Supporting Information

Rhodium-Catalyzed Hydrocarboxylation: Mechanistic Analysis Reveals Unusual Transition State for Carbon-Carbon Bond Formation

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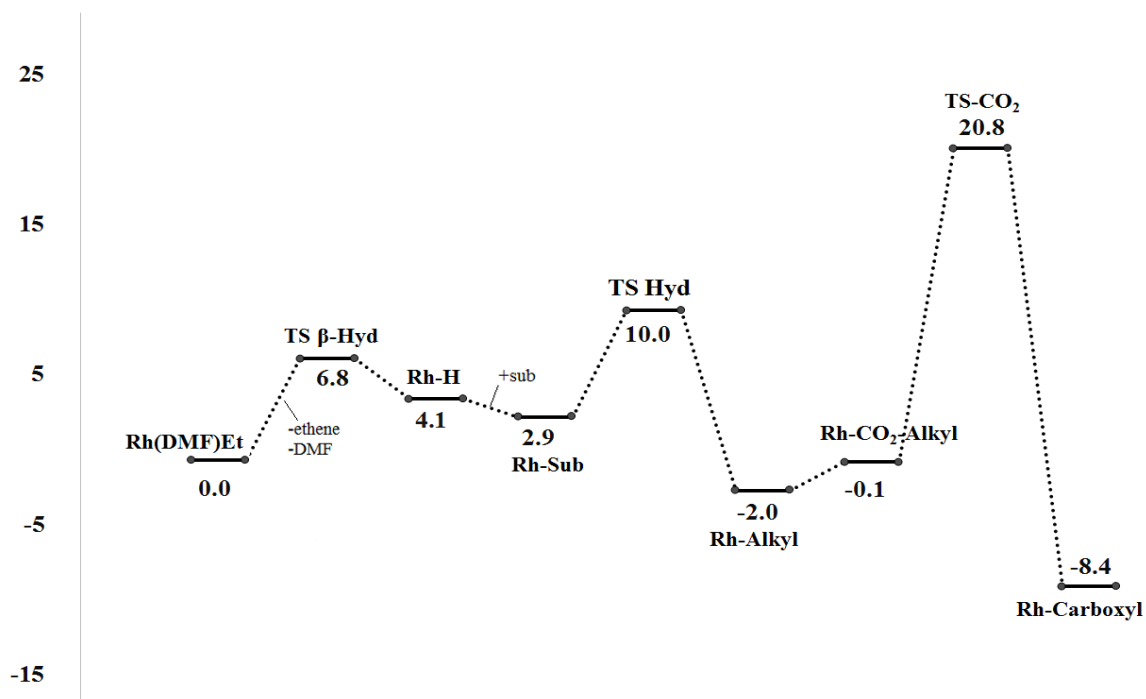
[&]Hylleraas Centre for Quantum Molecular Sciences, Department of Chemistry, University of Tromsø - The Arctic University of Norway, N-9037 Tromsø, Norway
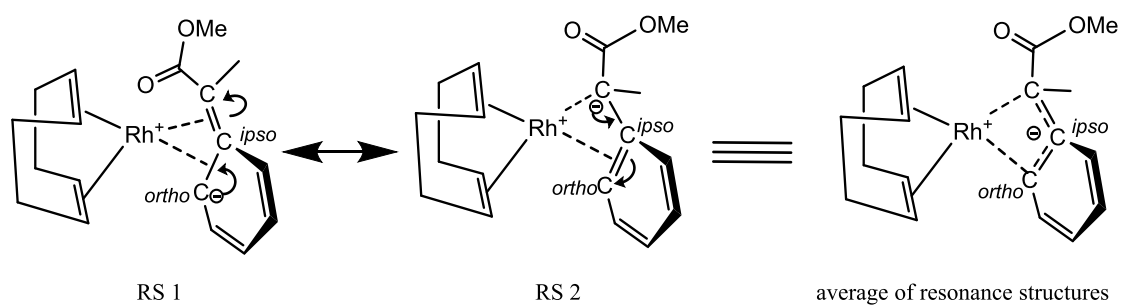
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β-carboxylation pathway

Figure S1. Computed free energy profile (kcal/mol, 273 K, PBE-D2/BS2[IEFPCM]//PBE-D2/BS1[IEFPCM] level of theory) of the catalytic cycle for rhodium-COD catalyzed hydrocarboxylation of the ester substrate methyl 2-phenylacrylate leading to the β-aryl carboxylic acid.

Possible resonance structures of Rh-Alkyl

RS 1   RS 2   average of resonance structures

Figure S2. Proposed resonance structures of Rh-Alkyl intermediate that contribute to η^2-binding mode.

Alternative geometry of Rh-Alkyl

Figure S3. The optimized geometry of the Rh-Alkyl intermediate with alternative binding mode of the substrate involving the carbonyl of the ester.

Possible resonance structures of C-C bond formation TSs

RS 1   RS 2   RS 3   RS 4   average of resonance

Figure S4. Possible resonance structures of C-C bond formation TSs, displaying an η^6 coordination mode with charge delocalization over seven carbon atoms.

A) TS$_{CO2\_III}$

B) TS$_{CO2\_IV}$

Figure S5. Optimized geometries with the ester substrate, methyl 2-phenylacrylate, for the CO_2 insertion TS where CO_2 is placed closer to rhodium, with A) η^6-coordination of the substrate, and B) coordination of the substrate via the ester group.

TS$_{CO2\_V}$

Figure S6 . Optimized geometry with the ester substrate, methyl 2-phenylacrylate, for the CO_2 insertion TS, where an η^2-interaction between CO_2 and rhodium takes place.

TS_CO$_2$_I_Et$_2$Zn

Figure S7. The optimized geometry of TS_CO$_2$_I_ZnEt$_2$ with diethyl-zinc, where the interaction between CO$_2$ and Zn is negligible.

Rh_CO2_Zn

Figure S8. The optimized geometry of the Rh_CO$_2$_Zn intermediate where both Zn and Rh interact with the carboxyl group.

Evaluation of rhodacycle

Figure S9. Evaluation of formation of a metallacycle via oxidative coupling between CO_2 and an ester substrate at the rhodium center (energy at the PBE/BS1[IEFPCM]) level of theory).

