Manipulating radicals
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Co^{III}-Carbene Radical Approach to Substituted 1H-Indenes

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Abstract

A new strategy for the catalytic synthesis of substituted 1H-indenes via metalloradical activation of o-cinnamyl N-tosyl hydrazones is presented, taking advantage of the intrinsic reactivity of a Co^{III} carbene radical intermediate. The reaction uses readily available starting materials and is operationally simple, thus representing a practical method for the construction of functionalized 1H-indene derivatives. The cheap and easy to prepare low spin cobalt(II) complex [Co^{II}(MeTAA)] (MeTAA = tetramethyltetraaza[14]annulene) proved to be the most active catalyst among those investigated, which demonstrates catalytic carbene radical reactivity for a non-porphyrin cobalt(II) complex.

The methodology has been successfully applied to a broad range of substrates, producing 1H-indenes in good to excellent yields. The metallo-radical catalyzed indene synthesis in this paper represents a unique example of a net (formal) intramolecular carbene insertion reaction into a vinylic C(sp^2)-H bond, made possible by a controlled radical ring-closure process of the carbene radical intermediate involved. The mechanism was investigated computationally and the results were supported by a series of radical-scavenging experiments. DFT calculations reveal a stepwise process involving activation of the diazo compound leading to formation of a Co^{III}-carbene radical, followed by radical ring-closure to produce an indanyl/benzyl radical intermediate. Subsequent indene product elimination involving a 1,2-hydrogen transfer step regenerates the catalyst.

Trapping experiments using 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) radical or dibenzoylperoxide (DBPO) confirm the involvement of cobalt(III) carbene radical intermediates. Deuterium labelling experiments show statistical scrambling of the allylic/benzylic and vinylic protons under the applied reaction conditions. EPR spectroscopic spin-trapping experiments using phenyl N-tert-butynitrone (PBN) reveal the radical nature of the reaction.
1. Introduction

Substituted indenes and their closely related indane derivatives are important structural motifs found in many natural products such as taiwaniaquinol, cyanosporaside A/B, biological active molecules such as endothelin receptors antagonist enrasentan, an antipruritic dimetindene, melatonin receptor, anti-inflammatory sulindac, aldosterone synthase inhibitors, and anti-tubecular agents. Some of them are market-leading drugs and/or key intermediates for the synthesis of natural products, pharmaceuticals and other bio-active compounds, as well as functional materials and metallocene complexes for olefin polymerization. Because of their importance and usefulness, construction of the indene skeleton has attracted interest of synthetic organic and medicinal chemists for several years. Several synthetic methodologies have been developed over the past years, including intra- and intermolecular cyclization reactions, each with their specific advantages and disadvantages. Representative intramolecular reactions include ring expansion of suitably substituted cyclopropenes, Friedel Crafts cyclization of allyl and properglyc alcohol derivatives, aromatic 1,3 dienes, and α,β unsaturated ketones. Other methods include oxidative cyclizations, palladium catalysed intramolecular Heck type couplings, ring-closing metathesis, aromatic C-H bond functionalization, intramolecular Morita–Baylis–Hillman approaches, and gold and iodine catalysed rearrangements.

![Figure 1. Representative natural products and drug molecules containing indene moieties and some related indane derivatives.](image-url)
A series of intermolecular approaches have also been developed for indene synthesis, including [3 + 2] annulation of aryl alkynes with benzyl derivatives, carbonyls, allenes and dienophiles, palladium-catalysed carbocyclization of aryl halides or boronic acid esters and alkynes, Fe-catalyzed cyclization of benzyl compounds or allenes with substituted alkynes, noble metal catalysed aromatic C-H bond activation cyclization, and copper catalysed radical cyclizations. However, several of these existing methods suffer from functional group intolerance, the necessity of expensive (noble) transition metal catalysts, harsh reaction conditions and/or are limited to the synthesis of specific indenes with a particular substitution pattern. Hence, in need of a broader pallet of synthetic methodologies the development of new, short, efficient, and broadly applicable catalytic routes to expand the currently available methods for indene synthesis from readily available starting materials is certainly in demand, especially those employing benign, readily available and inexpensive base metal catalysts.

Low-spin planar cobalt(II) complexes have recently emerged as a new class of catalysts capable of ‘carbene-transfer’ reactions proceeding via radical mechanisms involving discrete CoIII-carbene radical intermediates (Figure 2). Metalloradical activation of carbene precursors (such as diazo compounds or N-tosylhydrazones) produces carbenoids with radical-character at the respective ‘carbene’ carbon, enabling catalytic radical-type organometallic transformations. These carbene-radical intermediates are best described as one-electron reduced Fischer-type carbenes, and as a result they have characteristics of both electrophilic Fischer- and
nucleophilic Schrock-type carbenes; besides their radical character they have a reduced tendency to undergo undesirable carbene dimerization reactions.\(^{31}\)

While the mechanistic details and unusual radical-type electronic structure of the key carbene radical intermediates were only recently disclosed,\(^ {31}\) their unique electronic properties have been successfully applied in a variety of interesting metalloradical approaches of synthetic value, including enantioselective alkene cyclopropanation,\(^ {32}\) C-H functionalization,\(^ {33}\) β-ester- γ-amino ketones synthesis,\(^ {34}\) and in the regioselective synthesis of β-lactams\(^ {35}\) and 2H-chromenes.\(^ {36}\)

In this chapter, we report our efforts to develop a new metalloradical approach for the synthesis of substituted 1H-indenes, taking advantage of the unique reactivity of Co\(\text{III}\)-carbene radical intermediates. The method involves a net, overall carbene insertion into a vinylic C(sp\(^3\))-H bond and uses safe and easily accessible N-tosyl hydrazones as ‘carbene’ precursors.\(^ {37}\) This unprecedented methodology has a broad substrate scope and can be applied to a variety of aromatic substituted N-tosyl hydrazones and conjugated vinyl-groups containing several different functionalities. The cheap and easy to prepare low spin cobalt(II) complex [Co\(\text{II}(\text{MeTAA})\)] (MeTAA = tetramethyltetraaza[14]annulene) proved to be the most active catalyst among those investigated. Notably, while [Co\(\text{II}(\text{MeTAA})\)] was already synthesized and characterized in 1976,\(^ {38}\) it has thus far been used successfully as a catalyst only in our group (see Chapters 2,3 and 5). Here we report that it has a superior activity over [Co(TPP)] in catalytic 1H-indene synthesis. Furthermore, we disclose a plausible reaction mechanism based on control reactions, radical trapping and deuterium labeling experiments, EPR spectroscopy and computational studies (DFT).

### 2. Results and discussion

Our initial attempt to synthesize a substituted 1H-indene involved reaction of o-cinnamyl N-tosyl hydrazone (1a) in presence of the commercially available [Co\(\text{II}(\text{TPP})\)] catalysts (at a temperature of 60 °C, unless indicated otherwise). Although various bases such as LiO\(\text{tBu}\), KO\(\text{tBu}\), NaO\(\text{tBu}\), K\(_2\)CO\(_3\), NaOMe (Table 1, entries 1-5) can be used to activate the N-tosyl hydrazone in chlorobenzene, with LiO\(\text{tBu}\) the highest yield of the desired 1H-indene product 2a was obtained (51%; entry 1).

Upon increasing the amount of base (LiO\(\text{tBu}\)) from 1.2 to 3 equivalents the yield dropped substantially (Table 1, entries 1, 6-7). This is probably caused by decomposition or poisoning of the catalyst in presence of excess base. To improve the yield of the reaction different cobalt(II) sources were investigated. The use of
fluorinated porphyrin and salen based cobalt catalysts (Table 1, entry 8, 10) did not lead to formation of the desired product. However when the cheap and easy to prepare [CoII(MeTAA)] catalyst (Figure 2) was used, 1H-indene 2a was formed in excellent yield (83%) using toluene as the solvent (Table 1, entry 9).

