Supporting Information

Effector Regulated Catalytic Cyclization of Alkynoic Acids Using Pt$_2$L$_4$ Cages

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Supporting information

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Materials and methods

General procedures: All synthetic procedures were carried out under a nitrogen atmosphere using standard Schlenk techniques. All commercially available chemicals were used as received without further purification. Solvents used for synthesis were dried, distilled and degassed with the most suitable method. Column chromatography was performed open to air using solvents as received.

Cryospray-ionization MS (CSI-MS): Mass spectra were collected on a HR-ToF Bruker Daltonik GmbH (Bremen, Germany) Impact II, an ESI-ToF MS capable of resolution of at least 40000 FWHM, which was coupled to a Bruker cryo-spray unit. Detection was in positive-ion mode and the source voltage was between 4 and 6 kV. The sample was introduced with a syringe pump at a flow rate of 18 ul/hr. The drying gas (N₂) was held at 40°C and the spray gas was held at 60°C. The machine was calibrated prior to every experiment via direct infusion of a TFA-Na solution, which provided a m/z range of singly charged peaks up to 3500 Da in both ion modes. Software acquisition Compass 2.0 for Otof series. Software processing m- mass.

Materials: Deuterated solvents were purchased from Sigma Aldrich (D₂O : 151822-25g, 99.9 atom % D; Dichloromethane-d₂ : 444324-25g, 99.9 % atom D) and used without further purification exclusively for the catalytic experiments presented in this work (to prevent any contaminations). Maleic anhydride (M188-25G-A, 99%) and Maleic acid (M0375-100G, >99%) were also obtained from Sigma Aldrich and used without any further purification. 4-Pentyonic acid (164204, 5g), p-Benzoquinone (094629, 25g), 1,4-dizyanobenzene (079107, 25g) were purchased from fluorochem. The metal precursor [Pt(BF₄)₂(CH₃CN)₄] was synthesized according to literature.[1] Furanone was cyclized according to literature and purified by column chromatography according to literature procedure.[2]
Synthesis of building block (SI1)

Scheme S1. Synthetic route for the building block L^{OMe}.

1,3-Dibromo-5-methoxybenzene (2.42 mmol, 634.5 mg, 1 eq) was dissolved in freshly distilled THF (4 mL). Di-isopropyl amine (16 mL), 3-ethynylpyridine (6.00 mmol, 618.6 mg, 2.5 eq) and PdCl$_2$(PPh$_3$)$_2$ (0.055 mmol, 44 mg, 0.02 eq) were added under a stream of N$_2$. After stirring for 5 minutes, CuI (0.24 mmol, 46 mg, 0.1 eq) was added and the mixture was heated to 50 °C for 16 hours. After cooling down, the mixture was diluted with EtOAc (200 mL), dried with Na$_2$SO$_4$, filtered and concentrated in vacuo. The product was then further purified by flash column chromatography (2-10% methanol in DCM) to yield the product as a colorless solid (236.2 mg, 31% yield).

$^1$H NMR (400 MHz, Acetonitrile-d$_3$) δ 8.76 (dd, $J = 2.1$, 0.9 Hz, 2H), 8.65-8.55 (m, 2H), 7.93 (dt, $J = 7.9$, 2.0 Hz, 2H), 7.47-7.34 (m, 4H), 7.20 (d, $J = 1.4$ Hz, 2H), 3.87 (s, 3H).

$^{13}$C NMR (126 MHz, Acetonitrile-d$_3$) δ 159.75, 151.96, 149.17, 138.45, 126.76, 124.05, 123.43, 117.66, 90.88, 86.44, 55.44.

Synthesis of sphere C$^\text{Pt}$ and of molecular catalyst M$^\text{Pt}$ (SI2)

Scheme S2. Synthetic route for the [Pt$_2$L$^{OMe}$]$_4^{4+}$(BF$_4$)$_4$ assembly.

The sphere was synthesized according to a modified literature procedure.$^{[3,4]}$ Pt(BF$_4$)$_2$(CH$_3$CN)$_4$ (4.9 µmol, 2.6 mg, 0.49 eq) and L$^{OMe}$ (3.1 mg, 10 µmol, 1 eq) were put under N$_2$ in a high pressure tube. Acetonitrile-d$_3$ (dry, 1 mL) was added and the solution was heated to 150 °C for 16 hours. The $^1$H-NMR spectra of the crude material shows, in agreement to the excess of ligand used, signals of the free building block next to the desired cage signals. The product was first dissolved in diethyl ether and then precipitated in pentane to yield C$^\text{Pt}$BF$_4$ (4.7 mg, 95%) and used as such for the salt exchange (after the precipitation, excess building block is removed). Single crystals of the cage were obtained by slow vapor diffusion of Et$_2$O to a solution of the cage in CH$_3$CN at room temperature. $^1$H NMR (400 MHz, Acetonitrile-d$_3$) δ 9.34 (d, $J = 1.8$ Hz, 2H), 9.06 (dd, $J = 5.9$, 1.3 Hz, 2H), 8.09 (dt, $J = 8.2$, 1.6 Hz, 2H), 7.65 (dd, $J = 8.1$, 5.8 Hz, 2H), 7.53 (d, $J = 1.4$ Hz, 1H), 7.28 (d, $J = 1.4$ Hz, 2H), 3.85 (s, 3H).$^{13}$C NMR (126 MHz, Acetonitrile-d$_3$) δ
159.95, 154.01, 150.78, 143.07, 127.77, 126.70, 123.94, 123.19, 118.95, 93.94, 83.92, 55.57.

**Figure S1.** Crude \( \text{C}^{\text{Pt}}\text{BF}_4 \) assembly, \(^1\)H NMR in CD\(_3\)CN. Signals corresponding to free building block \( \text{L}^{\text{OMe}} \) indicated by blue ellipsoids.

