Open-shell nitrene- and carbene-complexes of cobalt

Characterisation and reactivity

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Chapter 6

*Cobalt(II) porphyrin catalysed synthesis of indolines via a 1,5-H atom transfer pathway.*

*We thank Alexander Karns (UC Irvine) for his valuable contribution to this chapter (concepts and experiments).*
Introduction

Direct C-H activation is a highly desirable way to functionalise molecules. In this context, metal-catalysed carbene and nitrene transfer reactions provide unique possibilities. In these transformations metal catalysts that can activate carbene or nitrene precursors are employed, typically leading to the formation of metal-carbenoid or -nitrenoid species.\(^1\) Depending on the reactivity of the thus formed metal-carbenoids and -nitrenoids, they can add to a variety of saturated (C-H bonds) or unsaturated bonds (alkenes and alkynes, for example). Transition-metal-catalysed carbene insertion into a saturated X-H (X= C, Si, O, N etc.) bond is an appealing methodology for construction of carbon-carbon or carbon-heteroatom bonds. Many of these methods find application in natural product synthesis and pharmaceuticals.\(^2\) Metal-catalysed carbene insertion into C-H bonds has proven to be an effective strategy for stereo- and enantioselective synthesis of five- and four-membered heterocycles.\(^3\) Significant advances in this area have been made with the Rh-/Ru-catalysed decomposition of diazo esters;\(^4\) reactions which are postulated to proceed via reactive metal-carbene intermediates. A special type of reactivity involving related carbene transfer pathways is displayed by cobalt. In its +2 oxidation state porphyrin complexes of cobalt exist as stable metalloradicals with well-defined open-shell doublet d\(^7\)-electronic configuration. These [Co\(^{II}\)(Por)] complexes have been successfully employed in carbene transfer reactions with unique activities. For example, cyclopropanation reactions mediated by [Co\(^{II}\)(Por)] catalysts have been proven to be very effective and selective for conversion of electron-deficient olefins.\(^5\) Their activities are not only limited to cyclopropanation/cyclopropanation but they have recently also been applied in a variety of other ring-closing reactions to form heterocycles.\(^6\) Mechanistically, these reactions proceed via radical mechanisms involving Co\(^{III}\)-carbene radical intermediates, which can be viewed as one-electron reduced Fischer-type carbene complexes (Figure 1).\(^7\) Consequently, the substrate acquires radical-character at the carbene-carbon, enabling controlled radical type reactivity in the coordination sphere of the metal. These carbene-radical intermediates also have a reduced tendency to undergo undesirable carbene dimerization reactions that are typical of free carbones. The other added advantage of the [Co\(^{II}\)(Por)] systems is that N-tosylhydrazones can be directly used as carbene precursors in combination with a suitable base. This obliterates the need to isolate the toxic and potentially explosive diazo compounds, unlike many Rh and Ru catalysts used in carbene transfer reactions.

Despite distinct advantages and unique reactivities of the [Co\(^{II}\)(Por)] catalysts in carbene transfer reactions, so far they haven’t been employed in the construction of N-containing heterocycles via the Co\(^{III}\)-carbene radical intermediates.\(^7\) Given the ubiquity of nitrogen atoms in biologically active compounds it is desirable to find ways in which N-containing heterocycles can be formed by such [Co\(^{II}\)(Por)] addition or insertion reactions of carbones. We were particularly interested in the synthesis of indolines. The indoline heterocycle is one of the most commonly observed among natural product and pharmaceutical scaffolds.\(^8\) Consequently indole and indoline synthesis is an important field of
A variety of strategies using metal-catalysed reactions have been reported (Figure 2). For example, Ru catalyst in ring-closing olefin metathesis (RCM)/elimination sequence or an RCM/tautomerization sequence of functionalized pyrrole precursors\[^{10}\], \([\text{RuCl}_2(\text{CO})_3]_2/\text{dppp}\) for the intramolecular oxidative amination of various aminoalkenenes in presence of \(\text{K}_2\text{CO}_3\) and allyl acetate to give the corresponding cyclic imines and indoles.\[^{11}\] Inter and intra-molecular cross-couplings with \(\text{Pd}\),\[^{12}\] \(\text{Cu}\),\[^{13}\] and \(\text{Rh(III)}\)- and \(\text{Rh(II)}\)-catalysed reactions,\[^{14}\] and many related synthetic protocols have also been developed. Carbene precursors have also previously been used in the synthesis of indolines with precious metals. Che and co-workers discovered the propensity of in-situ generated ruthenium carbenoids to undergo 1,2-insertion,\[^{15}\] a fundamental reaction of metal carbenes, to form indolines. Additionally, the Che group has also disclosed a method for indoline synthesis from nitrene precursors,\[^{16}\] involving a 1,5-hydrogen atom abstraction and subsequent formation of the key C-N bond using an iron catalyst. These strategies are summarised in Figure 2.

**Figure 2.** (Top) General strategies towards synthesis of the indoline heterocycle. (Bottom) Carbene and nitrene insertion pathways towards synthesis of indolines reported by Che and co-workers.

However, many of them are not tolerant to all functional groups and mostly employ expensive noble metals. Other disadvantages are use of harsh reaction conditions and sometimes use of protecting groups which are difficult to remove. In particular, only a few existing methods provide efficient and regio-controlled access to indolines that have a variety of substituents on the aromatic ring. Hence, new, robust, efficient, and broadly applicable catalytic routes to expand the currently available methods for indoline synthesis from readily available starting materials are welcome. In addition, the development of catalysts for these reactions based on earth-abundant metals is also highly desirable.

We argued that Co\[^{III}\]-carbene radicals could also be useful for the synthesis of five-membered \(N\)-containing heterocycles like indolines. While the Co\[^{III}\]-carbene radical has been shown to participate in traditional radical reactions like 1,2-addition and radical recombination (Scheme 1, left), there are no reported examples concerning indoline synthesis involving 1,5-hydrogen atom transfer (1,5-HAT) by Co\[^{III}\]-carbene radicals. The 1,5-HAT reaction is a fundamental and often under-appreciated reaction step, shown here to be a highly useful and versatile elementary step in the catalytic synthesis of \(N\)-heterocycles as a strategy in C-C bond formation. We herein disclose a method for the formation of indolines by exploiting the susceptibility of Co\[^{III}\]-carbene radicals to undergo 1,5-HAT. In organic
synthesis the susceptibility of free radicals to undergo 1,5-HAT is often an unwanted pathway. Herein, we turn the 1,5-HAT reactivity Co(III)-carbene radical intermediate to our advantage. The general concept of the approach used in this work is shown in Scheme 1 (right).