Experimental Studies of Rhodium Catalyzed Hydrocarboxylation:

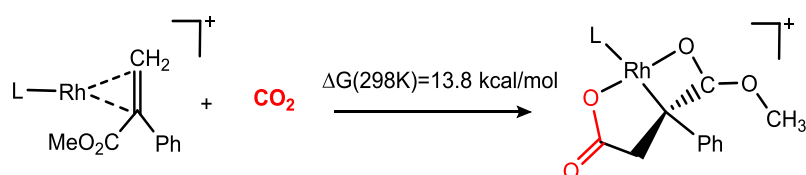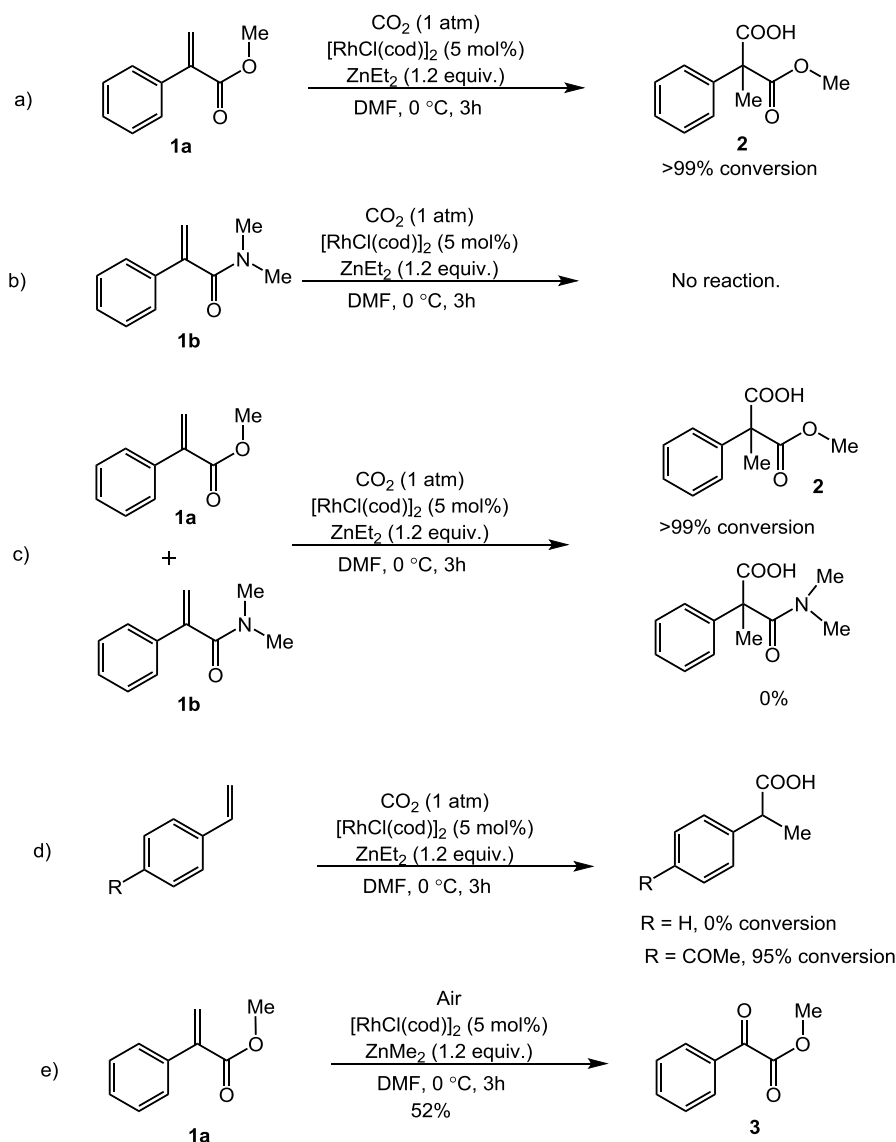### [I] General Information:

Diethylzinc (1.0 M in hexane solution) and [RhCl(cod)]$_2$ were purchased from Aldrich. DMF was dried from 4Å molecular sieves. Chemical shifts were reported in ppm compared to CDCl$_3$ [δ 7.26 (singlet), for ^{1}H NMR, and δ 77.16 (triplet) for ^{13}C NMR] and DMF-D$_7$ [δ 8.03 (singlet), δ 2.92 (quintet), δ 2.75 (quintet) ^{1}H NMR, and 163.15 (triplet), 34.89 (heptet), 29.76 (heptet) for ^{13}C NMR]. Important NMR data were tabulated in following order: multiplicity (s: singlet, d: doublet, t: triplet, tt: triplet of triplet,) and coupling constant (J (Hz)). Reactions were monitored by thin-layer chromatography (TLC) with Merck pre-coated silica gel plates (60 F$_{254}$). Visualization was accomplished with either UV light or by immersion in potassium permanganate or 5% alcoholic phosphomolybdic acid (PMA) followed by light heating with a heating gun. High-resolution mass spectra (HRMS) were recorded from MeOH solutions on an LTQ Orbitrap XL (Thermo Scientific) in positive electrospray ionization (ESI) mode. Methyl 2-phenylacrylate (**1a**) and N,N-dimethyl-2-phenylacrylamide (**1b**) were prepared according to the literature.[3]

[II] Experimental studies:

Figure S10. Rhodium catalyzed carboxylation and oxidative cleavage of double bond

a) Following the reported procedure,[3] [RhCl(cod)]$_2$ (2.4 mg, 0.005 mmol) was weighed into an oven-dried two-neck rb flask, which was sealed with a septum, evacuated and refilled with CO_2. The Rh catalyst was dissolved in DMF (0.5 mL), and then methyl 2-phenylacrylate (**1a**) (16 mg, 0.1 mmol) was added. Then, ZnEt$_2$ (0.12 ml, 0.12 mmol) was added dropwise at 0 °C. After 3 h, the reaction mixture was diluted with Et$_2$O (5 mL) and quenched with 1N HCl (5 mL). The crude reaction mixture was monitored by TLC and HRMS. Methyl 2-phenylacrylate (**1a**) was completely converted into

hydrocarboxylated product **2,** which was confirmed by HRMS (calculated $[M+Na]^+$ for $C_{11}H_{12}O_4Na^+$ is 231.0628 and observed value is 231.0622).
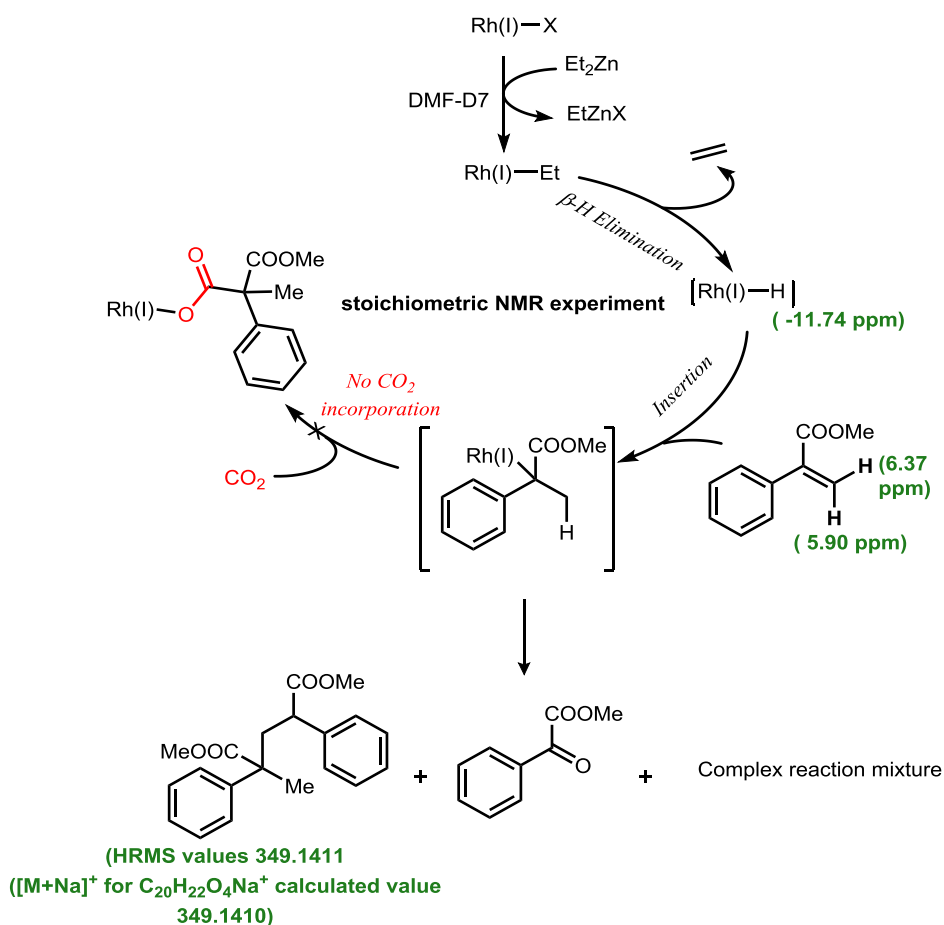
b) Following the above conditions for hydrocarboxylation, N,N-dimethyl-2-phenylacrylamide (**1b**) (17 mg, 0.1 mmol) was subjected to $[RhCl(cod)]_2$ (2.4 mg, 0.005 mmol) and $ZnEt_2$ (0.12 ml, 0.12 mmol) under CO_2 atmosphere. After 3 hours, the reaction mixture was diluted with Et_2O (5 mL) and quenched with 1N HCl (5 mL). TLC and HRMS (the only detected mass was m/z 222.1110 corresponding to $[M+H]^+$ of **1b**) analyses indicated that the reaction was not progressed.

c) Following the above conditions for hydrocarboxylation of **1a**, N,N-dimethyl-2-phenylacrylamide (**1b**) (9 mg, 0.05 mmol) and methyl 2-phenylacrylate (**1a**) (8 mg, 0.05 mmol) were subjected to $[RhCl(cod)]_2$ (2.4 mg, 0.005 mmol) and $ZnEt_2$ (0.12 ml, 0.12 mmol) under CO_2 atmosphere. After 3 hours, the reaction mixture was diluted with Et_2O (5 mL) and quenched with 1N HCl (5 mL). TLC and HRMS (m/z 231.0628 and 222.1110 corresponding to hydrocarboxylated product of **1a** and unreacted **1b)** indicated that the hydrocarboxylation reaction is selective for α,β-unsaturated esters.

d) Following the above procedure, 4-acetyl styrene was converted into carboxylated product while styrene was unreacted (monitored by GCMS).

e) Following the above conditions for hydrocarboxylation of **1a**, methyl 2-phenylacrylate (**1a**) (16mg, 0.1 mmol) was subjected to $[RhCl(cod)]_2$ (2.4 mg, 0.005 mmol) and $ZnMe_2$ (0.12 ml, 0.12 mmol) under open air atmosphere. After 3 hours, the reaction mixture was diluted with Et_2O (5 mL) and quenched with 1N HCl (5 mL). After separation, the aqueous layer was extracted with EtOAc (2 × 5 mL). The combined organic layers were dried over MgSO4 and evaporated under reduced pressure. The crude product was purified by flash chromatography with EtOAc/hexane (10:90) to afford methyl 2-oxo-2-phenylacetate **3** (9 mg, 52%). ^{1}H and ^{13}C NMR data was matching with the reported values of **3**.[4]