**Scheme S3.** \( \text{C}^{\text{Pt}} \) sphere synthesis.

1 ml DCM-\( \text{d}_2 \) was added to the \( \text{C}^{\text{Pt}}\text{BF}_4 \) (4.94 mg, 2.5 µmol, 1 eq). NaBARF (8.86 mg, 10 µmol, 4 eq) was added and the emulsion was sonicated for one hour. The emulsion then was filtered over a syringe filter and the filtrate was used as a stock solution for catalysis (concentration determined by internal standard, typical yields 90-95%). \(^1\)H NMR (300 MHz, Methylene Chloride-\( \text{d}_2 \)) \( \delta \) 8.82 (d, \( J = 1.8 \) Hz, 2H), 8.67 – 8.56 (m, 2H), 8.00 (dt, \( J = 8.2, 1.6 \) Hz, 2H), 7.80 – 7.69 (m, 18H), 7.59 – 7.47 (m, 12H), 7.22 (d, \( J = 1.4 \) Hz, 2H), 6.82 (s, 5H), 3.80 (s, 4H).
Figure S2. C\textsuperscript{Pt} assembly, \textsuperscript{1}H NMR in DCM-d\textsubscript{2}.

Figure S3. C\textsuperscript{Pt} assembly, DOSY NMR in DCM-d\textsubscript{2} at 300K.
**Figure S4.** \( \text{C}^{\text{Pt}} \) assembly, full HR-ESI MS spectrum, top measured; bottom, simulated spectra of different charged states of the self-assembly.

**Table S1.** Zoom into different charged species of \( \text{C}^{\text{Pt}} \text{n}^+ \) assembly (for \( n = 2-4 \)).

**Synthesis of \( \text{M}^{\text{Pt}} \)**

**Scheme S4.** \( \text{M}^{\text{Pt}} \text{BF}_4 \) synthesis.

Pt(\( \text{BF}_4 \))\(_2\)(\( \text{CH}_3\text{CN} \))\(_4\) (0.188 mmol, 100 mg, 1 eq) was dissolved in acetonitrile (dry, 5 mL) under \( \text{N}_2 \). 4-picoline (3.76 mmol, 0.366 mL, 20 eq) was added and the reaction mixture was stirred for 40 hours at 50 °C. After cooling the emulsion down to room temperature,
it was precipitated in diethyl ether (dry, under N₂, 50 mL). After filtering and drying under air, the product was collected as a white powder (90.5 mg, 65% yield). ¹H NMR (300 MHz, DMSO-d₆, ppm) δ 8.83 (d, J = 6.1 Hz, 8H), 7.50 (d, J = 5.9 Hz, 8H), 2.37 (s, 12H).

Scheme S5. MₚPt synthesis.

The counterion exchange of MₚBF₄ was performed according to the procedure described above for CₚPt. MₚPt was obtained as a colorless stock solution in DCM. ¹H NMR (500 MHz, Methylene Chloride-d₂) δ 8.15 (d, J = 6.0 Hz, 8H), 7.76 (m, 21H), 7.59 (s, 9H), 7.29 (d, J = 5.8 Hz, 8H), 2.42 (s, 12H). ¹³C NMR (126 MHz, CD₂Cl₂) δ 156.27, 151.28, 151.28, 149.97, 134.78, 129.25, 128.97, 128.73, 125.63, 123.46, 117.48, 21.13.

Synthesis of Substrate SₚPh (SI3)

Scheme S6. Synthesis route for the substrate SₚPh.

The substrate SₚPh was synthesized according to a modified literature procedure.[⁵] A Schlenck was cooled to -78 °C and n-BuLi (35 mmol, 14 mL in hexane, 2.5 M, 1.1 eq) was added. Diisopropylamine (64 mmol, 4.64 mL, 2 eq) was added dropwise, the mixture was allowed to warm up to room temperature, THF (10 mL) was added and the mixture was stirred for 15 minutes until no solid was visible. The colorless solution was cooled to -78 °C again, methyl diphenylacetate (32.7 mmol, 7.4 g, 1 eq, dissolved in 25 mL THF) was added dropwise and the solution was stirred for three hours. Propargyl bromide (75 mmol, 7.1 mL, 80% in toluene, 2.3 eq) was added dropwise and the solution was stirred overnight at room temperature. The mixture was then poured into ice water (400 mL) and stirred until all ice was melted. The two layer system was then extracted with Et₂O (3x 150 mL) which was then washed with water (150 mL) and brine (150 mL). The combined organic layers were dried over Na₂SO₄ and filtered over cotton. The filtrate was concentrated in vacuo and further purified by flash column chromatography (4-20% EtOAc in heptane). The product was collected as a white solid (6.84g, 79% yield). ¹H NMR (300 MHz, Chloroform-d) δ 7.34 (d, J = 2.7 Hz, 10H), 3.77 (s, 3H), 3.32 (d, J = 2.7 Hz, 2H), 1.95 (t, J = 2.6 Hz, 1H).
Methyl 3,3-diphenyl-4-pentynoic acetate (25.8 mmol, 6.84 g, 1 eq) was dissolved in THF (100 mL) and KOH solution (aq, 45 mmol, 2M, 22.5 mL) was added. The solution was heated to 80 °C and stirred for 48h. The solution was cooled to room temperature, the solvent was evaporated in vacuo and water (50 mL) was added. The solution was acidified with HCl (aq, concentrated) and the product was then extracted to DCM (3x 40 mL). The combined organic layers were dried over Na₂SO₄, concentrated in vacuo to yield the crude product S¹Ph as a white solid (2.5 g, 39% yield). The crude product was crystallized by dissolving the material in a minimum amount of DCM and layering the DCM phase with pentane. After 10 days, colorless crystals of the product were obtained. The crystalline material was further purified by column chromatography (hexane : ethyl acetate; 80:20) to afford the substrate S¹Ph as a colorless solid. 

\[ ^1H \text{ NMR (300 MHz, Chloroform-}d\text{)} \delta 7.43 – 7.29 \text{ (m, 10H), 3.32 (d, } J = 2.6 \text{ Hz, 2H), 1.95 (t, } J = 2.6 \text{ Hz, 1H).}\]

On a site note: when we attempted to perform the deprotection in EtOH, we observed formation of an unidentified site product (which does not have the alkyne peak in \(^1H\)-NMR) and resembles likely an adduct between ethanol and S¹Ph. It was not possible to separate this site product from the desired material S¹Ph by means of column chromatography or crystallization. Catalytic experiments using an impure material, yields similar results as the pure material (obtained through the described procedure). All herein presented catalytic studies were performed with the pure material obtained by the method described above.

