Palladium-catalyzed carbonylative synthesis of carboxylic acid anhydrides from Alkenes

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Appendix I

Supporting Information for Chapter 2

Palladium-Catalyzed Synthesis of Carboxylic Acid Anhydrides from Alkenes

AI.1. General experiment details and materials

Reactions and chemicals related: All reactions and operations involving air- or moisture-sensitive compounds were performed using standard Schlenk techniques in heated and vacuum dried glassware or in N_2-filled glove box. Chemicals were purchased from Sigma-Aldrich, TCI, Acros, Brunschwig or Bio-connect and used without further purification unless otherwise stated. Anhydrous 1,2-dichloroethane (DCE) was purchased from Biosolve and dried over flame dried 4Å molecular sieves. Toluene and dichloromethane (DCM) were purchased from Honeywell and dispensed *via* Pure Solv solvent dispenser by Innovative Technologies. Solvents were freeze-pump-thawed (FPT) before all catalytic reactions. All ligands except 1,2-bis(diphenylphosphanylmethyl)benzene were purchased from Sigma-Aldrich and Strem Chemicals. 1,2-bis(diphenylphosphanylmethyl)benzene was synthesized in-house.

a. Autoclaves: 100 mL stainless steel (316) autoclaves equipped with temperature probe and pressure adapter were used. For heating and stirring, an H.E.L. Polyblock PB4 was used.

b. NMR Spectroscopy: ^{1}H NMR and ^{13}C NMR were recorded on Bruker Avance 400 (operating at 400 MHz for ^{1}H, 101 MHz for ^{13}C) NMR spectrometer. ^{19}F and ^{31}P NMR spectra were referenced against $CFCl_3$ and 85% H_3PO_4 (external references) Multiplets were assigned as s (singlet), d (doublet), t (triplet), , q (quartet), p (quintet), dd (doublet of doublet), ddt (doublet of doublet of triplet) and m (multiplet). All measurements were carried out at room temperature. NMR yields were calculated using dibromomethane as internal standard.

c. GC Analysis: Gas chromatography (GC) was measured on Shimadzu GC-2010, equipped with DB-5MS UI column (length 60 m, diameter: 0.250 mm, film thickness: 1.0 µm), coupled to Flame Ionization Detector (FID). Gas chromatography-mass spectrometry (GC-MS) was measured on Agilent Technologies 7820A equipped with DB-5MS UI column (length 30 m, diameter: 0.250 mm, film thickness: 1.0 µm) column and coupled to mass detector MSD 5975. Helium was used as the mobile phase.

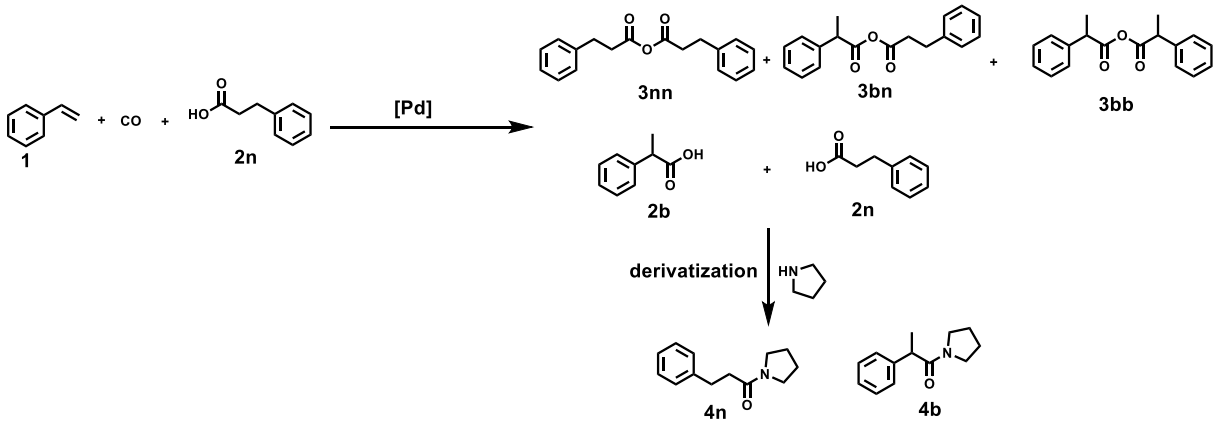
d. UPLC Analysis: Ultra Pressure Liquid Chromatography (UPLC) was measured using Waters ACQUITY UPLC equipped with a ACQUITY UPLC® BEH C18 1.7µm, 2.1 × 50 mm column and coupled to TUV detector.

e. HRMS: High resolution mass spectra (HRMS) were recorded on Q-Exactive HF Orbitrap (Thermo Scientific) equipped with an electrospray ion source (ESI) in positive mode, injection of 2 µL of a 1 µM solution *via* Ultimate 3000 nano UPLC (Dionex) system, with an external calibration (Thermo Scientific). Parameters used: Source voltage of 3.5 kV, capillary temperature 275 °C, no sheath gas, Resolution = 240.000 at m/z=400. Mass range

m/z=160-2000 or until a maximum of 6000. Eluents used: ACN:H_2O (1:1 v/v) supplemented with 0.1% formic acid. The data are given as mass units per charge (m/z).

AI.2. General reaction scheme, methods of analysis and calculations

AI.2.1. General reaction scheme showing reactants, all possible products of catalysis and products obtained on derivatization



Scheme AI.1. Overall reaction scheme showing substrates and products.

AI.2.2. Methods of analysis of substrates and products

a. GC : **1**, **4n**, **4b**

b. UPLC : **2n** + **2b** (total carboxylic acid; **2**) ; **3nn** + **3bn** + **3bb** (total anhydride; **3**)

c. NMR : **3nn**, **3bn**, **3bb**

AI.2.3. Calculations

a. Mass Balance:

The Mass Balance was calculated in terms of "number of phenyl groups" present in the reaction mixture after catalysis as follows:

$$\frac{phenyls\ of\ \mathbf{1}\ + phenyls\ of\ \mathbf{2} + \ phenyls\ of\ \mathbf{3}}{total\ initial\ phenyls} \times 100$$

Where,

Phenyls of **1** = mmol of **1** unreacted ; determined by GC

Phenyls of **2** = mmol of (**2n**+**2b**) ; determined by UPLC

Phenyls of **3** = 2 × mmol of **3**; determined by UPLC

Total initial phenyls = mmol of (**1**+**2n**) introduced in the reaction

An error margin of ±10% is considered to be acceptable for the mass balance.

b. Total Anhydride Yield %:

The total anhydride yield % was calculated as follows:

$$\frac{mmol\ of\ \mathbf{3}}{mmol\ of\ limiting\ substrate} \times 100$$

Where,

Limiting substrate can be either **1** or **2n** based on the equivalents used

mmol of **3** was determined by UPLC

c. Regioselectivity:

3nn:**3bn:3bb** was calculated as follows:

$$\frac{\boldsymbol{3nn}\ or\ \boldsymbol{3bn}\ or\ \boldsymbol{3bb}}{Total\ anhydride\ yield} \times 100$$

Where,

mmol of **3nn**, **3bn**, **3bb** were determined by NMR using dibromomethane as internal standard

4n:**4b** was calculated as follows:

$$\frac{\boldsymbol{4n}\ or\ \boldsymbol{4b}}{\boldsymbol{4n} + \boldsymbol{4b}} \times 100$$

Where,

mmol of **4n**, **4b** were determined by GC

d. Conversion %

Conversion % with respect to styrene (**1**) was calculated as follows:

$$\left[1 - \frac{\mathbf{1}\ unreacted}{initial\ \mathbf{1}\ charged}\right] \times 100$$

Where,

mmol of **1** was determined by GC

An error margin of ±5% is considered to be acceptable for the conversion.

e. Concentrations mentioned in mol% are always given with respect to the limiting reagent in cases where one of the reagents is used in excess.

AI.3. General catalytic procedure (GP) and analysis

Palladium acetate (0.05 mmol; 11.2 mg), 1,4-bis(diphenylphosphanyl)butane, dppb, (0.10 mmol; 42.7 mg) and 3−phenylpropionic acid (**2n**, 10.0 mmol; 1.50 g) were weighed into a clean and dried glass liner containing an oven−dried stirring bar. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. The required volume of degassed and dried solvent (6.0 mL) was added using standard Schlenk techniques and the mixture was stirred for one hour to allow for catalyst formation. Then the required volume of degassed and dried styrene (**1**, 10.5 mmol; 1.2 mL) was added using standard Schlenk procedures and the autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to a HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with nitrogen (N_2) (3 × 30 bar). The autoclave was flushed with carbon monoxide (CO) (1 × 30 bar) and then was charged with CO to 50 bar. The autoclave was stirred at 350 rpm and heated for 15 h at the desired temperature. At the end of the reaction time, the autoclave was brought to room temperature, cooled further for 30 minutes using an ice-bath and then was slowly depressurized. After 30 minutes of thawing, the contents of the glass liner were transferred to a 10 mL volumetric flask (**A**) and the total volume was adjusted to 10 mL using dichloromethane (DCM).

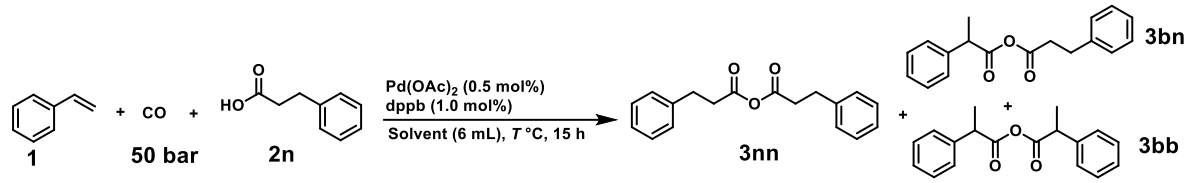
a. *GC Analysis*: 1 mL of the reaction mixture in flask **A** was transferred to a 10 mL volumetric flask (**B**), to which 0.3 mL undecane (internal standard for GC analysis) was added and was diluted up to 10 mL with DCM. The resulting solution was then analyzed using GC. The amount of styrene (**1**) present in the GC sample was determined using calibration lines with undecane as the internal standard. A 60 m × 0.250 mm ; 1.0 µm thickness DB-5MS GC column was used for analysis. 2.0 µL of each sample was injected and the following temperature program was used: injector at 350 °C, FID at 350 °C, oven at 40 °C for 3 min, increasing to 300 °C with 10 °C/min and hold at 300 °C for 10 min.
b. *UPLC Analysis*: 0.5 mL of the reaction mixture in flask **A** was transferred to a 10 mL volumetric flask (**C**) containing 20 mg benzamide (internal standard for UPLC analysis) and diluted up to 10 mL DCM. The resulting solution was then analyzed using UPLC. The amounts of phenylpropionic acid (**2**) and phenylpropionic anhydride (**3**) present in the reaction sample were determined using calibration lines with benzamide as the internal standard. The column used was an ACQUITY UPLC® BEH C18 1.7 µm, 2.1 × 50 mm column and the wavelength of the UV-Vis detector was set at 260 nm. An ACN/Milli-Q (MQ) water with 0.1% TFA gradient with a flow rate of 0.5 ml/min was used. The run was initiated with 98% solvent A (MQ water with 0.1% TFA) and 2% solvent B (ACN with 0.1% TFA) followed by a linear gradient to 100% solvent B in 5 min, staying at 100% B until 6 min and back to the initial 98% solvent A at 6.1 min. The total run time was 8.0 min. Injection volume was 2.0 µL.
c. *Derivatization Procedure*: In a capped microwave vial, 2.5 mL of the reaction mixture from flask **A** was added under N_2 to a cooled solution of pyrrolidine (0.5 mL; 6.1 mmol) and triethylamine (1.0 mL; 7.3 mmol) in DCM (1.0 mL). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h in an aluminium block.
d. *GC Analysis after derivatization*:1 mL of the derivatization reaction mixture was transferred to a 5 mL volumetric flask (**D**), 0.3 mL undecane (internal standard for GC analysis) was added and the volume was adjusted to 5 mL with DCM. The resulting solution was then analyzed using GC. The pyrrolidine-derivatized products (**4n** and **4b**) present in the GC sample were quantified using calibration lines with undecane as the internal standard. A 60 m × 0.250 mm ; 1.0 µm thickness DB-5MS GC column was used for analysis. 2.0 µL of each sample was injected and the following temperature program was used: injector at 350 °C, FID at 350 °C, oven at 40 °C for 3 min, increasing to 300 °C with 10 °C/min and hold at 300 °C for 10 min. The resulting yield of product was further calculated for the initial 10 mmol scale hydrocarbonylation reaction.

AI.4. Results: Optimization of reaction conditions

AI.4.1. Temperature and solvent screening

a. *Procedure same as GP*

Table AI.1. Temperature and solvent screening studies for anhydride synthesis from alkenes. See Scheme AI.1 for the derivatization reaction forming **4**.



Entry	Temperature (°C)	Solvent	Conversion %[a]	Total anhydride (3) Yield (%) [b]	Yield (4) (%) and regioselectivity (4n:4b) based on derivatization[a]
1	120	Toluene	90	Trace	0
2	120	DCE	90	Trace	0
3	105	Toluene	88	Trace	0
4	105	DCE	94	Trace	0
5	105	Diglyme	73	Trace	0
6	105	Anisole	82	Trace	0
7	85	Toluene	55	42	40 (90:10)
8	85	DCE	74	38	40 (95:5)
9	85	Diglyme	47	17	18 (>99:-)
10	85	Anisole	56	37	36 (92:8)
11	70	Toluene	30	26	26 (89:11)
12	70	DCE	63	65	62 (94:6)
13	70	Diglyme	12	0	0
14	70	Anisole	19	20	20 (>99:-)
15	55	DCE	21	23	25 (>99:-)
16	40	DCE	0	0	0

Reaction conditions: **1** (10.5 mmol), **2n** (10 mmol), $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), CO (50bar), *T* °C, Solvent (6 mL), 15 h. [a] Conversion% based on **1**, yield% (based on **2n**) and regioselectivity based on derivatization determined by GC using undecane as internal standard. [b] Total anhydride yield % (based on **2n**) determined by UPLC using benzamide as internal standard.

b. Mass Balance

Table AI.2. Mass Balance of the temperature and solvent screening studies for anhydride synthesis from alkenes.

