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Mechanism of Cobalt-Porphyrin−Catalyzed Aziridination

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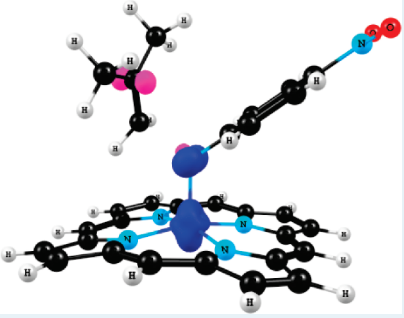
S *Supporting Information*

ABSTRACT: Density functional theory (DFT; OLYP) calculations clearly indicate the involvement of a cobalt nitrene in cobalt-porphyrin−catalyzed alkene aziridinations, as well as in allylic aminations. The transition state for the cobalt-nitrene−alkene interaction may be described as triradicaloid. A subsequent carbon radical, if it exists at all as an intermediate, collapses in an essentially barrierless manner to the aziridine product.

KEYWORDS: cobalt, porphyrin, nitrene, amination, aziridination, rebound mechanism

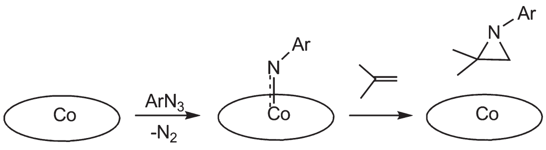


Late transition metal-nitrene complexes are typically rare and unstable species, as a result of severe metal(d_π)-nitrogen(p_π) antibonding interactions.[1−3] Yet, in recent years, such species have been synthesized and fully characterized,[4,5] exploiting low-coordinate ligand architectures that sidestep the offending orbital interactions.[6−8] Reactive metal-nitrene intermediates with conventional square-pyramidal[9,10] and octahedral[11] geometries remain of interest, however, as nitrene delivery agents in organic chemistry.[12,13] Thus ruthenium, rhodium, and copper complexes have long been known to be effective as catalysts for aziridination[12] and cyclopropanation.[14,15] The use of cobalt complexes, by contrast, has been only relatively recently explored, and cobalt porphyrins have been found to be excellent catalysts for aziridination, C−H amination, and cyclopropanation.[16−20] Particularly impressive are Zhang and coworkers' highly enantioselective adaptations of the reactions, based on chiral picket-fence−type porphyrins.[21,22] Despite the practical advances, the mechanism of cobalt-porphyrin−catalyzed aziridination has not been elucidated in depth, and a number of key questions remain: (a) Does the azide reagent, the nitrene donor, form a complex with cobalt porphyrin? (b) Is a discrete cobalt nitrene intermediate formed, as shown in Scheme 1? (c) If so, what is the nature of the cobalt-nitrene bonding in such an intermediate? (d) What is the nature of the aziridination transition state? (e) To what extent is allylic amination energetically competitive with aziridination?

We addressed these questions with OLYP[23−25]/6-311G(d,p) density functional theory (DFT) calculations.[26] Our models consisted of cobalt porphine as the catalyst, *p*-nitrophenyl azide as the nitrene source, and four different alkene substrates: 2-methylpropene (isobutene), (*Z*)-2-butene, (*E*)-2-butene, and 2-methyl-1-butene. The discussion below centers around isobutene, but details of our results on the other alkenes, which are fully consistent with the isobutene results, are presented in the Supporting Information.

Bringing the aryl azide into contact with the cobalt leads to spontaneous dissociation of N_2; no Co−aryl-azide complex could be detected.[27] The transition state (TS) is $\Delta G^\ddagger$ = 31.8 kcal/mol ($\Delta E^\ddagger$ = 28.3 kcal/mol) above the reactants, a reasonable value considering that the latter are stable compounds. The TS retains a substantial amount of the Co d_{z^2}-based spin density that is typical of cobalt porphyrins, but also shows incipient p_π spin density on the nitrene nitrogen. The calculations unequivocally indicate a cobalt nitrene intermediate (Figure 1), which forms in a thermodynamically favorable manner, with ΔG = −14.0 kcal mol^{-1} (ΔE = −12.1 kcal mol^{-1}). The geometric and electronic structure of this intermediate, which is yet to be detected experimentally, is of considerable interest. Its molecular geometry is consistent with C_s symmetry, and the unpaired electron resides in an a″-symmetry Co(d_π)-nitrene(p_π) antibonding orbital, with much of the spin density on the nitrene moiety. The intermediate may thus be described as a low-spin cobalt(III) nitrene anion-radical complex.[28,29]

Scheme 1. Co-Porphyrin−Catalyzed Aziridination Reaction Proceeding via a Postulated Nitrene Intermediate