**Scheme 1.** (left) Radical reactivity from carbene precursors and application in formal 1,2-addition. (right) Envisioned Co^{III}-carbene radical catalysed synthesis of indolines via 1,5 HAT.

**Results and discussion**

The substrates required for the envisioned cobalt-catalysed radical type C-C bond ring-closing reaction shown in Scheme 1 (right) were synthesised using the generalised synthetic scheme shown in Scheme 2.

**Scheme 2.** General strategy for synthesis of diazo-precursors employed in the [Co^{III}(TPP)]-catalysed ring-closing reaction to give indolines.

Starting from the commercially available (2-aminophenyl)methanol reagents A we first protected the amino functionality with Boc-anhydride (di-tert-butyl dicarbonate) to give B. Oxidation of the Boc-protected anilines B using MnO₂ gave the corresponding aldehydes C. This was followed by benzylation of the protected amines to give D. Refluxing D with tosyl-hydrazide then produces the
desired substrates $S$ with the $N$-tosylhydrazone functionality. Substrate $S$ can be treated with base to produce the corresponding diazo functionality \textit{in-situ}. The final step in the sequence is the cobalt-catalysed ring-closing step; the focus of the work described in this chapter.

The cobalt-catalysed radical type ring-closing reaction was then tested with substrate $S_1$ ($R=\text{Ph}, R'=\text{H}$) using LiO' Bu (1.7 equiv.) as base, benzene as solvent and 5 mol\% catalyst loading at 60 °C. We were pleased to see that under these reaction conditions the reaction proceeded cleanly to give the 5-membered indoline $P_1$ within 18 hours. We also tested the ring-closing of substrate $S_1$ with some other cobalt(II) catalysts that are known to be active in carbene insertion reactions. The results are summarised in Table 1.

\textit{Table 1.} Screening of various cobalt(II) catalysts for the ring-closing reaction to give indolines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Solvent</th>
<th>Temperature</th>
<th>Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Co$^{\text{II}}$(TPP)] (5 mol%)</td>
<td>LiO' Bu (1.7 equiv.)</td>
<td>C$_6$H$_6$</td>
<td>60 °C</td>
<td>18 h</td>
<td>99%</td>
</tr>
<tr>
<td>2</td>
<td>(none)</td>
<td>LiO' Bu (1.7 equiv.)</td>
<td>C$_6$H$_6$</td>
<td>60 °C</td>
<td>18 h</td>
<td>--</td>
</tr>
<tr>
<td>3</td>
<td>CoCl$_2$ (25 mol%)</td>
<td>LiO' Bu (1.7 equiv.)</td>
<td>C$_6$H$_6$</td>
<td>60 °C</td>
<td>18 h</td>
<td>trace</td>
</tr>
<tr>
<td>4</td>
<td>[Co$^{\text{II}}$(MeTAA)] (5 mol%)</td>
<td>LiO' Bu (1.7 equiv.)</td>
<td>C$_6$H$_6$</td>
<td>60 °C</td>
<td>18 h</td>
<td>83%</td>
</tr>
<tr>
<td>5</td>
<td>[Co$^{\text{II}}$(salen)] (5 mol%)</td>
<td>LiO' Bu (1.7 equiv.)</td>
<td>C$_6$H$_6$</td>
<td>60 °C</td>
<td>18 h</td>
<td>76%</td>
</tr>
</tbody>
</table>

The [Co$^{\text{II}}$(TPP)], [Co$^{\text{II}}$(MeTAA)] and [Co$^{\text{II}}$(Salphen)] complexes used as catalysts in this reaction are shown in Figure 3. [Co$^{\text{II}}$(TPP)], [Co$^{\text{II}}$(MeTAA)] and [Co$^{\text{II}}$(Salphen)] were all active in this reaction, while CoCl$_2$ showed no reactivity. This shows that the ligand plays a significant role in the activity of this class of catalysts. For reasons of superior activity, availability and ease of handling, we chose to perform further optimisations with the air- and moisture stable complex [Co$^{\text{II}}$(TPP)].

\textit{Figure 3.} [Co$^{\text{II}}$(TPP)], [Co$^{\text{II}}$(Salphen)] and [Co$^{\text{II}}$(MeTAA)] catalyst applied in the ring closing reaction shown in Table 1.
Next, we investigated the effect of different base equivalents in this reaction (Table 2). 1.7 equiv. of base was found to be optimal amount for this reaction. While lower equivalents (entry 1) didn’t lead to full conversion, higher equivalents (entry 2) gave other unidentified products. Thus, using [Co\textsuperscript{II}(TPP)] (5 mol %) as the catalyst, 1.7 equiv. of LiOtBu as the base, and benzene as the solvent, 95% of the product could be obtained in 6 hours reaction time. Finally, we could lower the catalyst loading to 1 mol% by increasing the reaction time, so to obtain excellent yields of the indoline product P1 (98%). Screening of different solvents (with [Co\textsuperscript{II}(Salen)] as the catalyst) showed that the reaction proceeded in good to moderate yields in apolar solvents like toluene and cyclohexane. Lower yields were obtained in more polar solvents like THF. The best solvent was benzene where the indoline product was formed selectively with no other side products. These results are summarised in Table 5 (see additional information).

Thus, with the optimised reaction conditions in hand we moved on to synthesise substrates with varying substituents, both at the aromatic ring, as well as substituents on the N-atom (Table 3). In all cases where an activated C-H bond was present next to the N-atom, the reaction proceeded smoothly. The electron-donating or withdrawing nature of the substituent on the benzyl ring on the N-atom didn’t affect the reaction much. To our delight, even furanyl (entry 6, Table 3) and o-pyridine substituents (entry 5, Table 3) are tolerated in the reaction.

Less activated C-H bonds proved unsuitable for the radical-type ring closing reaction. With a methyl or ethyl substitution on the N-atom ring-closure did not occur (entry 7 and 8, Table 3). The only identified products in these cases were results of unwanted carbene dimerisation. This shows that C-H activation in this system is possible only for activated C-H with a (radical) stabilising group connected to the activated position. Different substituents on the aromatic ring were also tested and these reactions also gave moderate to excellent yields. When an electron-withdrawing CF\textsubscript{3} group was present close to the in-situ formed diazo functionality (entry 11), the yield dropped to 68%.