**Binding Constant (SI4)**

Each titration was performed by addition of a solution containing guest and C\(^{Pt}\) to a solution of C\(^{Pt}\), maintaining a constant concentration of C\(^{Pt}\). The observable peak positions of C\(^{Pt}\) were plotted against the equivalents of guest in a 1:1 binding model.

![Figure S5](image.png)

**Figure S5.** Changes in the \(^1H\) NMR spectra of C\(^{Pt}\) upon addition of increasing amounts of benzoquinone, \(^1H\) NMR in DCM-d\(_2\).
**Figure S6.** Benzoquinone titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.

**Figure S7.** Changes in the $^1$H NMR spectra of C$^{pt}$ upon addition of increasing amounts of maleic anhydride, $^1$H NMR in DCM- d$_2$. 
Figure S8. Maleic anhydride titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.

Figure S9. Changes in the $^1$H NMR spectra of C$^{pt}$ upon addition of increasing amounts of 1,4 dicyano benzene, $^1$H NMR in DCM-d$_2$. 
Figure S10. 1,4 dicyano benzene titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.

Figure S11. Furanone PH titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.
**Figure S12.** Changes in the $^1$H NMR spectra of C\textsuperscript{Pt} upon addition of increasing amounts of maleic acid, $^1$H NMR in DCM-d\textsubscript{2}.

**Figure S13.** Maleic acid titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.
Figure S14. Changes in the $^1$H NMR spectra of $C^p$ upon addition of increasing amounts of acrylic acid, $^1$H NMR in DCM-d$_2$.

Figure S15. Acrylic acid titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.
Figure S16. Changes in the $^1$H NMR spectra of CPt upon addition of increasing amounts of levulinic acid, $^1$H NMR in DCM-d$_2$.

Figure S17. Levulinic acid titration data fitted to a 1:1 model; the residual from the fit; and parameters extracted from the fitting.
**Effector Catalysis (SI5)**

After the preparation of $\text{C}^\text{Pt}$, the solution of $\text{C}^\text{Pt}$ was let standing over night and catalytic experiments were performed during the following 5 days after $\text{C}^\text{Pt}$ has been prepared. Typical procedure for catalytic experiment as used in the effector experiments:

To an NMR tube containing the described amount of effector (see Table S2), 40 or 200 µl (of 2.5 mM solution of $\text{C}^\text{Pt}$ in DCM, 0.1 or 0.5 µmol catalyst) was added and the tube gently shaken. Then, 50 µl of DCM containing 5 µmol mesitylene (used as an internal standard) was added and the tube again gently shaken. 510 µl DCM containing the described amount of $\text{SPh}$ were added, followed by 50 µl D$_2$O. The tube was closed and shaken for 2 minutes. $^1$H NMR was recorded at 300 K to obtain the kinetic rates and to determine the turnover numbers (TON). For the reaction without any effector, nothing was added to the NMR tube prior the addition of the cage $\text{C}^\text{Pt}$. The molecular catalyst $\text{M}^\text{Pt}$ was screened accordingly using the same platinum amount (0.2 µmol). Due to deuterium in cooperation in the product, the signal at 3.6 ppm (a) was used for quantification instead of the signals at 4.5 ppm and 4.8 ppm (b/c).

**Note:** Amongst many catalytic performance experiments, we observed that the absolute TOF of the nanocage varied by a factor of 0.5-2 times of the herein reported values either by change of the platinum precursor batch, deuterated solvent batch or ligand batch. All herein reported TOF represent runs of multiple batches which matched well and could be reproduced using the same Pt precursor and ligand with same deuterated solvent and same substrate with different batches of individual cages formed according to the described methodology. Furthermore, the reported values are also the middle values of all batches containing also outliers. Importantly, the tuning effect of the investigated effectors remained always the same, regardless of the absolute TOF obtained with different Pt, solvent or ligand batches, e.g. TOFs obtained with maleic acid effector were always 18-20 times higher than without effector. Same holds for all other investigated effectors (e.g., TOF of Lactone effector 3.94-4.3 times and TOF of Dicyano benzene 0.4-0.6 times the TOF of no effector) and their relative rete between each other and in comparison, to the effector free catalysis. As different solvent, precursor and ligand batches may contain trace impurities, these can have a substantial effect on the observed TOF but were found to have a neglectable effect on the relative enhancing performance by addition of effectors.
Table S2. An overview of the amount of effector added to the solutions with C\textsuperscript{Pt}.

<table>
<thead>
<tr>
<th>Effector</th>
<th>Equivalents with respect to C\textsuperscript{Pt}</th>
<th>Amount [mg] used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maleic Anhydride</td>
<td>50</td>
<td>0.5</td>
</tr>
<tr>
<td>Furanone</td>
<td>100</td>
<td>0.98</td>
</tr>
<tr>
<td>1,4-Dicyanobenzene</td>
<td>1333</td>
<td>17</td>
</tr>
<tr>
<td>Benzoquinone</td>
<td>4</td>
<td>0.04</td>
</tr>
<tr>
<td>Maleic Acid</td>
<td>50</td>
<td>0.58</td>
</tr>
<tr>
<td>Acrylic Acid</td>
<td>100</td>
<td>0.72</td>
</tr>
<tr>
<td>Levulinic Acid</td>
<td>100</td>
<td>1.16</td>
</tr>
<tr>
<td>Pentynoic Acid</td>
<td>100</td>
<td>0.98</td>
</tr>
</tbody>
</table>

No Effector (10-20µmol S\textsuperscript{Ph}; 0.5 µmol C\textsuperscript{Pt})

Figure S18. The zoomed in \textsuperscript{1}H NMR of S\textsuperscript{Ph} transformation to P\textsuperscript{Ph} using C\textsuperscript{Pt}, displaying selective deuterium in cooperation into the product when D\textsubscript{2}O is used.