^{1}H NMR (400 MHz, Chloroform-d) δ 8.03 (d, $J = 7.8$ Hz, 2H), 7.67 (tt, $J = 7.6, 1.4$ Hz, 1H), 7.52 (t, $J = 7.6$ Hz, 2H), 3.98 (s, 1H). **^{13}C NMR (101 MHz, CDCl₃) δ** 186.18, 164.17, 135.13, 132.57, 130.24, 129.05, 52.94.
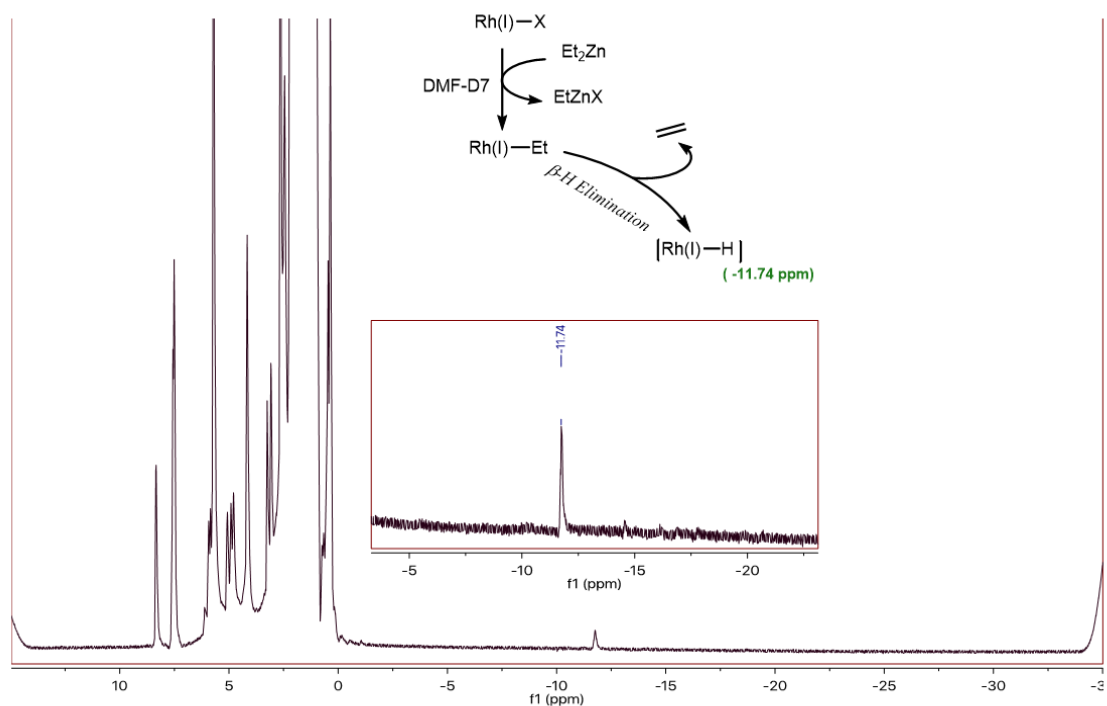
[III] Mechanistic Studies:

The rhodium complex (24 mg, 0.05 mmol) was weighed into an NMR tube, which was filled with DMF-D_7 (0.5 ml) and cooled to 0 °C. Then, $ZnEt_2$ (50 µL, 0.05 mmol) was added dropwise at 0 °C. The color of the solution changed from pale yellow to dark red immediately with evolution of ethylene bubbles. After 2 min, the NMR tube was introduced into the NMR spectrometer for identification of Rh-H intermediate. After 10 min, the tube was removed from NMR spectrometer. Subsequently, methyl 2-phenylacrylate (20 mg, 0.125 mmol) was added into the NMR tube and sonicated for 10 min. The NMR tube was introduced into the NMR spectrometer for evaluation if substrate insertion into the Rh-H had taken place. After 10min, the tube was removed from NMR spectrometer and CO_2 gas (quality >99 %) was introduced through a long stainless-steel needle at flow rates between 2 to 5 mL/min at 0 °C. After 10 min, the stainless- steel needle was replaced with NMR septum and the NMR tube was introduced into the NMR spectrometer for detection of carboxylated product.
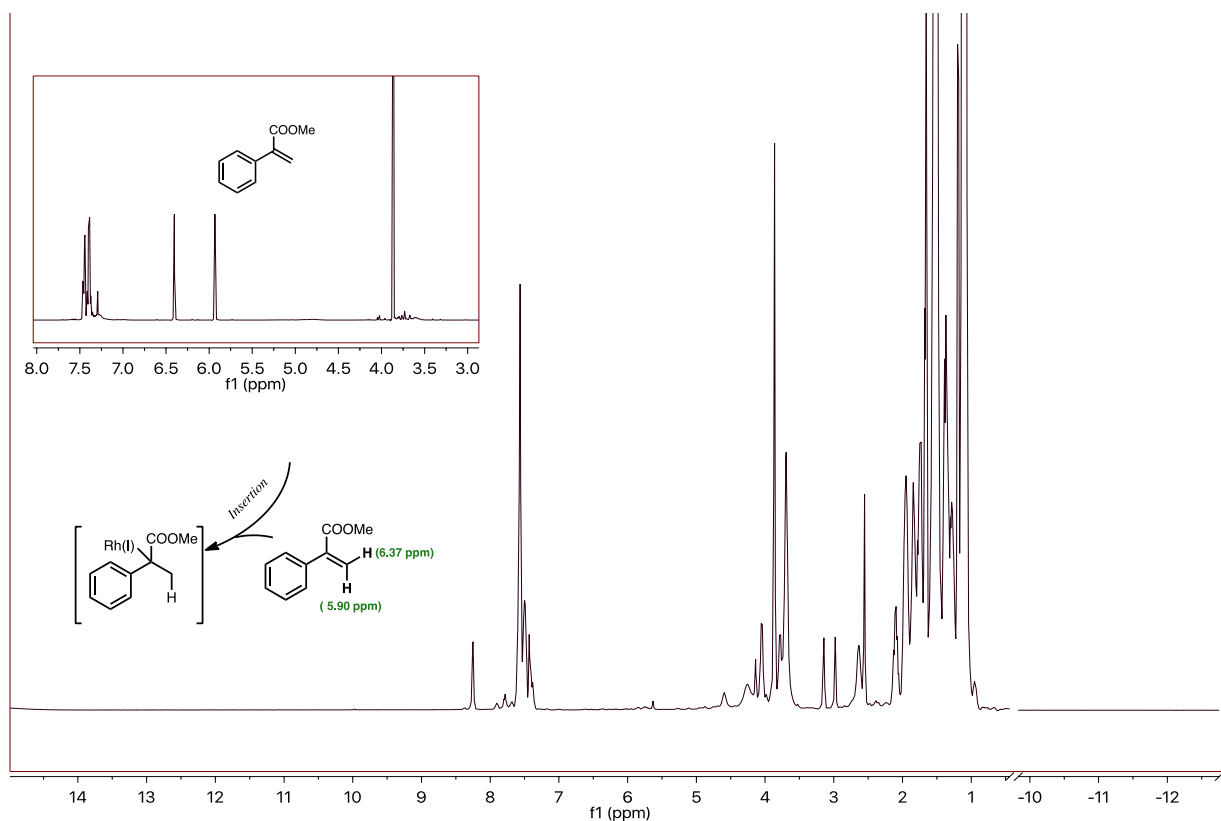