Table 2. Evaluation of different base equiv. for the [Co\textsuperscript{II}(TPP)]-catalysed ring-closing reaction to give indolines.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Solvent</th>
<th>Temperature</th>
<th>Time</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Co\textsuperscript{II}(TPP)] (5 mol%)</td>
<td>LiO’Bu (1.2 equiv.)</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>60 °C</td>
<td>18 h</td>
<td>35%</td>
</tr>
<tr>
<td>2</td>
<td>[Co\textsuperscript{II}(TPP)](5 mol%)</td>
<td>LiO’Bu (3 equiv.)</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>60 °C</td>
<td>18 h</td>
<td>65%</td>
</tr>
<tr>
<td>3</td>
<td>[Co\textsuperscript{II}(TPP)] (5 mol%)</td>
<td>LiO’Bu (1.7 equiv.)</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>60 °C</td>
<td>6 h</td>
<td>95%</td>
</tr>
<tr>
<td>4</td>
<td>[Co\textsuperscript{II}(TPP)] (1 mol%)</td>
<td>LiO’Bu (1.7 equiv.)</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>60 °C</td>
<td>18 h</td>
<td>98%</td>
</tr>
</tbody>
</table>
Table 3. Substrate scope for the [Co\textsuperscript{II}(TPP)]-catalysed ring-closing reaction to give indolines (substituents on N-atom and phenyl ring).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>S1</td>
<td>P1</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td>R = Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>S2</td>
<td>P2</td>
<td>96%</td>
</tr>
<tr>
<td></td>
<td>R = -(p-O\text{Me})-Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>S3</td>
<td>P3</td>
<td>92%</td>
</tr>
<tr>
<td></td>
<td>R = -(p-CF\text{3})-Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>S4</td>
<td>P4</td>
<td>97%</td>
</tr>
<tr>
<td></td>
<td>R = -(o-Me)-Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>S5</td>
<td>P5</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>R = Pyridyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>S6</td>
<td>P6</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>R = Furanyl</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Product</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>S7</td>
<td>P7</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>R = Me</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>S8</td>
<td>P8</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>R = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = H</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>S9</td>
<td>P9</td>
<td>81%</td>
</tr>
<tr>
<td></td>
<td>R = Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = \text{4-O\text{Me}}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>S10</td>
<td>P10</td>
<td>80%</td>
</tr>
<tr>
<td></td>
<td>R = Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = 5-Me</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>S11</td>
<td>P11</td>
<td>68%</td>
</tr>
<tr>
<td></td>
<td>R = Ph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>R' = \text{4-CF}_3 \text{3}</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Enantioselective synthesis of indolines via cobalt(II)-metalloradical catalysis

Next we explored a few chiral catalysts for the enantioselective indoline synthesis. Because the reaction also proceeded with [Co\textsuperscript{II}(Salophen)] we chose two chiral salophens and two chiral [Co\textsuperscript{II}(Por)] complexes to perform the reaction enantioselectively. These catalysts are shown in Figure 4. Unfortunately, very high enantioselectivities could not be achieved in this reaction using these catalysts. The best outcome from each catalyst is summarised in Table 4. While enantioselectivities were higher at room temperature, the yields dropped drastically below 60° C. At best an ee of 25% could be achieved at RT on using [Co\textsuperscript{II}(Salophen)] \textbf{1}, but the yield for this reaction was only 11%.
Table 4. Summary of results of enantioselective synthesis of indolines using some chiral catalysts (Figure 4).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Temperature</th>
<th>Yield</th>
<th>ee</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Co\textsuperscript{II}(Salophen)] 1</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>rt</td>
<td>11%</td>
<td>25%</td>
</tr>
<tr>
<td>2</td>
<td>[Co\textsuperscript{II}(Salophen)] 2</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>60 °C</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>3</td>
<td>[Co\textsuperscript{II}(Por)] 3</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>rt</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>4</td>
<td>[Co\textsuperscript{II}(Por)] 4</td>
<td>C\textsubscript{6}H\textsubscript{6}</td>
<td>rt</td>
<td>27%</td>
<td>22%</td>
</tr>
</tbody>
</table>

Figure 4. Different chiral [Co\textsuperscript{II}(Salophen)] and [Co\textsuperscript{II}(porphyrin)] complexes used in the enantioselective synthesis of indolines.

DFT mechanistic studies

Next, to shed some light on the mechanism, we explored this reaction computationally using DFT methods. In line with the similar systems that have been previously studied extensively, we considered a radical-type pathway involving activation of the in-situ formed diazo compound by the [Co\textsuperscript{II}(Por)] catalyst.\textsuperscript{5} The computations were performed at the BP86 and def2-TZVP level using the non-functionalised [Co\textsuperscript{II}(Por)] system. The choice for this computational method is based on previous realistic mechanistic pathways calculated by us on such systems. We further incorporated Grimme’s dispersion corrections (DFT-D3) for these systems. For the substrate, we included a full model for the diazo compound formed from substrate S1. Based on the energies obtained from these calculations we propose the mechanistic cycle depicted in Figure 5. Coordination of the diazo substrate on the catalyst to form a substrate-bound adduct B is exergonic by -5.0 kcal mol\textsuperscript{-1}. From this adduct B, elimination of dinitrogen via TS\textsubscript{1} (barrier: \(\Delta G^\ddagger = +8.6\) kcal mol\textsuperscript{-1}) leads to the formation of a carbenic-radical intermediate C (\(\Delta G^*= -13.8\) kcal mol\textsuperscript{-1}). From this intermediate C the key step of HAT proceeds readily via a low barrier TS\textsubscript{2} (barrier: \(\Delta G^\ddagger = +2.9\) kcal mol\textsuperscript{-1}) to give intermediate D (\(\Delta G^*= -21.5\) kcal mol\textsuperscript{-1}).
mol$^{-1}$). Ring-closing by radical rebound and homolysis of the Co-carbene bond proceeds through a slightly higher barrier TS3 ($\Delta G^\ddag = +11.5$ kcal mol$^{-1}$).

![Diagram](image)

**Figure 5.** (A) DFT-D3 calculated (Turbomole BP86, def2-TZVP) free energies ($\Delta G_{298K}^\ddag$ in kcal mol$^{-1}$) for the proposed reaction pathway. Energies of all intermediates are reported with respect to species A as the reference point (barriers for the transition states are reported in brackets). (B) Spin density plot of intermediate C showing maximum spin density at the carbene carbon. (C) Spin density plot of intermediate D after the 1,5-HAT step showing maximum spin density on the benzylic carbon and some delocalisation over the adjacent phenyl ring.

