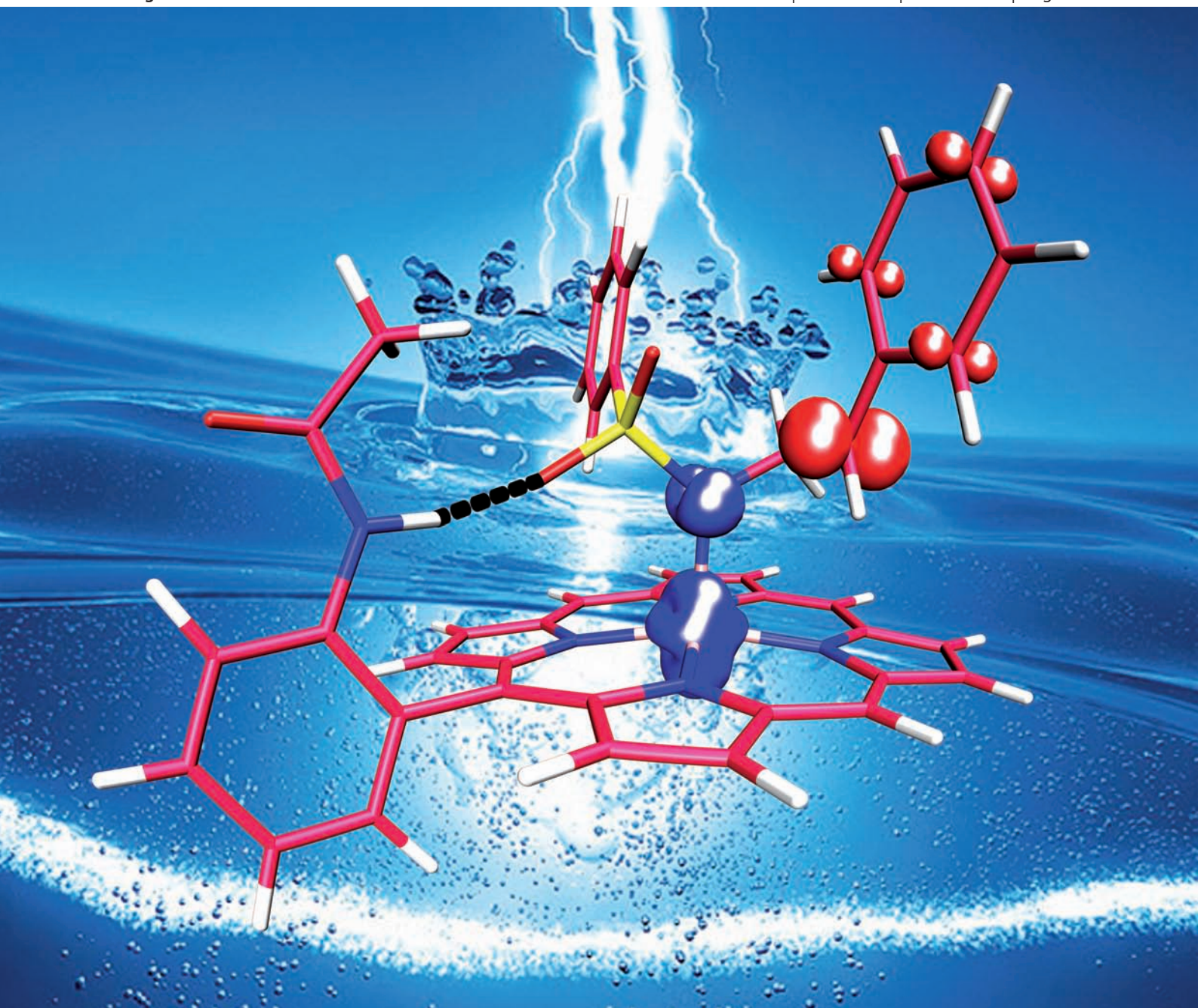


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PAPER

The radical mechanism of cobalt(II) porphyrin-catalyzed olefin aziridination and the importance of cooperative H-bonding†

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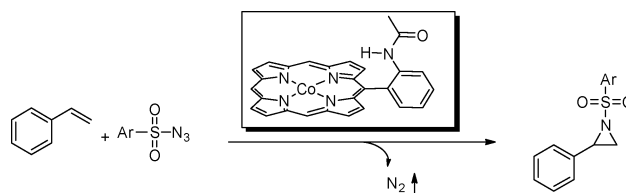
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The mechanism of cobalt(II) porphyrin-mediated aziridination of styrene with PhSO_2N_3 was studied by means of DFT calculations. The computations clearly indicate the involvement of a cobalt 'nitrene radical' intermediate in the $\text{Co}^{\text{II}}(\text{por})$ -catalyzed alkene aziridination. The addition of styrene to this species proceeds in a stepwise fashion *via* radical addition of the 'nitrene radical' C to the C=C double bond of styrene to form a γ -alkyl radical intermediate D. The thus formed tri-radical species D easily collapses in an almost barrierless ring closure reaction (TS3) to form the aziridine, thereby regenerating the cobalt(II) porphyrin catalyst. The radical addition of the 'nitrene radical' C to the olefin (TS2) proceeds with a comparable barrier as its formation (TS1), thus providing a good explanation for the first order kinetics in both substrates and the catalyst observed experimentally. Formation of C is clearly accelerated by stabilization of C and TS1 *via* hydrogen bonding between the S=O and N-H units. The computed radical-type mechanism agrees well with all available mechanistic and kinetic information. The computed free energy profile readily explains the superior performance of the $\text{Co}^{\text{II}}(\text{porAmide})$ system with H-bond donor functionalities over the non-functionalized $\text{Co}(\text{TPP})$.