Figure S19. \textsuperscript{1}H NMR progress of no-effector catalyzed cyclization of S\textsuperscript{Ph} (10 µmol) by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 200 min; 480 min. (Top) Zoom in into sphere signals region of \textsuperscript{1}H-NMR under catalytic conditions with no-effector catalyzed cyclization of S\textsuperscript{Ph} by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 200 min; 480 min.
Figure S20. Kinetic profile of $S^\text{ph}$ cyclization by $C^\text{Pt}$ in absence of any effector using 10 µmol $S^\text{ph}$.

Figure S21. Kinetic profile of $S^\text{ph}$ cyclization by $C^\text{Pt}$ in absence of any effector using different concentrations of $S^\text{ph}$. For comparison of different effectors same acid concentration was used in the individual experiments. Therefore, the data displayed in Fig. 3D is with 20 µmol $S^\text{ph}$, in Fig. 2B, 5A and 6 with 10 µmol $S^\text{ph}$. 
**Figure S22.** Kinetic profile of $S^{\text{Ph}}$ cyclization by $C^{\text{Pt}}$ in absence of any effector using different concentrations of $C^{\text{Pt}}$.

**Maleic Acid (10µmol $S^{\text{Ph}}$; 0.1 µmol $C^{\text{Pt}}$)**

**Figure S23.** $^1$H NMR progress of maleic acid-effector catalyzed cyclization of $S^{\text{Ph}}$ by $C^{\text{Pt}}$. Datapoints from bottom to top: 0 min; 60 min; 240 min. Zoom in into sphere signals region of $^1$H-NMR under catalytic conditions with maleic acid-effector catalyzed cyclization of $S^{\text{Ph}}$ by $C^{\text{Pt}}$. Datapoints from bottom to top: 0 min; 60 min; 240 min.
Figure S24. Kinetic profile of $S^{\text{Ph}}$ cyclization by $C^{\text{Pt}}$ in presence of 50 eq. maleic acid (in respect to $C^{\text{Pt}}$).

**Levulinic Acid (10$\mu$mol $S^{\text{Ph}}$; 0.1 $\mu$mol $C^{\text{Pt}}$)**

![Graph showing TON profile over time with data points for TON maleic acid 1, TON maleic acid 2, and TON maleic acid 3.]

Figure S25. $^1$H NMR progress of levulinic acid-effector catalyzed cyclization of $S^{\text{Ph}}$ by $C^{\text{Pt}}$. Datapoints from bottom to top: 0 min; 60 min; 180 min. Zoom in into sphere signals.
region of $^1$H-NMR under catalytic conditions with levulinic acid-effector catalyzed cyclization of $S^{ph}$ by $C^{Pt}$. Datapoints from bottom to top: 0 min; 60 min; 180 min.

**Figure S26.** Kinetic profile of $S^{ph}$ cyclization by $C^{Pt}$ in presence of 100 eq. levulinic acid (in respect to $C^{Pt}$).

**Acrylic acid (10µmol $S^{ph}$; 0.1 µmol $C^{Pt}$)**

**Figure S27.** $^1$H NMR progress of acrylic acid-effector catalyzed cyclization of $S^{ph}$ by $C^{Pt}$. Datapoints from bottom to top: 0 min; 60 min; 120 min. Zoom in into sphere signals region of $^1$H-NMR under catalytic conditions with acrylic acid-effector catalyzed cyclization of $S^{ph}$ by $C^{Pt}$. Datapoints from bottom to top: 0 min; 60 min; 120 min.
Figure S28. Kinetic profile of S\textsuperscript{ph} cyclization by C\textsuperscript{Pt} in presence of 100 eq. acrylic acid (in respect to C\textsuperscript{Pt}).

p-Benzooquinone (20µmol S\textsuperscript{ph}; 0.1 µmol C\textsuperscript{Pt})

Figure S29. \textsuperscript{1}H NMR progress of p-benzoquinone-effector catalyzed cyclization of S\textsuperscript{ph} by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 60 min; 240 min. Zoom in into sphere signals region of \textsuperscript{1}H-NMR under catalytic conditions with p-benzoquinone-effector catalyzed cyclization of S\textsuperscript{ph} by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 60 min; 240 min.
Figure S30. Kinetic profile of $S^{\text{Ph}}$ cyclization by $C^{\text{Pt}}$ in presence of 4 eq. p-benzoquinone (in respect to $C^{\text{Pt}}$).

1,4-dicyanobenzene (20µmol $S^{\text{Ph}}$; 0.1 µmol $C^{\text{Pt}}$)

Figure S31. Kinetic profile of $S^{\text{Ph}}$ cyclization by $C^{\text{Pt}}$ in presence of 1330 eq. 1,4-dicyanobenzene (in respect to $C^{\text{Pt}}$).
Maleic Anhydride (10-80µmol S<sub>Ph</sub>; 0.1 µmol C<sub>Pt</sub>)

Figure S32. <sup>1</sup>H NMR progress of maleic anhydride-effector catalyzed cyclization of S<sub>Ph</sub> by C<sub>Pt</sub>. Datapoints from bottom to top: 0 min; 60 min; 240 min. Zoom in into sphere signals region of <sup>1</sup>H-NMR under catalytic conditions with maleic anhydride-effector catalyzed cyclization of S<sub>Ph</sub> by C<sub>Pt</sub>. Datapoints from bottom to top: 0 min; 60 min; 240 min. The dataset shows development of a new active species (likely due to hydrolysis of maleic anhydride to maleic acid with proceeding reaction time).