Entry	Temperature (°C)	Solvent	1 (mmol) [a]	2 (mmol) [b]	3 (mmol)[b]	4 (mmol) / (4n:4b) [a]	Mass Balance %
1	120	Toluene	1.1	8.4	Trace	0	46
2	120	DCE	1.1	7.7	Trace	0	43
3	105	Toluene	1.3	10.5	Trace	0	58
4	105	DCE	0.6	10.7	Trace	0	55
5	105	Diglyme	2.8	9.7	Trace	0	61
6	105	Anisole	1.9	9.3	Trace	0	55
7	85	Toluene	4.7	5.5	4.2	4.0 (90:10)	91
8	85	DCE	2.7	7.3	3.8	4.0 (95:5)	86
9	85	Diglyme	5.6	8.4	1.7	1.8 (>99:-)	85
10	85	Anisole	4.6	6.9	3.7	3.6 (92:8)	92

11	70	Toluene	7.3	7.8	2.6	2.6 (89:11)	99
12	70	DCE	3.9	3.7	6.5	6.2 (94:6)	101
13	70	Diglyme	9.2	10.2	0	0	95
14	70	Anisole	8.5	8.1	2.0	2.0 (>99:-)	100
15	55	DCE	8.3	8.1	2.3	2.5 (>99:-)	102
16	40	DCE	10.4	9.9	0	0	99

[a] Determined by GC using undecane as internal standard. [b] Determined by UPLC using benzamide as internal standard. Total number of phenyls at the start of the reaction: **1** (1.2 mL = 10.5 mmol) + **2** (1.50 g = 10.0 mmol) = 20.5 mmol.

c. CO pressure drop graphs

Time for the reaction temperature to reach 70 °C is 1.5 h. The reaction time is 15 h (1.5 to 16.5 h).

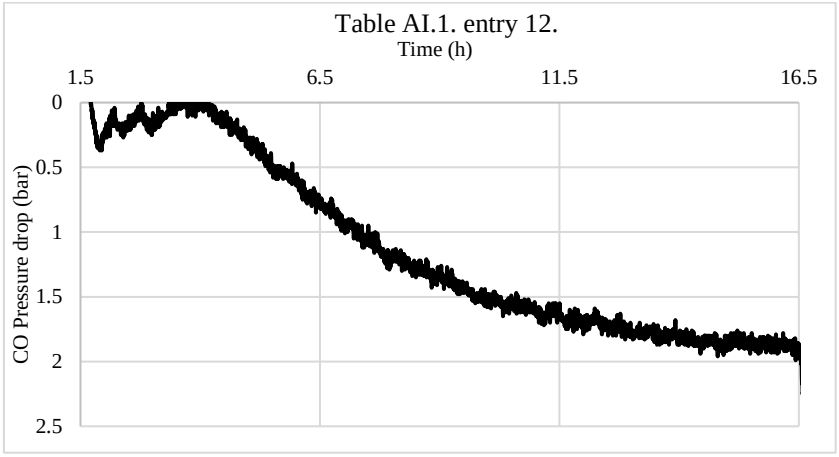
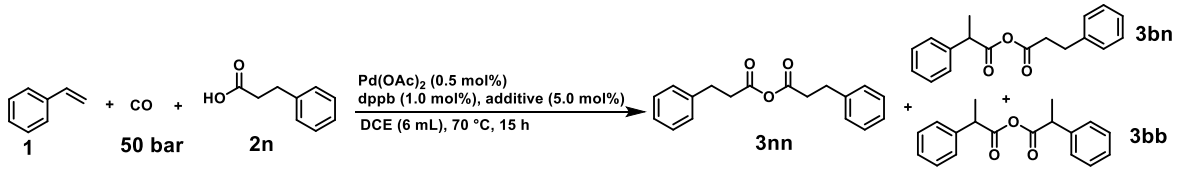


Figure AI.1. CO pressure drop for the reaction in Table AI.1. entry 12.

AI.4.2. Additive screening

a. *GP followed with a deviation*: additive (0.5 mmol) weighed in air and added along with $Pd(OAc)_2$, dppb and **2n**.

Table AI.3. Additive screening studies for anhydride synthesis from alkenes.



Entry	Additive	Total anhydride (3) Yield %[a]
1	None	65
2	$HOTs.H_2O$	0
3	Camphorsulfonic acid	0
4	2,4,6-trimethylbenzoic acid	49[b]
5	LiCl	0
6	LiOAc	60

Reaction conditions: **1** (10.5 mmol), **2n** (10 mmol), $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), additive (0.5 mmol), CO (50bar), 70 °C, DCE (6 mL), 15 h. [a] Total anhydride yield % determined by UPLC using benzamide as internal standard. [b] Additional peak of mixed anhydride observed.

b. Mass Balance

Table AI.4. Additive screening studies for anhydride synthesis from alkenes.

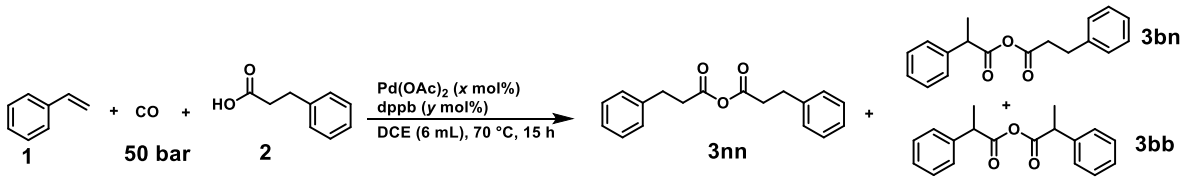
Entry	Additive	1 (mmol)[a]	2 (mmol)[b]	3 (mmol)[b]	Mass Balance %
1	None	3.9	3.7	6.5	101
2	$HOTs.H_2O$	3.7	8.7	0	61
3	Camphorsulfonic acid	5.1	9.2	0	70
4	2,4,6-trimethylbenzoic acid	2.8	5.7	4.9[c]	89
5	LiCl	9.0	10.6	0	96
6	LiOAc	3.3	5.2	6.0	100

[a] Determined by GC using undecane as internal standard. [b] Determined by UPLC using benzamide as internal standard. [c] Additional peak of mixed anhydride observed. Total number of phenyls at the start of the reaction: **1** (1.2 mL = 10.5 mmol) + **2** (1.50 g = 10.0 mmol) = 20.5 mmol.

AI.4.3. Effect of increased catalyst concentration

a. GP followed with a deviation: $Pd(OAc)_2$ (22.4 mg instead of 11.2 mg), dppb (85.4 mg instead of 42.7 mg).

Table AI.5. Catalyst loading studies for anhydride synthesis from alkenes.



Entry	Pd / L (mol%)	Total Anhydride (3) Yield %[a]	Yield % and regioselectivity (4n:4b) based on derivatization[b]
1	0.5 / 1.0	65	62 (94:6)
2	1.0 / 2.0	67	65 (94:6)

Reaction conditions: **1** (10.5 mmol), **2n** (10 mmol), $Pd(OAc)_2$ (0.05 / 0.10 mmol), dppb (0.1 / 0.2 mmol, CO (50bar), 70 °C, DCE (6 mL), 15 h. [a] Total anhydride yield % determined by UPLC using benzamide as internal standard. [b] Yield% and regioselectivity based on derivatization determined by GC using undecane as internal standard.

b. Mass balance

Table AI.6. Catalyst loading studies for anhydride synthesis from alkenes.

Entry	Pd / L (mol%)	1 (mmol) [a]	2 (mmol) [b]	3 (mmol)[b]	4 (mmol) / (4n:4b) [a]	Mass Balance %
1	0.5 / 1.0	3.9	3.7	6.5	6.2 (94:6)	101
2	1.0 / 2.0	4.0	3.6	6.7	6.5 (94:6)	102

[a] Determined by GC using undecane as internal standard. [b] Determined by UPLC using benzamide as internal standard. Total number of phenyls at the start of the reaction: 1 (1.2 mL = 10.5 mmol) + 2 (1.50 g = 10.0 mmol) = 20.5 mmol.

c. CO pressure drop graphs

Time for the reaction temperature to reach 70 °C is 1.5 h. The reaction time is 15 h (1.5 to 16.5 h)

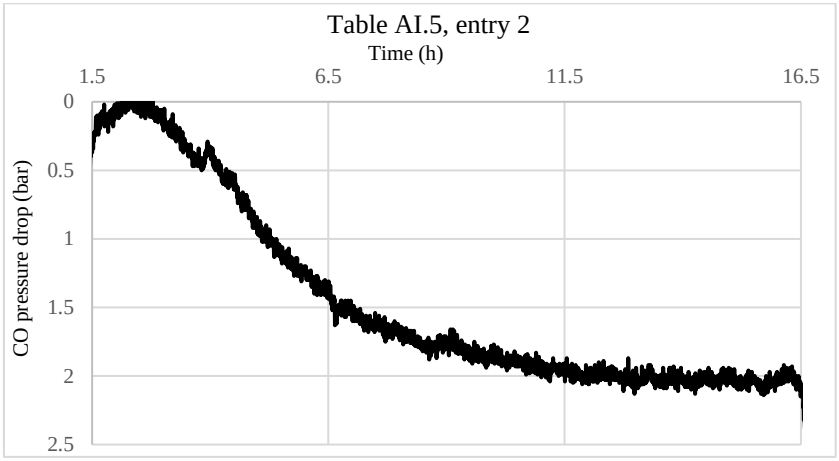


Figure AI.2. Doubling the catalyst loading (Table AI.5, entry 2) shows a quicker rate in CO consumption indicating faster reaction but the consumption of CO reaches stagnancy and no further reaction occurs.

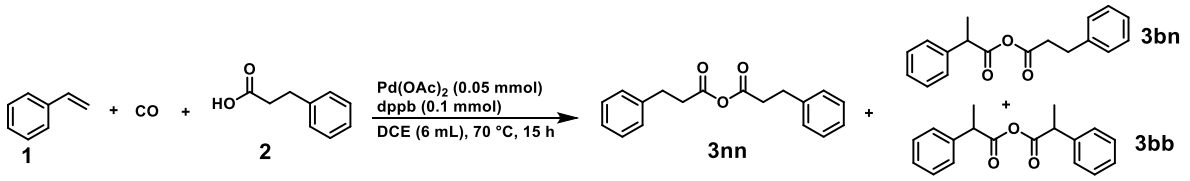
AI.4.4. Effect of substrate concentration and CO pressure

a. GP followed with a deviation in cases where equivalents of the substrates were changed:

1:2n	1	2n
10:20	1.2 mL (10.5 mmol)	3.0 g (20.0 mmol)
20:10	2.3 mL (20.2 mmol)	1.5 g (10.0 mmol)

b. 65 bar used instead of 50 bar CO wherever mentioned

Table AI.7. Varying substrate ratio for anhydride synthesis from alkenes.



Entry	CO pressure (bar)	1 : 2n (mmol)	Conversion% w.r.t 1[a]	Conversion% w.r.t 2n[b]	Total Anhydride (3) Yield %[c] (3nn:3bn)[d]	Yield % and regioselectivity (4n:4b) based on derivatization (4)[e]
1	50	10 : 10	63	63	65 (79:21)	62 (94:6)
2	50	20 : 10	50	82	95 (74:26)	95 (92:8)
3	50	10 : 20	69	38	74 (83:17)	74 (95:5)
4	50	10 : 30	71	29	74 (89:11)	75 (96:4)
5	35	20 : 10	60	66	81	76 (92:8)
6	35	10 : 20	65	27	58	60 (>99:1)
7	65	10 : 10	70	69	75 (77:23)	75 (93:7)
8	65	20 : 10	52	80	97 (74:26)	96 (93:7)
9	65	10 : 20	74	38	74 (85:15)	76 (96:4)
10	65	10 : 50	71	12	66 (89:11)	69 (96:4)

Reaction conditions: $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), 70 °C, DCE (6 mL), 15 h. [a] Conversion% w.r.t **1** determined by GC using undecane as internal standard. [b] Conversion% w.r.t **2n** determined by UPLC using benzamide as internal standard (**2b** formation was calculated to be 1 to 3% in entries 1, 2, 7, 8 and 6 to 8% in entries 3, 4, 9, 10 as per NMR analysis; to calculate conversion of **2n**, we considered concentration of **2** derived from UPLC data equal to **2n** since **2b** formation is minimal). [c] Total anhydride yield (%, based on the limiting reagent) determined by UPLC using benzamide as internal standard. [d] **3nn**:**3bn** determined by NMR, **3bb** found in trace amounts in all cases. [e] Yield (%, based on the limiting reagent) and regioselectivity based on derivatization determined by GC using undecane as internal standard.

c. Mass Balance:

Table AI.8. Varying substrate ratio for anhydride synthesis from alkenes.