1.1 Introduction

Aziridines are important building blocks and versatile synthons in organic synthesis. Furthermore, they exhibit a number of *in vivo* biological activities,¹ and find applications as anti-tumour and anti-bacterial agents (some of which are naturally occurring antibiotics such as mitomycins).²

There are several methods to prepare aziridines (*e.g.* cyclisation of 2-chloro-alkylamines, transformation of epoxides, 'cyclopropanation' of imines), most of which have important limitations and some of which generate substantial amounts of waste products. A well-established and quite general method to prepare aziridines is catalytic nitrene (N-R) transfer to olefins (Scheme 1). Several porphyrin- and salen-based transition metal catalysts (Mn, Co, and Ru) are known to enable (enantioselective) nitrene transfer to olefins, as well as some systems based on Cu complexes of other N-donor ligands.³ Nonetheless, the full potential of transition-metal mediated aziridination⁴ has not yet been exploited. This is mainly because the most frequently applied nitrene precursor is (*N*-(*p*-tolylsulfonyl)imino)phenyl iodine (PhI=NTs). This nitrene source easily generates a nitrene ligand at transition



Scheme 1 Schematic representation of the catalytic olefin aziridination.

metal catalysts ($\text{M}=\text{NR}$) for subsequent cycloaddition to olefins. However, the synthesis of $\text{PhI}=\text{NTs}$ is a high energy process, and the use of this reagent generates stoichiometric amounts of PhI , which is undesirable from an atom and energy efficiency point-of-view. Further disadvantages are the poor solubility and synthetic limitations to prepare these reagents, thus limiting their applicability and the substrate scope. Therefore, less expensive and more effective nitrene sources are required, as well as new catalysts that are capable of handling them.⁵ Organic azides are among the most promising and environmentally friendly alternatives, for which a large substrate scope is already available. Similar to diazo reagents, these compounds can generate nitrene ligands at transition metals by a simple loss of dinitrogen. This activation process is however troublesome in most cases, and quite harsh reaction conditions (high temperatures or photochemical activation) are generally required for nitrene transfer from organic azides to organic substrates. This makes it difficult to achieve high chemo- and enantioselectivities.

One of the early reports of the use of organic azides in olefin aziridination deals with the photochemical activation of tosyl

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† Electronic supplementary information (ESI) available: DFT optimized geometries (.pdb and .xyz) and Tables containing ΔE , ΔE_{ZPE} , ΔG , ΔH and ΔS values of all DFT optimized geometries. See DOI: 10.1039/c1dt10027k

azide (TsN_3) in the presence of Cu-based catalysts.⁶ More recently, the potential of thermal catalytic activation of organic azides was demonstrated. Besides some expensive Rh⁷ and Ru⁸ based catalysts, even some base metal catalysts based on Fe,⁹ Cu¹⁰ and Co¹¹ complexes have shown activity in nitrene transfer, including those from organic azides.

Among the most successful ligands applied in metal-based nitrene transfer catalysis are porphyrins. The first metalloporphyrin-catalyzed nitrene transfer reactions using iminoiodanes as the nitrene source were based on Mn and Fe complexes.¹² Only recently, Co(por) systems were developed for the activation of organic azides.^{11,13} Quite remarkably, simple non-functionalized tetraphenylporphyrin (TPP) based systems perform quite poorly in this reaction, while porphyrin systems appended with amide-based H-bond donors (such as 3,5-Di^tBu-IbuPhyrin and related D_2 -symmetric chiral porphyrins) are much more efficient in the aziridination of styrenes with tosyl azide (Fig. 1), and these systems are among the most efficient and cost-effective catalysts for this reaction. This allowed the development of unique (por)Co^{II}-based catalysts for aziridination (and C–H amination) reactions using different types of azides, including phosphoryl azides, arylsulfonyl azides and trichloroethoxysulfonyl azide.¹³

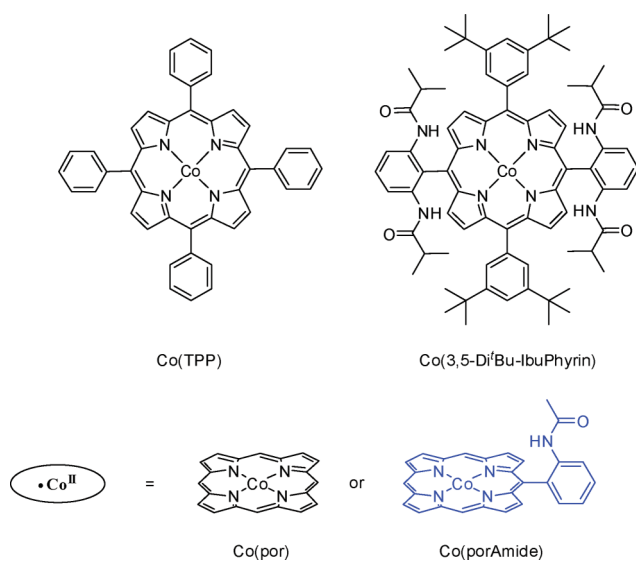


Fig. 1 Experimental cobalt(II) porphyrin complexes used for nitrene transfer from organic azides to olefins (top) and their simplified model systems used in this computational study (bottom).

Clearly, the H-bond donating substituents of the 3,5-Di^tBu-IbuPhyrin facilitate the reactions, but the reasons behind this behaviour are not fully understood.^{13b} The same holds for the exact reaction mechanism of the aziridination reaction. Understanding these reactions in terms of a detailed reaction mechanism, thus explaining the effect of the H-bonding on the unique reactivity of these systems, will be important for future developments in (stereo)selective aziridination reactions with these eco-friendly nitrene sources, and should assist in expanding the substrate scope to other organic azides and different olefins.

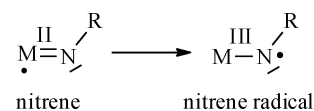
Herein we disclose a full and detailed DFT mechanistic study of the Co^{II}(por)-mediated aziridination of styrene using the unsubstituted Co^{II}(por) as well as the H-bond donor appended Co^{II}(porAmide) systems as simplified models for the experimental

Co(TPP) and Co((3,5-Di^tBu-IbuPhyrin) systems (Fig. 1). Before we describe the details of this computational study, we will first summarize the available mechanistic information concerning olefin aziridination reactions (section 1.2).

