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Cobalt(II)-tetraphenylporphyrin-catalysed carbene transfer from acceptor–acceptor iodonium ylides via N-enolate–carbene radicals

Roel F. J. Epping, Mees M. Hoeksma, Eduard O. Bobylev, Simon Mathew and Bas de Bruin

_square-planar cobalt(II) systems have emerged as powerful carbene transfer catalysts for the synthesis of numerous (hetero)cyclic compounds via cobalt(III)–carbene radical intermediates. Spectroscopic detection and characterization of reactive carbene radical intermediates is limited to a few scattered experiments, centered around monosubstituted carbene catalysts. Two interconnected catalytic cycles are involved in the overall mechanism, with a monocarbene radical and an N-enolate–carbene radical intermediate at the heart of each respective cycle. Notably, N-enolate formation is not a deactivation pathway but a reversible process, enabling transfer of two carbene moieties from a single N-enolate–carbene radical intermediate. The findings are supported by extensive experimental and computational studies._

Metal carbenes have emerged over several decades as highly versatile intermediates, enabling synthetic chemists to access a wide variety of structural motifs. Their synthetic utility ranges from cyclopropanes to numerous C–H and X–H insertion reactions as well as several ring-closing and expansion transformations. Previous work has focused mostly on platinum-group metals and such systems are still among the most successful ones. Over the past decades, attention has shifted largely towards first-row transition metals, which have a higher abundance and lower toxicity compared to their second- and third-row counterparts. Akin to their noble-metal analogues, these systems typically react via classical Fischer-type carbene pathways but a reversible process, enabling transfer of two carbene moieties from a single N-enolate–carbene radical intermediate at the heart of each respective cycle. Notably, N-enolate formation is not a deactivation pathway but a reversible process, enabling transfer of two carbene moieties from a single N-enolate–carbene radical intermediate. The findings are supported by extensive experimental and computational studies._

Metal carbene intermediates are major synthetic reagents in the preparation of a wide variety of organic compounds. However, the reactive nature of carbene radical intermediates limits the spectroscopic detection and characterization to a few scattered experiments. Typically these reports feature the detection of minor amounts at low temperatures, along with other species (including ‘bridging carbones’), or indirect detection with spin trapping agents. The difficulty in observing carbene radical intermediates largely originates from the use of monosubstituted carbene precursors with limited steric protection and/or electronic stabilization of the reactive core. Disubstituted acceptor–acceptor carbones have a (radical) stabilizing effect, facilitating detection and characterization of intermediates. However, activation of disubstituted acceptor–acceptor diazo compounds is far more difficult. The Zhang group developed enantioselective porphyrins equipped with hydrogen-bond donor motifs that facilitate carbene radical formation. Some of these can activate specific disubstituted diazo compounds, but the complexity of the required catalysts demands lengthy syntheses. This complexity, coupled with the inherent toxicity and potentially explosive nature of diazo compounds, calls for the development of alternative approaches.

As such, hypervalent iodine(III) analogues (that is, iodonium ylides) are useful alternative precursors for carbene formation. These substrates are readily prepared from acidic methylenes bearing two acceptor groups via condensation onto (diacetoxyiodo)benzene or related hypervalent iodo reagents. To the best of our knowledge, there are no reported examples of homogeneous cobalt systems capable of catalytic carbene transfer from iodonium ylides. For FeII- and closed-shell CoIII–porphyrin-based systems, a likely reason for this behaviour is the observed formation of catalytically inactive N-enolate species. In diatomic systems, the cyclic diester carbones rapidly rearrange to mono- or bis-N-enolate-modified porphyrins with the pendant carbonyl group serving as a fifth or sixth ligand. None of these reported N-enolate structures exhibit catalytic activity, suggesting that reactions of the type shown in Fig. 1c are catalyst deactivation pathways. Herein, we demonstrate that this assumption is incorrect for open-shell cobalt systems. By investigating the catalytic carbene transfer from acceptor–acceptor iodonium ylides mediated by homogeneous cobalt(II)-based systems, we uncovered an efficient protocol for styrene cyclopropanation via unique radical-type intermediates.