Figure S11. NMR investigation of stoichiometric reactions

We have carried out same NMR experiment with initial addition of excess amount of Et$_2$Zn (75 μL, 1.5 equiv). However, also in this case we did not observe any hydrocarboxylated product, but the presence of side products only.
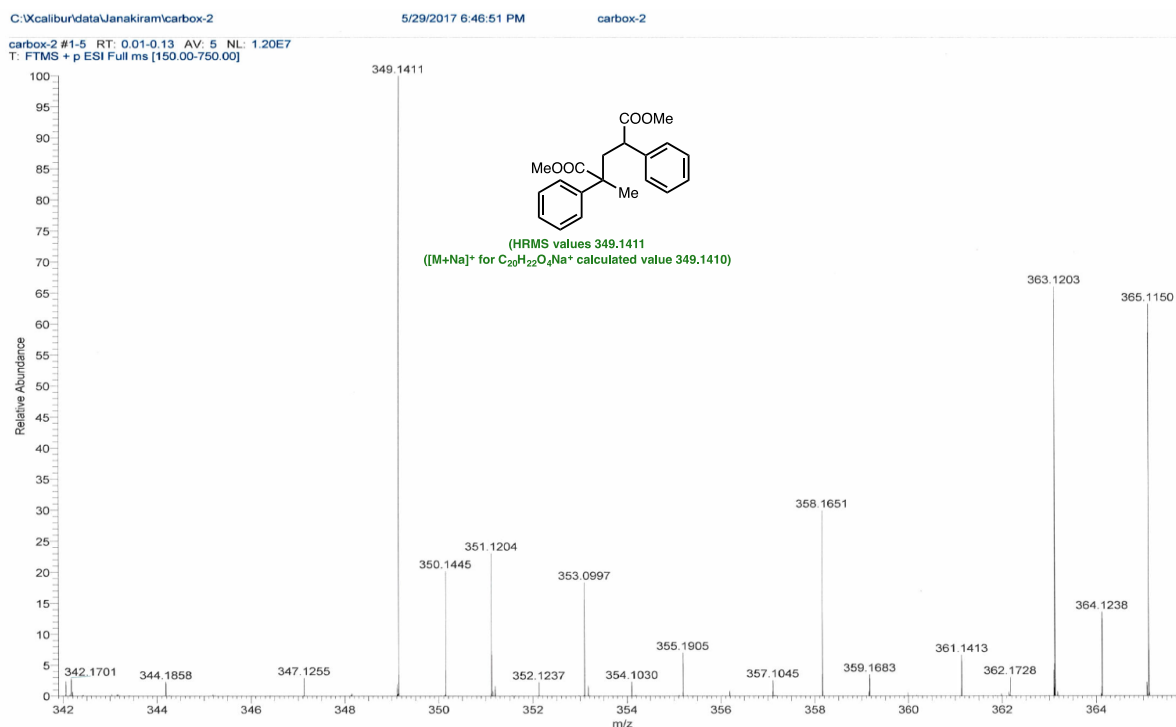
NMR investigation carboxylation process:

Figure S12. 1H NMR of Rh-H complex: (conditions: [RhCl(cod)]2 (1 equiv.) and Et$_2$Zn (1.0 M in Hexane) (1 equiv) in DMF-D7 (0.5 ml))

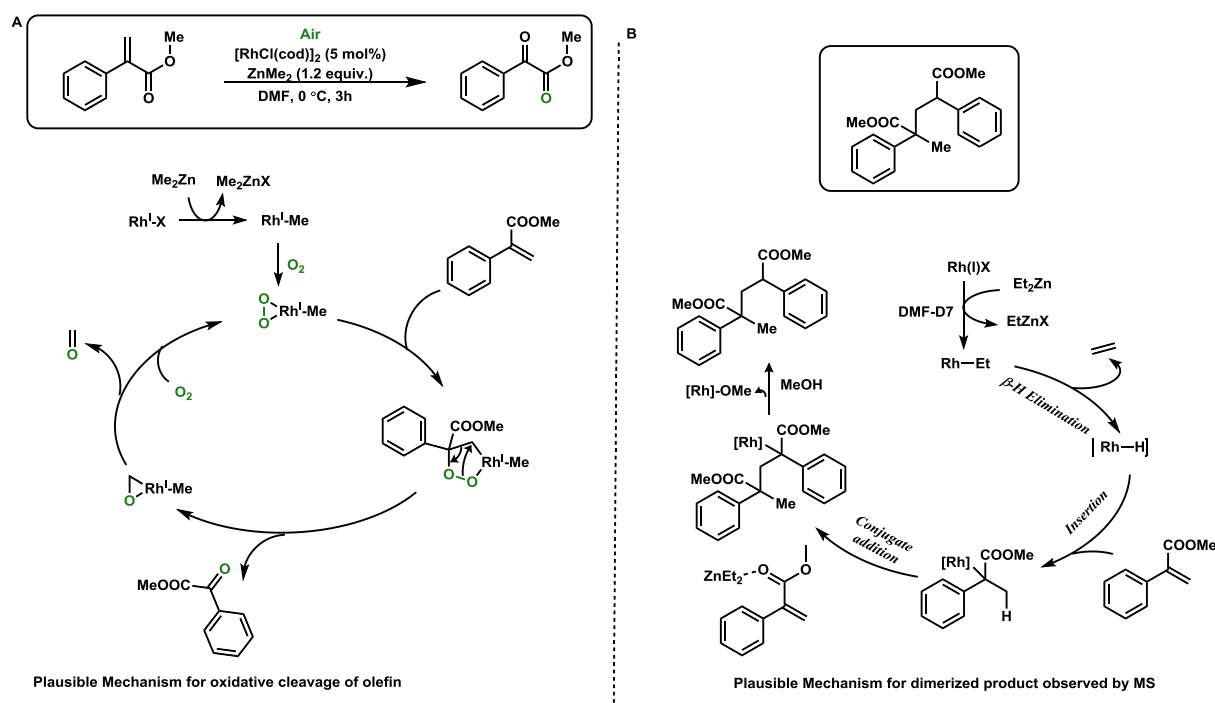**Figure S13.** 1H NMR of hydride inserted complex of Methyl 2-phenylacrylate

Figure S14. HRMS of crude reaction mixture of hydride inserted complex.