Table 1. Standardization of reaction conditions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base</th>
<th>Eq.</th>
<th>Solvent</th>
<th>Yielda (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Co(TPP)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>PhCl</td>
<td>51</td>
</tr>
<tr>
<td>2</td>
<td>[Co(TPP)]</td>
<td>KO'Bu</td>
<td>1.2</td>
<td>PhCl</td>
<td>41</td>
</tr>
<tr>
<td>3</td>
<td>[Co(TPP)]</td>
<td>NaO'Bu</td>
<td>1.2</td>
<td>PhCl</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>[Co(TPP)]</td>
<td>K₂CO₃</td>
<td>1.2</td>
<td>PhCl</td>
<td>39</td>
</tr>
<tr>
<td>5</td>
<td>[Co(TPP)]</td>
<td>NaOMe</td>
<td>1.2</td>
<td>PhCl</td>
<td>27</td>
</tr>
<tr>
<td>6</td>
<td>[Co(TPP)]</td>
<td>LiO'Bu</td>
<td>2</td>
<td>PhCl</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>[Co(TPP)]</td>
<td>LiO'Bu</td>
<td>3</td>
<td>PhCl</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>[Co(TPP-F₂₀)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>toluene</td>
<td>0</td>
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<td>9</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>toluene</td>
<td>83</td>
</tr>
<tr>
<td>10</td>
<td>[Co(salen)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>toluene</td>
<td>00</td>
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<td>11</td>
<td>[CuI]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>toluene</td>
<td>27</td>
</tr>
<tr>
<td>12</td>
<td>[Rh₂(OAc)₄]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>toluene</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>PhCl</td>
<td>78</td>
</tr>
<tr>
<td>14</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>PhH</td>
<td>86</td>
</tr>
<tr>
<td>15</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>THF</td>
<td>85</td>
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<tr>
<td>16</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>CH₂Cl₂</td>
<td>46</td>
</tr>
<tr>
<td>17</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>CH₃CN</td>
<td>55</td>
</tr>
<tr>
<td>18</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>hexane</td>
<td>70</td>
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<tr>
<td>19</td>
<td>--</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>PhH</td>
<td>0</td>
</tr>
<tr>
<td>20b</td>
<td>[Co(MeTAA)]</td>
<td>LiO'Bu</td>
<td>1.2</td>
<td>PhH</td>
<td>35</td>
</tr>
</tbody>
</table>

a Yields were determined by integration of the ¹H NMR signals in the presence of acenaphthene as internal standard. b Reaction carried out at room temperature.

[CoII(MeTAA)] is the cobalt(II) complex of the tetramethyltetraaza[14]annulene (MeTAA) ligand (Figure 3). The complex was first prepared in 1976,38 which involved two simple steps to obtain the complex in near quantitative yield. This is in sharp
contrast to the synthesis of porphyrin complexes, which is in general labor-intensive, low yielding, time consuming and produces large amounts of unwanted side products, thus demanding elaborate (column chromatography) purification steps. The MeTAA ligand has similar bonding properties as porphyrins, which reflects in its ability to bind a variety of transition metals. However, there are also some differences which likely explain its increased reactivity as compared to [Co(II)(TPP)]. While porphyrins have an aromatic (4n+2) delocalized π-cloud, MeTAA is Hückel anti-aromatic (4n), which increases the flexibility of the ligand. Another difference between these two macrocyclic structures is their ring size (14- vs 16-membered ring). The increased flexibility and smaller ring-size of MeTAA as compared to a porphyrin leads to deviation from planarity, and as such [Co(II)(MeTAA)] adopts a saddle shaped configuration.

Other catalysts such as [CuI] or [Rh2(OAc)4] (Table 1, entries 11-12) proved less or not effective. Quite surprisingly the carbene transfer catalyst [Rh2(OAc)4], which is well-known to be operative in a variety of carbene C-H bond insertion reactions, produced no indene at all. In general, carbene insertion into vinylic C(sp2)-H bonds appears to be entirely unprecedented, likely because cyclopropanation is favored for other (non-metalloradical) carbene transfer catalysts. Notably however, CuI did catalyze the reaction to some extent but produced only 27% of the desired indene, with mainly the carbene-carbene dimerized product being formed in the undesired side reaction.

Figure 3. Structures of the cobalt(II) catalysts used in this study.

Extended solvent screening revealed that the reaction works best in non-polar solvents such as benzene, toluene, or hexane (entries 9, 14, 18) or in low-polarity THF (entry 15). The use of more polar solvents such as CH2Cl2 or CH3CN (entries 16-17) led to comparatively low yields, . The reaction does not produce 2a without a catalyst (entry 19), and the yield of the reaction drops drastically when performing the reaction at room temperature (entry 20). Conversion of the N-tosyl hydrazone
into the corresponding diazo compound accounts for at least part of the required activation energy.\textsuperscript{37}

To explore the scope of the metalloradical catalyzed indene synthesis, several different functional groups were introduced at the vinylic double bond (Table 2). Several \(\alpha,\beta\)-unsaturated esters are tolerated (i.e. the Et-, \(n\)Bu-, tBu-, and Ph-esters \(1a-e\)), producing indenes \(2a-e\) in good to excellent yields (78–86%, entries 1-5) using the standardized reaction conditions shown in Table 2. Surprisingly, \(\alpha,\beta\)-unsaturated amide \(1f\) produced indene \(2f\) in even higher yield (98%; entry 6), and also styrene derivative \(1h\) furnished the corresponding indene product \(2h\) in good yield (85%; entry 8). The \(\alpha,\beta\)-unsaturated nitrile substrate \(1g\) works less well, producing indene \(2g\) in moderate yield (52%; entry 7).

\textbf{Table 2. Substrates scope varying functional groups at the vinylic double bond.}^a

<table>
<thead>
<tr>
<th>Entry</th>
<th>R- Products</th>
<th>Yield$^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-COOMe (1a) (\textit{2a})</td>
<td>86</td>
</tr>
<tr>
<td>2</td>
<td>-COOEt (1b) (\textit{2b})</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>-COO(n)Bu (1c) (\textit{2c})</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>-COO(t)Bu (1d) (\textit{2d})</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>-COOPh (1e) (\textit{2e})</td>
<td>82</td>
</tr>
<tr>
<td>6</td>
<td>-CONMe(_2) (1f) (\textit{2f})</td>
<td>98</td>
</tr>
<tr>
<td>7</td>
<td>-CN (1g) (\textit{2g})</td>
<td>52</td>
</tr>
<tr>
<td>8</td>
<td>-Ph (1h) (\textit{2h})</td>
<td>85</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: N-tosylhydrazone \(1a-h\) (0.2 mmol, 1.0 equiv), LiO\(\text{Bu}\) 0.24 mmol, 1.2 equiv), [Co(MeTAA)] (5 mol%), benzene (3 mL), 60 °C, overnight. $^b$ Isolated yields after column chromatography.
Table 3. Substrates scope bearing various functional group on aromatic ring.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrates</th>
<th>Products</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(1i)</td>
<td>(2i)</td>
<td>87 (^c)</td>
</tr>
<tr>
<td>2</td>
<td>(1j)</td>
<td>(2i)</td>
<td>85 (^c)</td>
</tr>
<tr>
<td>3</td>
<td>(1k)</td>
<td>(2j)</td>
<td>82 (^c)</td>
</tr>
<tr>
<td>4</td>
<td>(1l)</td>
<td>(2k)</td>
<td>84 (^c)</td>
</tr>
<tr>
<td>5</td>
<td>(1m)</td>
<td>(2l)</td>
<td>84 (^c)</td>
</tr>
<tr>
<td>6</td>
<td>(1n)</td>
<td>(2m)</td>
<td>93 (^c)</td>
</tr>
<tr>
<td>7</td>
<td>(1o)</td>
<td>(2n)</td>
<td>88 (^c)</td>
</tr>
<tr>
<td>8</td>
<td>(1p)</td>
<td>(2o)</td>
<td>72 (^c)</td>
</tr>
<tr>
<td>9</td>
<td>(1q)</td>
<td>(2p)</td>
<td>70</td>
</tr>
<tr>
<td>10</td>
<td>(1s)</td>
<td>(3)</td>
<td>95</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: \(N\)-tosylhydrazone (1a–h) (0.2 mmol, 1.0 equiv), LiO\(^t\)Bu (0.24 mmol, 1.2 equiv), CoMeTAA (5 mol%), benzene (3 mL), 60 °C, overnight. \(^b\) Isolated yields after column chromatography. \(^c\) Nearly 1:1 ratio of both isomers formed.
The substrate scope was further explored and broadened by investigating the effect of varying the substituents on the aromatic ring (Table 3). Substitution at the 5- or 6-position of the aromatic ring does not affect the yield of the products 2i (Table 3, entries 1-2). Electron withdrawing substituents such as -F, -Cl, -CF₃, and -NO₂ are all effective, affording the corresponding indenes 2i-l in good to excellent yields (Table 3, entries 1–5). Reactions proceeded even better with neutral electron-donating groups on the aromatic ring such as naphthyl (1n) and methyl (1o) groups producing the corresponding indenes 2m-n in excellent yields (Table 3, entries 6–7). Substrates 1p-q bearing 5-methoxy and 4,5-dimethoxy substituents produced indenes 2o-p in a somewhat lower yield (~70%).