Entry	CO pressure (bar)	1 : 2n (mmol)	Total exact no. of phenyls	1 (mmol)[a]	2 (mmol)[b]	3 (mmol)[b]	4 (mmol) (4n:4b)[a]	Mass Balance %
1	50	10 : 10	20.5	3.9	3.7	6.5	6.2 (94:6)	101
2	50	20 : 10	30.2	10.2	1.8	9.5	9.5 (92:8)	103
3	50	10 : 20	30.5	3.3	12.5	7.8	7.8 (95:5)	103
4	50	10 : 30	40.5	3.1	21.3	7.8	7.9 (96:4)	99
5	35	20 : 10	30.2	8.0	3.4	8.1	7.6 (92:8)	91
6	35	10 : 20	30.5	3.7	14.6	6.1	6.3 (>99:1)	100
7	65	10 : 10	20.5	3.2	3.1	7.5	7.5 (93:7)	104
8	65	20 : 10	30.2	9.7	2.0	9.7	9.6 (93:7)	103
9	65	10 : 20	30.5	2.7	12.5	7.8	8.0 (96:4)	101
10	65	10 : 50	60.5	3.0	44.0	6.9	7.2 (96:4)	101

[a] Determined by GC using undecane as internal standard. [b] Determined by UPLC using benzamide as internal standard.

d. CO pressure drop graphs

Time for the reaction temperature to reach 70 °C is 1.5 h. The reaction time is 15 h (1.5 to 16.5 h).

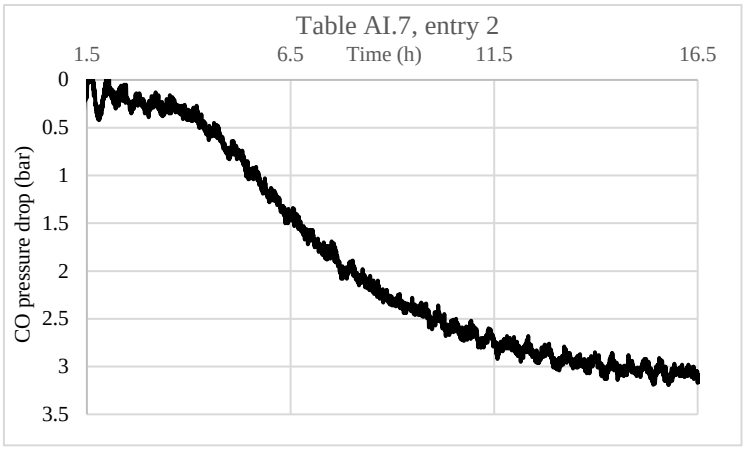


Figure AI.3. Relative CO pressure drop of Table AI.7, entry 2 when **1**:**2n** at 20:10 mmol at 50 bar CO pressure.

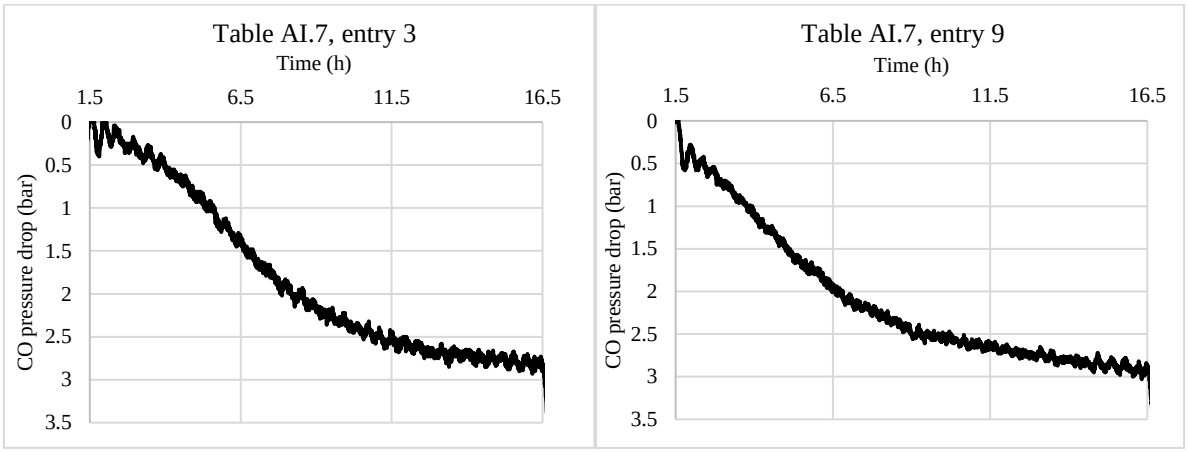


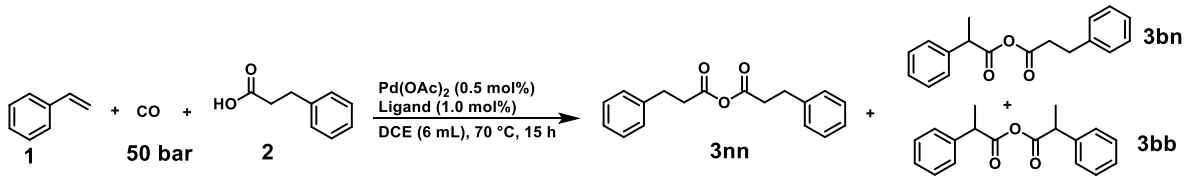
Figure AI.4. Relative CO pressure drop when **1:2n** at 10:20 mmol at 50 (left graph, Table AI.7, entry 3) and 65 bar (right graph, Table AI.7, entry 9) CO pressure.

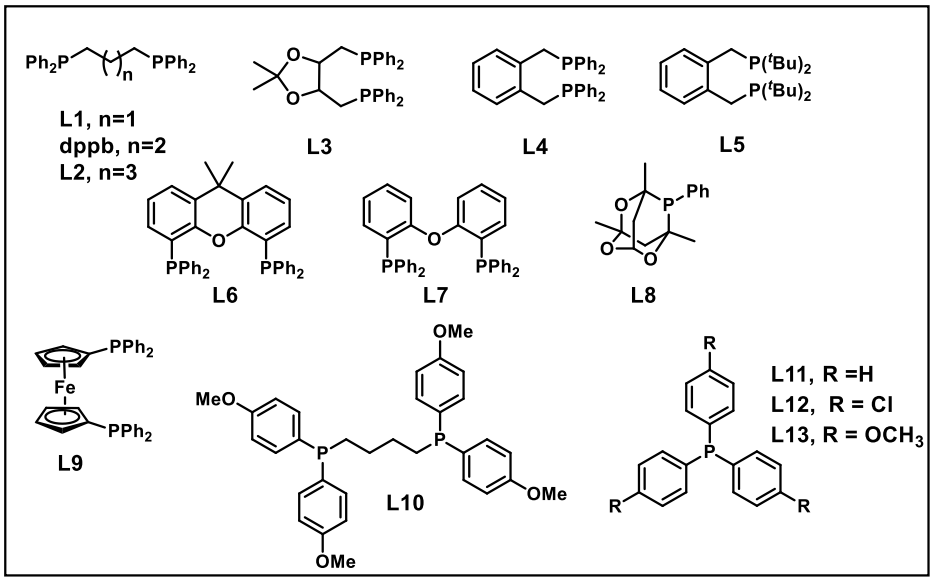
AI.4.5. Influence of ligands

a. GP followed with a deviation: Diphosphine (0.05 mmol) or monophosphine ligand (0.20 mmol) was weighed in air if air stable. Otherwise, air-sensitive ligands along with palladium acetate were weighed in a Schlenk flask in the glovebox and dissolved with DCE (6.0 mL).

b. Mass balance

Table AI.9. Influence of ligands on synthesis of anhydrides from alkenes.



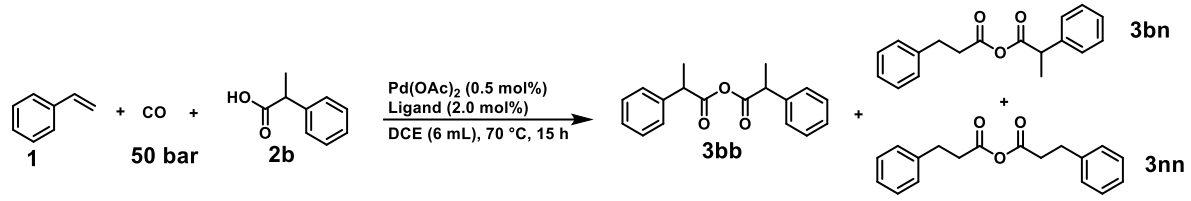


Entry	1 (mmol)[a]	2 (mmol)[b]	3 (mmol)[b]	4 (mmol) / (4n:4b)[a]	M.B. %	NMR Yield % (3)[c]			Total NMR Yield %	3nn: 3bn: 3bb
						3nn	3bn	3bb		
dppb	10.2	1.8	9.5	9.5 (92:8)	103	68	24	Trace	92	74:26: -
L1	9.6	6.2	4.0	4.0 (>99:-)	79	37	0	Trace	37	>99:-:-
L2	13.0	5.6	5.8	5.9 (93:7)	100	43	15	Trace	58	74:26: -
L3	9.5	2.1	9.1	9.2 (91:9)	99	60	29	Trace	89	67:33: -
L4[d]	13.0	8.0	3.2	3.3 (>99:1)	91	31	0	0	31	>99:-:-
L4[d][e]	6.5	7.5	2.8	2.8 (>99:1)	65	32	0	0	32	>99:-:-
L5[d]	16.5	10.5	0	0	89	0	0	0	0	-
L6	15.7	7.6	3.2	3.2 (>99:-)	99	31	0	0	31	>99:-:-
L6[e]	11.7	3.6	7.8	7.9 (94:6)	102	61	15	Trace	76	80:20: -
L7	11.3	4.1	7.0	7.1 (95:5)	97	56	12	Trace	68	82:18: -
L8	14.7	2.4[c]	6.2[c]	6.2 (80:20)	98	26	27	9	62	42:44: 14
L9	12.7	5.8	6.1	6.0 (93:7)	102	44	15	Trace	59	75:15: -
L10	9.1	4.1	6.4	6.9 (94:6)	86					

[a] Determined by GC using undecane as internal standard. [b] Determined by UPLC using benzamide as internal standard. [c] Determined by NMR analysis using dibromomethane as internal standard. [d] 0.075 mmol of ligand used instead of 0.10 mmol. [e] reaction temperature = 85 °C instead of 70 °C. Total number of phenyls at the start of the reaction: 1 (2.3 mL = 20.2 mmol) + 2 (1.5 g = 10.0 mmol) = 30.2 mmol. Abbreviation: M.B: Mass balance.

AI.4.6. Attempts to test influence of ligands on branched selectivity

Table AI.10. Influence of ligands on branched selectivity for synthesis of **3bb**.



Entry	3bb Yield%	Yield % and regioselectivity (4n:4b) based on derivatization (4)[a]
L11	-did not determine-	51 (18:82)
L12	-did not determine-	34 (12:88)
L13	-did not determine-	60 (23:76)
L8[b]	65[c]	65 (-:>99)

Reaction conditions: **1** (20.2 mmol), **2b** (10 mmol), $Pd(OAc)_2$ (0.05 mmol), **L** (0.20 mmol), CO (50bar), 70 °C, DCE (6 mL), 15 h. [a] Yield (%, based on the limiting substrate, **2b**) and regioselectivity based on derivatization determined by GC using undecane as internal standard. [b] reaction time = 20 h instead of 15 h. [c] **3bb** yield (%, based on the limiting substrate, **2b**) determined by NMR using dibromomethane as internal standard; **3nn** was not found, **3bn** was found in trace.

Table AI. 11. Mass Balance of catalytic reaction with **L8**.

Entry	1 (mmol) [a]	2b (mmol) [b]	3bb (mmol)[b][c]	4 (mmol) (4n:4b) [a]	Mass Balance %
L8[d]	14.0	4.3	6.5	6.5 (-:>99)	103

[a] Determined by GC using undecane as internal standard. [b] determined by NMR using dibromomethane as internal standard. [c] **3nn** was not found, **3bn** was found in trace. [d] reaction time= 20 h instead of 15 h.

AI.4.7. Derivatization of mixed anhydride and validation of UPLC and GC results with NMR data

a. Synthesis and derivatization of mixed anhydride: In a capped microwave vial with a stir bar, 5.0 mL $CDCl_3$ was charged to which 2-phenyl propionic acid (696 µL; 5.0 mmol) and triethylamine (732 µL; 5.5 mmol) were added. The mixture was cooled in an ice-bath and to it, 3-phenylpropionyl chloride (740 µL; 5.0 mmol) was added dropwise. After addition, the reaction mixture was stirred at room temperature overnight. 2.5 mL of the reaction mixture was added to a cooled solution of pyrrolidine (0.5 mL; 6.1 mmol) and triethylamine (1.0 mL; 7.3 mmol) in DCM (1.0 mL) under N_2. The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h. On GC analysis of the derivatization performed as described in GP, the selectivity of **4n**:**4b** was found to be 69:31.

b. Calculation applied to catalytic reaction mixtures:

Estimated **4n** selectivity: $\frac{\boldsymbol{3nn}+(0.69\times\boldsymbol{3bn})}{\boldsymbol{3nn}+\boldsymbol{3bn}}\times 100$

Estimated **4b** selectivity: $\frac{0.31\times\boldsymbol{3bn}}{\boldsymbol{3nn}+\boldsymbol{3bn}}\times 100$

Similarly, from the derivatization data, the composition of the catalytic mixture (**3nn**:**3bn**) can be estimated.