[IV] Plausible mechanism for oxidative cleavage of double bond and dimerization of 1a:

For oxidative cleavage of the double bond:[2] Transmetallation of the methyl group between [RhCl(cod)]$_2$ and dimethylzinc produces a Rh^I–Me species, which further reacts with oxygen in air to generate rhodium peroxide species.[5] Insertion of the methyl 2-phenylacrylate into the electron-poor peroxide species leads to 1,2-dioxa-3- rhodacyclopentane, which further undergoes rearrangement to give methyl benzoylformate and formaldehyde followed by generation of the catalyst as shown in Figure S15A.

For dimerization of 1a:[1] In the catalytic cycle as shown in Figure S15B, after insertion of methyl 2-phenylacrylate into the Rh^I–H species, the resulting intermediate can undergo conjugate addition with another methyl 2-phenylacrylate molecule to give dimerized product.

Figure S15. Plausible mechanism for **A)** oxidative cleavage of double bond and **B)** dimerization of **1a**.
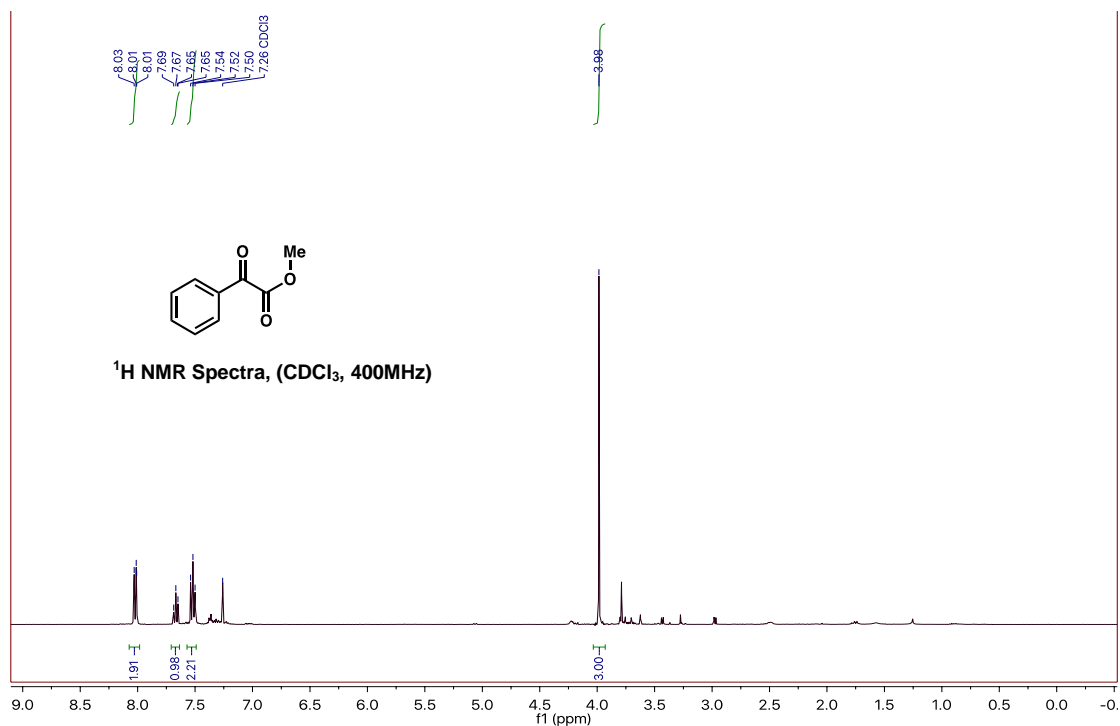
[V] NMR of Methyl benzoylformate:

8.03
8.01
7.69
7.67
7.65
7.54
7.52
7.50
7.26 CDCl3

3.98

¹H NMR Spectra, (CDCl₃, 400MHz)

1.91
0.98
2.21
3.00

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)

Figure S16. ¹H NMR of methyl benzoylformate

—186.18
—164.17
135.13
132.57
130.24
129.05
77.16 CDCl3
—52.94

¹³C NMR Spectra, (CDCl₃, 101MHz)