The aziridination transition states involving the interaction of the Co-nitrene and an alkene could be located for each of the four substrates examined. For isobutene, this TS is $\Delta G^\ddagger$ = 29.5 kcal mol^{-1} ($\Delta E^\ddagger$ = 24.7 kcal mol^{-1}, imag. freq. 490i cm^{-1}) relative to the reactants (Supporting Information, Figure S1). 2-Methyl-1-butene, another terminal alkene, exhibited a similar barrier: $\Delta G^\ddagger$ = 28.9 kcal mol^{-1} ($\Delta E^\ddagger$ = 24.6 kcal mol^{-1}, imag. freq. 485i cm^{-1},

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Supporting Information, Figure S1). The nonterminal alkenes (*Z*)-2-butene and (*E*)-2-butene exhibit slightly higher barriers: $\Delta G^{\ddagger}$ = 32.8 kcal mol^{-1} ($\Delta E^{\ddagger}$ = 28.8 kcal mol^{-1}, imag. freq. 486i cm^{-1}) and $\Delta G^{\ddagger}$ = 34.6 kcal mol^{-1} ($\Delta E^{\ddagger}$ = 28.7 kcal mol^{-1}, imag. freq. 497i cm^{-1}).

The detailed electron flow in this step is of unusual theoretical interest, for it appears not to conserve orbital symmetry. Thus the cobalt-nitrene intermediate has a $^{2}A''$ ground state, whereas the regenerated cobalt porphyrin catalyst has a fully symmetric $d_{z^2}{}^{1}$ ground state. To shed light on this conundrum, we attempted to optimize this TS for isobutene under a C_s symmetry constraint, which proved successful. This TS features an incipient bond between the nitrene nitrogen and the methylene carbon of the isobutene; the Co-nitrene bond is correspondingly weakened, en route to regeneration of the four-coordinate cobalt porphyrin catalyst. The spin density of this TS (Figure 2) may be described as triradicaloid, with three centers of spin density. The majority spin density is concentrated in the Co d_{z^2} orbital and as an a″ radical on the nitrene, and the minority spin density is largely localized in an a′-symmetry p orbital on the tertiary carbon of the isobutene.

To generate the aziridine, the carbon radical must rotate out of the mirror plane and couple with the nitrene radical; it is at this step when the system must break C_s symmetry. Figure 3 depicts the energy profile for this step, obtained by a series of constrained optimizations with stepwise shortening of the incipient C−N bond. It is clear that the putative carbon radical intermediate collapses in an essentially barrierless manner to the aziridine product. Optimization of this radical intermediate proved tricky. It could be located, however, for isobutene (Supporting Information, Figure S2), and we found an exceedingly soft (essentially barrierless) potential for rotation about the $CH_2-C(CH_3)_2$ bond. This raises the question whether the aziridination occurs with stereoretention or not; the fact that the carbon radical collapses in a barrierless

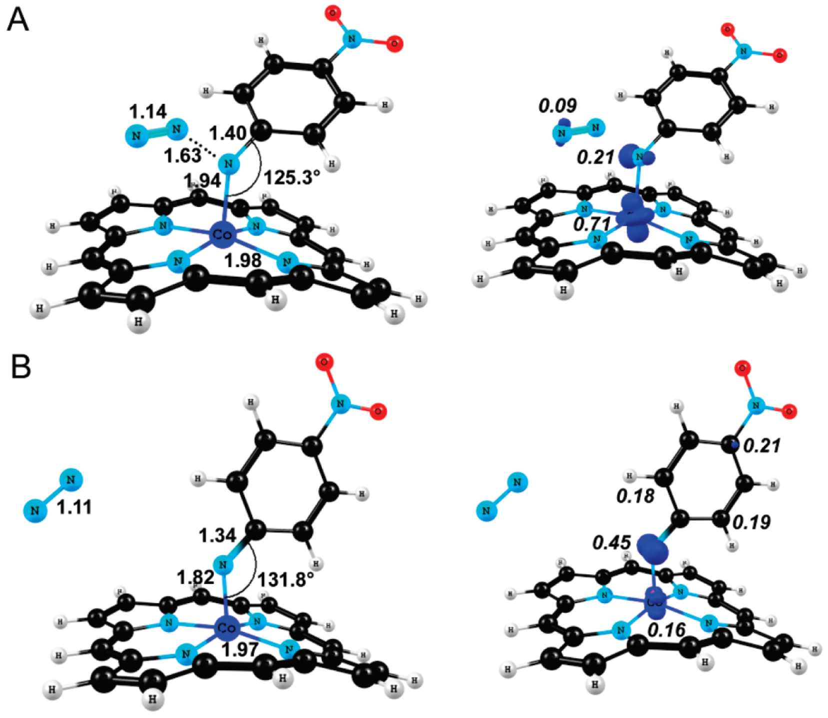

Figure 1. Structural highlights (left; Å, deg) and spin densities (right, spin populations in italics) of (A) the TS and (B) the products of the cobalt−aryl-azide reaction.