1.2 Background and available mechanistic information

In general, mechanistic studies of the aziridination reaction are associated with many contradicting reports, and the exact reaction mechanism is likely to be strongly dependent on variations in the catalyst, substrates and the precise reaction conditions. Most frequently, nitrene intermediates are proposed as the key intermediates, but such species are difficult to isolate or even detect spectroscopically. Hence, it is difficult to conclude from experimental data whether the reaction proceeds *via* a concerted or stepwise nitrene transfer to the olefin, and the intermediacy of the nitrene is sometimes even disputed.¹⁴ Most of these mechanistic studies focused on the use of $\text{PhI}=\text{NTs}$ as the nitrene source. Reported DFT studies are restricted to some examples of Fe¹⁵ and Cu.¹⁶

The redox non-innocence of the terminal nitrene ligands further adds to the complexity of our understanding of these reactions. One-electron reduction of the coordinated nitrene ligands by the metal (Scheme 2) has been proposed to lead to the formation of ‘nitrene radicals’ in several of the open-shell cases, hence leading to radical-type pathways.^{9e,16} Understanding the (electronic) structure of the ‘nitrene’ intermediate is thus an important issue to address.



Scheme 2 Redox non-innocent behaviour of nitrene ligands in open-shell transition metal complexes.

In early studies, Jacobsen *et al.* studied the effect of using differently substituted $\text{PhI}=\text{NTs}$ and TsN_3 nitrene sources on the outcome of (diimino)Cu^I-mediated aziridination reactions, and found no effect whatsoever on the (*enantio*)selectivity, which pointed to a stepwise (non-concerted) radical-type reaction mechanism for this system.⁶ This result was corroborated by the studies of Templeton, through a detailed Hammett-analysis of the influence of substituents at the styrene phenyl-ring.¹⁷ However, Norrby later pointed out that the mechanisms are possibly system dependent, and while radical pathways might be involved for radical stabilizing substrates, this might not be the case for other substrates. Theoretical studies of the Cu-catalyzed alkene aziridination revealed that the most likely mechanism follows a radical pathway involving nitrene radical addition to the olefin, leading to N-alkyl radical intermediates, which collapse to form the aziridines.^{16a}

Kinetic data were obtained for isolated (por)Ru^{IV}(tosylimido)₂ complexes by Che and co-workers. Secondary deuterium isotope effects revealed rehybridization from sp^2 to sp^3 only at the β -carbon atom, which is consistent with a carbo-radical intermediate generated from a nitrene radical intermediate and styrene derivatives.¹⁸ The effect of spin delocalization of the benzyl radical moiety was investigated by a kinetic Hammett analysis of varying *p*-substituted styrenes, which clearly required a

dual-parameter¹⁹ spin delocalisation parameterisation ($\log k_R$ vs. $(\sigma_{mb}, \sigma_{JJ'})$) pointing to a radical-type mechanism.¹⁸ Recently, Cenini and co-workers proposed a concerted mechanism for nitrene transfer from aromatic organic azides (ArN_3), wherein olefin attack on a cobalt-coordinated organic azide leads to simultaneous C–N bond formation and loss of N_2 .¹⁴ The putative nitrene intermediate was proposed to play a role only in the formation of side products.²⁰ The (por)Co mediated reaction proved to be first order in [catalyst], and both [styrene] and [ArN_3].¹⁴ The system dependency of this reaction is clearly illustrated by the very different results obtained with Mn^V (corrole) systems. Double labelling experiments with $ArI=NTs$ and $ArI=NTs^{tBu}$ established that the $ArI=NTs$ ligand of [(tpfc)Mn(=NTs^{tBu})(ArINTs)] is in fact the nitrene source in this case.²¹

It is clear that the mechanistic studies of aziridination reactions cannot be generalized, and hence we refrain from doing so. In this paper, we primarily focus on the Co^{II} (por) systems, and provide a computational model for the Co^{II} (por)-mediated aziridination of styrene with $PhSO_2N_3$. The results strongly point to a radical-type mechanism for this system, which involves a discrete nitrene radical species as the key intermediate. The computed pathway is in fact very similar to the recently proposed mechanism of olefin cyclopropanation with these same systems.²²

2. Results

The BP86 functional is generally accurate in predicting the geometries of transition metal complexes,²³ and has an excellent performance, especially for 3d metal compounds.²⁴ Extensive DFT computational studies of cobalt porphyrins and related cobalam derivatives have shown that Co–ligand bond dissociation enthalpies (BDE) and internuclear distances are best reproduced by the non-hybrid BP86. Hence, for reactions in which the making and breaking of cobalt–ligand bonds plays an important role, especially in cases where open-shell intermediates are involved, the use of the BP86 functional is preferred over B3LYP.²⁵ We have previously shown that the use of the BP86 functional gives fairly accurate predictions of the thermodynamic energies and kinetic barriers associated with catalytic chain transfer²⁶ and degenerative radical exchange processes of radical polymerization reactions controlled by Co(por) complexes.²⁷ We therefore consistently used the non-hybrid BP86 functional in our studies. The reported free energies in kcal mol⁻¹ are obtained from the calculated internal energies at the TZVP basis set on all atoms, adjusted for the zero-point energy, entropy, and approximately for the condensed phase reference volume (see Computational details section). We used the non-functionalized cobalt porphyrin Co(por) as a smaller model of the experimental Co(TPP) complex. In addition, we included calculations using the Co(porAmide) model containing a 2-acetamidophenyl substituted porphyrinato ligand as a smaller model of the experimental Co(3,5-Di^tBu-IbuPhyrin) system, in order to account for the effects of hydrogen bonding interactions between the sulfonyl moiety of $PhSO_2N_3$ and the ligand amide functionalities (Fig. 1).^{13b} The energy of each of the complexes in their doublet ($S = \frac{1}{2}$) and quartet ($S = 3/2$) states were compared. For most of the species the doublet state represents the ground state, and the discussion focuses mostly on the lowest energy doublet energy surface, unless stated otherwise.

2.1 Formation of ‘nitrene’ complexes from Co^{II} (por) and $PhSO_2N_3$

We first focused on the formation of the ‘nitrene’ species $Co(por)(NSO_2Ph)$ from $PhSO_2N_3$ and Co^{II} (por).

Experimentally, cobalt complexes with amide functionalised porphyrins exhibited higher activities in aziridination reactions as compared to Co(TPP).^{13b} In view of these higher activities, we also investigated the same reactions with the amide-functionalized Co^{II} (porAmide) model, in order to study the effect of hydrogen bonding interactions between the amide functionality of the porphyrin ligand and the sulfonyl group of the $PhSO_2N_3$ nitrene source on the rate of ‘nitrene’ formation (Fig. 2).