Results and discussion

We first set out to test the catalytic activity of [Co(TPP)] in the cyclopropanation of styrene using either dimethylidiazomalonate.
(DMM•N₂) or dimethylmalonate iodonium ylide (DMM•IY) as a model reaction (Table 1). The diazo substrate yielded little to no cyclopropane product (<10%, based on 1H NMR) even when heated to 60°C for 60 h (entries 1 and 2). This reactivity is consistent with previously reported attempts to activate acceptor–acceptor diazo compounds⁴²,⁴³. By marked contrast, the analogous reaction using the corresponding iodonium ylide yielded 99% cyclopropane in the analogous reaction using the corresponding iodonium ylide [Co(TPP)] in the absence of styrene. Using positive-mode cold electrospray ionization high-resolution mass spectrometry (CSI–HR–MS), quantitative yields can be obtained with a 5.0 mol% catalyst loading in just 5 minutes. Several control experiments confirmed a crucial role of the [Co(TPP)] catalyst as well as the ylide carbenoid species cannot be excluded solely based on these mass spectrometry experiments.

To shed more light on the stoichiometry of the reaction, ultraviolet–visible (UV/Vis) spectroscopy was used to probe changes in the porphyrin’s Soret bands and Q bands. Titrating the [Co(TPP)] catalyst with 0 to 2.5 equiv. DMM•IY in CH₂Cl₂ revealed a transition of the Soret peak at 410 nm to 430 nm (significantly lower intensity), with clear isosbestic points at 383, 424, 518 and 542 nm (Fig. 2e). Full conversion of [Co(TPP)] to a new species is observed upon the addition of 2 equiv. of iodonium ylide, and adding additional ylide does not lead to further perturbation of the UV/Vis spectrum. This reveals the rapid formation of a single, new species without a detectable second, long-lived intermediate. Spectral changes include the Soret peak at 410 nm to 430 nm (significantly lower intensity), with clear isosbestic points at 383, 424, 518 and 542 nm (Fig. 2e).

The reaction is not limited to styrene (Supplementary Figs. 66–68). Various substituted styrenes, vinylpyridine and methyl acrylate can be cyclopropanated. The system is very sensitive to steric hindrance through (preventing cyclopropanation of 1,2-substituted C=C bonds), and radical-stabilizing substituents are required (Supplementary Section 14).

Mechanistic investigations. Based on previous work regarding hypervalent iodine reagents in cobalt-catalysed nitrene transfer⁴⁴,⁴⁵, we suspected that biscarbenoid intermediates might play a role in the catalysis⁴⁶. This was first investigated by reacting DMM•IY and [Co(TPP)] in the absence of styrene. Using positive-mode cold electrospray ionization high-resolution mass spectrometry (CSI–HR–MS, positive mode), two major peaks at the mass to charge ratio m/z = 801 Da and m/z = 931 Da match those of mono- and biscarbenoid complexes, respectively (Fig. 2g). The isotopic patterns are in line with monocations, and subsequent reduction of the ionization voltage resulted in a complete collapse of both signals, suggesting the ionization of neutral species. Peaks at m/z = 671 Da and 1,620 Da, respectively, match those of the free [Co(TPP)] catalyst and a water adduct of a dimeric form of the monocarbenoid species (Supplementary Fig. 32). Tandem mass spectrometry analysis (Supplementary Fig. 43) shows m/z = 671 Da and m/z = 801 Da to be fragments of m/z = 931 Da. However, the presence of some monocarbenoid species cannot be excluded solely based on these mass spectrometry experiments.

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supported by time-dependent density functional theory (TD-DFT) calculations (Supplementary Section 16c).

Turning to X-band electron paramagnetic resonance (EPR) spectroscopy, an isotropic spectrum was observed at room temperature in benzene that was characteristic of an $S = \frac{1}{2}$ system (where $S$ is the effective spin quantum number) with small isotropic (iso) $^{59}$Co hyperfine interactions (HFIs; $A^{59}$Co = 85.6 MHz, where $A$ is the hyperfine coupling constant) and an isotropic (Lande) $g$ value ($g_{\text{iso}} = 1.998$). These values indicate a cobalt-bound, but organic-centred, radical undergoing restricted tumbling in solution (Fig. 2a). Additional EPR measurements at 40 K (Fig. 2b) in toluene glass corroborate these findings, showing a complex HFI pattern and a rhombic $g$ tensor ($g_{1} = 1.997; g_{2} = 2.006; g_{3} = 2.008$) in line with a cobalt-bound, organic-centred radical ($S = \frac{1}{2}$) with small $^{59}$Co HFIs ($A^{59}$Co$_{1} = 21; A^{59}$Co$_{2} = -173; A^{59}$Co$_{3} = -103$ MHz).