Table AI.12. Selectivity analysis based on NMR and GC data

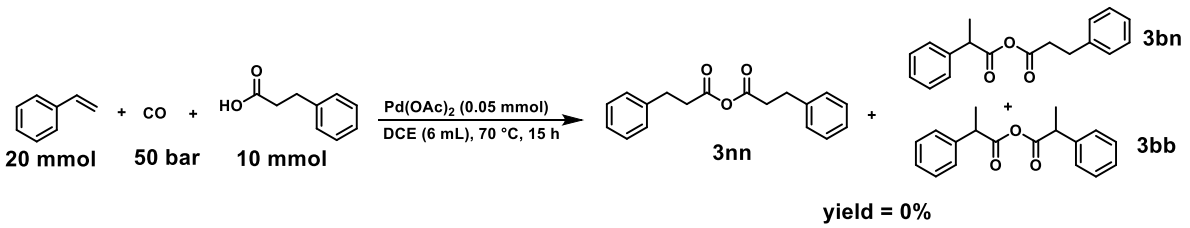
Condition	UPLC Yield%[a]	NMR Yield%[b]			3nn:3bn	Predicted selectivity on derivatization		Determined selectivity on derivatization (4n:4b)[c]
		3nn	3bn	3bb		4n	4b	
dppb	95	68	24	0	74:26	92	8	92:8
L1	40	37	0	0	>99:-	>99	-	>99:-
L2	58	43	15	0	74:26	92	8	93:7
L3	91	60	29	0	67:33	90	10	91:9
L4[d]	32	31	0	0	>99:-	>99	-	>99:-
L6[e]	78	61	15	0	80:20	94	6	94:6
L7	70	56	12	0	82:18	95	5	95:5
L9	61	44	15	0	75:25	92	8	93:7

Reaction conditions: **1** (20.2 mmol), **2n** (10 mmol), $Pd(OAc)_2$ (0.05 mmol), **L** (0.10 mmol), CO (50bar), 70 °C, DCE (6 mL), 15 h. [a] UPLC yield (%, based on **2n**) determined using benzamide as internal standard. [b] NMR yield (%, based on **2n**) determined using dibromomethane as internal standard; **3bb** found in trace amounts in all cases. [c] **4n**:**4b** based on derivatization determined by GC using undecane as internal standard. [d]] 0.075 mmol of ligand used instead of 0.10 mmol. [e] reaction temperature at 85 °C instead of 70 °C.

AI.4.8. Other control experiments and reaction considerations

AI.4.8.1. Without dppb

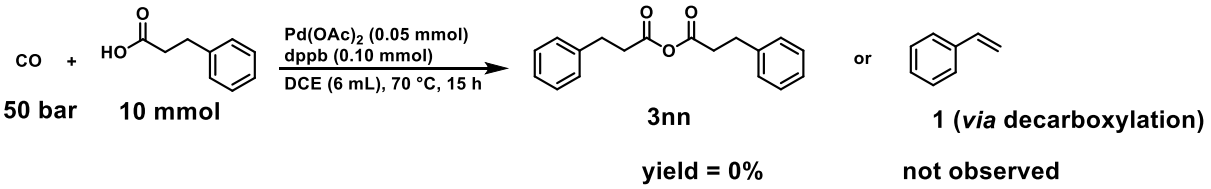
Palladium acetate (11.2 mg) and 3-phenylpropionic acid (**2n**, 1.50 g) were weighed in a clean and dried glass liner containing an oven-dried stirring bar in open air. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to the Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed and dried solvent DCE (6.0 mL, was added using standard Schlenk techniques and the mixture was stirred for one hour. After one hour, the required volume of degassed and dried styrene (**1**, 1.2 mL) was added using standard Schlenk procedures and the autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to the HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (30 bar × 3). The autoclave was flushed with CO (30 bar × 1) and then, charged with CO to 50 bar. The autoclave was stirred at 350 rpm and heated for 15 h at 70 °C. At the end of the reaction, the autoclave was cooled using an ice-bath for 30 minutes and depressurized slowly. After 30 minutes of thawing, the reaction mixture is transferred to a 10 mL volumetric flask and adjusted to 10 mL using dichloromethane (DCM). The anhydride yield was determined by UPLC.



Scheme AI.2. Control reaction in absence of ligand

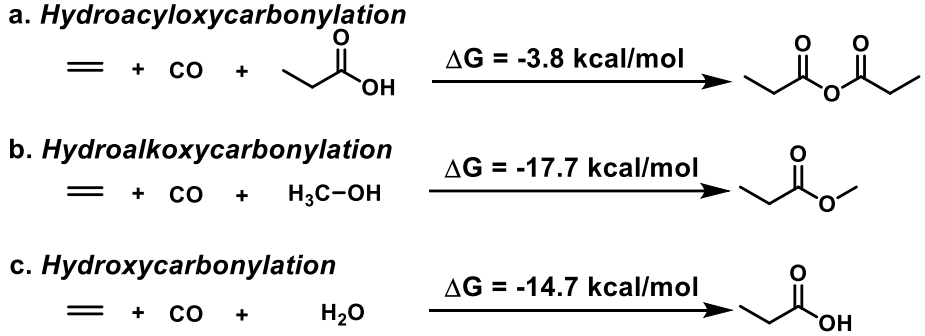
AI.4.8.2. Control reaction in absence of styrene; 2n in catalytic conditions

Palladium acetate (11.2 mg), dppb (42.7 mg) and 3-phenylpropionic acid (**2n**, 1.50 g) were weighed in a clean and dried glass liner containing an oven-dried stirring bar in open air. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to the Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed and dried solvent DCE (6.0 mL, was added using standard Schlenk techniques. The autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to the HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (30 bar × 3). The autoclave was flushed with CO (30 bar × 1) and then, charged with CO to 50 bar. The autoclave was stirred at 350 rpm and heated for 15 h at 70 °C. At the end of the reaction, the autoclave was cooled using an ice-bath for 30 minutes and depressurized slowly. After 30 minutes of thawing, the reaction mixture is transferred to a 10 mL volumetric flask and adjusted to 10 mL using dichloromethane (DCM). The anhydride yield was determined by UPLC. Presence of styrene was determined by GC.

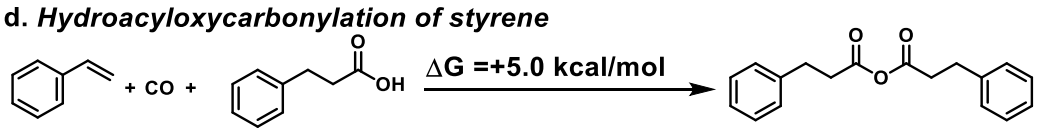


Scheme AI.3. Control reaction in absence of styrene.

AI.4.8.3. Computational calculation of Gibbs Free Energy (Δ*G*) of hydrocarbonylation reactions in gas-phase



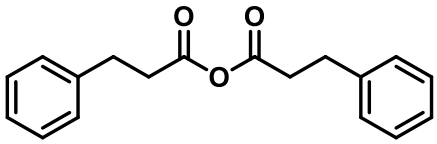
Scheme AI.4. Gibbs Free Energy (Δ*G*) in gas phase for hydrocarbonylation reactions of ethene: hydroacyloxycarbonylation, hydroalkoxycarbonylation, hydrocarboxylation.



Scheme AI.5. Gibbs Free Energy (Δ*G*) in gas phase for hydroacyloxycarbonylation reactions of styrene (**1**) with **2n**. The calculated $\Delta G_{\text{gas-phase}}$ shows the reaction to be endergonic but we do observe the reaction occurring, thus indicating a limitation in computational calculations.

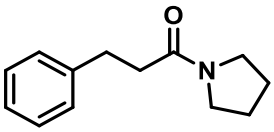
Computational details: Amsterdam Density Functional (ADF 2019.104), XC: GGA BLYP- Dispersion Grimme 3 BJDAMP, Basis set: TZ2P, Core: small

AI.5. Synthesis of standards and substrates



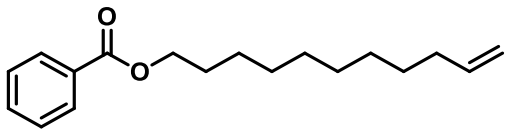
3-phenylpropionic anhydride

N,N'-Dicyclohexylcarbodiimide, DCC (2.8 g; 13.3 mmol) was dissolved in DCM (20 mL). The solution was cooled in an ice-bath and 3-phenylpropionic acid (4.0 g; 26.6 mol) was added. The solution was stirred at r.t. overnight. The reaction mixture was filtered, washed with half-saturated solution of Na_2CO_3 (2 x 10 mL) followed by water (10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed *in vacuo* to obtain a colourless oil (waxy solid at -20 °C), 2.4 g, 64% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.32-7.27 (m, 4H), 7.23 - 7.18 (m, 6H), 2.95 (t, *J* = 7.7 Hz, 4H), 2.74 (t, *J* = 7.8 Hz, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.51, 139.56, 128.63, 128.30, 126.55, 36.82, 30.17. The NMR spectra are in agreement with literature.[1]



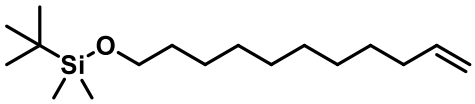
3-phenyl-1-pyrrolidin-1-yl-propane-1-one

To a cooled solution of pyrrolidine (0.5 mL, 6.0 mmol) and triethylamine (1.4 mL,10.0 mmol), 3-phenylpropionyl chloride (5.0 mmol) was added dropwise. The reaction mixture was stirred at r.t. overnight. The reaction mixture was quenched with water (2.0 mL), filtered, washed with 1N HCl (2 x 5 mL) followed by water (5 mL) and brine (5 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed *in vacuo*. The concentrate was purified by silica gel column chromatography using ethyl acetate/pentane (0 to 50%) to afford the corresponding pure product, as a yellow oil, 820 mg, 81% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.30 – 7.17 (m, 5H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.29 (t, *J* = 6.6 Hz, 2H), 3.01 – 2.97 (m, 2H), 2.58 – 2.54 (m, 2H), 1.93 – 1.78 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.80, 141.62, 128.52, 128.50, 126.13, 46.61, 45.70, 36.85, 31.27, 26.13, 24.45. The NMR spectra are in agreement with literature.[2]



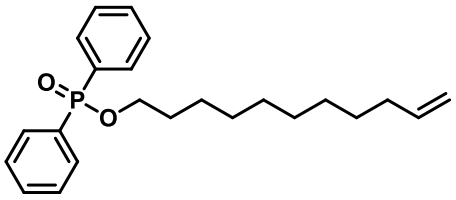
Undec-10-en-1-yl benzoate

To a solution of 10-undecen-1-ol (8.0 mL; 40 mmol), 4-dimethylaminopyridine (DMAP) (0.5 g, 4.0 mmol), and triethylamine (8.3 mL; 60 mmol) in anhydrous DCM, benzoyl chloride (5.8 mL; 50 mmol) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 30 min, and then at room temperature overnight. The reaction was quenched with water and extracted with DCM. The organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using ethyl acetate/pentane (0 to 20%) to afford the corresponding pure product, as a colourless oil, 9.9 g, 91% yield. The NMR spectra are in agreement with literature.[3] **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.06 – 8.04 (m, 2H), 7.57 – 7.54 (m, 1H), 7.46 – 7.42 (m, 2H), 5.81 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.04 - 4.89 (m, 2H), 4.31 (t, *J* = 6.7 Hz, 2H), 2.06 – 2.01 (m, 2H), 1.80 – 1.73 (m, 2H), 1.48 – 1.29 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 166.77, 139.28, 132.85, 130.59, 129.59, 128.38, 114.19, 65.20, 33.86, 29.53, 29.46, 29.32, 29.16, 28.98, 28.78, 26.10.



tert-Butyldimethyl-(undec-10-en-1-yloxy)-silane

To a solution of 10-undecen-1-ol (10.0 mL; 50 mmol), 4-dimethylaminopyridine (DMAP) (0.6 g, 5.0 mmol), and triethylamine (10.4 mL; 75 mmol) in anhydrous DCM, *tert*-butyldimethylsilyl trifluoromethanesulfonate (14.4 mL; 62.5 mmol) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 30 min, and then at room temperature overnight. The reaction was quenched with water and extracted with DCM. The organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using pentane to afford the corresponding pure product, as a colourless oil, 13.2 g, 93% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 5.84 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.05 – 4.94 (m, 2H), 3.62 (t, *J* = 6.6 Hz, 2H), 2.09 – 2.04 (m, 2H), 1.55 – 1.52 (m, 2H), 1.42 – 1.38 (m, 2H), 1.31 (s, 10H), 0.92 (s, 9H), 0.08 (s, 6H). **^{13}C NMR** (101 MHz, CDCl3) δ: 139.33, 114.15, 63.41, 33.88, 32.94, 29.64, 29.50, 29.49, 29.19, 29.00, 26.05, 25.85, 18.45, -5.19. **HRMS**: $[M + H]^+$ calculated for $C_{17}H_{37}O_1Si_1^+$ 285.2608; Found 285.2611



Undec-10-en-1-yl diphenylphosphinate

To a solution of 10-undecen-1-ol (10.0 mL; 50 mmol), 4-dimethylaminopyridine (DMAP) (0.6 g, 5.0 mmol), and triethylamine (10.4 mL; 75 mmol) in anhydrous DCM, diphenylphosphinic chloride (11.9 mL; 62.5 mmol) was added dropwise at 0 °C. The resulting mixture was stirred at 0 °C for 30 min, and then at room temperature overnight. The reaction was quenched with water and extracted with DCM. The organic layer was dried with Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography using ethyl acetate/pentane (0 to 50%) to afford the corresponding pure product, as a colourless oil, 16.5 g, 89% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.84 – 7.79 (m, 4H), 7.54 – 7.49 (m, 2H), 7.47 – 7.42 (m, 4H), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.02 - 4.91 (m, 2H), 4.04 – 3.99 (m, 2H), 2.06 – 2.01 (m, 2H), 1.75 – 1.68 (m, 2H), 1.40 – 1.26 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 139.27, 132.45, 132.14, 132.11, 131.75, 131.65, 131.08, 128.63, 128.49, 114.20, 65.10, 65.04, 33.86, 30.63, 30.57,29.48,29.43, 29.18, 29.14, 28.96, 25.66. **^{31}P NMR** (162 MHz, $CDCl_3$) δ: 31.70. **HRMS**: $[M + H]^+$ calculated for $C_{23}H_{32}O_2P_1^+$ 371.2134; Found 371.2131.