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
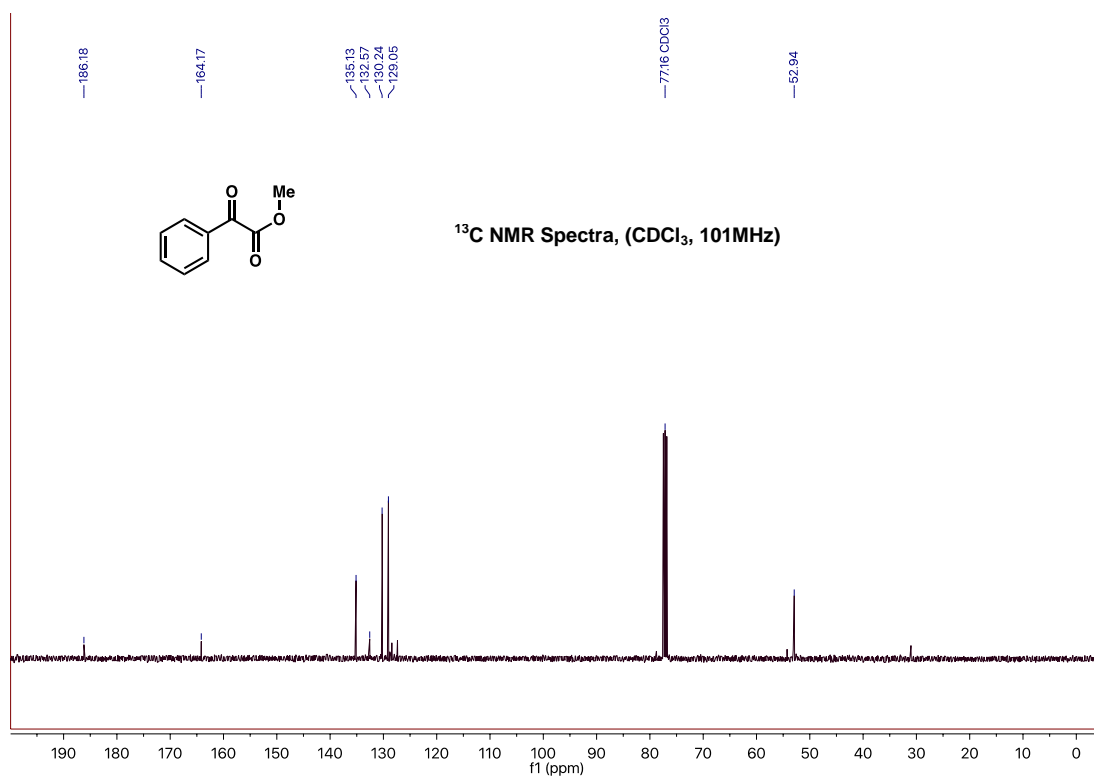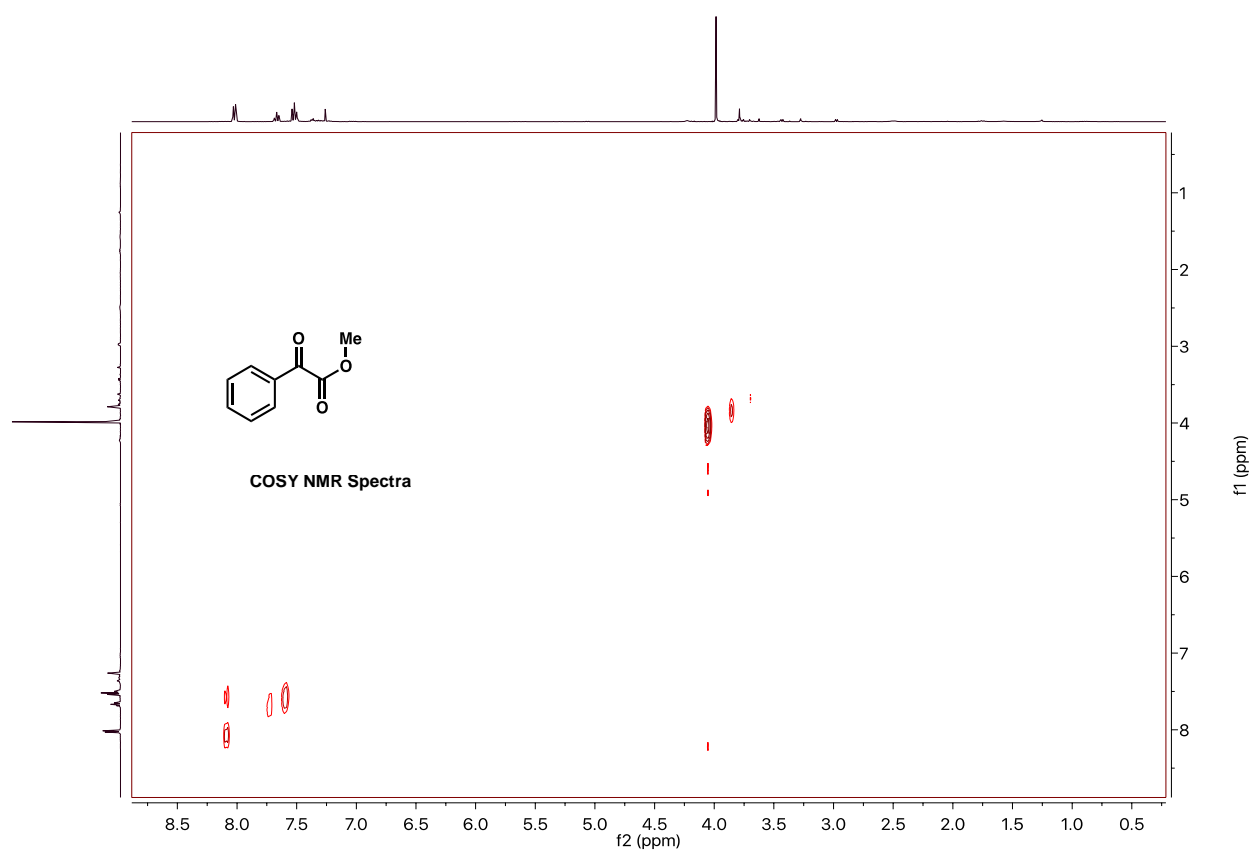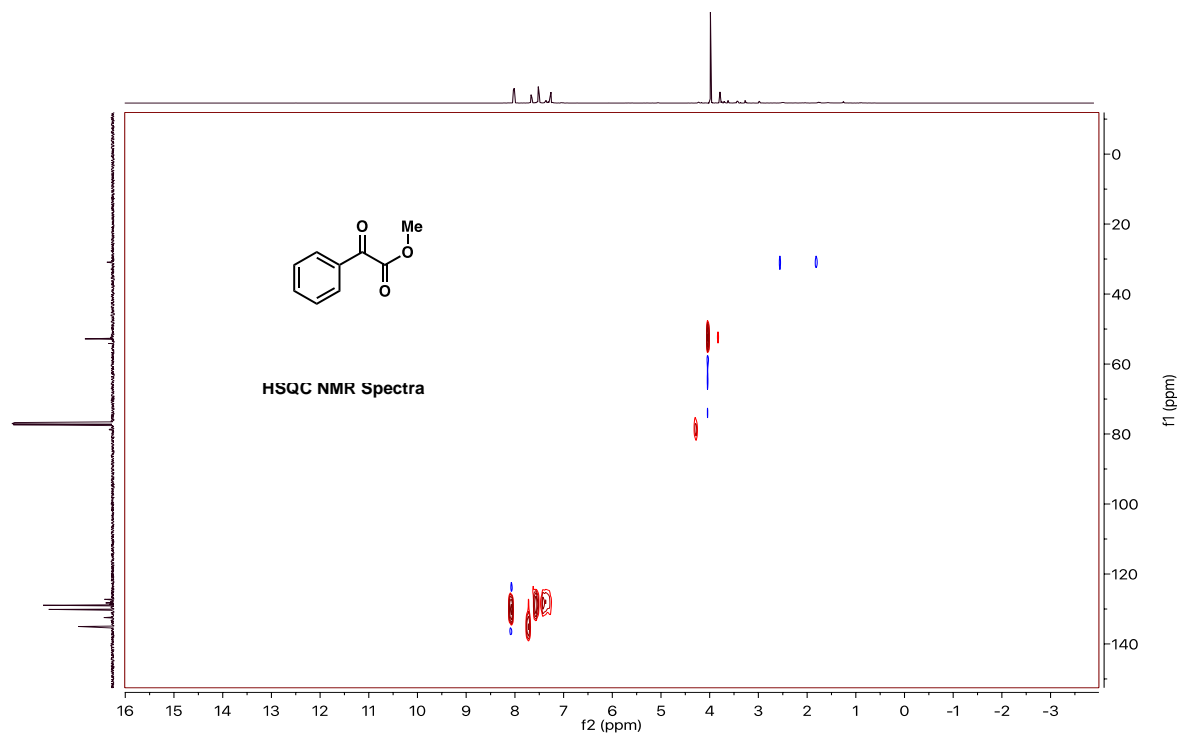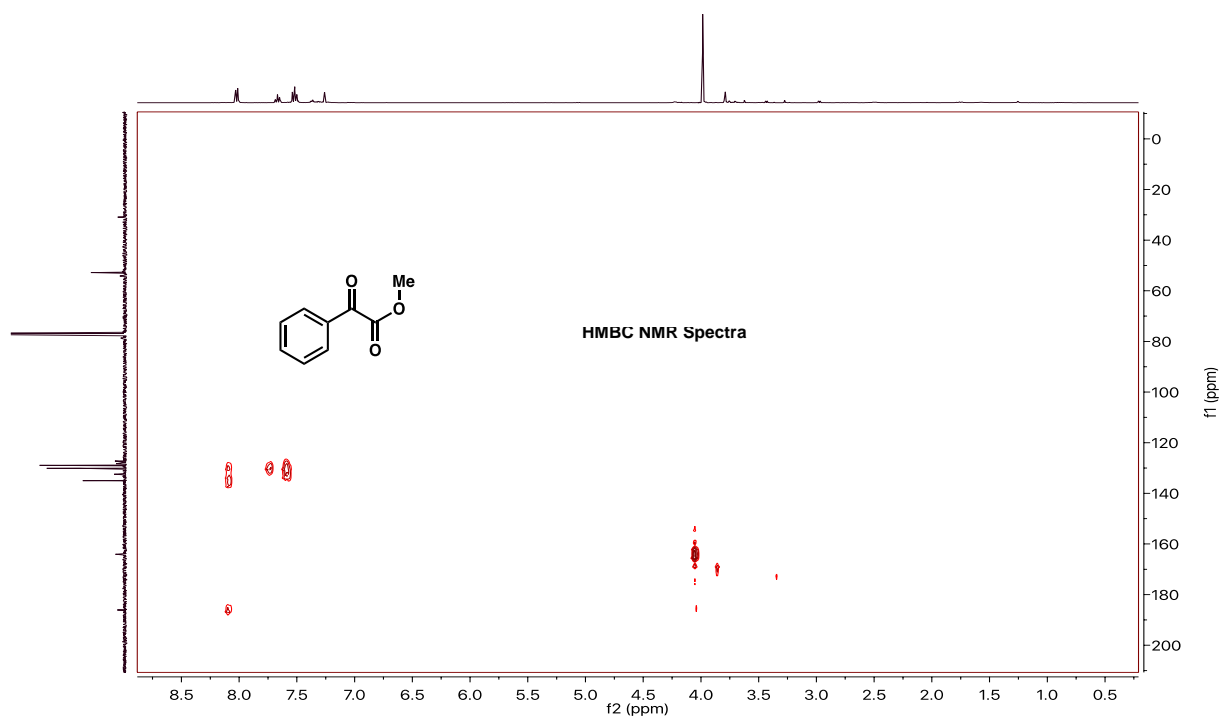f1 (ppm)