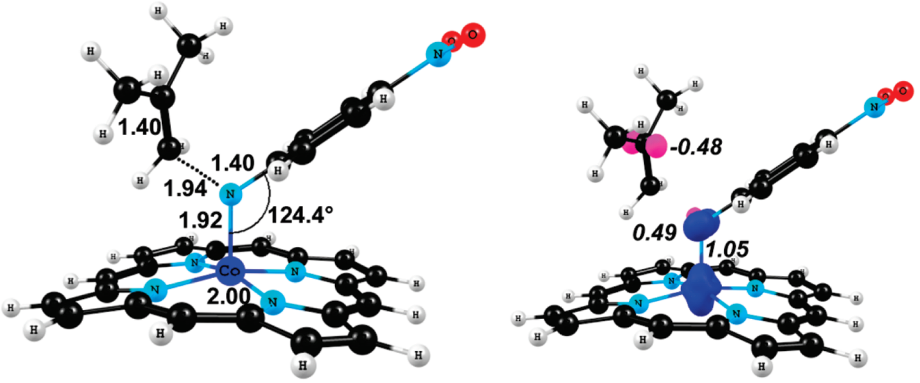

Figure 2. Structural highlights (left, Å, deg) and spin density (right, spin populations in italic) of the aziridination transition state (C_S symmetry). Majority and minority spin densities are indicated in blue and magenta, respectively.

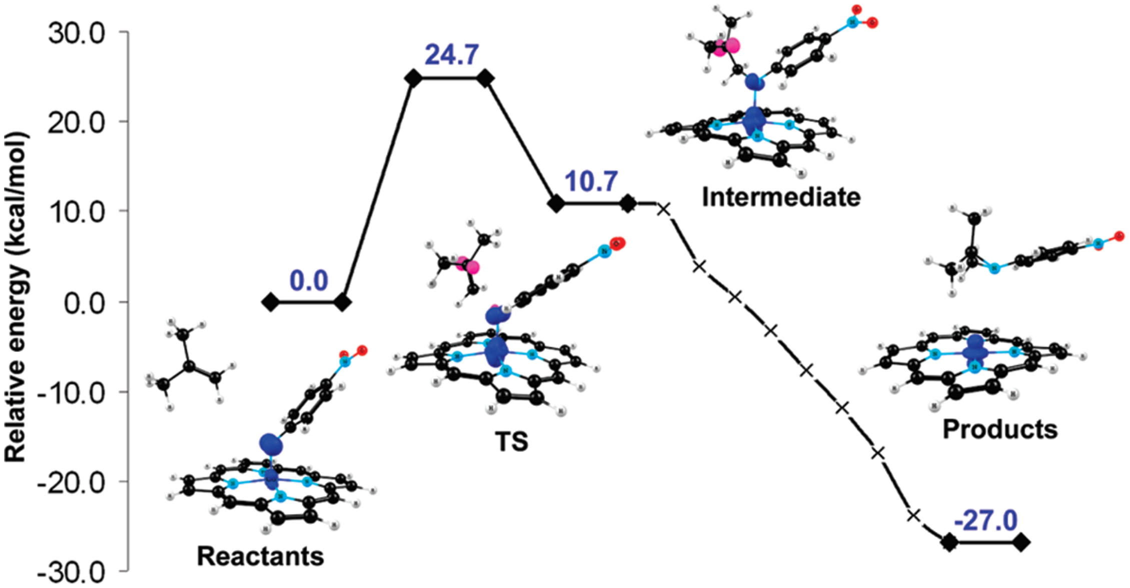

Figure 3. Relative energies (ΔE, kcal mol^{-1}) and optimized geometries with spin density profiles for Co-porphyrin−mediated aziridination of isobutene (C_1 symmetry).