AI.6. General procedure for substrate scope and applications

Palladium acetate (0.5 mol%), 1,4-diphenylphosphinobutane (dppb, 0.1 mol%) and carboxylic acid (if solid) were weighed in a clean and dried glass liner containing an oven-dried stirring bar in open air. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to the Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed and dried DCE (6.0 mL) and/or required volume of degassed liquid carboxylic acid was charged by standard Schlenk techniques and the mixture was stirred for one hour. After one hour, the required volume of degassed and dried alkene was added using standard Schlenk procedures and the autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to the HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with

N_2 (30 bar × 3). The autoclave was flushed with CO (30 bar × 1) and then, charged with CO to the 50 bar. The autoclave was stirred at 350 rpm and heated for a specified time at reaction temperature of 70 °C. At the end of the reaction, the autoclave was cooled using an ice-bath for 30 minutes and depressurized slowly. After 30 minutes of thawing, the reaction mixture is transferred to a 10 mL volumetric flask and adjusted to 10 mL using dichloromethane (DCM). The reaction mixture was subjected to one of the derivatization procedures as described below and the corresponding derivatized (linear) product was isolated. The scale and yield% mentioned are with respect to the carboxylic acid substrate.

a. Derivatization with pyrrolidine: To a cooled solution of pyrrolidine (0.5 mL; 6.1 mmol) and triethylamine (1.0 mL; 7.3 mmol) in DCM (1.0 mL), 2.5 mL reaction mixture was charged under N_2. The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (20 to 50%).

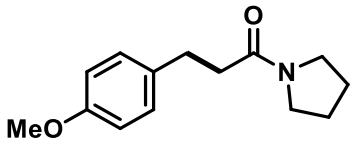
b. Derivatization with aniline: To a cooled solution of aniline (0.5 mL; 5.5 mmol), 4-dimethylaminopyridine, DMAP (3 mg) and triethylamine (1.0 mL; 7.3 mmol) in DCM (0.5 mL), 2.5 mL reaction mixture was charged under N_2. The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 50 °C for 15 h. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 20%).

c. Derivatization with benzyl alcohol: To a cooled solution of benzyl alcohol (0.5 mL; 4.63 mmol), 4-dimethylaminopyridine, DMAP (3 mg) and triethylamine (1.0 mL; 7.3 mmol) in DCM (0.5 mL), 2.5 mL reaction mixture was charged under N_2. The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 50 °C for 15 h. The reaction mixture was subjected to column chromatography using diethyl ether/pentane mixture (50%).

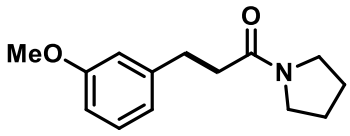
d. Derivatization with ammonia: To a cooled solution of 2.5 mL reaction mixture was added 7 N ammonia in methanol (0.1 mL; 11.9 mmol). The reaction mixture was left to thaw to room temperature overnight (15 h). The reaction mixture was subjected to column chromatography using methanol/DCM (2.5 to 10%).

e. Derivatization with benzyl mercaptan: Catalytic reaction mixture (2.5 mL) was added under N_2 to a cooled solution of benzyl mercaptan (0.3 mL; 2.75 mmol) and triethylamine (0.4 mL; 3.0 mmol) in DCM (0.5 mL),. The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h. The reaction mixture was subjected to column chromatography using diethyl ether/pentane mixture (0 to 1%).

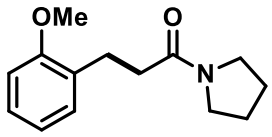
AI.7. Experimental data characterization of products (substrate scope and applications)



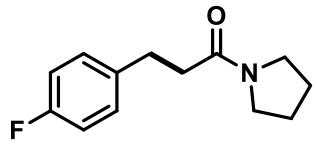
Followed procedure **AI.6a**. Colourless oil, 517 mg, 89% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.15 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H), 3.46 (t, J = 6.7 Hz, 2H), 3.29 (t, J = 6.6 Hz, 2H), 2.95 – 2.91 (m, 2H), 2.55 – 2.51 (m, 2H), 1.90 – 1.80 (m , 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.91, 157.99, 133.67, 129.45, 113.88, 55.33, 46.62, 45.68, 37.11, 30.37, 26.14. NMR spectra are in agreement with the literature.[4]



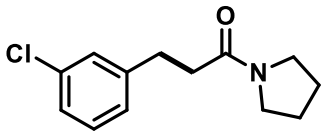
Followed procedure **AI.6a**. Yellow oil, 441 mg, 76% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.20 (t, J = 7.8 Hz, 1H), 6.83 – 6.73 (m, 3H), 3.79 (s, 3H), 3.47 (t, J = 6.8 Hz, 2H), 3.30 (t, J = 6.6 Hz, 2H), 2.98 – 2.94 (m, 2H), 2.58 – 2.54 (m, 2H), 1.93 – 1.79 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.78, 159.72, 143.27, 129.48, 120.86, 114.20, 111.45, 55.23, 46.62, 45.73, 36.76, 31.32, 24.46. **HRMS**: $[M + H]^+$ calculated for $C_{14}H_{20}NO_2^+$ 234.1489; Found 234.1488.



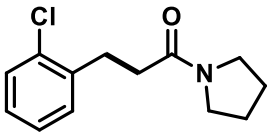
Followed procedure **AI.6a**. Pale yellow solid, 544 mg, 93% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 7.18 (m, 2H), 6.90 – 6.83 (m, 2H), 3.83 (s, 3H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.33 (t, *J* = 6.6 Hz, 2H), 2.99 – 2.95 (m, 2H), 2.55 – 2.51 (m, 2H), 1.92 – 1.79 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.46, 157.54, 130.27, 129.83, 127.47, 120.55, 110.22, 55.27, 46.56, 45.63, 35.14, 26.40, 26.17, 24.49. **HRMS**: $[M + H]^+$ calculated for $C_{14}H_{20}NO_2^+$ 234.1489; Found 234.1488.



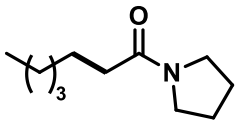
Followed procedure **AI.6a**. Pale yellow solid, 522 mg, 94% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.20 - 7.17 (m, 5.4 Hz, 2H), 6.99 – 6.94 (m, 2H), 3.46 (t, *J* = 6.8 Hz, 2H), 3.30 (t, *J* = 6.7 Hz, 2H), 2.98 – 2.94 (m, 2H), 2.55 – 2.52 (m, 2H), 1.91 – 1.81 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.53, 162.60, 160.18, 137.20, 137.17, 129.92, 129.84, 115.26, 115.05, 46.57, 45.67, 36.76, 30.32, 26.08, 24.40. **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -117.64. **HRMS**: $[M + H]^+$ calculated for $C_{13}H_{17}FNO^+$ 222.1289; Found 222.1288.



Followed procedure **AI.6a**. colourless oil, 447 mg, 75% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.23 – 7.16 (m, 3H), 7.13 – 7.10 (m, 1H), 3.47 (t, *J* = 6.8 Hz, 2H), 3.31 (t, *J* = 6.7 Hz, 2H), 2.99 – 2.95 (m, 2H), 2.57 – 2.53 (m, 2H), 1.94 – 1.80 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.33, 143.68, 134.17, 129.75, 128.61, 126.83, 126.32, 46.63, 45.76, 36.38, 30.82, 26.13, 24.45. **HRMS**: $[M + H]^+$ calculated for $C_{13}H_{17}ClNO^+$ 238.0993; Found 238.0991.

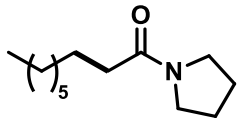


Followed procedure **AI.6a**. yellow oil, 366 mg, 62% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.35 – 7.29 (m, 2H), 7.21 – 7.13 (m, 2H), 3.46 (t, *J* = 6.8 Hz, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 3.12 – 3.08 (m, 2H), 2.60 – 2.56 (m, 2H), 1.93 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.56, 139.08, 133.94, 131.01, 129.49, 127.73, 126.98, 46.61, 45.72, 34.72, 29.37, 26.13, 24.45. HRMS: $[M + H]^+$ calculated for $C_{13}H_{17}ClNO^+$ 238.0993; Found 238.0993.

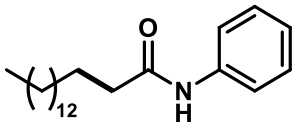


Followed procedure **AI.6a**. colourless oil, 424 mg, 92% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.46 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.9 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 – 1.91 (m, 2H), 1.88 – 1.81 (m, 2H), 1.68 – 1.61 (m, 2H),

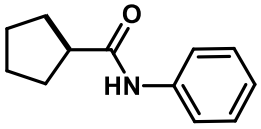
1.37 – 1.25 (m, 6H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.94, 46.67, 45.62, 34.93, 31.72, 29.28, 26.19, 24.98, 24.48, 22.61, 14.13. NMR spectra are in agreement with the literature.[5]



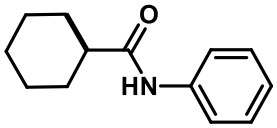
Followed procedure **AI.6a**. colourless oil, 345 mg, 65% (496 mg, 94% obtained when catalysis reaction time was 24 h) (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 – 1.91 (m, 2H), 1.88 – 1.81 (m, 2H), 1.68 – 1.61 (m, 2H), 1.35 – 1.23 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.95, 46.67, 45.62, 34.94, 31.91, 29.62, 29.49, 29.25, 26.20, 25.02, 24.48, 22.71, 14.16. NMR spectra are in agreement with the literature.[6]



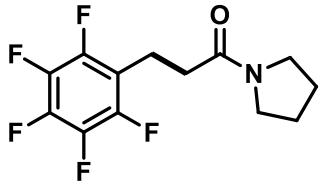
Followed procedure **AI.6b**. White solid, 191 mg, 46% (1.25 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 2H), 7.37 – 7.33 (m, 2H), 7.15 – 7.11 (m, 1H), 2.38 (t, *J* = 7.6 Hz, 2H), 1.79 – 1.72 (m, 2H), 1.29 – 1.41 (m, 24H), 0.91 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.41, 137.99, 129.06, 124.23, 119.77, 37.96, 31.99, 29.76, 29.74, 29.72, 29.68, 29.55, 29.45, 29.43, 29.34, 25.69, 22.76, 14.20. NMR spectra are in agreement with the literature.[7]



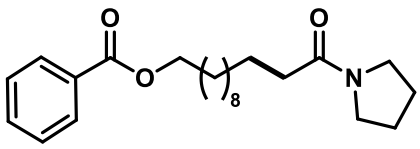
Followed procedure **AI.6b**. White solid, 372 mg, 78% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.52 (m, 2H), 7.32 – 7.26 (m, 2H), 7.10 - 7.06 (m, 1H), 2.68 (p, *J* = 8.1 Hz, 1H), 1.98 – 1.84 (m, 4H), 1.83 – 1.73 (m, 2H), 1.66 – 1.55 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 174.74, 138.24, 129.01, 124.08, 119.76, 46.93, 30.60, 26.08. NMR spectra are in agreement with the literature.[8]



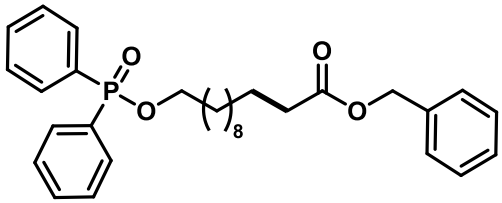
Followed procedure **AI.6b**. White solid, 181 mg, 36% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.54 – 7.52 (m, 2H), 7.33 – 7.26 (m, 2H), 7.10 – 7.07 (m, 1H), 2.27 – 2.19 (m, 1H), 1.96 – 1.93 (m, 2H), 1.84 – 1.81 (m, 2H), 1.71– 1.68 (m, 1H), 1.59 – 1.49 (m, 2H), 1.34 – 1.22 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 174.52, 138.18, 129.02, 124.13, 119.83, 46.61, 29.72, 25.73. NMR spectra are in agreement with the literature.[8]



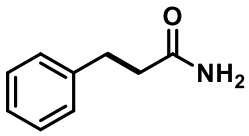
Followed procedure **AI.6a**. White solid, 105 mg, 29% (1.25 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.47 (t, *J* = 6.9 Hz, 2H), 3.37 (t, *J* = 6.8 Hz, 2H), 3.08 – 3.04 (m, 2H), 2.57 – 2.53 (m, 2H), 2.00 – 1.93 (m, 2H), 1.90 – 1.83 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 169.21, 46.48, 45.81, 33.61, 26.14, 24.42,17.91. **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -143.85, -157.85, 163.03. **HRMS**: $[M + H]^+$ calculated for $C_{13}H_{13}F_5NO^+$ 294.0912; Found 294.0910.