The computed barriers of all steps of the catalytic cycle depicted in Figure 5 are surprisingly low. This suggests that formation of the diazo compound from the tosyl hydrazone precursors, which requires heating, is the actual rate limiting step of the reaction. Once the diazo compound is generated, the next highest barrier in the catalytic reaction is the ring-closing step from species D to liberate the product and regenerate catalyst A. This is in agreement with the experimental observations, with chiral catalysts giving some chirality transfer in the ring-closing step. Release of product and regeneration of free catalyst is overall exergonic by $-30.0$ kcal mol$^{-1}$. Also, we calculated the spin densities on the intermediates C and D (Figure 5 B and C). Maximum spin-density in intermediate C is indeed located on the “carbene carbon” with some further delocalisation in the neighbouring phenyl ring (Figure 5B). The unpaired electron of the intermediate D formed after the HAT is delocalised on the benzylic carbon with considerable delocalisation also on the adjacent phenyl ring (Figure 5C).

In an attempt to prove the involvement of radical intermediates (as shown in Figure 5), we performed some radical trapping experiments using up to 10 equivalents of the radical scavenger TEMPO (TEMPO= 2,2,6,6-tetramethylpiperidinoxyl). However, in all the attempts to scavenge species C or D, the indoline product was still the major product. This is in agreement with the very low barriers of all
reaction steps shown in Figure 5, suggesting that the ring-closing steps are too fast to trap these intermediates. Kinetically, the intramolecular reaction seems to outcompete the inter-molecular radical trapping by TEMPO free radical, at least with the concentrations used in these experiments.

Summary and Conclusions

In this work we report a novel route for the synthesis of several substituted indolines which are substructures of a variety of natural products and pharmaceutically relevant compounds. It proceeds efficiently via a [Co\(^{II}\)(Por)]-catalysed pathway via activation of an in-situ formed diazo compound. The key-step in this reaction is a 1,5 HAT reaction, which is usually considered to be an undesirable pathway in organic free-radical chemistry. In this reaction, however, it is a desirable step, making catalytic synthesis of indolines possible. To the best of our knowledge, this is the first example of the synthesis of N-heterocycles via a cobalt(III)-carbene radical mediated C-H activation/rebound mechanism. The reaction uses commercially available starting materials and is thus a practical method to synthesise substituted indolines. Tosyl-hydrazone substrates can be used as precursors for the diazo functionality which can be generated in-situ in these reactions, thus precluding the need to isolate them. The metallo-radical catalysed indoline synthesis in this work represents an example of a net, formal (intramolecular) carbene insertion reaction into a benzylic C-H bond, but proceeds via a radical mechanism and displays highly controlled reactivity of the key Co\(^{III}\)-carbene radical intermediates involved.

Supporting information, experimental and computational details

1. General

All manipulations were performed under a nitrogen atmosphere using standard Schlenk techniques. All solvents used for catalysis were dried over and distilled from sodium (toluene, tetrahydrofuran (THF)) or CaH\(_2\) (dichloromethane (DCM), hexane, methanol).

All NMR spectra were recorded at 293 K.

\(^1\)H NMR: All \(^1\)H NMR spectra were measured on a Bruker Avance 400 (400 MHz) or Mercury 300 (300 MHz), referenced internally to residual solvent resonance of CDCl\(_3\) (δ = 7.26 ppm), or dms-o-d\(_6\) (δ = 2.5 ppm)

\(^{13}\)C\({}^{1}\)H) NMR: Bruker Avance 400 (101 MHz) or Bruker Avance 500 (126 MHz), referenced internally to residual solvent resonance of CDCl\(_3\) (δ = 77.2 ppm) or dms-o-d\(_6\) (δ= 39.52)

Individual peaks are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant in Hz.

High Resolution Mass spectra were measured on an AccuTOF LC, JMS-T100LP Mass spectrometer (JEOL, Japan). FD/FI probe (FD/FI) is equipped with FD Emitter, Carbotec or Linden (Germany), FD 10 \(\mu\)m. Current rate 51.2 mA/min over 1.2 min FI Emitter, Carbotec or Linden (Germany), FI 10 \(\mu\)m. Flashing current 40 mA on every spectra of 30 ms. Typical measurement conditions are: Counter electrode –10kV, Ion source 37V.

2. Chemicals used

All chemicals were purchased from commercial sources unless otherwise mentioned. Solvents for all catalytic reactions were freshly distilled from sodium (toluene) and for acetonitrile or over calcium
Hydride (acetonitrile). Reactions were performed using standard Schlenk techniques under an atmosphere of dinitrogen. [Co(HMeTAA)]\textsuperscript{5b}, [Co(Salophen)]\textsuperscript{1}\textsuperscript{7}, chiral catalysts [Co(Salophen)]\textsuperscript{2}\textsuperscript{18}, [Co(Por)]\textsuperscript{3}\textsuperscript{19} and [Co(Por)]\textsuperscript{4}\textsuperscript{20} were synthesised according to literature methods.

3. Synthesis of N-substituted substrates

Substrates S1-S8 compounds were synthesised starting from t-butyl(2-formyl phenyl)carbamate using the following generalised procedure. 1 mmol of t-butyl(2-formyl phenyl)carbamate, 1.3 mmol of RCH\textsubscript{2}Br (BnBr for S1, 2-methyl benzyl bromide for S2, 1-(bromomethyl)-4-methoxybenzene for S3, 4-trifluoro benzylbromide for S4, MeI for S5, ethyl iodide for S6, Bromomethyl pyridine.HBr for S7, Bromomethyl furan for S8) was dissolved in 1.5 mL DMF. This mixture was cooled to 0 °C. To this was added dropwise over 5 min a solution of 1 mmol of NaH in 670 μL of DMF. This reaction mixture was allowed to stir for 20h after which 5 mL of saturated NH\textsubscript{4}Cl solution was added slowly. The mixture was extracted three times with EtOAc. The organic layer was dried over MgSO\textsubscript{4}, filtered and concentrated to give the N-Boc-substituted aldehydes. These N-Boc-substituted aldehydes were reacted with tosyl hydrazide using the procedure described in literature to give the final compound.\textsuperscript{5b}

4. Synthesis of Substituted Anilines
Synthesis of substrate S9:

\[ \text{Carboxylic acid} \rightarrow \text{Benzyl alcohol} \rightarrow \text{Aldehyde} \]

6.6 mmol of the carboxylic 2-amino-6-methylbenzoic acid was dissolved in 14 mL of THF in a round bottom flask. The reaction mixture was cooled to 0 °C and 16 mmol of LiAlH₄ was added. Subsequently, additional 14 mL of THF was added and the reaction was let to stir for 6 hours, allowing it to warm to rt during this time. The reaction mixture was filtered through a plug of celite and concentrated to give the corresponding benzyl alcohol. Without further purification, 1.1 equiv. of Boc₂O was added in THF (13 mL) and refluxed for 16 hours. The reaction mixture was then concentrated to give a brown oil. This brown oil was directly refluxed with 10 equiv. of MnO₂ in DCM for 16 h. The crude reaction mixture was filtered through celite and the filtrate was concentrated. It was then chromatographed on silica (0-5% EtOAc/Hex) to give the corresponding aldehyde. The aldehyde was then benzylated according to procedure described in 5.