The $^{13}$C labelling of the ylidic carbon gave a similar isotropic X-band EPR spectrum in benzene at room temperature as for the $^{12}$C analogue ($^{12}$C-$^{15}$F$^{-}$: $g_{\text{iso}} = 1.998; A^{59}$Co$_{\text{iso}} = 85.6$ MHz; $A^{13}$C$_{\text{iso}} = 104.7$ MHz), but now with nine effective hyperfine lines instead of eight. This is caused by additional coupling with a single $I = \frac{1}{2}$ (I = nuclear spin) $^{13}$C nucleus (Fig. 2c). At 40 K in toluene glass (Fig. 2d), a rhombic spectrum was observed similar to that of $^{12}$C-$^{15}$F$^{-}$, indicating a cobalt-bound, carbene-centred radical species ($g_{1} = 1.998; g_{2} = 2.004; g_{3} = 2.006$). The $^{59}$Co HFIs match the previously obtained values ($A^{59}$Co$_{1} = 21; A^{59}$Co$_{2} = -173; A^{59}$Co$_{3} = -103$ MHz), but with additional $^{13}$C HFIs stemming from a single $^{13}$C nucleus ($A^{13}$C$_{1} = 260; A^{13}$C$_{2} = 30; A^{13}$C$_{3} = 30$ MHz). These values are in good agreement with the DFT-calculated (B3LYP/ZORA-def2-TZVPP) EPR parameters of N-enolate–carbene complex $^{15}$F$^{-}$ (Supplementary Table 9). Complementary data were obtained with in situ attenuated total reflection Fourier-transform infrared spectroscopy studies (Supplementary Section 7). On the basis of the combined spectroscopic evidence, we conclude that the reaction between DMM$^{11}$IY and [Co(TPP)] results in formation of the N-enolate–carbene radical species $^{15}$F$^{-}$ (Fig. 3). Additional proof for the structure of $^{15}$F$^{-}$ comes from NMR and single-crystal X-ray diffraction characterization of the diamagnetic N-enolate–alkyl species $^{15}$F$^{-}$, which is readily obtained by hydrogen atom transfer (HAT) to the carbene radical moiety of $^{15}$F$^{-}$ (Fig. 2f). More details about the formation and characterization of diamagnetic complex $^{15}$F$^{-}$ are in the following section ‘HAT-induced catalyst deactivation’.

Having characterized the N-enolate–carbene radical intermediate $^{15}$F$^{-}$, we proceeded to investigate its potential role in the catalytic reaction with styrene. [Co(TPP)] was exposed to 2 equiv. DMM$^{11}$IY to form $^{15}$F$^{-}$ quantitatively, after which an excess of styrene was added. To our surprise, this ‘single-turnover’ experiment produced 2 equiv. of cyclopropane 1, thus indicating that both the carbene radical moiety and the enolate moiety of $^{15}$F$^{-}$ can be transferred as a carbene group to styrene (Fig. 3). Clearly, this demonstrates that formation of the N-enolate moiety is reversible for the paramagnetic [Co$^{III}$(TPP)] and is not a catalyst deactivation pathway. This is in stark contrast with previous work pertaining to closed-shell Co$^{III}$-porphyrins, where N-enolate formation proved to be a thermodynamic sink$^{1–3}$.