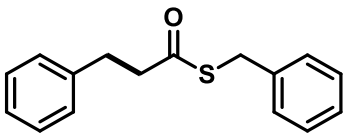
Followed procedure **AI.6a**. Colourless oil at r.t. and solidifies at -20 °C, 158 mg, 34% (338 mg, 73% when reaction performed at 2.0 mol% catalyst loading) (1.25 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.06 – 8.03 (m, 2H), 7.58 – 7.53 (m, 1H), 7.46 – 7.42 (m, 2H), 4.31 (t, *J* = 6.7 Hz, 2H), 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 – 1.91 (m, 2H), 1.88 – 1.80 (m, 2H), 1.80-1.73 (m, 2H), 1.68 – 1.60 (m, 2H), 1.47 – 1.42 (m, 2H), 1.37 - 1.25 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.92, 166.77, 132.85, 130.58, 129.59, 128.38, 65.21, 46.67, 45.63, 34.93, 29.61, 29.59, 29.57, 29.55, 29.52, 29.34, 28.78, 26.20, 26.10, 25.02, 24.49. **HRMS**: $[M + H]^+$ calculated for $C_{23}H_{36}NO_3^+$ 374.2689; Found 374.2686.



Followed procedure **AI.6c**. Colourless oil, 231 mg, 37% (*mixture with 9% branched product*; 1.25 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 4H), 7.54 – 7.49 (m, 2H), 7.47 – 7.42 (m, 4H), 7.37 – 7.29 (m, 5H), 5.11 (s, 2H), 4.02 (q, *J* = 6.7 Hz, 2H), 2.48 (q, *J* = 6.7 Hz, 0.11H; *belongs to branched product*), 2.35 (t, *J* = 7.5 Hz, 2H), 1.75 – 1.68 (m, 2H), 1.68 – 1.60 (m, 2H), 1.41 – 1.34 (m, 2H), 1.31 – 1.24 (m, 12H), 1.16 (d, *J* = 6.9 Hz, 0.36H; *belongs to branched product*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (*mixture with branched product*): 176.81, 173.78, 136.18, 132.44, 132.15, 132.12, 131.75, 131.65, 131.07, 128.63, 128.60, 128.57, 128.50, 128.23, 128.11, 66.13, 65.11, 65.05, 39.61, 34.39, 33.85, 30.64, 30.57, 29.77, 29.52, 29.51, 29.43, 29.45, 29.29, 29.20, 29.18,27.23, 25.67, 25.01,17.13. **^{31}P NMR** (162 MHz, $CDCl_3$) δ: 31.13. **HRMS**: $[M + H]^+$ calculated for $C_{31}H_{40}O_4P^+$ 507.2659; Found 507.2657.



Followed procedure **AI.6d**. White solid, 316 mg, 85% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.37 – 7.26 (m, 3H), 7.22 – 7.18 (m, 3H), 5.93 (br s, 1H), 5.50 (br s, 1H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.52 (t, *J* = 8 Hz, 2H). δ: 3.61(q, *J* = 7.2 Hz, 0.13H), 1.51 (d, *J* = 7.2 Hz, 0.40 H) belong to the branched amide. **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 174.99, 140.72, 128.65, 128.38, 126.38, 37.60, 31.44. δ: 177.10, 141.27, 129.05, 127.67, 127.46, 46.67, 18.38 belong to the branched amide. NMR spectra are in agreement with the literature.[9]



Followed procedure **AI.6e**. Colourless oil, 595 mg, 93% (2.5 mmol scale derivatization). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.31 – 7.27 (m, 4H), 7.26 – 7.15 (m, 6H), 4.12 (s, 2H), 3.01 – 2.97 (m, 2H), 2.90 – 2.85 (m, 2H). δ: 3.90 (q, *J* =7.1 Hz, 0.13H), 1.54 (d, *J* =7.1 Hz, 0.39H) belong to the branched thioester. **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 197.95, 140.03, 137.63, 128.89, 128.70, 128.62, 128.40, 127.33, 126.44, 45.31, 33.26, 31.49. δ: 200.63, 139.76, 137.40, 128.76, 128.66, 128.05, 127.58,127.29, 54.11, 33.57, 18.48 belong to the branched thioester. NMR spectra are in agreement with the literature.[10]

AI.8. Examples of typical GC, UPLC chromatograms and NMR spectra

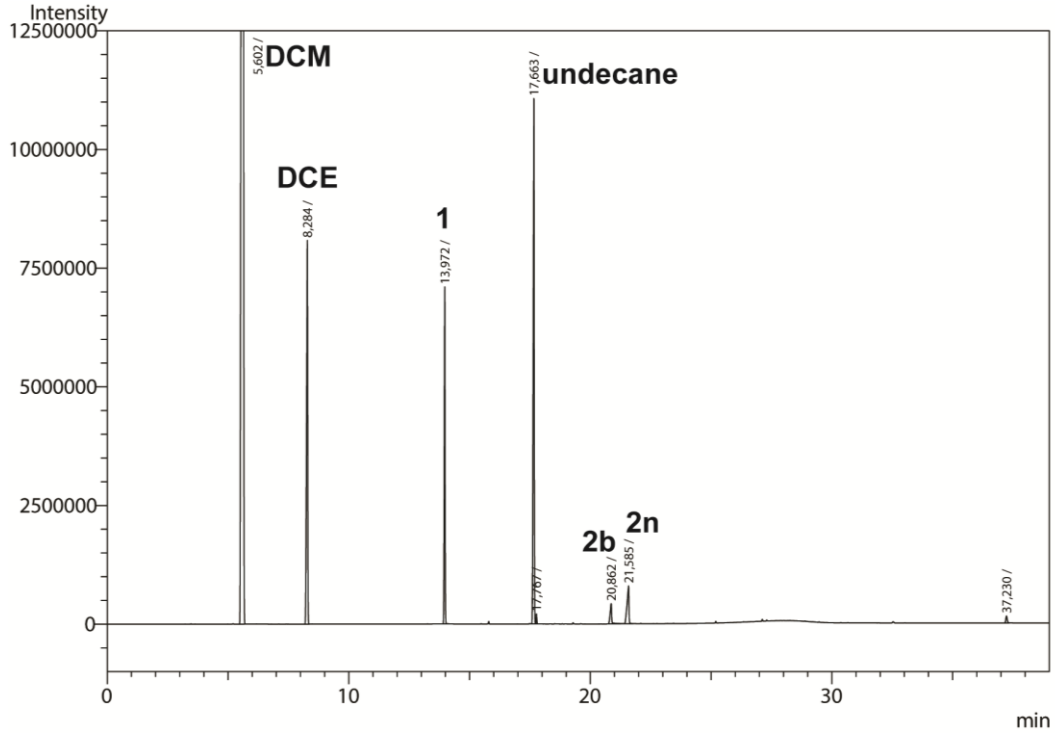


Figure AI.5. Typical GC-FID chromatogram of catalytic reaction mixture (example shown is of Table AI.7, entry 2).

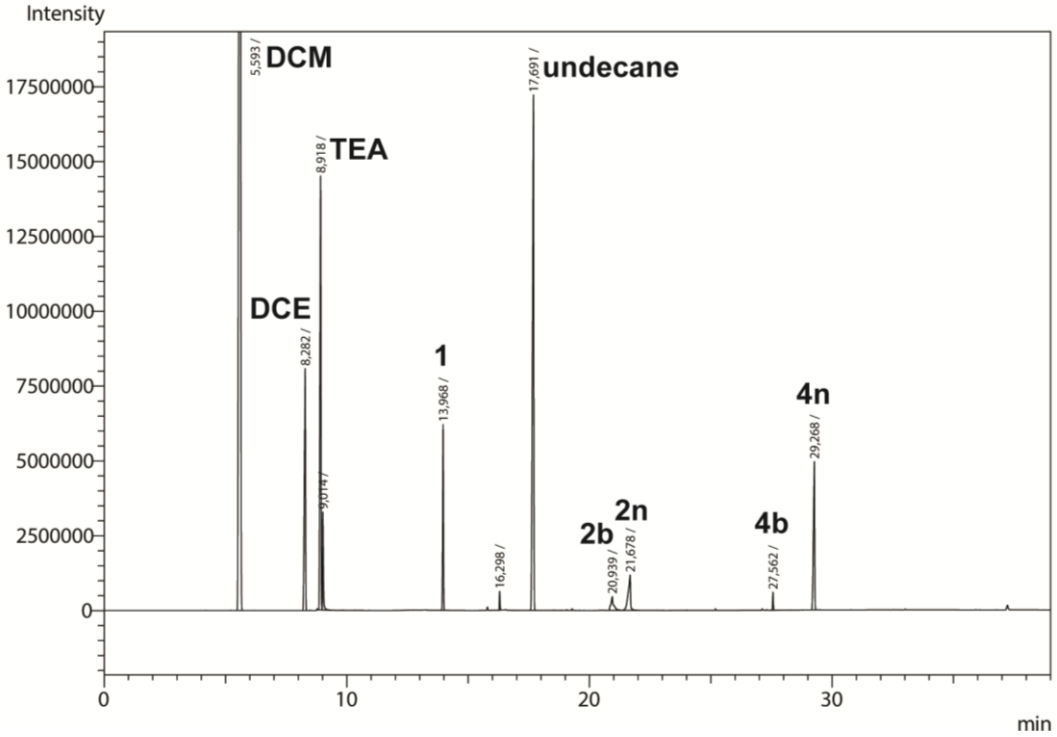


Figure AI.6. Typical GC-FID chromatogram of pyrrolidine derivatized catalytic reaction mixture (example shown is of Table AI.7, entry 2).

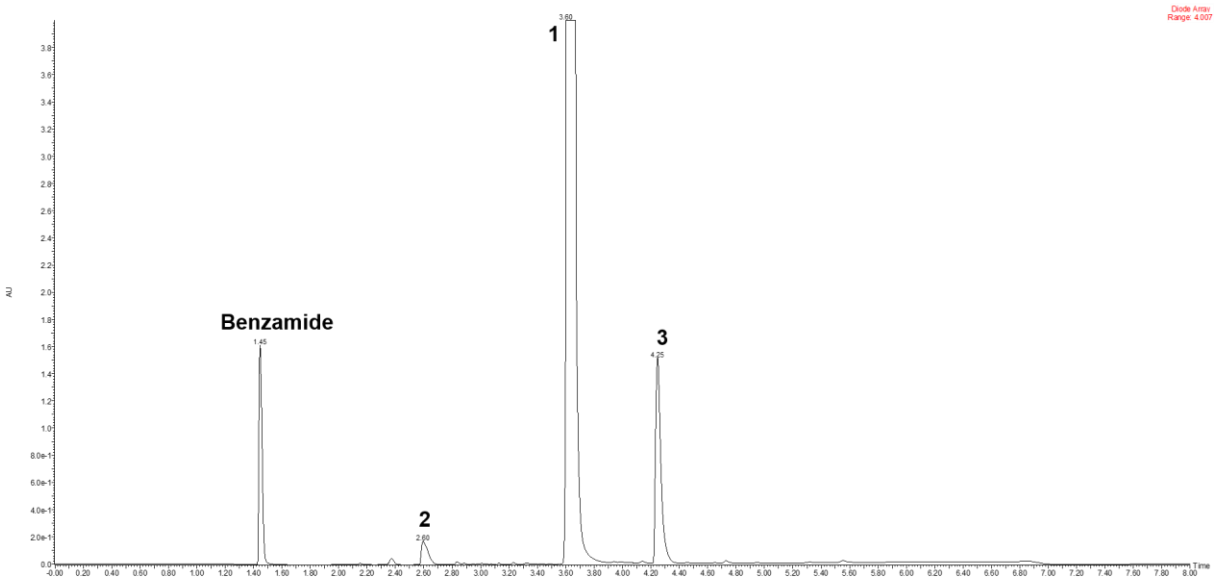


Figure AI.7. Typical UPLC chromatogram of catalytic reaction mixture (example shown is of Table AI.7, entry 2).

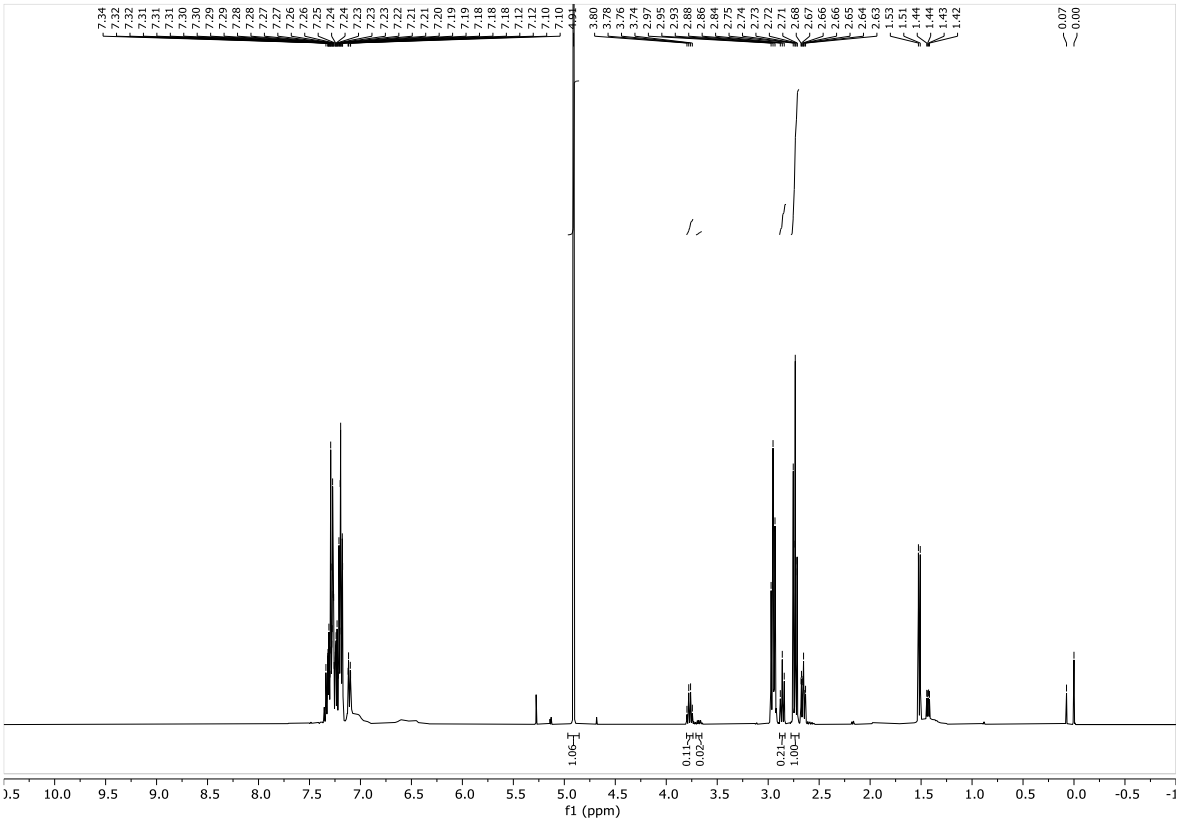


Figure AI.8. Typical NMR spectrum of catalytic reaction mixture (example shown is of Table AI.7, entry 2).