Synthesis of substrate S10:

\[ \text{Aniline} \rightarrow \text{Aldehyde} \]

1 g (~8 mmol) of 4-trifluoromethyl aniline was dissolved in 4 mL of THF. To this was added 1.9 g (~8.8 mmol) of Boc₂O. The mixture was refluxed for two days after which it was evaporated to dryness, taken up in EtOAc followed by washing with 1M HCl and H₂O. Concentrating the organic layer gave a white solid which was washed with hexanes to give a white solid. This white solid was dissolved in 14 mL of dry THF followed and cooled to -78 °C. To this was added 8mL tBuLi (1.7 M solution in pentane) followed by 2.9 mL of DMF. After the addition the mixture was stirred at -20 °C for 1 h and then at RT for two hours. The reaction was quenched by slowly adding ~100 mL of 5% HCl solution followed by 200 mL of Et₂O. The ether layer was washed with water and then concentrated to give a yellow solid which was the aldehyde. The aldehyde was then benzylated according to procedure described in 5.

Synthesis of substrate S11:

\[ \text{Aldehyde} \rightarrow \text{Aldehyde} \]

To a round bottom flask was sequentially added the aldehyde (1.00 g, 5.52 mmol, 1 equiv.), absolute ethanol (16.5 mL), iron powder (1.23 g, 22.1 mmol, 4 equiv.) and 0.1M HCl (2.8 mL, 0.28 mmol, 0.05 equiv.). The reaction mixture was heated to 65 °C for 2 hours, followed by heating at 75 °C for 2 hours. Following complete reduction, the reaction mixture was cooled to room temperature, quenched with saturated aqueous NaHCO₃ (10 mL), and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were dried with MgSO₄, filtered, and concentrated to a brown oil.
The crude product mixture was immediately dissolved in dry THF (5.5 mL), and Boc₂O (2.5 mL, 11.0 mmol, 2 equiv.) was added in one portion. The reaction mixture was heated at 50 °C for 24 hours, at which point thin-layer chromatography indicated low conversion. An additional 2 mL of Boc₂O was added, and the reaction mixture was heated to reflux for 72 hours. Upon completion, the reaction mixture was concentrated and immediately purified by silica gel chromatography. The aldehyde was then benzylated according to procedure described in 5.

5. General Procedure for the Synthesis of Hydrazone Precursors from the corresponding aldehydes (S9-11)

To a flame-dried Schlenk vial was added sodium hydride (217 mg, 5.42 mmol, 60% w/w dispersion in mineral oil, 1.2 equiv.). The vial was evacuated and filled with nitrogen three times, and DMF (3.3 mL) was added. The suspension was cooled to 0 °C, and a solution of the aldehyde (1.00 g, 4.52 mmol, 1 equiv.) and benzyl bromide (805 µL, 6.78 mmol, 1.2 equiv.) in DMF (7.5 mL) was added dropwise over 10 minutes. Following addition, the reaction mixture was removed from the water bath and stirred overnight. Upon completion, the reaction mixture was diluted with ethyl acetate (20 mL) and saturated aqueous ammonium chloride (10 mL) was added dropwise. The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 x 10 mL). The combined organic layers were dried with MgSO₄, filtered, and concentrated to a yellow oil.

The yellow oil was immediately dissolved in dry methanol (9 mL), and tosyl hydrazide (926 mg, 4.97 mmol, 1.1 equiv.) was added. The reaction mixture was capped and stirred vigorously overnight. Upon completion, the reaction mixture was filtered, and the precipitate was washed sequentially with methanol and hexanes, and dried under a stream of air to afford the product as a white solid.

6. General Procedure for Cobalt-Catalyzed Indoline Formation

To a flame dried Schlenk tube 0.3 mmol of the substrate was added followed by the catalyst (1 mol %). The Schlenk tube was evacuated and back-filled with nitrogen three times. Then inside a glove box 1.6 equiv of LiO'Bu was added to this schlenk flask. The solids were dissolved in 6 mL of benzene and set to react at 60°C for 18 h. After that the reaction mixture was opened to air and 6mL of water was added. The organic layer was separated and the water layer was extracted 3 times with hexane (3 X 6mL). The organic portions were collected, dried over MgSO₄, concentrated and chromatographed on silica.
Table 5. Screening of different solvents for the ring-closing reaction to give indolines.

![Chemical structure diagram]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temperature</th>
<th>Time</th>
<th>Yield</th>
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</thead>
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<td>18 h</td>
<td>76%</td>
</tr>
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<td>16%</td>
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<td>65%</td>
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<td>60 °C</td>
<td>18 h</td>
<td>70%</td>
</tr>
<tr>
<td>5</td>
<td>Cyclohexane</td>
<td>60 °C</td>
<td>18h</td>
<td>77%</td>
</tr>
</tbody>
</table>

7. Analytical data

Substrate S₁

![Structure of S₁]

1H NMR (500 MHz, Chloroform-d) δ 11.56 (s, 1H), 7.86 – 7.69 (m, 3H), 7.60 (d, J = 7.8 Hz, 1H), 7.40 (s, 2H), 7.31 (d, J = 7.3 Hz, 1H), 7.30 – 7.18 (m, 4H), 7.10 (dd, J = 19.2, 7.7 Hz, 3H), 4.72 (d, J = 15.4 Hz, 2H), 2.35 (s, 3H), 1.12 (s, 6H).

13C NMR (126 MHz, Chloroform-d) δ 153.99, 143.54, 143.48, 140.67, 137.39, 136.35, 131.25, 130.49, 129.85, 128.46, 127.47, 127.46, 127.30, 125.46, 80.04, 52.92, 27.90, 21.15.

HRMS (FD): Calculated for - 479.1879[M+], found- 479. 1875 Dalton

Substrate S₂

![Structure of S₂]
$^1$H NMR (500 MHz, DMSO-$d_6$) δ 11.57 (s, 1H), 7.85 – 7.67 (m, 3H), 7.58 (d, $J = 7.7$ Hz, 1H), 7.39 (s, 2H), 7.38 – 7.19 (m, 2H), 7.06 (s, 2H), 7.06 – 6.92 (m, 2H), 4.92 – 4.40 (m, 2H), 2.34 (s, 3H), 2.09 (s, 3H), 1.18 (d, $J = 44.7$ Hz, 7H).