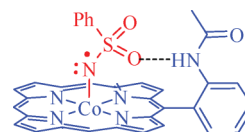
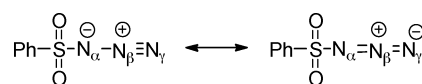


Fig. 2 Relevant hydrogen bonding interactions in formation and stabilisation of the ‘nitrene’ species.

The calculated free energies for the reaction of $PhSO_2N_3$ with $Co(por)$ and $Co(porAmide)$ are plotted in Fig. 3. Generally, Co^{II} (por) systems and their adducts Co^{II} (por)(L) have a low-spin d^7 doublet ($S = \frac{1}{2}$) ground state,²⁸ and reaction profiles at the doublet surface make most sense based on many experimental observations. Furthermore, related DFT calculations reported by Yamada and coworkers have shown that the contribution of higher (quartet) spin states to the cyclopropanation mechanism in reactions mediated by Co(salen) models can be neglected,²⁹ even at the hybrid B3LYP level, which is known to favour the stability of higher spin states.^{30,31} Hence, we started all calculations with complexes in their doublet spin states. Nonetheless, we also optimized the species in their quartet states to compare their energies (species labelled as ⁴X; see also the ESI†).

As for diazo compounds, organic azides have a resonance structure with a formal negative charge on their α -nitrogen atom (Scheme 3), thus allowing the coordination of this atom to transition metals. The first step of the cobalt-mediated reaction is generally considered to involve the coordination of the α -nitrogen atom of $PhSO_2N_3$ to the Co^{II} (por) species **A** (⁴A is >18 kcal mol⁻¹ higher in energy than ²A). This step is slightly endergonic (7.4 kcal mol⁻¹) according to the DFT calculations, and leads to the adduct **B**. The concentration of the azide in the experimental system will obviously have a large influence on the relative concentration of these species.



Scheme 3 Relevant resonance structures of $PhSO_2N_3$.

The coordination of the azide decreases the electron density at the α -nitrogen atom of $PhSO_2N_3$, and stabilizes the N_α -charged resonance structure (Scheme 3, left). At the same time, this will facilitate crossing the transition state barrier for N_2 loss (**TS1**),

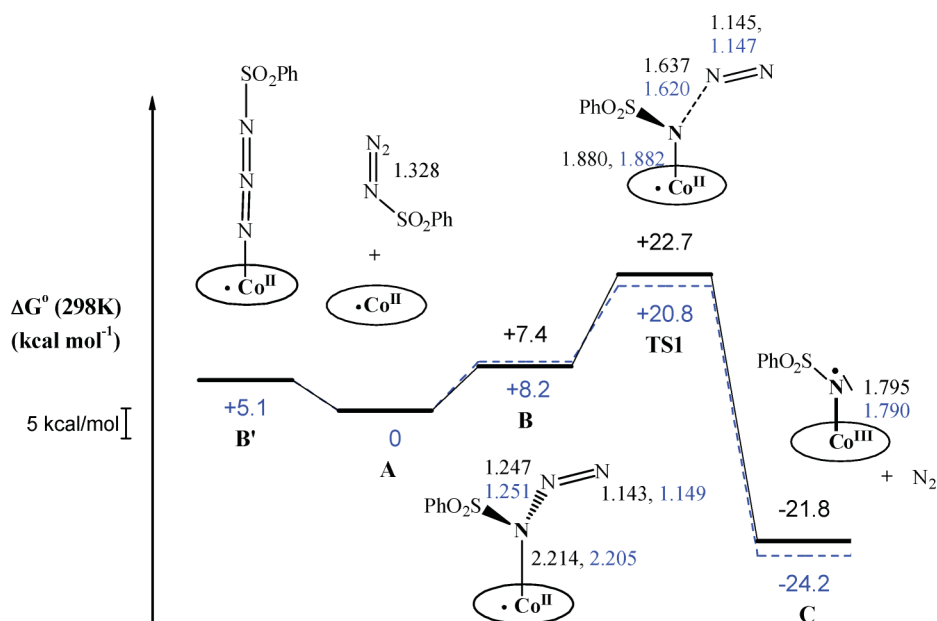


Fig. 3 Free energy changes for the reaction of PhSO_2N_3 with $\text{Co}^{\text{II}}(\text{por})$ (black) and with $\text{Co}^{\text{II}}(\text{porAmide})$ involving hydrogen bonding of the sulfonyl group with the amide moiety (dashed blue). Selected bond distances (Å) are presented as well.

because the azide in the adduct **B** is no longer linear but prefers a bent structure with an elongated $\text{N}_\alpha\text{-N}_\beta$ bond (from 1.25 to 1.64 Å). The energy barrier of the formation of the ‘nitrene’ species is relatively high, but accessible (+22.7 kcal mol⁻¹), which is in good agreement with the experimental results showing relatively slow reactions and a first order behaviour in [azide]. N_2 loss affords the ‘nitrene’ species **C**, which is a strongly exergonic process (-21.8 kcal mol⁻¹).³² This species clearly has a doublet ground state. The optimized geometries of the electronically excited quartet state ⁴**C** are +10–11 kcal mol⁻¹ higher in (free) energy for both the $\text{Co}(\text{por})$ and the $\text{Co}(\text{porAmide})$ models. At the quartet surface, both ⁴**B** (+26.1 kcal mol⁻¹ relative to ²**A**) and ⁴**TS1** (+37.7 kcal mol⁻¹ relative to ²**A**) are substantially higher in (free) energy than their comparative low spin doublet analogues. The formation of the nitrene species **C** thus seems to occur primarily at the low spin doublet ground state energy surface.