For most of the asymmetrically substituted substrates shown in Table 3 (except entry 10) both possible regio-isomers of products 2i-p are formed in a nearly 1:1 ratio. This points to allylic/benzylic double bond isomerization under the applied reaction conditions, as can be expected for 1H-indenes having rather acidic allylic/benzylic protons. Substitution at the allylic/benzylic position has also been investigated. Interestingly reacting N-tosylhydrazone 1s results in regio-selective formation of indene product 3 in high yield (Table 3, entry 10) with the double bond at the thermodynamically favored most substituted position.

![Scheme 1](image)

Scheme 1. Deuterium-labeling experiments showing complete scrambling of allylic and vinylic protons.
Full statistical (thermodynamically controlled) scrambling of the allylic and vinylic protons under the applied (alkaline) reaction conditions was confirmed by the deuterium-labeling experiments shown in Scheme 1. Starting either with a deuterium label at the azomethine position (1a-D) or at the vinylic position (1b-D) of the carbenoid precursor leads in both cases to a complete statistical distribution of the deuterium atoms over the allylic/benzylic and vinylic positions, as indicated by a 2:1 ratio of the -CDH- and =CD signals in the D-NMR spectra of deuterium-labeled indene products 2a-D/2a'-D and 2b-D/2b'-D (Scheme 1).

To shed more light on the catalytic reaction mechanism, we explored the mechanism computationally. Additionally, we performed a set of trapping and control experiments, combined with EPR spectroscopic investigations.

**Scheme 2. Proposed Mechanism of [Co(MeTAA)] Catalyzed 1H-indene Synthesis** (DFT-D3 calculated (Turbomole, BP86, def2-TZVP, disp3) mechanism for [Co(MeTAA)] catalyzed 1H-indene formation (free energies, ΔG_{298K}^o, in kcal mol^{-1}). All energies, including the transition states, are reported with respect to species A as the reference point.)
At first sight the reaction may seem to proceed via a direct carbene insertion into the vinylic C(sp²)-H bond. However, such reactions are unprecedented to the best of our knowledge, and [Rh₂(OAc)₄] (which is well-known for its reactivity in C-H bond functionalization by direct carbene insertion) is not active in 1H-indene formation (vide supra). In addition, attempts to find a transition state for this process for the [Co(MeTAA)] catalyst with DFT were unsuccessful, and the electronic structure of a CoIII-carbene radical in general (Figure 2) seems to be incompatible with any direct, concerted C-H insertion mechanism of the carbenoid. Hydrogen atom transfer from the vinylic C-H bond to the carbene radical followed by a radical rebound step could in principle be an alternative, but all attempts to optimize such a vinyl radical intermediate (D' in Scheme 2) converged back to carbene radical C, thus indicating that the route via D' is not a viable pathway. As such, a metalloradical pathway involving attack of the carbene radical at the vinylic double bond to form the cyclized γ-radical intermediate D seems to be the most plausible mechanism. This mechanism was fully explored for both the [Co(MeTAA)] and [Co(TPP)] catalysts with DFT-D₃ at the BP86, def2-TZVP level, using Grimme’s version dispersion corrections (disp3). The selected computational method is in agreement with our previous studies involving Co(III)-carbene radicals as intermediates in catalytic cyclizations, and is known to provide accurate Co-C BDEs.⁴²

The computed mechanism for the [Co(MeTAA)] catalyst is presented in Scheme 2. The corresponding mechanism for the [Co(TPP)] catalyst and the associated energy diagrams of the reactions with both catalysts are shown in Figure 4. All steps have accessible barriers, and each step is exergonic.

The first steps of the DFT computed reaction mechanism involve trapping and activation of the in situ generated diazo compound by the [Co(MeTAA)] catalyst (Scheme 2). Formation of the CoII-catalyst-diazo adduct B is exergonic (ΔG° = -11.6 kcal mol⁻¹), as is N₂-elimination from B to produce the CoIII-carbene radical species C (ΔG° = -14.7 kcal mol⁻¹). The transition state barrier for formation of C is low (TS1; ΔG⁺ = +7.4 kcal mol⁻¹). These steps are similar to those reported previously in the mechanisms for 2H-chromene formation³⁶ and cyclopropanation³¹ using CoII-porphyrin catalysts.

The next step involves addition of the carbene radical to the vinylic double bond producing the cyclized γ-radical intermediate D (ΔG° = -17.7 kcal mol⁻¹) via transition state TS2 (barrier: ΔG⁺ = +18.9 kcal mol⁻¹). This appears to be the rate limiting step of the catalytic cycle. Indene formation from D requires a low barrier 1,2-hydrogen atom transfer (TS3; ΔG⁺ = +13.8 kcal mol⁻¹), relocating the radical from the γ- to the β-position. The thus formed cobalt-bound β-radical species is so
unstable that it spontaneously dissociates in a barrierless manner to form indene product $E$. The overall process is strongly exergonic ($\Delta G^\circ = -58.4$ kcal mol$^{-1}$).

Figure 4. Energy Diagram for the computed mechanism for catalytic indene synthesis using [Co(MeTAA)] (black) and [Co(TPP)] (red).

An alternative pathway for indene formation from $D$ is possible, involving dissociation of the dearomatized (methide-like $2H$-chromene) $E'$ from $D$, followed by 1,2 hydride shift ($TS_4$) to produce the $1H$-indene product $E$ (Scheme 2). Dissociation of $E'$ from $D$ involving homolytic splitting of the Co-C bond to produce starting complex $A$ is endergonic by about +13 kcal mol$^{-1}$ according to DFT (the reverse reaction is barrierless), but coordination of substrate $1a'$ to $A$ producing $B$ makes the overall process virtually thermoneutral. Subsequent conversion of $E'$ to $E$ has a low barrier transition state ($TS_4; \Delta G^\ddagger = +10.4$ kcal mol$^{-1}$). The computed pathways for indene formation from $D$ via $E'$ ($\Delta G^\ddagger = +12.7$ kcal mol$^{-1}$; determined by dissociation of $E'$ to form $A$) and the direct pathway over $TS_3$ ($\Delta G^\ddagger = +13.8$ kcal mol$^{-1}$) have very similar overall barriers, and thus seem to be competing trails producing the same product.
Spin density plots of the key intermediates \textbf{C} and \textbf{D} are presented in Figure 5. Most spin density is ligand centered for both intermediates. For intermediate \textbf{C} the highest spin population is found on the carbenoid carbon atom, in agreement with a \textit{Co}^{III}-carbene radical electronic structure as presented in Figure 2. In intermediate \textbf{D} the largest spin population is found at the \( \gamma \)-position, with some delocalization over the adjacent phenyl moiety. Both structures have less than 10\% spin population at cobalt, thus showing that radical-type elementary steps involving coordinated substrate radicals play a key role in the catalytic mechanism.