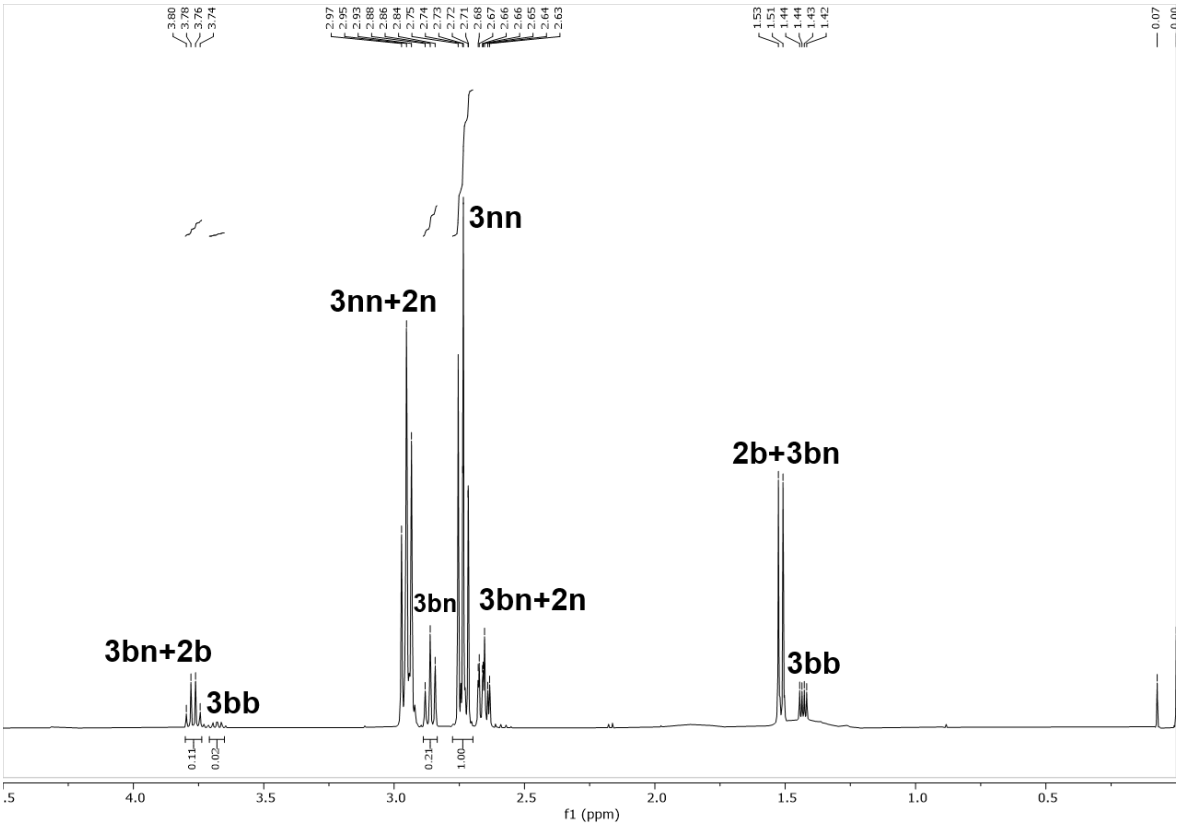


Figure AI.9. Typical NMR spectrum of catalytic reaction mixture, highlighting the important peaks to determine selectivity (example shown is of Table AI.7, entry 2).

AI.9. Computational calculations: Cartesian coordinates (in Å) and total energies ($G_{gas\text{-}phase}$)

Carbon Monoxide **CO** (-342.41 kcal mol^{-1})

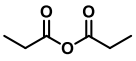
C	0.000000	0.000000	-0.568201
O	0.000000	0.000000	0.568201

Ethene ═ (-693.43 kcal mol^{-1})

C	-0.666527	0.000000	0.000000
C	0.666527	0.000000	0.000000
H	-1.238837	-0.925831	0.000000
H	-1.238837	0.925831	0.000000
H	1.238837	-0.925831	0.000000
H	1.238837	0.925831	0.000000

Propionic acid  (-1367.06 kcal mol^{-1})

C	-4.056625	-1.260868	-0.820949
C	-2.789528	-0.399554	-0.806764
C	-1.556965	-1.154524	-0.340822
O	-1.509072	-2.319199	-0.000214
O	-0.445232	-0.340061	-0.345535
H	-2.567342	0.007064	-1.802850
H	-3.938745	-2.120197	-1.488545
H	-4.911575	-0.668497	-1.163669
H	-4.279180	-1.646898	0.178792
H	-2.904320	0.475504	-0.152571
H	0.300068	-0.896065	-0.035531

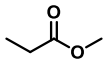
Propionic anhydride 
(-2406.66 kcal mol^{-1})

C	-3.111105	-3.451606	1.458275
C	-2.419276	-2.104488	1.434626
O	-2.898599	-1.041957	1.141188
O	-1.049218	-2.267191	1.764184
C	-0.342129	-1.219016	2.407207
O	-0.863395	-0.454078	3.173965
C	1.120599	-1.279946	2.019188
C	2.000040	-0.315108	2.821568
C	-4.543705	-3.405702	0.916359
H	-3.086784	-3.798837	2.501587
H	-2.484517	-4.159767	0.900163

H	1.168941	-1.066512	0.941318
H	1.452120	-2.321279	2.125795
H	3.040806	-0.388436	2.489242
H	1.960457	-0.546363	3.891026
H	1.664557	0.718461	2.692911
H	-4.557103	-3.078081	-0.128256
H	-5.156945	-2.705497	1.491673
H	-5.000697	-4.399121	0.974008

Methanol H_3C-OH (-655.44 kcal mol^{-1})

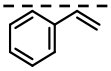
C	-4.882061	0.081262	0.000000
O	-3.439857	0.061455	0.000000
H	-5.300227	-0.400142	0.896496
H	-5.300227	-0.400142	-0.896496
H	-5.175718	1.134844	0.000000
H	-3.148729	-0.865737	0.000000

Methyl propionate 
(-1709.19 kcal mol^{-1})

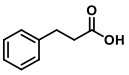
C	-4.056150	-1.259738	-0.821178
C	-2.787629	-0.399879	-0.806350
C	-1.555009	-1.160341	-0.339008
O	-1.519704	-2.327576	0.000129
O	-0.455349	-0.341778	-0.347822
C	0.787401	-0.968285	0.084055
H	-3.939239	-2.119444	-1.488610
H	-4.910849	-0.666648	-1.163930
H	-4.279413	-1.646360	0.178278
H	-2.904104	0.474476	-0.151831
H	-2.567178	0.006142	-1.802849
H	1.542633	-0.184240	0.015030
H	1.036458	-1.808680	-0.570700
H	0.692987	-1.329691	1.112372

Water H_2O (-316.23 kcal mol^{-1})

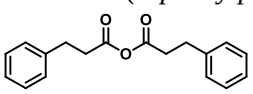
O	0.000000	0.000000	-0.284442
H	0.000000	-0.768786	0.311309
H	0.000000	0.768786	0.311309

Styrene  (-2170.80 kcal mol^{-1})

C	-0.62249869	-0.09049250	-0.12754874
C	0.68942543	0.03695300	0.12308939
H	0.55889121	-1.61910024	-2.11362469
H	-1.32281042	0.42905890	0.52891998
H	1.45293862	-0.44673773	-0.48151834
H	1.04099697	0.63961620	0.95569476
C	-1.25820443	-0.86297546	-1.20669054
C	-2.66377192	-0.87019538	-1.30263108
C	-3.31782321	-1.58666252	-2.30758357
C	-2.57721007	-2.31449560	-3.24292754
C	-1.17775919	-2.31824539	-3.16195689
C	-0.52679093	-1.60305244	-2.15899556
H	-3.24499453	-0.30484046	-0.57651060
H	-4.40413160	-1.57593207	-2.36011639
H	-3.08128940	-2.87380252	-4.02736873
H	-0.59466506	-2.88254934	-3.88640084

2n *(3-phenylpropionic acid)* 
(-2836.44 kcal mol^{-1})

C	-3.82582751	-1.26799962	-1.43026021
C	-3.02337421	-0.85983009	-0.17962084
C	-1.52650729	-0.80151002	-0.42211564
O	-0.95541171	-1.03362284	-1.46860317
O	-0.85302606	-0.44029169	0.72373950
H	-3.34626971	0.12316137	0.18854499
H	-3.61346680	-0.55787845	-2.23725936
H	-5.32293078	-3.39123197	-0.57242699
H	-3.47603146	-2.24760606	-1.77451857
H	-3.20707465	-1.55737619	0.64841430
H	0.09823200	-0.42445925	0.48712236
C	-5.31265841	-1.31111539	-1.14502525
C	-6.10545848	-0.16261631	-1.29361259
C	-7.47023014	-0.18827214	-0.99129012
C	-8.06521252	-1.36827243	-0.53281239
C	-7.28632899	-2.52031033	-0.38219325
C	-5.92192413	-2.48903326	-0.68593153
H	-5.65046025	0.75774026	-1.65642269
H	-8.06949836	0.71061659	-1.11808356
H	-9.12721370	-1.39133005	-0.30034259
H	-7.74183745	-3.44419879	-0.03267349

3nn *(3-phenylpropionic anhydride)*
 (-5344.69 kcal mol^{-1})

C	-3.11120411	-3.42601805	1.39514806
C	-2.39669679	-2.09508075	1.30878248

O	-2.83957789	-1.05205967	0.90754797	C	5.62191201	-1.47320361	2.79247453
O	-1.05109442	-2.25162816	1.72894030	C	6.15914341	-0.74746769	1.72423872
C	-0.35696470	-1.16402748	2.31906850	C	5.34575920	0.14429152	1.01725294
O	-0.90144486	-0.32615218	2.98712180	C	4.00422693	0.30540558	1.37636022
C	1.12105831	-1.28546120	2.01925972	H	3.86966160	-1.87197301	3.98420125
C	1.98729337	-0.27725492	2.79958059	H	6.24881335	-2.16380805	3.35214493
C	-4.50838453	-3.41204843	0.74437653	H	7.20366774	-0.87166257	1.44862484
H	-3.18027624	-3.69013885	2.46027840	H	5.75690684	0.71799785	0.18962865
H	-2.47020896	-4.19436470	0.94429644	C	-5.19188476	-4.75706602	0.87697663
H	1.24576836	-1.14918112	0.93536487	C	-5.99346729	-5.04735331	1.99168108
H	1.43284702	-2.31810751	2.22184086	C	-6.58884890	-6.30375920	2.13940352
H	3.37838713	1.00613209	0.82601503	C	-6.38996996	-7.29279605	1.17049521
H	1.83934311	-0.43644849	3.87395753	C	-5.59494206	-7.01493116	0.05366083
H	1.63722053	0.73727750	2.58033404	C	-5.00199901	-5.75690975	-0.08936175
H	-4.40652526	-3.14045889	-0.31271982	H	-6.15756438	-4.27998068	2.74650651
H	-5.11225197	-2.62818844	1.21416292	H	-7.21123472	-6.50869491	3.00758081
H	-4.38952942	-5.54541444	-0.96450836	H	-6.85489454	-8.26943612	1.28196535
C	3.45284598	-0.41856901	2.44469487	H	-5.44049989	-7.77572809	-0.70824692
C	4.27962741	-1.30852625	3.14741627				

AI.10. References

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Appendix II

Supporting Information for Chapter 3

Palladium-Catalyzed Synthesis of Symmetric Carboxylic Acid Anhydrides from Alkenes with *in situ* Generated Carboxylic Acids

AII.1. General experiment details and materials

Reactions and chemicals related: All reactions and operations involving air- or moisture-sensitive compounds were performed using standard Schlenk techniques in heated and vacuum dried glassware or in N_2-filled glove box. Chemicals were purchased from Sigma-Aldrich, TCI, Acros, Brunschwig or Bio-connect and used without further purification unless otherwise stated. Anhydrous 1,2-dichloroethane (DCE) was purchased from Biosolve and dried over flame dried 4Å molecular sieves. Toluene and dichloromethane (DCM) were purchased from Honeywell and dispensed *via* Pure Solv solvent dispenser by Innovative Technologies. Solvents were freeze-pump-thawed (FPT) before all catalytic reactions. All ligands except 1,2-diphenylphosphinomethyl benzene were purchased from Sigma-Aldrich and Strem Chemicals. 1,2-diphenylphosphinomethyl benzene was synthesized in-house.

a. Autoclaves: 100 mL stainless steel (316) autoclaves equipped with temperature probe and pressure adapter were used. For heating and stirring, an H.E.L. Polyblock PB4 was used.