Figure S33. Kinetic profile of 10µmol S<sub>Ph</sub> cyclization by C<sub>Pt</sub> in presence of 50 eq. maleic anhydride (in respect to C<sub>Pt</sub>).
Figure S34. Kinetic profile of 10-80µmol S\textsuperscript{Ph} (Ph100-800) cyclization by C\textsuperscript{Pt} in presence of 50 eq. maleic anhydride (in respect to C\textsuperscript{Pt}). Data displayed in maintest was taken from experiments containing 20 µmol S\textsuperscript{Ph} and 5mmol maleic anhydride to have the same quantity of acid as in the maleic acid effector reaction.
Figure S35. Structure and ESI-MS spectrum of maleic acid associated to $\text{C}^{\text{Pt}}$ observed after addition of maleic anhydride to $\text{C}^{\text{Pt}}$. MS spectrum showing signals associated to maleic acid-$\supset$C$^{\text{Pt}}$. Zoom in into sphere signals region of $^1\text{H}$-NMR of maleic acid-effector (top) and maleic anhydride effector (bottom) after 60 min under catalytic conditions showing similar catalytic species based on $^1\text{H}$-NMR shifts of the cage signals.
Furanone (20 µmol S<sup>Ph</sup>; 0.1 µmol C<sub>Pt</sub>)

**Figure S36.** <sup>1</sup>H NMR progress of furanone-effector catalyzed cyclization of S<sup>Ph</sup> by C<sub>Pt</sub>. Datapoints from bottom to top: 0 min; 60 min; 180 min. Zoom in into sphere signals region of <sup>1</sup>H-NMR under catalytic conditions with furanone-effector catalyzed cyclization of S<sup>Ph</sup> by C<sub>Pt</sub>. Datapoints from bottom to top: 0 min; 60 min; 180 min.

**Figure S37.** Kinetic profile of S<sup>Ph</sup> cyclization by C<sub>Pt</sub> in presence of 100 eq. furanone (in respect to C<sub>Pt</sub>).
Figure S38. ESI-MS spectra of a mixture of furanone and C\textsuperscript{Pt} displaying mainly hydrolyzed furanone being associated with the sphere C\textsuperscript{Pt}.

Pentynoic Acid (5\textmu mol S\textsuperscript{Ph}; 5\textmu mol S\textsuperscript{H}; 0.5 \textmu mol C\textsuperscript{Pt})

Figure S39. $^1$H NMR progress of pentynoic acid-effector catalyzed cyclization of S\textsuperscript{Ph} by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 120 min; 180 min. Zoom in into sphere signals region of $^1$H-NMR under catalytic conditions with pentynoic acid-effector catalyzed cyclization of S\textsuperscript{Ph} by C\textsuperscript{Pt}. Datapoints from bottom to top: 0 min; 120 min; 180 min.
Consecutive production of effector and $C^{pt}$ catalyzed $S^{Ph}$ cyclization

(A) The substrate $S^H$ (10 µmol, 0.98 mg, 20 eq.) was dissolved in CD$_2$Cl$_2$ (600 µL). The catalyst (0.5 µmol sphere $C^{pt}$, 0.05 eq) and D$_2$O (50 µL) were added and the mixture was heated at 300K for 12 h to form the product furanone PH quantitatively (See Fig. S39). Then, the second substrate $S^{Ph}$ (10 µmol, 2.5 mg, 20 eq.) was added and the conversion followed with NMR at 300K. The kinetic profile can be found at Fig. S36.

(B) The substrate $S^H$ (10 µmol, 0.98 mg, 20 eq.) was dissolved in CD$_2$Cl$_2$ (600 µL). The catalyst (0.5 µmol sphere $C^{pt}$, 0.05 eq) and D$_2$O (50 µL) were added and the mixture was heated at 300K for 5d to form levulnic acid (See Fig. S39). Then, the second substrate $S^{Ph}$ (5 µmol, 1.25 mg, 10 eq.) was added and the conversion followed with NMR at 300K.

Figure S40. Spectra of a catalytic transformation of pentynoic acid at different time points (from bottom to top: 0h, 2h, 12h, 5d).

Effector controlled conversion of pentynoic acid $S^H$

Figure S41. Spectra of a catalytic transformation of pentynoic acid at different time points with and without maleic anhydride effector.
Comparison of chemical shifts of Cage signals with different Effectors

**Figure S42.** Spectra of a catalytic mixtures (containing $S^{ph}$ and $C^{pt}$) showing the cage signals in presence of different effectors.

**Figure S43.** Spectra of a catalytic mixtures (containing $S^{ph}$ and $C^{pt}$) showing the cage signals in presence of different effectors.
Control Experiments (SI6)

Effector influence molecular catalyst M\textsuperscript{Pt} (SI6A)

**Figure S44.** Zoom in into molecular catalyst signals region of \textsuperscript{1}H-NMR of maleic acid-effector (top) and maleic anhydride effector (middle) and no effector (bottom) after 420 min under catalytic conditions showing similar catalytic species based on \textsuperscript{1}H-NMR shifts of the molecular catalyst signals.

**Figure S45.** Kinetic profile of S\textsuperscript{ph} cyclization by M\textsuperscript{Pt} in presence of 50 eq. maleic acid (in respect to M\textsuperscript{Pt}) and in absence of maleic acid at low catalyst concentrations (0.2 µmol M\textsuperscript{Pt}; same concentration of catalyst as used in cage experiments; TON and TOF are displayed per 2 Pt atoms for better comparison with the cage).
Figure S46. Kinetic profile of $S$Ph cyclization by M$^{\text{Pt}}$ at high catalyst concentrations (1 µmol M$^{\text{Pt}}$; 5 times higher catalyst loading as used in cage experiments; TON and TOF are displayed per 2 Pt atoms for better comparison with the cage).

Figure S47. Kinetic profile of $S$Ph cyclization by M$^{\text{Pt}}$ in presence of 50 eq. maleic acid (in respect to M$^{\text{Pt}}$) at high catalyst concentrations (1 µmol M$^{\text{Pt}}$; 5 times higher concentration of catalyst as used in cage experiments; TON and TOF are displayed per 2 Pt atoms for better comparison with the cage).
**Figure S48.** Comparison of best performing kinetic profiles of $S^\text{Ph}$ cyclization by $M^\text{Pt}$ in presence of 50 eq. maleic acid (in respect to $M^\text{Pt}$) and in absence of maleic acid at high catalyst concentrations (1 $\mu$mol $M^\text{Pt}$; 5 times higher concentration of catalyst as used in cage experiments; TON and TOF are displayed per 2 Pt atoms for better comparison with the cage).