![Figure 5](image)

**Figure 5.** (a) Spin density plots of the DFT-optimized \textit{Co}^{III}-carbene radical species \textbf{C} (left) and cyclized \( \gamma \)-radical intermediate \textbf{D} (right).

To obtain additional information about the mechanistic pathway we attempted to trap intermediates with radical scavengers.\textsuperscript{43} In agreement with the above DFT calculations indicating that \textit{Co}^{III}-carbene radical intermediate \textbf{C} is the catalytic resting state, these trapping experiments produced in all cases products stemming from species \textbf{C} (Scheme 3).

Reacting substrate \textit{1a} with [\textit{Co(MeTAA)}] in the presence of three equivalents of TEMPO under identical reaction conditions as used in catalytic indene synthesis led to formation of product \textit{5} (Scheme 3). Compound \textit{5} was isolated, purified by column chromatography and characterized by \( ^1 \text{H} \), \( ^{13} \text{C} \) and GCMS spectroscopy (see Supporting Information). The compound has a TEMPO moiety attached to the carbon stemming from the ‘carbene’, which is (over)oxidized to a carbonyl group. The use of dibenzoylperoxide as a radical-scavenger also led to trapping of carbene radical intermediate \textbf{C}, in this case leading to formation of product \textit{7} (Scheme 3). No ring-closed intermediates could be trapped, consistent with \textbf{TS2} being the rate limiting step in the DFT calculated mechanism with all follow-up steps after formation of \textbf{D} being fast (Scheme 1). Cold spray ESI-HRMS experiments of the
catalytic reaction mixture in absence of radical scavengers are in agreement with the presence of carbenenoid species C (Scheme 2). The detected mass m/z=576.1906 (calc. m/z=576.1936) corresponds to [C+H]⁺ (C₃₃H₃₃CoN₄O₂), and can be attributed to protonated species C.

Scheme 3. Radical scavenging experiments used to trap the CoІІІ-carbene radical intermediate.

Figure 6. Isotropic X-band EPR spectrum of the PBN-trapped carbon-centered radical (T= 298 K; microwave frequency: 9,36607 GHz; power: 6.33 mW; modulation amplitude: 1.0 G). Reaction conditions: N-tosylhydrazone (0.2 mmol, 1.0 equiv), LiOtBu (0.24 mmol, 1.2 equiv), [Co(MeTAA)] (5 mol%), PBN (0.4 mmol, 2.0 equiv), benzene (3 mL), 60 °C, 30 min.

Spin trapping experiments using phenyl N-tert-butyl nitroxide (PBN) as the spin trap support the proposed radical-type mechanism. Heating a mixture of 1a, [Co(MeTAA)], LiO'Bu in the presence of PBN led to formation of PBN-trapped carbon-centered radicals as detected with EPR spectroscopy (Figure 6). The
resulting EPR signal \((g = 2.0063, A_N = 14.4 \text{ G}, A_H = 2.8 \text{ G})\) is strong and similar to other reported PBN-trapped carbon centered radicals.\(^{44}\) Heating the reaction mixture in absence of cobalt (i.e. non-catalytic conditions, in which case no indene formation occurs) also some PBN-trapped radicals were detectable, but different ones with weaker intensity (see supporting information).

### 3. Summary and Conclusions

Metalloradical activation of a series of o-cinnamyl-N-tosyl hydrazones produces a variety of functionalized \(1H\)-indenones in high yields and with a broad functional group tolerance. The reaction uses readily available starting materials and is operationally simple, thus representing a practical method for the construction of substituted \(1H\)-indene derivatives. The cheap and easy to prepare low spin cobalt(II) complex [Co(MeTAA)] proved to be the most active catalyst among those investigated, showcasing for the first time catalytic activity of this complex in general. DFT studies reveal a stepwise process involving activation of the diazo compound leading formation of a Co\(^{III}\)-carbene radical, followed by a rate limiting radical ring-closure step to produce an indanyl-radical intermediate. Subsequent 1,2-hydrogen atom transfer leads to elimination of the \(1H\) indene product and regenerates the Co\(^{II}\)-catalyst. The computed mechanism was supported by a series of radical-scavenging experiments. Deuterium labelling experiments further reveal statistical scrambling of the allylic/benzylic and vinylic protons under the applied reaction conditions. The metallo-radical catalyzed indene synthesis in this chapter represents a unique example of a net, formal (intramolecular) carbene insertion reaction into a vinylic C(sp\(^2\))-H bond, made possible by taking advantage of the distinctive and controlled reactivity of the key Co\(^{III}\)-carbene radical intermediates involved.
4. Experimental Section

General Considerations: 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) or CaH₂ (dichloromethane, hexane, ethyl acetate, methanol). The catalyst [CoIII(MeTAA)] has been synthesized according to literature procedures. All chemicals were purchased from commercial suppliers (either from Sigma-Aldrich or Fluorochem) and used without further purification. NMR spectra (¹H and ¹³C) were measured on a Bruker AV400 (100 MHz for ¹³C). Unless noted otherwise, the NMR spectra were measured in CDCl₃. Individual peaks are reported as: multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, coupling constant in Hz. Mass spectra of the newly synthesized compounds were recorded on an Agilent-5973 GC-MS spectrometer, and the corresponding HRMS data were recorded on a JEOL AccuTOF 4G via direct injection probe using CSI (Cold Spray Ionization). EPR spectra were recorded on a Bruker EMXplus spectrometer at room temperature (298 K).

General Procedure for the synthesis of the aldehyde precursors: The o-bromobenzaldehyde (1.0 equiv.) was dissolved in toluene (2 mL/mmol aldehyde). Pd(OAc)₂ (0.02 equiv.), P(o-tol)₃ (0.04 equiv.), the required Heck acceptor (1.5 equiv.) and Et₃N (0.4 mL/mmol aldehyde) were added, and the reaction mixture was placed under an N₂ atmosphere and heated to reflux (115°C, oil bath) for 40 h. The reaction was then cooled to RT, diluted with H₂O and extracted with CH₂Cl₂. The organic phase was dried (MgSO₄), filtered and concentrated, and the crude material was purified by flash chromatography.

General Procedure for Synthesis of the N-tosylhydrazone substrates: An equimolar mixture of corresponding aldehyde and N-tosyl hydrazide were placed in a round bottom flask and dissolved in methanol (2 mL/mmol). The reaction mixture was stirred overnight at room temperature. The white precipitate was collected by filtration, and washed with methanol and hexane to obtain the pure product.

General Procedure for Synthesis of 1H-Indenes: Under a nitrogen atmosphere, the respective cinnamyl N-tosylhydrazone (1a–r) (0.2 mmol) was added to a flame-dried Schlenk tube. The tube was capped with a Teflon screw cap, evacuated, and backfilled with nitrogen. Base LiO’Bu (1.2 equiv; 0.22 mmol), [CoIII(MeTAA)] catalyst (5 mol%) and benzene (anhydrous and degassed, 3 mL) were added inside the glove box. The Schlenk tube was then placed in an oil bath and heated to the desired temperature under nitrogen for a set period. After the reaction finished, the resulting mixture was concentrated and the residue was purified by flash chromatography (silica gel).
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Characterization of N-tosylhydrazone substrates and 1H-indene products:

*(E)-Methyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1a):

Yield = 82%; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta 8.17 (d, J = 15.8 \text{ Hz}, 1H), 8.09 (d, J = 8.3 \text{ Hz}, 2H), 7.77 (dd, J = 7.8, 1.4 \text{ Hz}, 1H), 7.42 (s, 1H), 7.36 (s, 1H), 7.17 (dd, J = 7.8, 1.4 \text{ Hz}, 1H), 7.05 (t, J = 8.1 \text{ Hz}, 1H), 6.96 (t, J = 9.5 \text{ Hz}, 3H), 6.28 (d, J = 15.8 \text{ Hz}, 1H), 3.65 (s, 3H), 1.97 (s, 3H); \(^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta 167.11, 144.74, 144.07, 141.55, 135.23, 133.56, 131.81, 130.06, 129.87, 129.57, 127.88, 127.17, 126.92, 126.70, 120.91, 51.83, 21.48.