$^{13}$C NMR (126 MHz, DMSO-$d_6$) δ 153.96, 143.71, 143.47, 136.50, 135.23, 130.56, 130.39, 127.46, 125.99, 28.07, 21.32, 19.01.

HRMS (FD): Calculated for C$_{27}$H$_{31}$N$_3$O$_4$S$_1$ [M+] 493.2035, found 493.2038 Dalton

Substrate S3

$^1$H NMR (500 MHz, DMSO-$d_6$) δ 11.55 (s, 1H), 7.87 – 7.64 (m, 3H), 7.60 (d, $J = 7.9$ Hz, 1H), 7.38 (d, $J = 7.9$ Hz, 2H), 7.30 (d, $J = 7.7$ Hz, 1H), 7.23 (d, $J = 7.8$ Hz, 1H), 7.13 – 6.97 (m, 3H), 6.77 (d, $J = 8.1$ Hz, 2H), 4.64 (bs, 2H), 3.69 (s, 3H), 2.34 (s, 3H), 1.11 (s, 6H).

$^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 158.42, 153.79, 143.39, 140.52, 136.19, 131.12, 130.31, 129.69, 129.13, 127.74, 127.13, 125.28, 113.66, 79.79, 54.94, 52.12, 27.76, 20.99.

HRMS (FD): Calculated for C$_{27}$H$_{31}$N$_3$O$_5$ [M+] 509.1984, found 509.1994 Dalton

Substrate S4

$^1$H NMR (400 MHz, DMSO-$d_6$) δ 11.58 (d, $J = 2.6$ Hz, 1H), 7.81 (d, $J = 2.4$ Hz, 1H), 7.78 – 7.68 (m, 2H), 7.62 (t, $J = 8.1$ Hz, 3H), 7.47 – 7.30 (m, 5H), 7.27 (d, $J = 7.7$ Hz, 1H), 7.12 (d, $J = 7.8$ Hz, 1H), 5.05 – 4.60 (m, 2H), 2.34 (d, $J = 2.5$ Hz, 3H), 1.52 – 0.98 (m, 11H).

$^{13}$C NMR (75 MHz, DMSO-$d_6$) δ 143.42, 143.15, 142.21, 140.45, 136.15, 130.89, 130.51, 129.68, 128.80, 128.08, 127.66, 127.36, 127.12, 126.00, 125.20, 122.40, 80.22, 27.72, 20.97.

$^{19}$F NMR (282 MHz, DMSO-$d_6$) δ -60.87.

HRMS (FD): Calculated for C$_{27}$H$_{28}$F$_3$N$_3$O$_4$S [M+] 547.1753, found 547.1755 Dalton

Substrate S5
$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 11.52 (d, $J = 4.2$ Hz, 1H), 7.87 (d, $J = 4.4$ Hz, 1H), 7.83 – 7.61 (m, 3H), 7.40 (d, $J = 7.7$ Hz, 3H), 7.36 – 7.12 (m, 2H), 3.19 – 2.93 (m, 3H), 2.36 (d, $J = 4.5$ Hz, 3H), 1.11 (s, 7H).
$^{13}$C NMR (126 MHz, DMSO-$d_6$) $\delta$ 153.69, 143.43, 143.17, 142.36, 136.14, 130.70, 130.50, 129.69, 127.17, 125.27, 79.48, 37.22, 27.71, 20.99.
HRMS (FD): Calculated for C$_{20}$H$_{25}$N$_3$O$_4$S [M+] 403.1566, found - 403.1566 Dalton

Substrate S6

$^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 11.55 (s, 1H), 7.89 (s, 1H), 7.74 (d, $J = 8.1$ Hz, 2H), 7.69 (dd, $J = 7.8$, 1.6 Hz, 1H), 7.40 (d, $J = 8.1$ Hz, 3H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.20 (dd, $J = 7.9$, 1.2 Hz, 1H), 2.35 (s, 3H), 1.09 (s, 7H), 0.93 (t, $J = 7.1$ Hz, 4H).
$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 153.26, 143.48, 143.42, 136.14, 131.38, 130.66, 129.70, 127.23, 127.14, 79.36, 44.20, 27.77, 20.99, 13.07.
HRMS (FD): Calculated for C$_{21}$H$_{27}$N$_3$O$_4$S [M+] 417.1722, found - 417.1752 Dalton

Substrate S7

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 11.59 (s, 1H), 8.40 (s, 1H), 7.99 (s, 1H), 7.87 – 7.58 (m, 3H), 7.40 (d, $J = 8.0$ Hz, 2H), 7.25 (dq, $J = 20.2$, 7.4, 5.9 Hz, 4H), 4.80 (s, 2H), 2.35 (s, 3H), 1.20 (d, $J = 46.9$ Hz, 10H).
$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 156.81, 153.74, 148.91, 143.88, 143.39, 142.86, 141.06, 136.66, 136.23, 135.23, 131.12, 130.37, 129.69, 129.45, 128.03, 127.66, 127.17, 125.32, 122.36, 79.93, 54.75, 27.71, 21.00.
HRMS (FD): Calculated for C$_{25}$H$_{27}$N$_3$O$_5$S [M+] 480.1831, found - 481.1853 Dalton

Substrate S8

$^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 11.56 (s, 1H), 7.72 (d, $J = 7.5$ Hz, 3H), 7.62 (d, $J = 7.5$ Hz, 1H), 7.47 – 7.42 (m, 1H), 7.38 (d, $J = 8.2$ Hz, 2H), 7.33 (d, $J = 7.3$ Hz, 0H), 7.26 (d, $J = 7.6$ Hz, 1H), 7.07 (d, $J = 7.8$ Hz, 1H), 6.17 (d, $J = 49.5$ Hz, 2H), 4.69 (s, 2H), 2.34 (s, 3H), 1.09 (s, 7H).
$^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 190.03, 144.07, 142.43, 134.73, 133.12, 128.14, 127.64, 110.43, 109.99, 109.35, 81.54, 46.56, 28.13.
HRMS (FD): Calculated for C$_{24}$H$_{27}$N$_3$O$_5$S [M+] 469.1671, found - 469.1681 Dalton
Substrate S9

\[
\begin{align*}
&\text{H NMR (400 MHz, DMSO-}^d_6\text{) } \delta 11.55 (s, 1H), 7.94 (s, 1H), 7.73 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.0 Hz, 2H), 7.33 - 7.18 (m, 3H), 7.18 - 7.02 (m, 3H), 6.78 (d, J = 7.7 Hz, 1H), 4.80 (d, J = 15.3 Hz, 1H), 4.24 (s, 1H), 2.33 (s, 4H), 2.22 (s, 4H), 1.16 (s, 9H). \\
&\text{C NMR (75 MHz, DMSO-}^d_6\text{) } \delta 153.90, 144.85, 143.39, 141.60, 137.51, 136.15, 129.99, 129.62, 129.45, 129.04, 128.27, 127.32, 127.21, 79.70, 52.87, 27.80, 21.70, 20.97. \\
&\text{HRMS (FD): Calculated for C}_{27}\text{H}_{31}\text{N}_3\text{O}_4\text{S [M+]} 493.2035, found - 493.2059 \text{ Dalton}.
\end{align*}
\]