**Summary:**

Our brief study into the catalytic activity of the molecular counterpart ($M^\text{Pt}$) of the nanocage $C^\text{Pt}$ displayed 2 times lower catalytic activity under any condition (Figure S44-47). Whereas under identical concentration as the cage experiments (Figure S44) no influence of the effector was observed for $M^\text{Pt}$, at high concentrations we observed also increased catalytic activity for $M^\text{Pt}$ after a delay time (e.g., Figure S47). The increase of catalytic activity of $M^\text{Pt}$ in the presence of an effector is by a factor of $\sim2$-$4$ and thus much lower than the tuning of the nanocage (ca. 20-fold increase), highlighting the nanocage effect.
C\textsuperscript{Pt} Stability (SI6B)

**Figure S49.** Stability of C\textsuperscript{Pt} in the cyclization of S\textsuperscript{Ph} in presence of 100 eq. levunilic acid, zoom in into cage signal region (\textsuperscript{1}H NMR in DCM:D\textsubscript{2}O). Amount of cage present, determined by the internal standard in \textsuperscript{1}H NMR.

**Figure S50.** Stability of C\textsuperscript{Pt} in the cyclization of S\textsuperscript{Ph} in presence of 50 eq. maleic acid, zoom in into cage signal region (\textsuperscript{1}H NMR in DCM:D\textsubscript{2}O). Amount of cage present, determined by the internal standard in \textsuperscript{1}H NMR.
Figure S51. Stability of $\text{C}^{\text{Pt}}$ in the cyclization of $\text{S}^{\text{Ph}}$ in presence of 100 eq. acrylic acid, zoom in into cage signal region ($^1\text{H}$ NMR in DCM:D$_2$O). Amount of cage present, determined by the internal standard in $^1\text{H}$ NMR.

**Bulky acid influence on nanocage catalyst $\text{C}^{\text{Pt}}$ (SI6C)**

We briefly studied the influence of two bulky acids and their effect on the catalytic performance of $\text{C}^{\text{Pt}}$ catalyzed $\text{S}^{\text{Ph}}$ cyclization. Typical procedure for catalytic experiment as used in the effector experiments: To an NMR tube containing the described amount of bulky acid (see Table S3), 40 µl (of 2.5 mM solution of $\text{C}^{\text{Pt}}$ in DCM, 0.1 µmol catalyst) was added and the tube gently shaken. Then, 50 µl of DCM containing 5 µmol mesitylene (used as an internal standard) was added and the tube again gently shaken. 510 µl DCM containing the described amount of $\text{S}^{\text{Ph}}$ were added, followed by 50 µl D$_2$O. The tube was closed and shaken for 2 minutes. $^1\text{H}$ NMR was recorded at 300 K to obtain the kinetic rates and to determine the turnover numbers (TON).

**Table S3.** An overview of the bulky acids added to the solutions with $\text{C}^{\text{Pt}}$.

<table>
<thead>
<tr>
<th>Effector/Bulky Acid</th>
<th>Equivalents with respect to $\text{C}^{\text{Pt}}$</th>
<th>Amount [mg] used</th>
<th>$\text{S}^{\text{Ph}}$ Equivalents with respect to $\text{C}^{\text{Pt}}$</th>
<th>TOF</th>
<th>TOF/TOF$^\text{none}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>none</td>
<td>-</td>
<td>-</td>
<td>200</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>1-Adamantanecarboxylic acid</td>
<td>100</td>
<td>1.8</td>
<td>100</td>
<td>2.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Diphenylacetic acid</td>
<td>100</td>
<td>2.1</td>
<td>100</td>
<td>1.8</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Figure S52. Kinetic profile of S\textsuperscript{Ph} cyclization by C\textsuperscript{Pt} in presence of 100 eq. of bulky acids which do not fit into the nanocage as effectors.

We observe that bulky acids (if used under identical acid concentrations) do not enhance the catalytic rate of S\textsuperscript{Ph} cyclization but slow it down insignificantly. We anticipate that competition binding (instead of the S\textsuperscript{Ph}) of organic bulky acids to the exterior of the nanocage can slow down the catalysis slightly as observed. The two bulky acids do not bind inside of the nanocage as the chemical shifts of the nanocage remain identical to the reaction performed without bulky acids (see Figure S53). In contrast to the two studied bulky acids which do not fit inside of the nanocage, both, maleic acid and acrylic acid display significant enhancement of catalytic rate (Figure S24 and S28).
**Figure S53.** Spectra of a catalytic mixtures (containing $S_{Ph}$ and $C_{Pt}$) showing the cage signals in presence of different bulky acids (top two) in comparison to the spectra in absence of the bulky acids.
Computational Studies (SI7)

Computational analysis of $\text{C}^{\text{Pt}}$ or $\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}}$ catalyzed cyclization of $\text{S}^{\text{H}}$ was carried out using Grimme’s GFN2-xTB tight binding method with the $\text{xtb}$ software (v. 5.4.1).\cite{6} While $\text{S}^{\text{H}}$ and $\text{S}^{\text{Ph}}$ present similar computational requirements for the two systems, as the phenyl groups feature additional conformational complexity and are more difficult to use with the push-pull reaction path finder tool. To minimize potential errors in finding minimum reaction paths we used the simpler $\text{S}^{\text{H}}$ as a model system. We identified one possible transition state $\text{TS1}$ and $\text{TS2}$. For $\text{TS2}$, a very complex step, other transition states may occur. The obtained $\text{TS2}$ is in agreement with the kinetic isotope effect.

$\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}} \text{Int1}$: An initial structure prepared featuring an alkynyl-coordinated $\text{S}^{\text{H}}$ axially coordinated to a Pt center of $\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}}$. Upon initial optimization (see parameters below), a pyridyl moiety was displaced to restore the preferred square planar coordination of the metal center and the proton of the carboxylic acid was transferred to the same pyridyl group. This initial structure was subjected to molecular dynamics (MD) using $\text{xtb}$ in order to better explore conformational space. The final trajectory frame was then optimized with $\text{xtb}$ to produce a structure for $\text{Int1}$ (Figure S54).