Most interestingly, the H-bond appended $\text{Co}(\text{porAmide})$ system has a significantly lower transition state barrier **TS1** (lowered from +23 to +21 kcal mol⁻¹) for formation of the nitrene species **C**. This is in good agreement with the reported experimental data.¹³

Previously, a fully characterized nitrene complex has been isolated upon the reaction of $\text{Fe}^{\text{III}}(\text{TPP})\text{Cl}$ with $\text{PhI}=\text{NTs}$. The nitrene ligand in this complex is bridging between the metal centre and a pyrrole nitrogen of the porphyrin.³³ The reports of Che¹⁸ and Abu-Omar²¹ for Ru and Mn systems suggest further that bis-nitrene species and nitrene-azide species might be involved in the aziridination reactions. In this light, we also optimized some terminal and bridging (bis)nitrene and nitrene-azide analogues, in order to compare their energy with **C** (Fig. 4). From this study, however, it is clear that all of the possible bridging (bis)nitrene and nitrene-azide species are substantially higher in energy than **C**. Hence, **C** is the more likely intermediate to be involved in the aziridination of styrene.³⁴

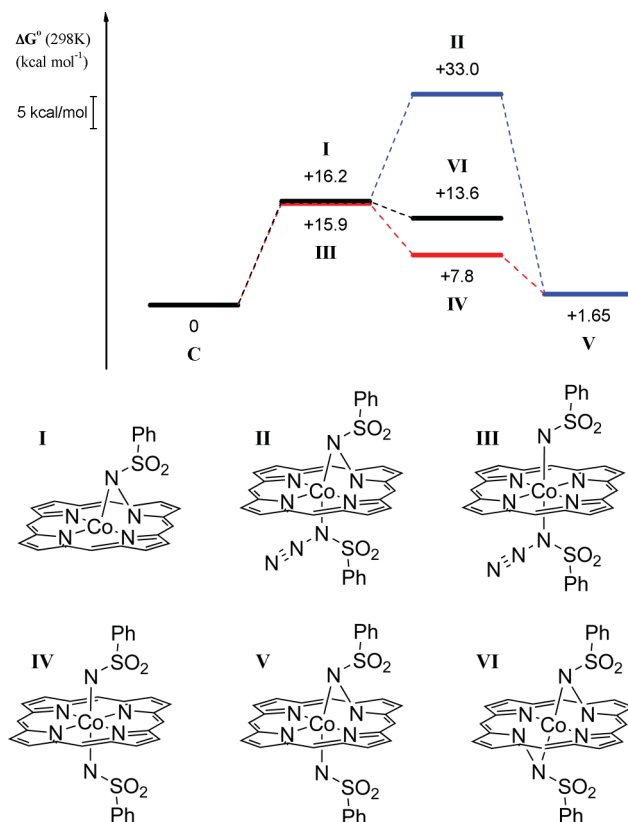


Fig. 4 The relative free energies (kcal mol⁻¹) of several nitrene-azide and terminal and bridging (bis)nitrene species as compared to **C**.

2.2 Electronic structure of the ‘nitrene species’

The SOMO and spin density plots of the ‘nitrene’ species $\text{Co}^{\text{II}}(\text{por})(\text{N}-\text{SO}_2\text{Ph})$ and $\text{Co}^{\text{II}}(\text{porAmide})(\text{N}-\text{SO}_2\text{Ph})$ as calculated by DFT are presented in Fig. 5.

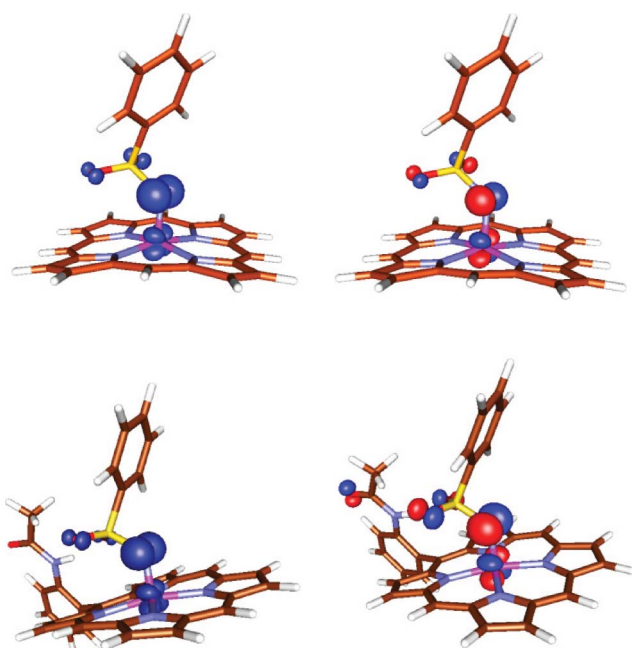


Fig. 5 The spin density (left) and SOMO (right) plots of the DFT optimized ‘nitrene radical’ species $\text{Co}^{\text{III}}(\text{por})(\cdot\text{N-SO}_2\text{Ph})$ (top) and $\text{Co}^{\text{III}}(\text{porAmide})(\cdot\text{N-SO}_2\text{Ph})$ (bottom).

According to these calculations, the ‘nitrene’ complexes are actually species with a ‘nitrene radical ligand’ (Fig. 5).³⁵ The unpaired electron resides mainly on the ‘nitrene’ nitrogen, *i.e.* the α -nitrogen of the $\text{N-SO}_2\text{Ph}$ moiety, and is slightly delocalized over the neighbouring cobalt and oxygen atoms. Hence the ‘nitrene ligands’ are best described as nitrogen-centred ligand radicals $\{\text{RN}^\bullet\}^-$ (‘nitrene radical ligands’) rather than true transition metal nitrene moieties in the classic sense. This should give rise to radical-type reactivity at their nitrogen atoms.