Substrate S10

\[
\begin{align*}
&\text{H NMR (400 MHz, DMSO-}^d_6\text{) } \delta 11.81 (s, 1H), 9.58 (s, 1H), 7.79 (d, J = 9.4 Hz, 2H), 7.71 (dd, J = 7.7, 5.7 Hz, 3H), 7.64 (d, J = 8.2 Hz, 1H), 7.43 - 7.33 (m, 5H), 7.27 - 7.16 (m, 3H), 7.16 - 7.09 (m, 2H), 4.72 (s, 1H), 2.39 (s, 2H), 2.34 (s, 3H), 1.12 (s, 8H). \\
&\text{C NMR (75 MHz, DMSO-}^d_6\text{) } \delta 153.25, 143.64, 143.44, 141.70, 136.87, 136.02, 135.48, 132.31, 129.77, 129.44, 128.43, 128.19, 127.81, 127.50, 127.10, 126.83, 125.48, 121.88, 121.69, 80.62, 48.62, 27.64, 21.05, 20.98. \\
&\text{F NMR (282 MHz, DMSO-}^d_6\text{) } \delta -61.26. \\
&\text{HRMS (FD) - Calculated for C}_{27}\text{H}_{28}\text{F}_3\text{N}_3\text{O}_4\text{S [M+] 547.1753, found - 547.1753 Dalton}.
\end{align*}
\]

Substrate S11

\[
\begin{align*}
&\text{H NMR (400 MHz, DMSO-}^d_6\text{) } \delta 11.55 (s, 1H), 7.72 (t, J = 4.1 Hz, 3H), 7.40 (d, J = 8.0 Hz, 2H), 7.20 (dd, J = 10.0, 6.7 Hz, 2H), 7.17 - 7.08 (m, 2H), 7.05 (d, J = 2.9 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 4.79 - 4.40 (m, 2H), 3.72 (s, 3H), 2.35 (s, 3H), 1.13 (s, 11H). \\
&\text{C NMR (75 MHz, DMSO-}^d_6\text{) } \delta 157.52, 154.20, 143.50, 143.20, 137.33, 136.12, 133.71, 132.04, 129.73, 129.04, 128.35, 127.34, 127.22, 116.18, 109.19, 79.74, 55.26, 53.00, 27.82, 21.03. \\
&\text{HRMS (FD) - Calculated for C}_{27}\text{H}_{33}\text{N}_3\text{O}_5\text{S-} 509.1984{[M+]}, \text{found - 509.1990 Dalton}.
\end{align*}
\]
Analytical data of synthesised indolines

**Product P1**

![Indoline Structure](image)

$^1$H NMR (300 MHz, Chloroform-$d$) δ 7.91 (s, 1H), 7.34 – 7.17 (m, 6H), 7.12 (d, $J$ = 7.4 Hz, 1H), 6.98 (td, $J$ = 7.4, 1.0 Hz, 1H), 5.37 (d, $J$ = 10.6 Hz, 1H), 3.68 (dd, $J$ = 16.3, 10.6 Hz, 1H), 2.97 (dd, $J$ = 16.3, 3.5 Hz, 1H), 1.30 (d, $J$ = 16.2 Hz, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$): δ = 28.1, 37.8, 62.6, 80.7, 114.6, 122.5, 124.8, 125.2, 127.1, 127.6, 128.5, 129.1, 143.3, 144.7, 152.3.

HRMS (FD): calculated for C$_{19}$H$_{21}$NO$_2$ [M+] 295.1572, found 295.1565 Dalton

**Product P2**

![Indoline Structure](image)

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.89 (br, 1H), 7.20 (dd, $J$ = 7.5, 7.5 Hz, 1H), 7.11—7.09 (m, 3H), 6.96 (dd, $J$ = 7.5, 7.0 Hz, 1H), 6.80—6.77 (m, 2H), 5.30 (br, 1H), 3.76 (s, 3H), 3.63 (dd, $J$ = 16.0, 11.0 Hz, 1H), 2.93 (dd, $J$ = 16.0, 3.0 Hz, 1H), 1.34 (br, 9H). Matched literature.$^{21}$

**Product P3**

![Indoline Structure](image)

$^1$H NMR (400 MHz, Chloroform-$d$) δ 7.95 (bs, 1H), 7.56 (d, $J$ = 8.1 Hz, 2H), 7.33 (s, 1H), 7.31 – 7.23 (m, 2H), 7.13 (d, $J$ = 7.4 Hz, 1H), 7.00 (t, $J$ = 7.4 Hz, 1H), 5.61 – 5.27 (m, 1H), 3.71 (dd, $J$ = 16.3, 10.7 Hz, 1H), 2.93 (dd, $J$ = 16.3, 3.5 Hz, 1H), 1.57 – 1.02 (m, 9H).

$^{13}$C NMR (101 MHz, Chloroform-$d$) δ 152.04, 129.53, 129.21, 127.75, 125.50, 125.37, 124.80, 122.78, 122.67, 114.66, 99.86, 62.03, 37.47, 28.06, 0.94. $^{19}$F NMR (282 MHz, Chloroform-$d$) δ -62.39.

HRMS FD Calculated for C$_{20}$H$_{20}$F$_3$NO$_2$ [M+] 363.1446, found 363.1450 Dalton

**Product P4**

![Indoline Structure](image)

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.98 (br, 1H), 7.23 (m, 1H), 7.14—7.01 (m, 5H), 6.96 (dd, $J$ = 7.5, 7.0 Hz, 1H), 5.57 (br, 1H), 3.68 (dd, $J$ = 16.0, 11.0 Hz, 1H), 2.82 (app. d, $J$ = 16.0 Hz, 1H), 2.38 (s, 3H), 1.23 (br, 9H). Matched literature.$^{21}$

**Product P5**

![Indoline Structure](image)
**Product P6**

![Structure of Product P6]

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 8.65 – 8.26 (m, 1H), 7.96 (s, 1H), 7.59 (td, $J = 7.7$, 1.6 Hz, 1H), 7.23 (dd, $J = 15.9$, 8.1 Hz, 1H), 7.12 (dt, $J = 13.6$, 6.9 Hz, 3H), 6.96 (t, $J = 7.4$ Hz, 1H), 5.52 (d, $J = 10.6$ Hz, 1H), 3.71 (dd, $J = 16.4$, 10.8 Hz, 1H), 3.08 (dd, $J = 16.2$, 3.7 Hz, 1H), 1.30 (s, 9H).