![Figure S54](image)

**Figure S54.** Rendering of the $\text{Int1}$ state of $\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}}$ showing the internal base activity of the $\text{C}^{\text{Pt}}$ pyridyl moiety and electrostatic interaction with the coordinated substrate.

$\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}} \text{Int2}$: A simple distance constraint was used to drive the cyclization of the coordinated $\text{S}^{\text{H}}$ into a coordinated intermediate. Then the intermediate model was subjected to an identical protocol of optimization, MD annealing, and secondary optimization as employed for $\text{Maleic acid}\rightleftharpoons \text{C}^{\text{Pt}} \text{Int1}$ (see above), affording the minimum structure of $\text{Int2}$ shown in Figure S55.
Figure S55. (a) Rendering of the Int2 state of Maleic acid−C\textsuperscript{Pt} showing the internal base activity of the C\textsuperscript{Pt} pyridyl moiety and electrostatic interaction with the coordinated intermediate.

**Maleic acid−C\textsuperscript{Pt} SM and Product:** Structures featuring the S\textsuperscript{H} substrate or P\textsuperscript{H} product located near the Pt center of Maleic acid−C\textsuperscript{Pt} were trivially constructed and subjected to an identical protocol of optimization, MD annealing, and secondary optimization as Maleic acid−C\textsuperscript{Pt} Int1 (see above). Notably, the lack of coordination between S\textsuperscript{H} or P\textsuperscript{H} and C\textsuperscript{Pt} lead to a significant distance the two species. For visualization the initially minimized structures (with proximate S\textsuperscript{H} or P\textsuperscript{H}) are shown below in Figure S56.

Figure S56. Renderings of the (a) SM and (b) Product state of S\textsuperscript{H} and P\textsuperscript{H} with Maleic acid−C\textsuperscript{Pt}.

**C\textsuperscript{Pt}SM−Product:** Equivalent model structures were developed for C\textsuperscript{Pt} without maleic acid substrate. Initial models were constructed by stripping the maleic acid from the appropriate Maleic acid−C\textsuperscript{Pt} SM−Product structure. These initial models were then subjected to the same protocol as Maleic acid−C\textsuperscript{Pt} Int1 (see above). Shown in Figure S57 are the four structures afforded for the C\textsuperscript{Pt} catalytic cycle.
**Figure S57.** Renderings of the (a) SM, (b) Int1, (c) Int2, and (d) Product state of C\textsubscript{Pt} catalytic cycle.

**T1:** The transition state for cyclization was investigated for both C\textsubscript{Pt} and Maleic acid\textless;C\textsubscript{Pt} using the meta-dynamics push-pull reaction path analysis facility of xtb.\textsuperscript{[6]} The S\textsubscript{2} and S\textsubscript{3} structures were used as the end points, providing a reaction path potential energy surface and transition state structure shown in Figure S58.

**Figure S58.** (a) Potential energy surface computed for the cyclization of coordinated S\textsubscript{H} for C\textsubscript{Pt} (green trace) and Maleic acid\textless;C\textsubscript{Pt} (purple trace). Renderings of (b) Maleic acid\textless;C\textsubscript{Pt} and (c) C\textsubscript{Pt} transition states for cyclization found using xtb.
Simulating the proto-demetallation of the cyclized intermediate to the product required the addition of water molecules to the model to accurately simulate proton transfer. The Int2 models were hydrated using packmol to randomly place 15 water molecules between the terminal carbon of the substrate and the protonated pyridine moiety.\textsuperscript{[7]} The packed structures were minimized using xtb and then the proton transfer was directed using a simple distance scan. After multiple attempts with randomly generated water networks, suitable models were found that enabled a complete proton transfer circuit between the pyridine and substrate to afford one of the possible transition states. The optimized models for these successful circuits before and after proton transfer were then processed using the meta-dynamics push-pull reaction path analysis facility of xtb to produce a free energy pathway for this reaction shown in Figure S59.

**Figure S59.** (a) Potential energy surface computed for the proto-demetallation of the cyclized intermediate for C\textsuperscript{Pt} (green trace) and Maleic acid≤C\textsuperscript{Pt} (purple trace). Renderings of (b) C\textsuperscript{Pt} and (c) Maleic acid≤C\textsuperscript{Pt} transition states (among other potential TS) for cyclization found using xtb with added water molecules. Proton transfer circuit is shown with highlight (pink).
Comparison to limited DFT results

The GFN2-xTB approach was used in order to accommodate the large size and complexity of the system within a reasonable calculation timescale, especially for the TS2 transition state. Given the approximate nature of this approach, we compared the energies of Int1, Int2, TS1, and Product relative to SM optimized using xtb and same structures optimized with DFT using Gaussian 16\cite{G16} and a bvp86/lanl2dz theory level, with the results plotted in Figure S60.

**Figure S60.** Energies obtained from xtb (x-axis) and DFT (y-axis) plotted with a linear fitting function independently for C\(_{\text{Pt}}\) (red) and Maleic acid\(\rightsquigarrow C_{\text{Pt}}\) (black).

We observe that xtb generally under-estimates the energy differences between states, but the errors appear consistent for each model system. Similarly, both DFT and xtb indicate the same direction of energy differences between for C\(_{\text{Pt}}\) and Maleic acid\(\rightsquigarrow C_{\text{Pt}}\), favoring C\(_{\text{Pt}}\) in state Int1 and Int2 while favoring Maleic acid\(\rightsquigarrow C_{\text{Pt}}\) in Product. The lack of solvation used in the DFT optimization and the difference in optimization engines used in either software for these calculations may account for the significant absolute differences between the two calculation approaches. Overall, this comparison suggests that xtb may be suitable for analysis of complex catalytic mechanisms in supramolecular confined spaces.
**Intermediate Int2 trapping (SI8)**

We attempted to trap Int2 in the presence of maleic acid as an effector and $S^{Ph}$ as substrate by mixing 0.5 µmol C$^{Pt}$ with 10 µmol maleic acid and 20 µmol $S^{Ph}$ in 0.65 ml DCM. The resulting mixture was directly injected into the mass machine (ESI-MS) to obtain information on the Int2. Although, we observe clearly nanocage with maleic acid inside, Int2 has the same molecular weight as Int1. We observe one or two $S^{Ph}$ associated to the maleic acid containing nanocage, indicating that the catalysis may take place on both Pt centers (or alternatively $S^{Ph}$ is bound to one side and catalysis only happens on one).