*(E)-Methyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1b):

Yield = 85%; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta 8.20 (s, 1H), 8.12 (d, J = 15.8 \text{ Hz}, 1H), 7.90 (d, J = 8.1 \text{ Hz}, 2H), 7.83 – 7.57 (m, 2H), 7.49 (dd, J = 5.3, 3.6 \text{ Hz}, 1H), 7.38 – 7.30 (m, 2H), 7.27 (d, J = 8.2 \text{ Hz}, 2H), 6.30 (d, J = 15.8 \text{ Hz}, 1H), 4.27 (q, J = 7.0 \text{ Hz}, 2H), 2.37 (s, 3H), 1.34 (t, J = 7.1 \text{ Hz}, 3H); \(^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta 166.85, 144.99, 143.95, 141.46, 135.33, 133.58, 131.94, 129.97, 129.81, 129.54, 127.88, 127.14, 121.25, 60.82, 21.45, 21.18, 14.15.

*(E)-Butyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1c):

Yield = 86%; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta 8.98 (s, 1H), 8.22 (s, 1H), 8.10 (d, J = 15.8 \text{ Hz}, 1H), 7.91 (d, J = 8.3 \text{ Hz}, 2H), 7.80 (dd, J = 6.1, 3.1 \text{ Hz}, 1H), 7.54 – 7.48 (m, 1H), 7.36 (dd, J = 5.7, 3.5 \text{ Hz}, 2H), 7.29 (d, J = 8.3 \text{ Hz}, 2H), 4.22 (t, J = 6.7 \text{ Hz}, 2H), 2.39 (s, 3H), 1.70 (p, J = 6.8 \text{ Hz}, 2H), 1.43 (h, J = 7.1 \text{ Hz}, 3H), 0.96 (t, J = 7.4 \text{ Hz}, 3H); \(^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta 166.90, 144.71, 144.00, 141.19, 135.26, 133.60, 131.89, 130.03, 129.84, 129.56, 127.89, 127.61, 127.12, 121.37, 64.74, 30.57, 21.47, 19.06, 13.63.

*(E)-tert-Butyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1d):

Yield = 81%; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta 8.85 (s, 1H), 8.19 (s, 1H), 7.99 (d, J = 15.8 \text{ Hz}, 1H), 7.91 (d, J = 8.3 \text{ Hz}, 2H), 7.79 (dd, J = 5.7, 3.5 \text{ Hz}, 1H), 7.49 (dd, J = 5.6, 3.5 \text{ Hz}, 1H), 7.36 (dd, J = 5.9, 3.4 \text{ Hz}, 2H), 7.29 (d, J = 8.1 \text{ Hz}, 2H), 6.24 (d, J = 15.7 \text{ Hz}, 1H), 2.39 (s, 3H), 1.55 (s, 9H); \(^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta 166.03, 144.78, 144.01, 140.15, 135.23, 133.91, 131.70, 130.02, 129.58, 129.55, 127.90, 127.55, 127.19, 123.42, 81.04, 28.05, 21.47.

*(E)-Phenyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1e):

Yield = 89%; \( ^1H \) NMR (400 MHz, CDCl\(_3\)): \( \delta 8.53 (s, 1H), 8.52 (s, 1H), 8.11 (s, 1H), 7.95 – 7.86 (m, 2H), 7.74 (dd, J = 5.8, 3.4 \text{ Hz}, 1H), 7.59 (dd, J = 5.7, 3.4 \text{ Hz}, 1H), 7.42 (dd, J = 10.3, 5.2 \text{ Hz}, 4H), 7.27 (d, J = 7.9 \text{ Hz}, 3H), 7.20 (d, J = 7.7 \text{ Hz}, 2H), 6.51 (d, J = 15.8 \text{ Hz}, 1H), 2.38 (s, 3H); \(^{13}C \) NMR (100 MHz, CDCl\(_3\)): \( \delta 165.04, 150.57, 144.86, 144.16, 143.40, 135.10, 133.39, 131.89, 130.15, 129.61, 129.37, 128.29, 127.89, 127.43, 125.81, 121.49, 120.43, 21.47.

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(E)-N’-(2-((E)-3-((Dimethylamino)oxy)-3-oxoprop-1-en-1-yl)benzylidene)-4-methylbenzenesulfonylhydrazide (1f):

Yield = 76%; 1H NMR (400 MHz, CDCl3): δ 9.33 (s, 1H), 8.27 (s, 1H), 7.88 (d, J = 8.4 Hz, 4H), 7.46 (dd, J = 5.8, 3.2 Hz, 1H), 7.36 (dd, J = 5.4, 3.8 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 6.74 (d, J = 15.3 Hz, 1H), 3.17 (s, 3H), 3.09 (s, 3H), 2.39 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 166.27, 144.21, 143.60, 138.70, 135.75, 134.66, 132.11, 129.78, 129.43, 129.25, 127.76, 126.95, 126.63, 121.21, 37.43, 36.06, 21.43.

(E)-N’-(2-((E)-2-Cyanovinyl)benzylidene)-4-methylbenzenesulfonylhydrazide (1g):

Yield = 80%; 1H NMR (400 MHz, CDCl3): δ 8.07 (s, 1H), 8.02 – 7.77 (m, 4H), 7.62 – 7.52 (m, 1H), 7.51 – 7.38 (m, 4H), 7.28 (d, J = 0.9 Hz, 2H), 5.76 (d, J = 16.5 Hz, 1H), 2.46 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 148.86, 145.05, 143.87, 135.66, 132.45, 131.90, 130.39, 129.70, 129.49, 127.75, 117.89, 98.53, 21.48.

(E)-4-Methyl-N’-(2-((E)-styryl)benzylidene)benzenesulfonohydrazide (1h):

Yield = 92%; 1H NMR (400 MHz, CDCl3): δ 8.13 (s, 1H), 7.89 – 7.74 (m, 3H), 7.71 (d, J = 7.9 Hz, 1H), 7.56 (dd, J = 13.0, 7.7 Hz, 4H), 7.44 – 7.29 (m, 5H), 7.24 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 16.1 Hz, 1H), 2.40 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 146.92, 144.12, 137.26, 136.96, 135.10, 132.61, 130.23, 130.13, 129.55, 129.08, 127.98, 127.87, 127.46, 126.90, 126.70, 126.51, 21.47.

(E)-Methyl 3-((4-fluoro-2-((E)-2-tosylhydrazono)methyl)phenyl)acrylate (1i):

Yield = 79%; 1H NMR (400 MHz, CDCl3): δ 8.26 (s, 1H), 8.09 (s, 1H), 8.05 (d, J = 15.8 Hz, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.80 (dd, J = 8.8, 5.7 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.24 – 7.17 (m, 1H), 7.10 (td, J = 8.3, 2.6 Hz, 1H), 6.32 (d, J = 15.8 Hz, 1H), 3.86 (s, 3H), 2.43 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 167.04, 144.32, 142.73, 142.70, 140.00, 135.04, 134.18, 134.10, 129.67, 129.29, 129.20, 127.88, 120.81, 117.69, 117.47, 113.70, 113.47, 51.92, 21.51.

(E)-Methyl 3-((5-fluoro-2-((E)-2-tosylhydrazono)methyl)phenyl)acrylate (1j):

Yield = 80%; 1H NMR (400 MHz, CDCl3): δ 8.19 (s, 1H), 8.09 (d, J = 1.5 Hz, 1H), 7.99 (d, J = 15.7 Hz, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.53 (dd, J = 9.2, 3.8 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.11 (t, J = 8.3 Hz, 1H), 6.29 (d, J = 15.7 Hz, 1H), 3.84 (s, 3H), 2.44 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 167.04, 144.32, 142.73, 142.70, 140.00, 135.04, 134.18, 134.10, 129.67, 129.29, 129.20, 127.88, 120.81, 117.69, 117.47, 113.70, 113.47, 51.92, 21.51.