Nitrene complexes are known to be preferred for metals favouring somewhat higher oxidation states, and for metals that are capable of filling the vacant nitrogen orbitals through π -back donation.³⁶ Notable examples include nitrene complexes of Ru, Fe,³³ Co,³⁷ Cu,³⁸ Mn,³⁹ and Ni⁴⁰ Concerning cobalt, paramagnetic five-coordinate amido complexes ($\text{Co}^{\text{III}}\text{-NHSiMe}_3$) have been isolated, which are presumably formed from a nitrene intermediate. Diamagnetic (closed-shell) nitrenes of cobalt have also been reported ($[\text{PhBP}_3]\text{Co}^{\text{III}}\equiv\text{N-}p\text{-tolyl}$), which are formed from a closed-shell Co^{I} species.^{37b}

The presence of substantial spin density at the nitrene is not completely unexpected. The approach of the coordinating electron pair at nitrogen pushes the energy of the metal d_z^2 orbital up, and after cleavage of the N-N bond, the electron transfer from this d-orbital to the empty p-orbital of the nitrene nitrogen can result in the formation of a one-electron reduced nitrene ligand, *i.e.* a ‘nitrene radical’ anionic ligand $\{\text{RN}^\bullet\}^-$ (see Fig. 6A/B). This is similar to the reduction of Fischer-type carbenes by Co^{II} , which we have previously reported to be important in (por)Co-mediated cyclopropanation reactions.²²

Exactly the same electronic structure arises if the bonding is considered as a triplet nitrene interacting with the $\text{Co}^{\text{II}}(\text{por})$ species (Fig. 6C). The formation of a Co-N σ -bonding pair from the unpaired electrons in the cobalt d_x^2 orbital and the

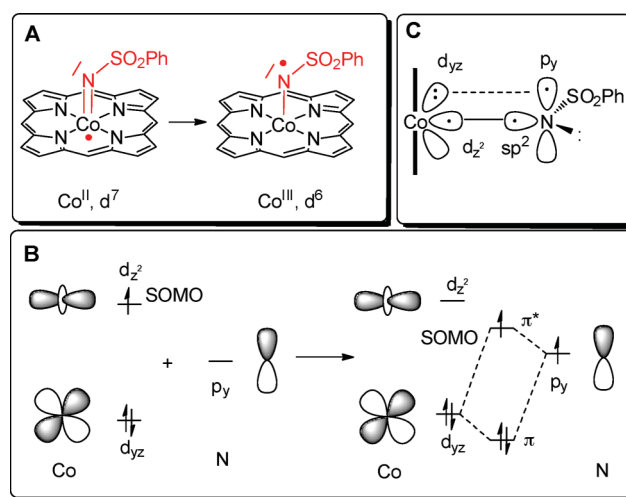


Fig. 6 The redox non-innocent behaviour of nitrene ligands coordinated to open-shell $\text{Co}^{\text{II}}(\text{por})$ species (A) and a simplified bonding scheme explaining this behaviour (B).

triplet carbene sp^2 orbital leaves an unpaired electron in the p_y orbital, effectively generating the same nitrene radical $\{\text{RN}^\bullet\}^-$. Formal oxidation state counting leads to a cobalt(III)-nitrene radical in each case. This redox non-innocent behaviour and the electron transfer from the electropositive metal centre to the nitrene is of crucial importance, because it weakens the Co-N bond and imposes a radical-type reactivity to the ‘nitrene’ moiety. Somewhat related chromium and iron complexes containing similar nitrogen-centred ligands of the type $\{\text{RN}^\bullet\}^-$ were recently disclosed by Lu and Wieghardt⁴¹ and Betley^{9f}.

2.3 Aziridination steps involving addition of the ‘nitrene radical ligand’ to styrene

We tried to find transition states for direct reactions of olefins with the PhSO_2N_3 adduct **B**, $\text{Co}^{\text{II}}(\text{por})(\text{N}_3\text{SO}_2\text{Ph})$, to investigate the possibility of aziridination proceeding *via* C–N coupling between the azide adduct **B** and styrene with simultaneous dinitrogen loss from the coordinated PhSO_2N_3 moiety, as proposed by Cenini and co-workers.¹⁴ Despite several attempts in approaching the problem with different constraint-geometry variations, we were, however, unable to find such a transition state.⁴² Therefore, we focused on the ‘nitrene radical’ species **C** as the remaining and most logical nitrene transfer intermediate in the aziridination mechanism.

The computed nitrene transfer mechanism from **C** clearly proceeds *via* a stepwise radical process (Fig. 7). The reaction involves the addition of the nitrogen-centred ‘nitrene radical’ **C** to the olefin, thus generating the $\text{Co}(\text{por})(\text{N}(\text{SO}_2\text{Ph})\text{-CH}_2\text{-CHR}^\bullet)$ species **D**.

The formation of this species is associated with a relatively high transition state barrier (**TS2**), which is somewhat lower for the $\text{Co}(\text{porAmide})$ ($\Delta G^\ddagger = 22.8 \text{ kcal mol}^{-1}$ with respect to **C**) systems than for $\text{Co}(\text{por})$ ($\Delta G^\ddagger = 24.1 \text{ kcal mol}^{-1}$ with respect to **C**). These **TS2** barriers for formation of **D** are thus nearly equally high as the **TS1** barriers for formation of **C**, and this provides a good explanation for the experimental fact that the reaction is first order in both [azide] and [styrene].¹⁴

The ⁴**TS2** barriers for the addition of the high-spin nitrene species ⁴**C** to styrene at the quartet surface (22.5 and 23.7 kcal mol^{-1}

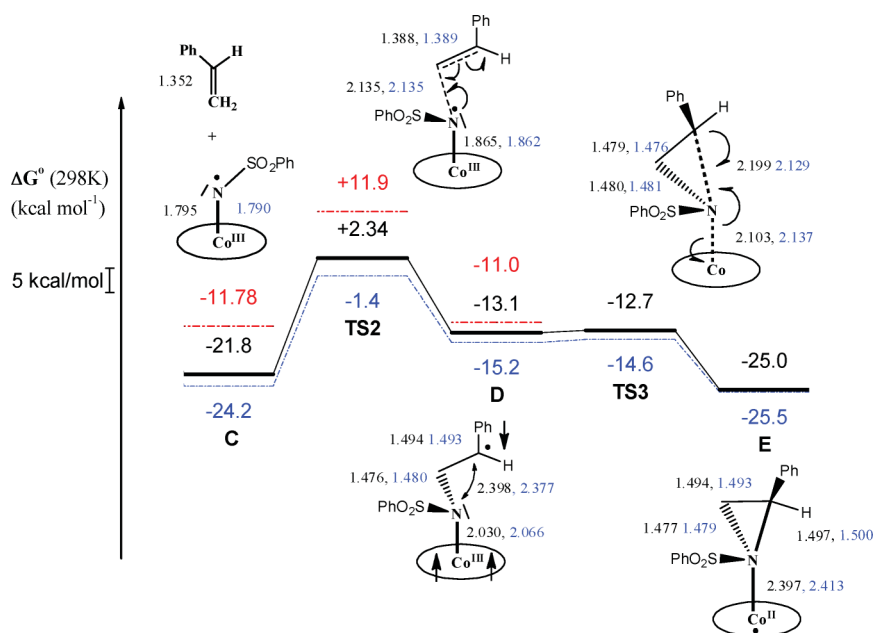


Fig. 7 The computed pathways for the aziridination of styrene. Free energies in kcal mol⁻¹ relative to species A (black for Co(por); dashed red for Co(por) quartet states, dashed blue for Co(porAmide). The structures and selected bond lengths are for the lower energy species in their doublet states (*S* = 1/2).