![Diagram of potential structures of the observed 748Da mass.](image)

**Figure S61.** Potential structures of the observed 748Da mass.

![ESI-MS spectra of a mixture of maleic acid, $S^{Ph}$ and C$^{Pt}$](image)

**Figure S62.** ESI-MS spectra of a mixture of maleic acid, $S^{Ph}$ and C$^{Pt}$ displaying mainly maleic acid being associated with the sphere C$^{Pt}$. Minor peaks are one or two $S^{Ph}$ associated to maleic acid C$^{Pt}$.
Figure S63. ESI-MS zoom in into one $S^{ph}$ associated to maleic acid-$C^\text{Pt}$ (top obtained, bottom simulated spectra).

Figure S64. ESI-MS zoom in into one $S^{ph}$ associated to maleic acid-$C^\text{Pt}$ (top obtained, bottom simulated spectra).
X-Ray Structure Analysis (SI9)

X-ray diffraction data of $\text{C}^{\text{Pt-BF}_4}$ were measured on a Bruker D8 Quest ECO three-circle diffractometer with a sealed tube using graphite-monochromated (Triumph) Mo Kα radiation ($\lambda = 0.71076$ Å) and a CPAD Photon III C14 detector. The sample was cooled with $\text{N}_2$ to 150(2) K with a Cryostream 700 (Oxford Cryosystems). Intensity data were integrated using the SAINT software.$^{[9]}$ Multi-scan absorption correction and scaling was executed with SADABS.$^{[10]}$ and the structure solve by direct methods with SHELXT 2018/2.$^{[11]}$

The crystal structure contained a large void (total solvent accessible volume = 1663 Å$^3$, 416 e$^-$), containing two highly disordered BF$_4^-$ counterions and residual solvents (CH$_3$CN and Et$_2$O) within the asymmetric unit that could not be refined reliably. Thus, the SQUEEZE$^{[12]}$ procedure in PLATON$^{[13]}$ (version 70422) was applied, accounting for 415 electrons per unit cell, congruent with the presence of 4 × BF$_4^-$ (40 e$^-$/molecule), 4 × CH$_3$CN (22 e$^-$/molecule) and 4 × Et$_2$O (42 e$^-$/molecule) solvent molecules in the unit cell.

Both before and after the SQUEEZE procedure, ADDSYM ($Fmmm$) or ADDSYM-EXT ($I/2m$) indicated the possibility of higher symmetry. However, the resulting higher-symmetry refinement revealed that the complete cage structure did not remain intact. Therefore, refinement was performed in space group $P\bar{1}$.

Least-squares refinement was performed with SHELXL-2018/3.$^{[14]}$ All non-hydrogen atoms were refined with anisotropic displacement parameters. The hydrogen atoms were refined isotropically on calculated positions using a riding model with their $U_{iso}$ values constrained to 1.5 times the $U_{eq}$ of their pivot atoms for terminal $sp^3$ carbon atoms and 1.2 times for all other carbon atoms. Disordered moieties were refined using bond lengths restraints and displacement parameter restraints.

Due to the characteristics of the crystal (i.e., large voids containing disordered solvent molecules, weak diffraction intensity, temporal instability), a few A-level and B-level alerts remain in the resulting CheckCIF$^{[15]}$ report.

The crystal data for $\text{C}^{\text{Pt-BF}_4}$ is summarized as shown in Table S4. The X-ray crystallographic data for $\text{C}^{\text{Pt-BF}_4}$ was deposited at the Cambridge Crystallographic Data Centre (CCDC), under the deposition number CCDC 2189698.
| **Table S4** |
|-----------------|----------------|
| **CCDC number** | 2189698 |
| **Empirical formula** | $\text{C}_{42}\text{H}_{28}\text{N}_{4}\text{O}_{2}\text{Pt}$ |
| **Formula weight** | 815.77 |
| **Temperature [K]** | 150(2) |
| **Crystal system** | triclinic |
| **Space group (number)** | $P\overline{1}$ (2) |
| **a [Å]** | 14.79(9) |
| **b [Å]** | 14.69(8) |
| **c [Å]** | 17.79(11) |
| **α [°]** | 113.91(9) |
| **β [°]** | 114.07(9) |
| **γ [°]** | 91.00(10) |
| **Volume [Å$^3$]** | 3147(33) |
| **Z** | 2 |
| **$\rho_{\text{calc}}$ [gcm$^{-3}$]** | 0.861 |
| **μ [mm$^{-1}$]** | 2.253 |
| **$F(000)$** | 804 |
| **Crystal size [mm$^3$]** | 0.246×0.170×0.054 |
| **Crystal colour** | colourless |
| **Crystal shape** | plate |
| **Radiation** | MoKα ($\lambda=0.71076$ Å) |
| **2θ range [°]** | 4.79 to 50.00 (0.84 Å) |
| **Index ranges** | $-17 \leq h \leq 17$ |
| | $-17 \leq k \leq 17$ |
| | $-21 \leq l \leq 21$ |
| **Reflections collected** | 62453 |
| **Independent reflections** | 11096 |
| | $R_{\text{int}} = 0.1609$ |
| | $R_{\text{sigma}} = 0.1255$ |
| **Completeness to $\theta = 24.999°$** | 99.9 % |
| **Data / Restraints / Parameters** | 11096/381/465 |
| **Goodness-of-fit on $F^2$** | 1.022 |
| **Final $R$ indexes [$\geq2\sigma(I)$]** | $R_1 = 0.0995$ |
| | $wR_2 = 0.2370$ |
| **Final $R$ indexes [all data]** | $R_1 = 0.1677$ |
| | $wR_2 = 0.2871$ |
| **Largest peak/hole [eÅ$^{-3}$]** | 4.01/-1.26 |
References