(E)-Methyl 3-((5-chloro-2-((E)-2-tosylhydrazono)methyl)phenyl)acrylate (1k):

Yield = 86%; 1H NMR (400 MHz, CDCl3): δ 8.18 (s, 1H), 8.06 (s, 1H), 8.00 (d, J = 15.8 Hz, 1H), 7.92 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 2.3 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.36 (d, J = 8.0 Hz, 3H), 6.32 (d, J = 15.8 Hz, 1H), 3.85 (s, 3H), 2.44 (s, 3H); 13C NMR (100 MHz, CDCl3): δ 166.90, 144.34,
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142.73, 140.04, 136.15, 135.02, 133.26, 131.82, 130.16, 129.68, 128.46, 127.88, 127.20, 121.38, 51.95, 21.52.

(E)-Methyl 3-(2-((E)-(2-tosylhydrazono)methyl)-5-(trifluoromethyl)phenyl)acrylate (1l):

\[
\text{Yield = 84%; } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta 8.24 (s, 1H), 8.08 (d, } J = 17.1 \text{ Hz, 2H), 8.00 (s, 1H), 7.93 (d, } J = 8.3 \text{ Hz, 2H), 7.63 (d, } J = 1.2 \text{ Hz, 2H), 7.36 (d, } J = 8.1 \text{ Hz, 2H), 6.38 (d, } J = 15.9 \text{ Hz, 1H), 3.87 (s, 3H), 2.44 (s, 3H); } ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta 166.53, 144.50, 142.85, 140.05, 136.69, 134.88, 132.32, 131.56, 129.69, 127.94, 124.71, 123.21, 52.03, 21.50.
\]

(E)-Methyl 3-(5-nitro-2-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1m):

\[
\text{Yield = 82%; } ^1H \text{ NMR (400 MHz, DMSO-d}_6): \delta 11.85 (s, 1H), 8.39 (d, } J = 2.4 \text{ Hz, 1H), 8.30 (s, 1H), 8.18 (dd, } J = 8.6, 2.4 \text{ Hz, 1H), 8.07 (d, } J = 15.9 \text{ Hz, 1H), 7.99 (d, } J = 8.6 \text{ Hz, 2H), 7.80 (d, } J = 8.0 \text{ Hz, 2H), 7.41 (d, } J = 8.0 \text{ Hz, 2H), 6.67 (d, } J = 15.8 \text{ Hz, 1H), 3.79 (s, 3H), 2.36 (s, 3H); } ^{13}C \text{ NMR (100 MHz, DMSO-d}_6): \delta 166.22, 148.33, 144.11, 143.51, 139.58, 139.06, 136.24, 133.61, 130.10, 129.98, 127.57, 124.60, 124.23, 122.17, 52.23, 21.36.
\]

(E)-Methyl 3-(2-((E)-(2-tosylhydrazono)methyl)naphthalen-1-yl)acrylate (1n):

\[
\text{Yield = 78%; } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta 8.23 (d, } J = 16.1 \text{ Hz, 1H), 8.18 (s, 1H), 8.14 (s, 1H), 8.05 (d, } J = 8.8 \text{ Hz, 1H), 8.00 - 7.95 (m, 1H), 7.93 (d, } J = 8.3 \text{ Hz, 2H), 7.87 - 7.79 (m, 2H), 7.60 - 7.50 (m, 2H), 7.35 (d, } J = 8.1 \text{ Hz, 2H), 6.09 (d, } J = 16.1 \text{ Hz, 1H), 3.89 (s, 3H), 2.42 (s, 3H); } ^{13}C \text{ NMR (101 MHz, CDCl}_3): \delta 166.35, 145.65, 144.11, 143.51, 139.58, 139.06, 136.24, 133.61, 130.10, 129.98, 127.57, 124.60, 124.23, 122.17, 52.23, 21.36.
\]

(E)-Methyl 3-(2-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1o):

\[
\text{Yield = 93%; } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta 8.21 (s, 1H), 8.14 - 8.06 (m, 2H), 7.92 (d, } J = 8.0 \text{ Hz, 2H), 7.69 (d, } J = 8.0 \text{ Hz, 1H), 7.32 (d, } J = 8.0 \text{ Hz, 3H), 7.21 (d, } J = 8.1 \text{ Hz, 1H), 6.31 (d, } J = 15.9 \text{ Hz, 1H), 3.85 (s, 3H), 2.42 (s, 3H), 2.38 (s, 3H); } ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta 167.20, 145.00, 144.01, 141.64, 140.37, 135.24, 133.42, 130.88, 129.54, 129.20, 127.88, 127.82, 127.59, 120.62, 51.82, 21.47, 21.26.
\]

(E)-Methyl 3-(4-methoxy-2-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1p):

\[
\text{Yield = 89%; } ^1H \text{ NMR (400 MHz, CDCl}_3): \delta 8.40 (s, 1H), 8.18 (s, 1H), 8.01 (d, } J = 15.7 \text{ Hz, 1H), 7.95 - 7.89 (m, 2H), 7.50 (d, } J = 8.7 \text{ Hz, 1H), 7.36 - 7.30 (m, 3H), 6.94 (dd, } J = 8.7, 2.7 \text{ Hz, 1H), 6.25 (d, } J = 15.7 \text{ Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.42 (s, 3H); } ^{13}C \text{ NMR (100 MHz, CDCl}_3): \delta 167.57, 160.87, 144.22, 144.10, 140.51, 135.21, 133.53, 129.56, 128.48, 127.88, 126.18, 118.36, 117.43, 110.57, 55.43, 51.77, 21.47.
\]
(E)-Methyl 3-(4,5-dimethoxy-2-((E)-(2-tosylhydrazono)methyl)phenyl)acrylate (1q): 
Yield = 88%; 'H NMR (400 MHz, CDCl₃): δ 8.25 (s, 1H), 8.18 (s, 1H), 7.99 (d, J = 15.7 Hz, 1H), 7.91 (d, J = 8.4 Hz, 2H), 7.40 – 7.30 (m, 3H), 6.96 (s, 1H), 6.26 (d, J = 15.5 Hz, 1H), 3.96 (s, 3H), 3.93 (s, 3H), 3.84 (s, 3H), 2.43 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 167.38, 150.82, 150.77, 144.16, 144.08, 140.14, 135.26, 129.53, 127.89, 126.79, 125.88, 118.59, 108.26, 108.11, 56.00, 55.85, 51.83, 21.48.

(1E)-Methyl 3-((E)-(2-tosylhydrazono)methyl)phenyl)but-2-enoate (1r): 
Yield = 86%; 'H NMR (400 MHz, CDCl₃): δ 8.24 (s, 1H), 7.95 – 7.82 (m, 4H), 7.42 – 7.30 (m, 4H), 7.15 (dd, J = 7.1, 1.8 Hz, 1H), 5.70 (s, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.43 (s, 3H), 2.40 (s, 3H), 1.32 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 166.29, 155.31, 145.37, 143.98, 143.75, 135.37, 129.88, 129.59, 129.53, 128.01, 127.81, 126.44, 121.07, 60.19, 21.54, 21.49, 14.13.

1a-D: 
Yield = 83%; 'H NMR (400 MHz, CDCl₃): δ 8.58 (s, 1H), 8.12 (d, J = 15.8 Hz, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.85 – 7.75 (m, 1H), 7.57 – 7.46 (m, 1H), 7.43 – 7.34 (m, 2H), 7.32 (d, J = 8.1 Hz, 2H), 6.33 (d, J = 15.8 Hz, 1H), 3.85 (s, 3H), 2.41 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 167.11, 144.15, 141.43, 135.18, 133.57, 131.69, 130.14, 129.92, 129.61, 127.91, 127.76, 127.18, 121.00, 106.18, 106.17, 51.87, 21.50.

