can also fulfill this role).

Figure 7.

Depiction of two low energy conformers of **3**. The global minimum structure, (a), is shown with its carbonyl group (-C=O) rotated nearly perpendicular relative to the carbene p_y orbital, while the nitro (-NO₂) group is in-plane. A slightly higher energy structure, (b), has its nitro group rotated out-of-plane with respect to the p_y orbital and the carbonyl aligned.

Electrostatic Potential (ESP) and Natural Bond Orbital (NBO) results. Bond distances (BD), charges (Q), spin densities (SD), and bond orders (BO) of representative metal-carbene complexes (Fischer-type, FC, and Schrock-type, SC) and a series of [Co(Por)]-carbene complexes are presented. Charges and spin densities are reported in units of (*e*) with bond distances in Å and unit-less bond orders, M refers to the metal and C refers to the carbene carbon.

Table 1

Label	Complex	MSD	M Q	C SD	C Q	M-C BD	M-C BO
FC	(CO) ₅ W-C(CH ₃)OCH ₃	–	–1.91	–	0.701	2.01	0.702
SC	(C ₃ H ₅) ₂ Ti-CH ₂	–	0.655	–	–0.860	1.93	1.58
1	[Co(Por)]-CHCO ₂ Et	0.0224	0.516	0.798	–0.357	1.86	0.898
2	[Co(Por)]-CHSO ₂ Ph	0.0246	0.471	0.920	–0.185	1.85	0.886
3	[Co(Por)]-C(NO ₂)CO ₂ Et	0.0725	0.502	0.649	–0.113	1.85	0.858
4	[Co(Por)]-CHSO ₂ H	0.0770	0.427	0.863	–0.439	1.86	0.882
5	[Co(Por)]-C(CF ₃)CO ₂ Et	0.00998	0.549	0.825	–0.347	1.89	0.842
6	[Co(Por)]-CH ₂	0.109	0.396	0.931	–0.425	1.86	0.947
7	[Co(Por)]-CF ₂	0.711	0.119	0.282	0.0977	1.93	0.779
8	[Co(Por)]-C(CH ₃)CO ₂ Et	0.0130	0.395	0.771	–0.0274	1.90	0.898
9	[Co(Por)]-C(CH ₂ CH ₃)CO ₂ Et	0.0380	0.430	0.793	–0.349	1.90	0.849

Table 2

CDA analysis for the [Co(Por)]-CHCO₂Et (**1**), Tungsten (W) Fischer carbene and Titanium (Ti) Schrock carbene complexes. Values shown are donation/backdonation ratio, repulsive charge polarization and rest term (Δ). Significant deviations of Δ from zero are indicative of covalent bonding character.

Label	Complex	<i>d/b</i>	<i>r</i>	Δ
FC	(CO) ₅ W-C(CH ₃)OCH ₃	2.28	-0.242	0.004
SC	(C ₅ H ₅) ₂ Ti-CH ₂	3.71	-0.294	0.165
1	[Co(Por)]-CHCO ₂ Et	2.61	0.079	0.024
7	[Co(Por)]-CF ₂	1.94	-0.182	0.010