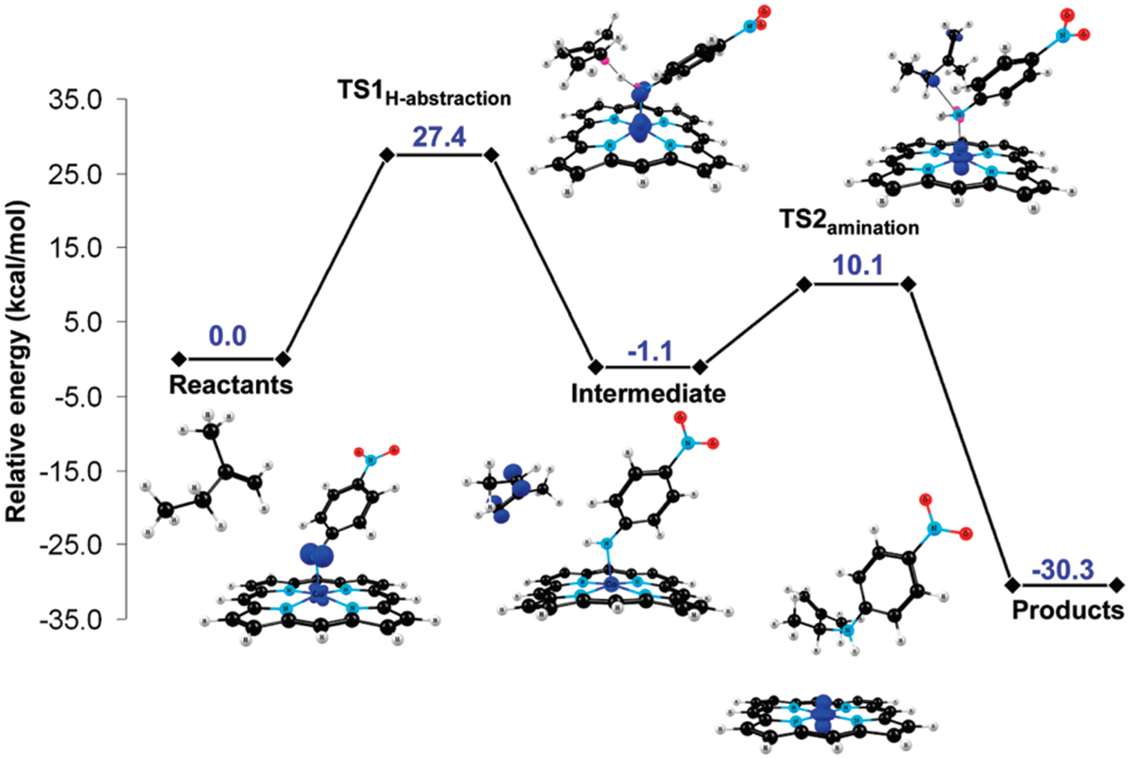

Figure 4. Relative energies (ΔG, kcal mol^{-1}) and optimized geometries with spin density profiles for Co-porphyrin−mediated allylic amination of 2-methyl-1-butene (C_1 symmetry).

manner and might not even exist as a true minimum suggests that the reaction might well be stereoretentive. Unfortunately, experimental data are at present lacking with respect to this point.

Because Co-catalyzed aziridination is often accompanied by allylic amination,[19] we also examined the latter pathway for 2-methyl-1-butene, as shown in Figure 4. The first, hydrogen-abstraction step is rate-limiting, with a barrier of $\Delta G^{\ddagger} = 27.4$ kcal/mol ($\Delta E^{\ddagger} = 24.9$ kcal mol^{-1}, imag. freq. 1538i cm^{-1}), which is comparable to the aziridination barrier. The second, C−N bond formation step has a low barrier of only 10.1 kcal/mol ($\Delta E^{\ddagger} = 5.6$ kcal mol^{-1}, imag. freq. 172i cm^{-1}) and can occur via two enantiomeric pathways; only the (*S*) product is shown in Figure 4 (additionally, resonance implies that amination should also be possible on the terminal double bond carbon; the TS for that reaction has a similar barrier and is not shown here). Our calculations thus nicely reproduce the experimental observation that aziridination and amination are competing reaction channels.[19]

Thus, gratifyingly, we have been able to answer each of the mechanistic questions that we set out to address. Overall, the aziridination mechanism resembles the rebound mechanism of cytochrome P450 and of a number of model systems. This is of interest because Goldberg and Abu-Omar have recently shown that a number of manganese-catalyzed group transfer reactions in fact do not involve the rebound mechanism.[14,15] Thus, epoxidation by a manganese corrolazine catalyst does not involve direct oxene transfer from manganese;[30] likewise, manganese corrole-catalyzed aziridination by PhINTs does not involve manganese-based nitrene transfer.[31] Unpublished DFT calculations in our laboratory, on the other hand, suggest that FeCl-corrole—catalyzed aziridination does involve a rebound-like mechanism.[32] DFT calculations thus clearly have a major role to play in elucidating details of nitrene transfer pathways, which remain much less explored than analogous oxene transfer processes.

■ ASSOCIATED CONTENT

Ⓢ **Supporting Information.** Details of additional TSs and Cartesian coordinates for all optimized structures (14 pages). This material is available free of charge via the Internet at http://pubs.acs.org.

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(27) With the PW91 functional (unlike with OLYP), however, an exceedingly weakly bound Co—aryl-azide complex could be discerned. See Supporting Information, Figure S3 for details.

(28) The $^2A''$ ground state is clear-cut; the alternative $^2A'$ state is about 0.7 eV higher in energy.

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