Armed with this knowledge, $^{15}$F$^{-}$ generated in situ was exposed to 1 equiv. of styrene in a single-turnover reaction and studied by X-band EPR spectroscopy (Fig. 4a). Interestingly, this produced a spectrum indicative of a cobalt-bound organic-centred radical that is distinctly different from $^{15}$F$^{-}$. Simulation of the EPR spectrum suggests the formation of mono-terminal carbene species $^{1}$ (g$_{1} = 2.018; g_{2} = 1.988; g_{3} = 2.047; A^{59}$Co$_{1} = 15; A^{59}$Co$_{2} = 30; A^{59}$Co$_{3} = 135$ MHz), in agreement with the computed EPR parameters (Supplementary Fig. 17 and Supplementary Table 9). The $^{59}$Co hyperfine coupling is very similar to that reported for the monoester Co$^{III}$-corrole carbene radical reported by Musselman et al.$^{8}$ (135 MHz for $^{15}$F versus 136 MHz for $^{1}$) (ref. 22). However, $^{1}$ has a more anisotropic g tensor, comparable to that reported for the transient monocarbene radical formed upon reaction of [Co(TPP)] with ethyl diazo acetate$^{9}$.

These findings suggest that the initial carbene transferred from $^{15}$F$^{-}$ to styrene is the carbene radical moiety, after which the N-enolate moiety of the newly formed Co$^{III}$-N-enolate adduct $^{1}$ rearranges to $^{1}$. In the presence of additional styrene, the latter reacts to produce a second equivalent of cyclopropane (Fig. 3).

When running the catalytic reaction by adding the reagents in the order (1) DMM$^{11}$IY, (2) styrene, (3) [Co(TPP)], followed by freeze-quenching the reaction mixture after 20 seconds, a mixture was obtained containing mainly [Co(TPP)] and the monocarbene radical species $^{1}$ (Supplementary Fig. 19), while upon reversing the order of addition to (1) DMM$^{11}$IY, (2) [Co(TPP)], (3) styrene, we detected a (to the best of our knowledge) new, previously unencountered species (Fig. 4b and Supplementary Fig. 20). The relatively large g anisotropy of the latter species points to a cobalt-centred radical. Upon comparison with the DFT-calculated EPR parameters (Supplementary Table 9), we assign this spectrum to the N-enolate adduct $^{1}$ (g$_{1}$ = 2.051; g$_{2}$ = 2.168; g$_{3}$ = 2.027; A$^{59}$Co$_{1} = -109; A^{59}$Co$_{2} = -124; A^{59}$Co$_{3} = 390$ MHz; Fig. 4b). These data suggest that carbene transfer proceeds mostly from the N-enolate–carbene radical intermediate $^{15}$F$^{-}$ in reactions where the catalyst reacts first with the ylide. Conversely, the monocarbene radical $^{1}$ is the dominant carbene transfer intermediate in reactions where styrene is present from the start.

We decided to gather more mechanistic information via Hammett analysis of the carbene transfer reactions (Supplementary Section 13). To account for radical contributions to the Hammett
parameters, the $\sigma_{\pi}^*$ (Jiang & Ji's spin-delocalization Hammett constant) radical spin-delocalization substituents$^{47}$ were included as well as the classical $\sigma^{+}$ Hammett constants (Fig. 4c)$^{68}$. Changing the order of addition of reagents does not have a noticeable influence on the obtained Hammett parameters (Supplementary Figs. 62 and 63 and Supplementary Tables 14 and 15), suggesting that both carbene radicals ($I^T$ and $I^E$) have similar electronic properties. Interestingly, the large $|\rho/\sigma|$ values ($|\rho|=0.43$ and $|\sigma|=0.14$ are the reaction-specific Hammett values correlated to $\sigma$ and $\sigma_{\pi}^*$, respectively, obtained from multiple linear regression analysis) suggest a significant build-up of negative charge in the transition state, implying that the carbene radicals are distinctly nucleophilic$^{49,50}$.

**HAT-induced catalyst deactivation.** Cobalt(III)–carbene radicals are known to deactivate rapidly through HAT from either the starting diazo reagent or the solvent$^{1,2,4}$. Detailed spectroscopic (EPR, NMR, UV/Vis and attenuated total reflection Fourier-transform infrared spectroscopy) and mass spectrometric studies (Supplementary Section 9) revealed that HAT from the solvent (toluene) or other hydrogen sources (for example, trace impurities) indeed leads to deactivation of both monocarbene radical intermediate $I^t$ and N-enolate–carbene radical intermediate $I^E$ to produce the alkyl species $1^+$ and biscarbenoid complexes $1^+$ (Fig. 3). HAT deactivation is observed to be significantly faster for $I^t$ than for $I^E$-T, in good agreement with supporting DFT studies (Supplementary