1b-D: 
Yield = 88%; 'H NMR (400 MHz, CDCl₃): δ 8.51 (d, J = 3.0 Hz, 1H), 8.16 (d, J = 2.5 Hz, 1H), 8.10 (s, 1H), 7.92 (d, J = 7.9 Hz, 2H), 7.87 – 7.75 (m, 1H), 7.59 – 7.47 (m, 1H), 7.39 (dt, J = 5.9, 3.9 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 4.30 (d, J = 7.0 Hz, 2H), 2.42 (d, J = 3.2 Hz, 3H), 1.36 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 144.69, 144.22, 140.97, 135.11, 133.78, 131.53, 130.19, 129.77, 129.61, 127.92, 127.87, 127.30, 60.74, 21.50, 14.19.

Methyl 1H-indene-2-carboxylate (2a): 
Yield = 86%; 'H NMR (400 MHz, CDCl₃): δ 7.75 (s, 1H), 7.54 (q, J = 4.7 Hz, 2H), 7.42 – 7.31 (m, 2H), 3.98 – 3.79 (s, 3H), 3.71 (s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 165.35, 144.67, 142.59, 141.12, 136.93, 127.47, 126.76, 124.17, 123.29, 51.53, 38.25; HRMS (EI, m/z): Calculated for [M⁺] C₁₁H₁₀O₂: 174.0681; found: 174.0671.

Ethyl 1H-indene-2-carboxylate (2b): 
Yield = 78%; 'H NMR (400 MHz, CDCl₃): δ 7.75 (s, 1H), 7.54 (dd, J = 7.8, 3.9 Hz, 2H), 7.40 – 7.30 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.72 (s, 2H), 1.39 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 164.96, 144.68,
n-Butyl 1H-indene-2-carboxylate (2c):

Yield = 80%; ¹H NMR (400 MHz, CDCl₃): δ 7.79 – 7.70 (m, 1H), 7.54 (d, J = 3.3 Hz, 2H), 7.41 – 7.31 (m, 2H), 4.28 (t, J = 6.6 Hz, 2H), 3.71 (s, 2H), 1.75 (dd, J = 8.5, 6.4 Hz, 2H), 1.55 – 1.42 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.02, 144.68, 142.67, 140.79, 137.41, 127.36, 126.72, 124.14, 123.21, 64.21, 38.25, 30.71, 19.18, 13.68, 0.92; HRMS (EI, m/z): Calculated for [M⁺] C₁₂H₁₂O₂: 188.0837, found: 188.0834.

N,N-Dimethyl-1H-indene-2-carboxamide (2f):

Yield = 98%; ¹H NMR (400 MHz, CDCl₃): δ 7.51 (d, J = 7.0 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.37 – 7.27 (m, 2H), 7.04 (s, 1H), 3.78 (s, 2H), 3.15 (d, J = 13.5 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 167.99, 143.16, 143.05, 140.63, 133.42, 126.59, 126.10, 123.82, 122.08, 40.48, 38.35, 35.37. HRMS (EI, m/z): Calculated for [M⁺] C₁₂H₁₃NO: 187.0997, found: 187.1005.

1H-Indene-2-carbonitrile (2g):

Yield = 52%; ¹H NMR (400 MHz, CDCl₃): δ 7.64 (d, J = 2.2 Hz, 1H), 7.59 – 7.48 (m, 2H), 7.47 – 7.33 (m, 2H), 3.72 (d, J = 2.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 146.13, 142.99, 141.29, 128.27, 127.37, 124.00, 123.16, 116.99, 114.09, 40.82; HRMS (EI, m/z): Calculated for [M⁺] C₁₀H₇N: 141.0578, found: 141.0578.
Methyl 6-fluoro-1H-indene-2-carboxylate (2i):

Yield = 87%; 1H NMR (400 MHz, CDCl₃): δ 7.69 (d, J = 6.1 Hz, 1H), 7.46 (td, J = 8.8, 5.0 Hz, 1H), 7.23 (ddd, J = 8.5, 5.9, 2.4 Hz, 1H), 7.12 – 7.00 (m, 1H), 3.87 (d, J = 3.4 Hz, 3H); 13C NMR (100 MHz, CDCl₃): δ 165.02, 164.98, 164.14, 163.38, 161.68, 160.96, 146.96, 146.87, 144.21, 144.12, 140.25, 140.23, 139.93, 139.91, 139.11, 138.61, 138.58, 136.75, 136.71, 125.08, 124.99, 124.24, 124.15, 114.57, 114.34, 114.28, 114.05, 111.92, 111.69, 110.07, 109.84, 51.65, 51.56, 38.47, 38.44, 37.69; HRMS (EI, m/z): Calculated for [M⁺] C₁₁H₉FO₂: 192.0587, found: 192.0593.

Methyl 5-chloro-1H-indene-2-carboxylate (2j):

Yield = 82%; 1H NMR (400 MHz, CDCl₃): δ 7.68 (d, J = 10.6 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H), 7.45 (dd, J = 8.1, 4.4 Hz, 1H), 3.87 (d, J = 1.8 Hz, 3H), 3.73 – 3.64 (m, 2H); 13C NMR (100 MHz, CDCl₃): δ 165.00, 146.18, 144.16, 142.69, 141.04, 139.87, 138.71, 137.32, 133.70, 132.74, 127.41, 127.19, 125.12, 124.62, 124.02, 123.23, 51.68, 51.64, 38.23, 37.93; HRMS (EI, m/z): Calculated for [M⁺] C₁₁H₉ClO₂: 208.0291, found: 208.0294.

Methyl 5-(trifluoromethyl)-1H-indene-2-carboxylate (2k):

Yield = 84%; 1H NMR (400 MHz, CDCl₃): δ 7.89 – 7.71 (m, 2H), 7.63 (d, J = 1.4 Hz, 2H), 3.89 (d, J = 1.0 Hz, 3H), 3.77 (d, J = 1.9 Hz, 2H); 13C NMR (100 MHz, CDCl₃): δ 164.81, 164.75, 147.94, 145.76, 144.65, 142.99, 139.82, 139.72, 138.83, 125.66, 124.43, 124.27 – 124.03 (m, 1C), 123.30, 121.06, 121.03, 120.03, 119.48, 118.15, 51.91, 38.79, 38.59; HRMS (EI, m/z): Calculated for [M⁺] C₁₂H₉F₃O₂: 242.0555, found: 242.0557.

Methyl 5-nitro-1H-indene-2-carboxylate (2l):

Yield = 84%; 1H NMR (400 MHz, CDCl₃): δ 8.39 (s, 1H), 8.32 – 8.24 (m, 1H), 7.82 – 7.74 (m, 1H), 7.67 (d, J = 8.4 Hz, 1H), 3.91 (dd, J = 2.3, 0.9 Hz, 3H), 3.87 – 3.81 (m, 2H); 13C NMR (100 MHz, CDCl₃): δ 164.32, 150.92, 148.57, 147.23, 145.04, 143.69, 142.47, 140.08, 139.23, 139.06, 124.65, 124.35, 122.97, 122.54, 119.48, 118.15, 51.91, 38.79, 38.59; HRMS (EI, m/z): Calculated for [M⁺] C₁₁H₉NO₄: 219.0532, found: 219.0536.

Methyl 3H-cyclopenta α-naphthalene-2-carboxylate (2m):

Yield = 93%; 1H NMR (400 MHz, CDCl₃): δ 8.15 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.91 (dd, J = 13.6, 7.8 Hz, 1H), 7.83 (dd, J = 14.9, 7.7 Hz, 2H), 7.68 – 7.47 (m, 3H), 4.00 (d, J = 1.9 Hz, 1H), 3.92 (d, J = 4.3 Hz, 3H), 3.84 (d, J = 2.0 Hz, 1H); 13C NMR (100 MHz, CDCl₃): δ 165.22, 165.15, 143.48, 142.53, 141.86, 139.96, 138.86, 138.77, 136.69, 136.37, 132.75, 132.47, 129.77, 128.77, 128.46, 128.13, 127.79, 126.60, 126.47, 125.92, 125.47, 123.80, 123.33, 122.37, 121.24, 51.56, 51.54, 39.51, 37.41; HRMS (EI, m/z): Calculated for [M⁺] C₁₅H₁₂O₂: 224.0837, found: 224.0837.
Methyl 5-methyl-1H-indene-2-carboxylate (2n):

Yield = 88%; ¹H NMR (400 MHz, CDCl₃): δ 7.71 (d, J = 7.0 Hz, 1H), 7.42 (t, J = 7.3 Hz, 1H), 7.35 (s, 1H), 7.18 (dd, J = 8.0, 3.8 Hz, 1H), 3.87 (t, J = 1.3 Hz, 3H), 3.72 – 3.63 (m, 2H), 2.44 (d, J = 5.7 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.45, 145.09, 142.83, 141.80, 141.16, 139.99, 137.70, 137.06, 136.44, 135.84, 128.47, 127.66, 124.97, 123.81, 122.95, 51.48, 38.01, 21.61, 21.26; HRMS (EI, m/z): Calculated for [M+] C₁₂H₁₂O₂: 188.0837, found: 188.0837.