for Co(porAmide) and Co(por), respectively) are very comparable to the corresponding **TS2** barriers at the doublet surface. However, the high spin species **⁴C** and **⁴TS2** are consistently >10 kcal mol⁻¹ higher in energy than their low spin counterparts **C** and **TS2** (see Fig. 7 and ESI†).

The species **D** clearly has unpaired electron spin density at the γ -carbon of the 'alkyl' moiety (Fig. 8). It is noteworthy that the cobalt centre of **D** has undergone a spin-flip as a result of the addition of styrene to **C**, and has transformed from low-spin Co^{III} (*S* = 0) to intermediate spin Co^{III} (*S* = 1).⁴³ As a result, **D** exists in two possible spin states; a doublet **²D** (in which the γ -carbon radical is antiferromagnetically coupled to one of the two unpaired

electrons at cobalt) and a quartet **⁴D** (in which the γ -carbon radical is ferromagnetically coupled with the two unpaired electrons at cobalt). The optimized geometries of these spin-states have nearly equal (free) energies, with **⁴D** being only +2.1 kcal mol⁻¹ higher in (free) energy than **²D**.

The unpaired spin density of cobalt is partly delocalized over the amido-fragment (see Fig. 8), and antiferromagnetic coupling with the unpaired electron at the γ -carbon in the doublet **²D** greatly facilitates the C–N bond formation. Accordingly, the ring closure to give the aziridine adduct **E** *via* **TS3** on the doublet energy surface is nearly barrierless ($\Delta G^\ddagger \sim 0.4$ kcal mol⁻¹).⁴⁴ See Fig. 7. Aziridine ring closure from **⁴D** requires a preceding spin-flip to **²D** in order to reach **TS3**. The dissociation of the aziridine from **E** is strongly exergonic (–7.8 kcal mol⁻¹ for Co(por); –7.3 kcal mol⁻¹ for Co(porAmide); see Fig. 9), which renders the reaction of **C** with styrene irreversible. The thus formed product is not the most stable form of the aziridine, and pyramidal inversion at nitrogen leads to a further free energy gain of 4.9 kcal mol⁻¹. Aziridines are ring strained compounds, for which the energy barrier for pyramidal inversion at nitrogen is considerably higher than in acyclic amines. However, the barrier for this process is generally low enough to occur at room temperature for unsubstituted aziridines. In cases where the aziridine nitrogen bears an electronegative substituent the inversion barrier is much augmented.⁴⁵ We did not consider the barrier of this process with DFT.

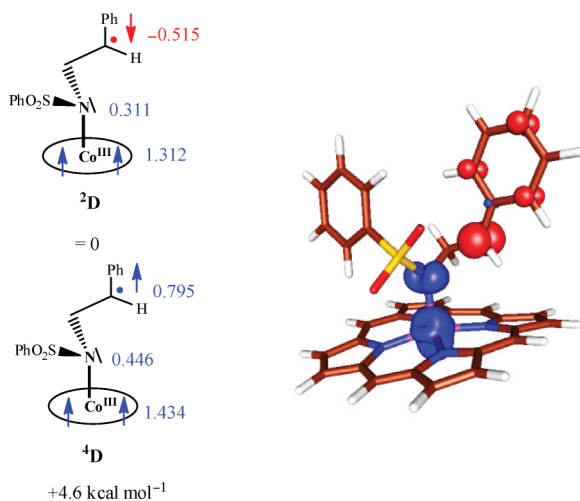


Fig. 8 Schematic representation of the two spin states of the Co(por)(N(SO₂Ph)–CH₂–CHR') species (**²D** and **⁴D**; left) (Mulliken spin densities: positive in blue, negative in red) and the spin density plot of doublet **²D** (right).

3. Details of the applied computational methods

The geometry optimizations were carried out with the Turbomole program package⁴⁶ coupled to the PQS Baker optimizer⁴⁷ *via* the BOpt package,⁴⁸ at the spin unrestricted ri-DFT level using the BP86⁴⁹ functional and the resolution-of-identity (ri) method.⁵⁰ We used the SV(P) basis set⁵¹ for the geometry optimizations of all

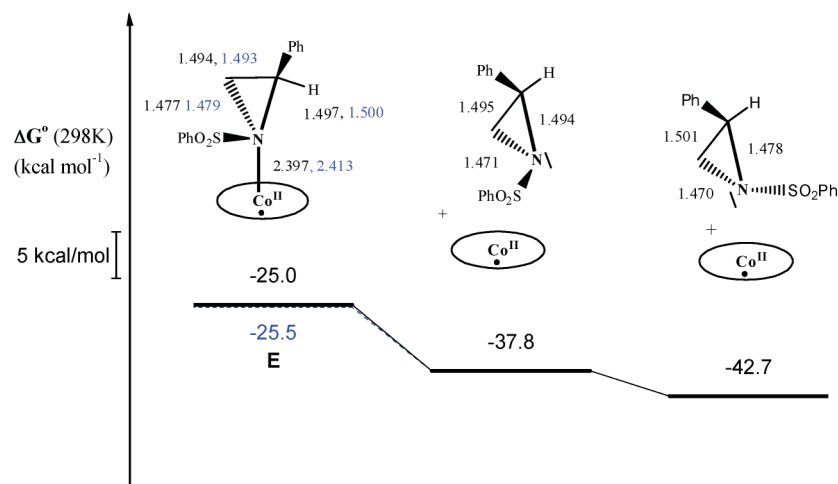


Fig. 9 Exergonic aziridine dissociation from Co(por)(aziridine) species **E** and subsequent pyramidal inversion at N of the aziridine. Free energies in kcal mol⁻¹ relative to Co(por) species **A**.