Figure S17. ¹³C NMR of methyl benzoylformate

Figure S18. COSY NMR of methyl benzoylformate

Figure S19. HSQC NMR of methyl benzoylformate

Figure S20. HMBC NMR of methyl benzoylformate

[VI] References:

(1) Kumaraswamy, G.; Rambabu, D., Hydroxy-rhodium(I) catalyzed regioselective Michael addition of cyclic enones *Tetrahedron Letters* **2012,** *53*, 1042-1044.

(2) Bönnemann, H.; Nunez, W.; Rohe, D. M. M., Rhodium-Catalyzed C,C-Double Bond Cleavage by Molecular Oxygen *Helv. Chim. Acta* **1983,** *66*, 177.

(3) Kawashima, S.; Aikawa, K.; Mikami, K., Rhodium-Catalyzed Hydrocarboxylation of Olefins with Carbon Dioxide *Eur. J. Org. Chem.* **2016,** *2016*, 3166-3170.

(4) Moriyama, K.; Takemura, M.; Togo, H., Direct and Selective Benzylic Oxidation of Alkylarenes via C–H Abstraction Using Alkali Metal Bromides *Org. Lett.* **2012,** *14*, 2414-2417.

(5) De Bruin, B.; Budzelaar, P. H.; Gal, A. W., Functional Models for Rhodium-Mediated Olefin-Oxygenation Catalysis *Angew. Chem. Int. Ed.* **2004,** *43*, 4142-4157.