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**Fig. 2 | Spectroscopic detection and characterization of the N-enolate–carbene radical $I^T$. a, Experimental (Exp; black) and simulated (Sim; red) X-band EPR spectrum of species $P^T$ obtained in a reaction between DMM•IY and [Co(TPP)] in benzene at room temperature. B, magnetic field; dX'/dB, first derivative of the absorption signal. b, Spectrum of $^{13}C$-$I^T$ measured at room temperature, generated in a reaction between $^{13}C$-DMM•IY and [Co(TPP)] in benzene at room temperature. c, Spectrum of $I^T$ measured in toluene glass at 40 K, respectively (Fig. 3). HAT-induced catalyst deactivation. Cobalt(III)–carbene radicals are known to deactivate rapidly through HAT from either the starting diazo reagent or the solvent$^{1,2,4}$. Detailed spectroscopic (EPR, NMR, UV/Vis and attenuated total reflection Fourier-transform infrared spectroscopy) and mass spectrometric studies (Supplementary Section 9) revealed that HAT from the solvent (toluene) or other hydrogen sources (for example, trace impurities) indeed leads to deactivation of both monocarbene radical intermediate $I^t$ and N-enolate–carbene radical intermediate $I^E$ to produce the alkyl species $1^+$ and biscarbenoid complexes $1^+$ (Fig. 3). HAT deactivation is observed to be significantly faster for $I^t$ than for $I^E$-T, in good agreement with supporting DFT studies (Supplementary
The N-enolate moiety clearly has a protective function, making the barrier for HAT deactivation higher. The diamagnetic alkyl species $\text{IE}^{-}\text{A}$ could be isolated and was characterized in detail by UV/Vis spectroscopy as well as $^1\text{H}$ NMR, $^{13}\text{C}$ NMR, $^1\text{H}$-$^1\text{H}$ correlation spectroscopy (NMR), $^1\text{H}$-$^{13}\text{C}$ heteronuclear single quantum coherence NMR, heteronuclear multiple bond correlation NMR (Supplementary Section 3a) and single-crystal X-ray diffraction studies (Fig. 2f and Supplementary Section 3b).

NMR, infrared studies, bond-length analysis and use of the harmonic oscillator model for aromaticity51 reveal that TPP N-enolate functionalization leads to desymmetrization of the macrocycle. However, the overall aromaticity is largely retained (harmonic oscillator model for aromaticity value, 0.91; Supplementary Section 3b). The modified pyrrole ring still binds to cobalt, but has a substantially elongated Co–N bond.

**Fig. 3** | Schematic overview of spectroscopically detected catalytic intermediates and deactivation products. Schematic overview with $\text{I}^\text{X}$ = intermediate $\text{X}$, where $\text{X}=\text{A}$ (alkyl); $\text{B}$ (bridging carbene); $\text{E}$ (enolate) or $\text{T}$ (terminal carbene). Note that the mono-terminal carbene radical intermediate $\text{I}^\text{T}$ is not detectable during UV/Vis titrations leading to direct formation of $\text{I}^\text{T}$, but can be detected in single-turnover experiments between $\text{I}^\text{T}$ and 1 equiv. styrene. Complexes $\text{I}^\text{T}$ and $\text{I}^\text{T}$ deactivate to diamagnetic alkyl species $\text{IE}^{-}\text{A}$ and $\text{I}^\text{A}$ via HAT (for example, from toluene). Phenyl rings of the TPP ligand have been omitted for clarity. FTIR, Fourier-transform infrared spectroscopy.

**Fig. 4** | Trapping and reactivity studies. a, X-band EPR spectrum of $\text{I}^\text{T}$ obtained in toluene-$d_8$ glass at 40 K after reacting $\text{I}^\text{E}$ with 1 equiv. styrene. b, EPR spectrum of $\text{I}^\text{E}$ measured after freeze-quenching the catalytic reaction mixture obtained in the ‘reverse order’ of addition: (1) DMM$\bullet$Iy, (2) $[\text{Co(TPP)}]$, (3) styrene. c, Hammett plot for the $[\text{Co(TPP)}]$-catalysed cyclopropanation of styrene using DMM$\bullet$Iy. $k_x$, rate of substituted styrene; $k_H$, rate of styrene; $R^2$, coefficient of determination; $\rho$, Hammett reaction constant. Styrene first means order of addition (1) DMM$\bullet$Iy, (2) styrene, (3) $[\text{Co(TPP)}]$.
Computational DFT studies. To gain further insight into the mechanism of the metallo-radical-catalysed cyclopropanation reaction, we turned to DFT calculations. The results are shown in Fig. 5. A detailed account is provided in the Supplementary Information. Herein we summarize the main results, which are in excellent agreement with the experimental data:

(a) Reaction mechanism: The overall reaction mechanism for [Co(TPP)]-catalysed styrene cyclopropanation is quite intricate and consists of two interconnected catalytic cycles with low reaction barriers—a ‘monocarbene cycle’ in which monocarbene radical $I^\bullet$ is the key intermediate, and a ‘biscarbene cycle’ in which N-enolate–carbene radical $I^{\bullet-T}$ is the key carbene transfer species.

(b) Ylide activation: The first and second addition of DMM●Y both proceed via low barrier transition states to produce $I^\bullet$ and $I^{\bullet-T}$. Interestingly, the order of stability for the monocarbene and bis-carbenoids is $I^\bullet > I^\bullet$ (bridging carbene intermediate) $\approx I^{\bullet-T}$ whereas for the bis-carbenoids, the relation is reversed ($I^{\bullet-T} > I^\bullet$ (bridging-terminal carbene intermediate) $> I^{\bullet-T}$ (bis-terminal carbene intermediate)).

(c) N-enolate to carbene radical rearrangement: The ‘biscarbene cycle’ is reconnected to the ‘monocarbene cycle’ via intramolecular rearrangement of $I^\bullet$ to $I^\bullet$ and subsequent formation of $I^\bullet$. Although slow, the highest barrier of this process (TS10: $\Delta \Delta G^\dagger = 23.1$ kcal mol$^{-1}$, where $\Delta \Delta G^\dagger$ is equal to the energy of the transition state relative to the precursor) is readily accessible in room temperature. This explains why $I^\bullet$ is detectable with EPR spectroscopy (Fig. 4b), why N-enolate formation is reversible and why treatment of $I^{\bullet-T}$ with excess styrene produces 2 equiv. of cyclopropane.

(d) Ylide versus styrene activation: The barrier for styrene addition to $I^\bullet$ is substantially lower than the barrier for styrene addition to $I^{\bullet-T}$ (+10.8 versus +18.3 kcal mol$^{-1}$), and the ‘monocarbene cycle’ should be faster than the ‘biscarbene cycle’. Combined with the fact that the ylide is much less soluble than styrene, this explains why the monocarbene cycle is the dominant catalytic pathway under reaction conditions where all components are present before adding the catalyst.

(e) Kinetic trapping: Formation of $I^{\bullet-T}$ from monocarbene radical $I^\bullet$ is competitive with styrene addition to $I^\bullet$ at equimolar concentrations.
concentrations (+11.2 versus +10.8 kcal mol⁻¹), and hence both cycles are relevant. While accessible at room temperature, the computed barrier for formation of Φ from Φ⁺ is relatively high. Hence, under conditions where the ylide reacts with the catalyst before styrene is added, the catalytic reaction should be largely trapped in the ‘biscarbone cycle’. Experimental detection of Φ⁺ with EPR spectroscopy for a reaction carried out by adding the reagents in the order (1) DMM•IY, (2) [Co(TPP)], (3) styrene (Fig. 4b and Supplementary Fig. 20), confirms this.

**NEVPT2–CASSCF electronic structure calculations.** To check for possible multireference/multiconfigurational contributions to the electronic structures of the key carbene transfer intermediates Φ and Φ⁺-T (ref. 57), and to provide an accurate description of their frontier molecular orbitals, we also performed NEVPT2-corrected CASSCF calculations (Supplementary Information). These calculations confirm that these species have a doublet (S = ½) ground state without significant multireference character, well separated from higher spin states, and that their electronic structures are properly described by DFT (Supplementary Tables 28 and 29 and Supplementary Figs. 87 and 88).