stationary points. All minima (no imaginary frequencies) and transition states (one imaginary frequency) were characterized by numerically calculating the Hessian matrix. The ZPE and gas-phase thermal corrections (entropy and enthalpy, 298 K, 1 bar) from these analyses were calculated. Improved energies were obtained with single point calculations at the spin unrestricted DFT/BP86 level using the Turbomole def-TZVP basis set.⁵² Estimated condensed phase (1 L mol⁻¹) free energies, entropies and enthalpies were obtained from these data by neglecting the enthalpy RT term and subsequent correction for the condensed phase reference volume ($S_{CP} = S_{GP} + R \ln(1/24.5)$) for all steps involving a change in the number of species, except for steps involving gaseous N₂. The energies of each of the complexes in their doublet ($S = \frac{1}{2}$) and quartet ($S = 3/2$) states were compared. For all species, the doublet state represents the ground state, with the quartet states being >10 kcal mol⁻¹ higher in energy (except **D**, for which ⁴**D** is only +2 kcal mol⁻¹ higher in energy than ³**D**). The discussion thus focuses on the lowest energy doublet energy surface, unless stated otherwise.

4. Summary & conclusions

A radical pathway for the Co^{II}(por)-catalyzed aziridination of styrene is proposed on the basis of the above computational (DFT) study. The reaction involves several unusual key intermediates as summarized in Fig. 10.

The reaction proceeds *via* a two-step radical addition-substitution pathway, in which the redox non-innocent behaviour of the nitrene ligand in intermediate **C** plays a key role (Fig. 10). The Co^{II}(por) catalyst **A** reacts with the azide PhSO₂N₃ to form a transient adduct **B**, which loses dinitrogen (**TS1**) to form the 'nitrene radical' **C**. The electronic structure of the 'nitrene radical' **C** is best described as a cobalt(III) species with a one-electron reduced nitrene ligand, or alternatively a triplet nitrene interacting covalently with the doublet cobalt(II) centre. This underlines the general importance of redox non-innocent ligands,⁵³ and the results are in good agreement with the proposed mechanisms for aziridination with Ru, Fe and Cu species.

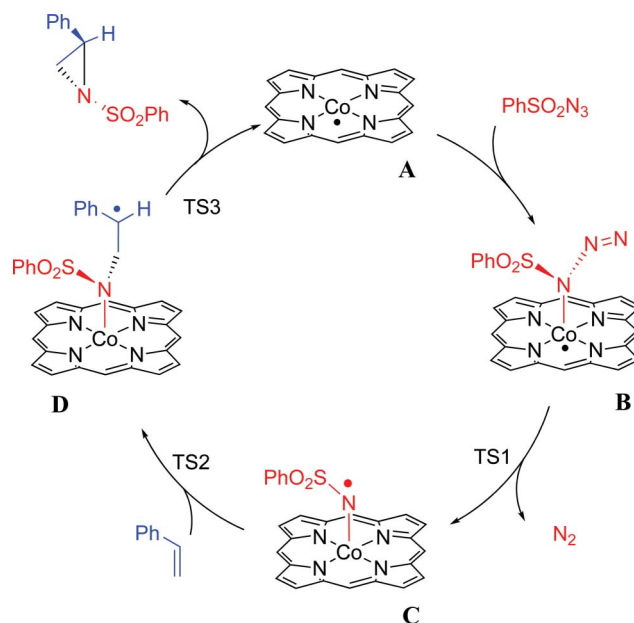


Fig. 10 Summary of the catalytic cycle for the Co^{II}(por)-catalyzed aziridination of styrene with PhSO₂N₃.

The radical addition of the 'nitrene radical' **C** to the C=C double bond of styrene yields a metastable γ -alkyl radical intermediate **D**. This species (in its doublet spin state) readily collapses in an almost barrierless ring closure reaction (**TS3**) to form the aziridine. The addition of the 'nitrene radical' **C** to the olefin (**TS2**) proceeds with a comparable barrier as its formation (**TS1**), thus providing a good explanation for the experimentally observed first-order kinetics in both substrates and the catalyst.¹⁴

Interestingly, the formation of **C** is clearly accelerated by the stabilization of **C** and **TS1** *via* hydrogen bonding with the amide-appended porphyrin in the Co(porAmide) model. All the intermediates following the formation of **C** are also stabilised by H-bonding, and all the follow-up reaction steps in the reaction of **C** with styrene proceed with somewhat lower barriers due to the presence of this same H-bond donor. The computed radical-type mechanism (Fig. 10) thus agrees well with all the available

mechanistic and kinetic information, and readily explains the excellent performance of the H-bond donor appended Co^{II}(por) systems developed in the group of Zhang. The new insights obtained from these studies should shed light on how to address further selectivity issues in catalytic aziridination and will aid future developments to expand the substrate scope and the design of new catalytic systems.

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- 35 The hydrogen bond significantly stabilises the SOMO of the Co(porAmide) nitrene radical **C** (−5.397 eV) as compared to the SOMO of the Co(por) analog **C'** (−5.094 eV). This likely contributes to the lower **TS1** barrier shown in Fig. 3. Calculated Mulliken spin densities at both the BP86/def-TZVP level (Co 27%, N: 65%, O 6% and 7%) and at the b3-lyp, def-TZVP level (Co 2%, N: 87%, O 5% and 7%) reveal a nitrogen-centred radical.
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- 43 The 'nitrene radical' ligand in **C** is both a π -donor (filled p_x-orbital) and a weak π -acceptor (half-filled p_y acceptor orbital). The latter keeps cobalt in a low spin configuration in **C**, but upon the transformation of **C** into species **D** the π -accepting properties are lost and the π -donating properties of the resulting 'amido' nitrogen donor in **D** raises the energy of one of the π -type d_{xy} orbitals of cobalt, and lowers the overall orbital splitting. At the same time, the σ -donation of the 'amido' nitrogen with the metal d_z orbital is weaker as a result of higher steric demands around the nitrogen atom, hence lowering the energy of the metal d_z orbital. The combination leads to a spin-flip from low-spin (S = 0) to intermediate-spin (S = 1) cobalt.
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