$^{13}$C NMR (75 MHz, Chloroform-$d$) $\delta$ 149.42, 136.84, 127.74, 124.96, 122.87, 122.16, 119.20, 114.90, 28.28.

HRMS (FD): Calculated for C$_{20}$H$_{23}$NO$_2$ [M+] 309.1729, found 309.1740 Dalton

**Product P9**

![Structure of Product P9]

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.81 (br, 1H), 7.27 (s, 1H), 7.19 (dd, $J = 6.5$, 6.5 Hz, 1H), 7.15 (d, $J = 6.0$ Hz, 1H), 6.96 (dd, $J = 6.5$, 6.5 Hz, 1H), 6.26 (m, 1H), 6.12 (s, 1H), 5.47 (br, 1H), 3.52 (dd, $J = 13.5$, 9.0 Hz, 1H), 3.15 (dd, $J = 13.5$, 2.5 Hz, 1H), 1.47 (br, 9H). Matched literature $^{21}$

$^{13}$C NMR (75 MHz, Chloroform-$d$) $\delta$ 155.70, 152.35, 128.52, 127.15, 125.31, 112.14, 111.21, 77.49, 77.07, 76.65, 55.68, 37.92, 28.21.

HRMS (FD): Calculated for C$_{20}$H$_{23}$NO$_3$ [M+] 325.1678 Dalton, found 325.1788 Dalton

**Product P10**

![Structure of Product P10]

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.79 (s, 1H), 7.32 – 7.25 (m, 3H), 7.19 (d, $J = 7.5$ Hz, 2H), 6.87 – 6.53 (m, 2H), 5.36 (s, 1H), 3.78 (s, 3H), 3.66 (dd, $J = 16.4$, 10.5 Hz, 1H), 2.93 (dd, $J = 16.3$, 3.4 Hz, 1H), 1.29 (s, 9H).

$^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 152.32, 144.93, 142.75, 134.05, 130.24, 128.44, 127.70, 127.00, 125.14, 123.59, 112.02, 77.28, 76.96, 76.64, 62.47, 36.75, 29.63, 28.07, 18.49.

HRMS (FD): Calculated for C$_{20}$H$_{23}$NO$_2$ [M+] 309.1729, found 309.1679 Dalton
Product P11

\[ \text{Product P11} \]

\[ \text{F}_3\text{C} \]

\[ \text{Ph} \]

\[ \text{Boc} \]

\[^1\text{H} \text{NMR (300 MHz, Chloroform-}d\text{)} \delta 7.97 (s, 1H), 7.55 - 7.47 (m, 1H), 7.36 (s, 1H), 7.33 - 7.23 (m, 3H), 7.16 (dd, } J = 7.7, 1.8 \text{ Hz, 2H}), 5.41 (dd, } J = 10.8, 3.5 \text{ Hz, 1H}), 3.70 (dd, } J = 16.6, 10.7 \text{ Hz, 1H}), 3.01 (dd, } J = 16.6, 3.6 \text{ Hz, 1H}), 1.29 (d, } J = 17.4 \text{ Hz, 9H}). \]

\[^{13}\text{C NMR (101 MHz, Chloroform-}d\text{)} \delta 151.99, 143.86, 128.55, 127.36, 125.73, 125.37, 125.33, 125.30, 125.26, 125.05, 124.62, 124.30, 123.97, 123.03, 121.71, 121.67, 120.34, 114.10, 77.23, 76.91, 76.60, 62.97, 37.32, 29.60, 29.27, 27.93, 22.60. \]

\[^{19}\text{F NMR (282 MHz, Chloroform-}d\text{)} \delta -61.42. \]

HRMS (FD) Calculated for C\text{_{20}}H\text{_{20}}F\text{_{3}}N\text{O}_{2} [M+] 363.1446, found 363.1765 Dalton

8. Computational details

Geometry optimizations were carried out with the Turbomole program package coupled to the PQS Baker optimizer via the BOpt package. We used unrestricted ri-DFT-D3 calculations at the BP86 level, in combination with the def2-TZVP basis set, and a small (m4) grid size. Grimme’s dispersion corrections (version 3, disp3, ‘zero damping’) were used to include Van der Waals interactions. All minima (no imaginary frequencies) and transition states (one imaginary frequency) were characterized by calculating the Hessian matrix. ZPE and gas-phase thermal corrections (entropy and enthalpy, 298 K, 1 bar) from these analyses were calculated. The nature of the transition states was confirmed by following the intrinsic reaction coordinate.

**Figure 6.** Energy Diagram for the computed mechanism for catalytic indoline synthesis using [Co\text{II}(Por)]. DFT-D3 calculated (Turbomole BP86, def2-TZVP) free energies (ΔG\text{298K}° in kcal mol\text{\textasciicircum{-1}}) are reported for each step.
**Table 6.** Energies of optimised geometries shown in Figure 6

<table>
<thead>
<tr>
<th>Ring-closing for indolines BP86-def2TZVP_disp3</th>
<th>Total Energy (SCF) Hartree</th>
<th>Total free energy (G) Hartree</th>
<th>H_correction Hartree</th>
<th>H (SCF+H_correction) Hartree</th>
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</thead>
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<tr>
<td>Diazo_substrate</td>
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<td>Co(Por)</td>
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<td>N₂</td>
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<td>-109.593</td>
<td>0.00543</td>
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<td>B</td>
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<td>TS1_N2_Loss</td>
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<tr>
<td>C</td>
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<td>-3313.69311</td>
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**Acknowledgements**

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References and notes


(7) Aziridine (three membered N-heterocycles) synthesis via nitrene transfers have been reported using cobalt(II) porphyrins. See chapter 1 of this thesis and references therein.


(22) (a) PQS version 2.4, 2001, Parallel Quantum Solutions, Fayetteville, Arkansas, USA (the Baker optimizer is available separately from PQS upon request); b) Baker, J. J. Comput. Chem.; 1986, 7, 385.