**Conclusions**

In this work we demonstrated that the acceptor–acceptor iodonium ylide DMM•IY is a highly suitable precursor to generate, detect and characterize disubstituted carbene radicals at [Co(TPP)], which are productive in carbene transfer catalysis and enable efficient and fast catalytic cyclopropanation of styrenes. Reaction of [Co(TPP)] with 2 equiv. DMM•IY produces the N-enolate–carbene radical intermediate Φ⁺-T, containing a CoIII–carbene radical moiety and an enolate-modified porphyrin ring generated by carbene attack at one of the pyrrole rings of the TPP ligand. In contrast to what might be expected, formation of the N-enolate is a reversible process and not a route to catalyst deactivation. The carbene radical and (indirectly) the N-enolate moieties are both carbene-delivering functionalities capable of carbene transfer to other substrates.

The mechanism of the cyclopropanation reaction proceeds via two interconnected catalytic cycles. The key carbene transfer intermediate in one cycle is monocarbene Φ⁺, and in the other cycle it is the unusual N-enolate–carbene radical Φ⁺-T. Catalyst deactivation involves HAT from the solvent or trace impurities to the carbene radical moieties of these intermediates. The N-enolate moiety clearly has a protective function, making the barrier for HAT deactivation higher. Facile and energetically favourable carbene formation coupled to comparably high deactivation barriers leads to the observed selective formation of donor–acceptor cyclopropanes from iodonium ylide DMM•IY and a variety of styrenes in quantitative yield.

The interplay of opposing stabilities between terminal and N-bridging carbene (radical) moieties dictated by the CoIII redox cycle plays an important role and explains the unique active participation of the otherwise catalytically inactive N-enolate species. We envision that further application of these unique CoIII–carbene radicals has the potential to unlock new scaffolds via the superior activation of acceptor–acceptor iodonium ylides over diazo compounds.

**Online content**

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41557-022-00905-4.

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**References**

Methods

**General procedure for the cyclopropanation of alkenes.** A 4 ml glass vial with a 10 mm Teflon-coated stir bean was flame-dried. After cooling and leaving it open to air, DMM•IY (36.1 mg; 108 µmol; 1.2 equiv.) and 1,3,5-trimethoxybenzene (5.0 mg; 30 µmol; 0.33 equiv.) were added. The vial was added to an Ar bucket, in which it was cycled three times with Ar/vacuum (vacuum for ≥2 min). To this was added styrene (10.3 µl; 9.4 mg; 90 µmol; 1 equiv.), which was filtered over basic alumina, degassed and then added via a Gilson pipette (which was cycled beforehand >20 times rapidly in and out of the Ar bucket and flushed with degassed alkenes twice before addition). Quickly afterward, 1 ml of a stock solution of [Co(TPP)] in deuterated solvent (3.0 mg ml⁻¹) was added to the vial, and the vial was sealed with a cap. The reaction mixture was then stirred at 400 r.p.m. for 10 min in the centre of the stirring plate. Afterward, the reaction was quenched by cycling the mixture through a syringe in open air and filtering the mixture via a syringe filter (polytetrafluoroethylene, hydrophobic, 0.45 µm) into an NMR tube. A ^1H NMR spectrum was recorded and used for yield determination.

Data availability

All processed data that support the findings of this study are available within the article and its Supplementary Information (experimental details; synthetic procedures; catalytic studies; X-ray diffraction, EPR, NMR, UV/Vis, in situ attenuated total reflection Fourier-transform infrared spectroscopy and CSI–HR–MS data; and (additional) DFT and NEVPT2–CASSCF calculations). All raw data that support the findings of this study have been deposited at the FigShare repository with https://doi.org/10.6084/m9.figshare.17528879. The X-ray crystallographic data for I^A was deposited at the Cambridge Crystallographic Data Centre (CCDC) under deposition number CCDC 2091203.

References


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Author contributions

R.F.J.E. and B.d.B. conceived and designed the project. R.F.J.E. and M.M.H. performed the experimental work, and R.F.J.E. and B.d.B., the spectroscopic work. Quantum chemical calculations were carried out by R.F.J.E., M.M.H. and B.d.B. Mass spectrometry measurements were performed by E.O.B. and R.F.J.E. Crystallographic measurements and characterization were carried out by S.M. The authors discussed all results and the manuscript in detail.

Competing interests

The authors declare no competing interests.

Additional information

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