Methyl 6-methoxy-1H-indene-2-carboxylate (2o):

Yield = 72%; ¹H NMR (400 MHz, CDCl₃): δ 7.70 (d, J = 2.0 Hz, 1H), 7.42 (dd, J = 10.8, 8.2 Hz, 1H), 7.14 – 7.03 (m, 1H), 6.98 – 6.86 (m, 1H), 3.89 – 3.83 (m, 6H), 3.66 (dd, J = 12.5, 1.9 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 165.39, 165.28, 160.02, 147.00, 143.82, 141.04, 138.13, 136.89, 135.63, 134.54, 124.66, 123.97, 114.27, 113.12, 109.94, 107.92, 55.42, 51.53, 51.40, 38.30, 37.54; HRMS (EI, m/z): Calculated for [M+] C₁₂H₁₄O₃: 204.0786, found: 204.0792.

Methyl 5,6-dimethoxy-1H-indene-2-carboxylate (2p):

Yield = 70%; ¹H NMR (400 MHz, CDCl₃): δ 7.70 – 7.63 (m, 1H), 7.08 (s, 1H), 7.04 (s, 1H), 3.95 (s, 3H), 3.93 (s, 3H), 3.84 (s, 3H), 3.64 (d, J = 1.1 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 165.25, 149.64, 148.57, 141.36, 138.19, 135.12, 107.42, 105.83, 56.01, 51.38, 38.26; HRMS (EI, m/z): Calculated for [M+] C₁₃H₁₄O₄: 234.0892, found: 234.0897.

Ethyl 3-methyl-1H-indene-2-carboxylate (3):

Yield = 95%; ¹H NMR (400 MHz, CDCl₃): δ 7.52 (ddddd, J = 8.5, 5.3, 2.8, 0.8 Hz, 2H), 7.42 – 7.33 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.69 (d, J = 2.5 Hz, 2H), 2.58 (t, J = 2.4 Hz, 3H), 1.40 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 165.90, 151.20, 145.21, 143.38, 129.74, 127.49, 126.44, 123.84, 120.98, 106.12, 59.83, 38.67, 14.34, 12.32; HRMS (EI, m/z): Calculated for [M+] C₁₃H₁₄O₂: 202.0994, found: 202.0977.

Methyl 1H, 1D-indene-2-carboxylate (2a-D):

Yield = 88%; ¹H NMR (400 MHz, CDCl₃): δ 7.76 (s, 1H), 7.54 (q, J = 4.6 Hz, 2H), 7.36 (dd, J = 5.4, 3.2 Hz, 2H), 3.87 (s, 3H), 3.71 (s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 165.35, 144.67, 142.59, 141.19, 141.12, 136.93, 127.47, 126.76, 124.17, 123.28, 51.53, 38.26; ²H NMR (60 MHz, CDCl₃): δ 7.54, 3.46; HRMS (EI, m/z): Calculated for [M+] C₁₁H₁₀D₂O: 175.0744, found: 175.0762.

Ethyl 1H, 1D-indene-2-carboxylate (2b-D):

Yield = 85%; ¹H NMR (400 MHz, CDCl₃): δ 7.88 – 7.63 (m, 1H), 7.62 – 7.46 (m, 2H), 7.43 – 7.30 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.71 (s, 1H), 1.39 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 164.97, 144.68, 142.66, 140.85, 137.38, 127.38, 126.73, 124.15, 123.22, 60.31, 38.25, 14.28;
**CoIII-Carbene Radical Approach to Substituted 1H-Indenes**

**1H NMR (60 MHz, CHCl₃):** δ 8.24, 4.16; HRMS (EI, m/z): Calculated for [M+] C₆₃H₁₀₂O₂: 189.0900, found: 189.0924.

**Synthetic procedure for compound 5 and 7:** Under a nitrogen atmosphere, cinnamyl N-tosylhydrazone (1a-b) (0.1 mmol) and TEMPO/DBP (0.2 mmol) were added to a flame-dried Schlenk tube. The tube was capped with a Teflon screw cap, evacuated, and backfilled with nitrogen. Base LiO'Bu (1.2 equiv; 0.12 mmol), [CoII(MeTAA)] catalyst (5 mol %) and benzene (anhydrous and degassed, 2 mL) were added inside the glove box. The Schlenk tube was then placed in an oil bath and heated to the desired temperature under nitrogen for a set period. After the reaction finished, the resulting mixture was concentrated and the residue was purified by flash chromatography (silica gel).

**(E)-2,2,6,6-Tetramethylpiperidin-1-yl-2-(3-ethoxy-3-oxoprop-1-en-1-yl)benzoate (5):**

Yield = 14%; ¹H NMR (400 MHz, CDCl₃): δ 8.44 (d, J = 15.9 Hz, 1H), 7.98 (dd, J = 7.8, 1.4 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.61 – 7.54 (m, 1H), 7.48 (td, J = 6.4, 1.4 Hz, 1H), 6.35 (d, J = 15.9 Hz, 1H), 3.81 (s, 3H), 1.86 – 1.62 (m, 5H), 1.48 (dd, J = 7.8, 5.2 Hz, 1H), 1.27 (s, 6H), 1.18 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 166.74, 166.70, 143.50, 136.14, 132.04, 130.01, 129.72, 129.30, 127.79, 120.78, 60.33, 51.59, 39.09, 31.88, 20.84, 16.88; HRMS (GC, m/z): Calculated for [M+] C₂₀H₂₇NO₄: 345.1940, found: 345.

**(E)-2-(3-ethoxy-3-oxoprop-1-en-1-yl)benzyl benzoate (7):**

Yield = 08%; ¹H NMR (400 MHz, CDCl₃): δ 8.13 (d, J = 15.8 Hz, 1H), 8.10 – 8.03 (m, 2H), 7.69 – 7.63 (m, 1H), 7.61 – 7.52 (m, 2H), 7.48 – 7.38 (m, 4H), 6.45 (d, J = 15.8 Hz, 1H), 5.53 (s, 2H), 3.82 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 166.90, 166.06, 141.27, 134.73, 133.87, 133.02, 130.03, 129.99, 129.74, 129.61, 128.87, 128.29, 126.82, 120.33, 64.26, 51.68, 29.60; HRMS (GC, m/z): Calculated for [M+] C₁₈H₁₆O₄: 296.1049, found: 296.

**Computational Section:** Geometry optimizations were carried out with the Turbomole program package coupled to the PQS Baker optimizer via the BOpt package. We used unrestricted r-DF-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. The relative (free) energies obtained from these calculations and the energy diagram are reported in Figure 4 and Table 4.
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<th>SPECIES</th>
<th>&lt;S&lt;sup&gt;2&lt;/sup&gt;&gt;</th>
<th>SCF (au)</th>
<th>ZPE (au)</th>
<th>SCF+ZPE (au)</th>
<th>ENTHALPY Y (au)</th>
<th>FREE ENERGY (298) (au)</th>
<th>FREE ENERGY (298) (kcal)</th>
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5. Acknowledgements

We thank Ed Zuidinga for MS measurements, Jan Meine Ernsting for NMR advice, Tim Storr for providing [Co(salen)] and Braja Das for help with experiments (design and labwork).

6. References


[49] (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.