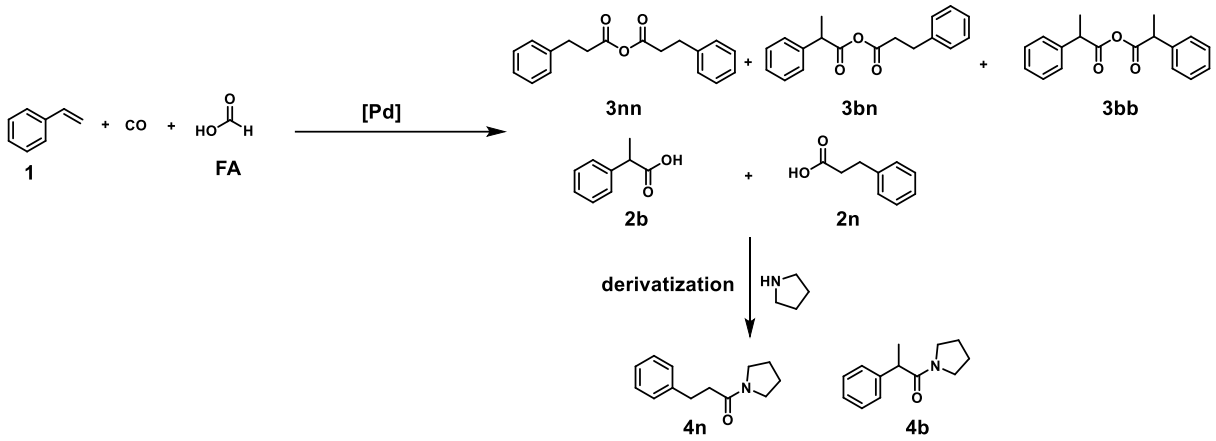
b. NMR Spectroscopy: ^{1}H NMR and ^{13}C NMR were recorded on Bruker Avance 400 (operating at 400 MHz for ^{1}H, 101 MHz for ^{13}C) NMR spectrometer. ^{19}F and ^{31}P NMR spectra were referenced against $CFCl_3$ and 85% H_3PO_4 (external references). Multiplets were assigned as s (singlet), d (doublet), t (triplet), , q (quartet), p (quintet), dd (doublet of doublet), ddt (doublet of doublet of triplet) and m (multiplet). All measurements were carried out at room temperature. NMR yields were calculated using dibromomethane as internal standard.

c. GC Analysis: Gas chromatography (GC) was measured on Shimadzu GC-2010, equipped with DB-5MS UI column (length 60 m, diameter: 0.250 mm, film thickness: 1.0 µm), coupled to Flame Ionization Detector (FID). Gas chromatography-mass spectrometry (GC-MS) was measured on Agilent Technologies 7820A equipped with DB-5MS UI column (length 30 m, diameter: 0.250 mm, film thickness: 1.0 µm) column and coupled to mass detector MSD 5975. Helium was used as the mobile phase.

d. HRMS: High resolution mass spectra (HRMS) were recorded on Q-Exactive HF Orbitrap (Thermo Scientific) equipped with an electrospray ion source (ESI) in positive mode, injection of 2 µL of a 1 µM solution *via* Ultimate 3000 nano UPLC (Dionex) system, with an external calibration (Thermo Scientific). Parameters used: Source voltage of 3.5 kV, capillary temperature 275 °C, no sheath gas, Resolution = 240.000 at m/z=400. Mass range m/z=160-2000 or until a maximum of 6000. Eluents used: ACN:H_2O (1:1 v/v) supplemented with 0.1% formic acid. The data are given as mass units per charge (m/z).

AII.2. General reaction scheme, methods of analysis and calculations

AII.2.1. General reaction scheme showing reactants, all possible products of catalysis and products obtained on derivatization



Scheme AII.1. Overall reaction scheme showing substrates and products.

AII.2.2. Methods of analysis of substrates and products

a. GC : **1**, **4n**, **4b**

b. NMR : **2n**, **2b**, **3nn**, **3bn**, **3bb**

AII.2.3. Calculations

a. Mass Balance:

The Mass Balance was calculated in terms of "number of phenyl groups" present in the reaction mixture after catalysis as follows:

$$\frac{phenyls\ of\ \mathbf{1}\ + phenyls\ of\ \mathbf{2} + \ phenyls\ of\ \mathbf{3}}{total\ initial\ phenyls} \times 100$$

Where,

Phenyls of **1** = mmol of **1** unreacted ; determined by GC

Phenyls of **2** = mmol of (**2n**+**2b**) ; determined by NMR

Phenyls of **3** = 2 × mmol of **3**; determined by NMR

Total initial phenyls = mmol of **1** introduced in the reaction

An error margin of ±10% is considered to be acceptable for the mass balance.

b. Total Anhydride Yield %:

The total anhydride yield % was calculated as follows:

$$\frac{mmol\ of\ \mathbf{3}}{mmol\ of\ limiting\ reagent} \times 100$$

Where,

mmol of **3** (**3nn** + **3bn** + **3bb**) was determined by NMR

c. Regioselectivity:

3nn:**3bn:3bb** was calculated as follows:

$$\frac{\boldsymbol{3nn}\ or\ \boldsymbol{3bn}\ or\ \boldsymbol{3bb}}{Total\ anhydride\ yield} \times 100$$

Where,

mmol of **3nn**, **3bn**, **3bb** were determined by NMR using dibromomethane as internal standard

4n:**4b** was calculated as follows:

$$\frac{\boldsymbol{4n}\ or\ \boldsymbol{4b}}{\boldsymbol{4n}+\boldsymbol{4b}} \times 100$$

Where,

mmol of **4n**, **4b** were determined by GC

d. Conversion %

Conversion % with respect to styrene (**1**) was calculated as follows:

$$\left[1-\frac{\mathbf{1}\ unreacted}{initial\ \mathbf{1}\ charged}\right] \times 100$$

Where,

mmol of **1** was determined by GC

An error margin of ±5% is considered to be acceptable for the conversion.

e. Concentrations mentioned in mol% are always given with respect to the limiting reagent in cases where one of the reagents is used in excess.

AII.3. General catalytic procedure (GP) and analysis

Palladium acetate (0.05 mmol; 11.2 mg) and 1,4-bis(diphenylphosphanyl)butane, dppb, (0.10 mmol; 42.7 mg) were weighed into a clean and dried glass liner containing an oven−dried stirring bar. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. A freeze-pump-thawed solution of formic acid in dried 1,2-dichloroethane (DCE) was added using standard Schlenk techniques and the mixture was stirred for 30 mins. Then the required volume of degassed and dried styrene (**1**) was added using standard Schlenk procedures and the autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to a HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with nitrogen (N_2) (3 × 30 bar). The autoclave was flushed with carbon monoxide (CO) (1 × 30 bar) and then was charged with CO to 50 bar. The autoclave was stirred at 350 rpm and heated for 15 h at the desired temperature. At the end of the reaction time, the autoclave was brought to room temperature, cooled further for 30 minutes using an ice-bath and then was slowly depressurized. After 30 minutes of thawing, the contents of the glass liner were transferred to a 10 mL volumetric flask (**A**) and the total volume was adjusted to 10 mL using dichloromethane (DCM).

a. GC Analysis: 1 mL of the reaction mixture in flask **A** was transferred to a 10 mL volumetric flask (**B**), to which 0.3 mL undecane (internal standard for GC analysis) was added and was diluted up to 10 mL with DCM. The resulting solution was then analyzed using GC. The amount of styrene (**1**) present in the GC sample was determined using calibration lines with undecane as the internal standard. A 60 m × 0.250 mm ; 1.0 µm thickness DB-5MS GC column was used for analysis. 2.0 µL of each sample was injected and the following

temperature program was used: injector at 350 °C, FID at 350 °C, oven at 40 °C for 3 min, increasing to 300 °C with 10 °C/min and hold at 300 °C for 10 min.

b. NMR Analysis: NMR samples were prepared by drying 0.4 mL of the reaction mixture *in vacuo*, diluted with $CDCl_3$ and dibromomethane added as internal standard.

c. Derivatization Procedure: In a capped microwave vial, 2.5 mL of the reaction mixture from flask **A** was added under N_2 to a cooled solution of pyrrolidine (0.5 mL; 6.1 mmol) and triethylamine (1.0 mL; 7.3 mmol) in DCM (1.0 mL). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h in an aluminium block.

d. GC Analysis after derivatization:1 mL of the derivatization reaction mixture was transferred to a 5 mL volumetric flask (**C**), 0.3 mL undecane (internal standard for GC analysis) was added and the volume was adjusted to 5 mL with DCM. The resulting solution was then analyzed using GC. The pyrrolidine-derivatized products (**4n** and **4b**) present in the GC sample were quantified using calibration lines with undecane as the internal standard. A 60 m × 0.250 mm ; 1.0 µm thickness DB-5MS GC column was used for analysis. 2.0 µL of each sample was injected and the following temperature program was used: injector at 350 °C, FID at 350 °C, oven at 40 °C for 3 min, increasing to 300 °C with 10 °C/min and hold at 300 °C for 10 min. The resulting yield of product was further calculated for the initial 10 mmol scale hydrocarbonylation reaction.

AII.4. Results of screening studies:

AII.4.1. Influence of relative substrate ratio

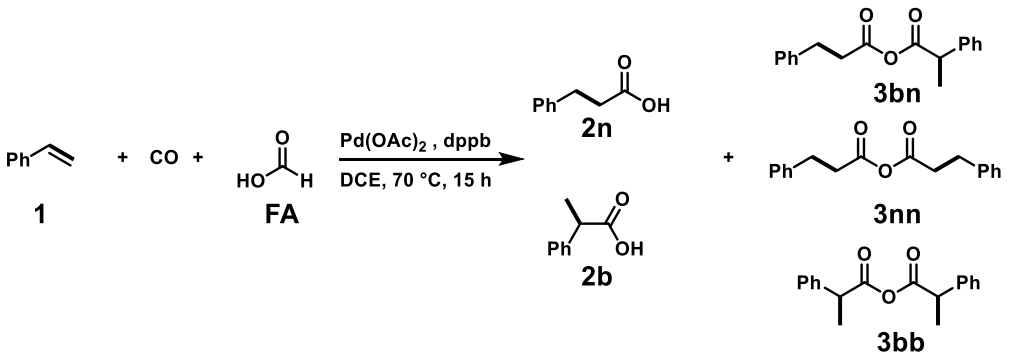
a. Procedure same as GP

b. Exact mmol of substrates used

1:FA	1	FA
5:10	572 µL (5.0 mmol)	378 µL (10.0 mmol)
5:5	572 µL (5.0 mmol)	190 µL (5.0 mmol)
10:5	1.2 mL (10.5 mmol)	190 µL (5.0 mmol)
15:5	1.7 mL (14.9 mmol)	190 µL (5.0 mmol)
30:10	3.4 mL (29.7 mmol)	378 µL (10.0 mmol)

c. Mass Balance:

Table AII.1. Mass balance: Influence of substrate ratio.



Entry	1:FA (mmol)	1[a] (mmol)	2n[b] (mmol)	2b[b] (mmol)	3nn[b] (mmol)	3bn[b] (mmol)	3bb[b] (mmol)	Yield% of 4/ (4n:4b)[a]	Mass Balance %
1	5:10	0	3.7	0.8	0	0	0	0	90
2	5:5	0	3.7	0.9	Trace	0	0	0	92
3	10:5	2.4	1.1	0.2	2.1	1.1	0.3	72 (89:11)	102
4	15:5	4.2	0.8	0.2	2.5	1.6	0.2	84 (86:14)	93
5	30:10[c]	8.0	1.5	Trace	4.7	3.5	0.6	86 (86:14)	91

Reaction conditions: **1** (x mmol), formic acid (y mmol), CO (50 bar), $Pd(OAc)_2$ (0.05 mmol), dppb (0.1 mmol), 70 °C, DCE (6 mL), 15 h. Yield% (based on limiting reagent). [a] Determined by GC analysis using undecane as internal standard. [b] Determined by NMR analysis using dibromomethane as internal standard. [c] t = 20 h instead of 15 h.

d. CO pressure drop graphs

Time for the reaction temperature to reach 70 °C is 1.5 h. The reaction time is 15 h (1.5 to 16.5 h).

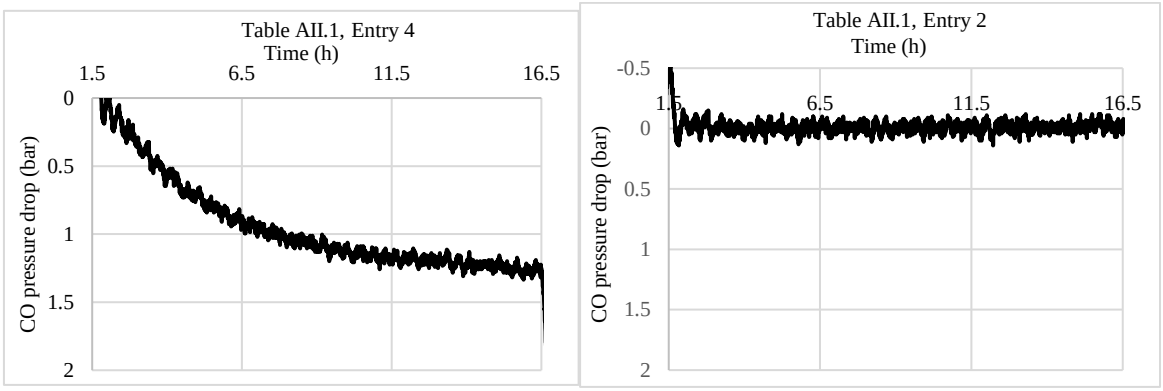


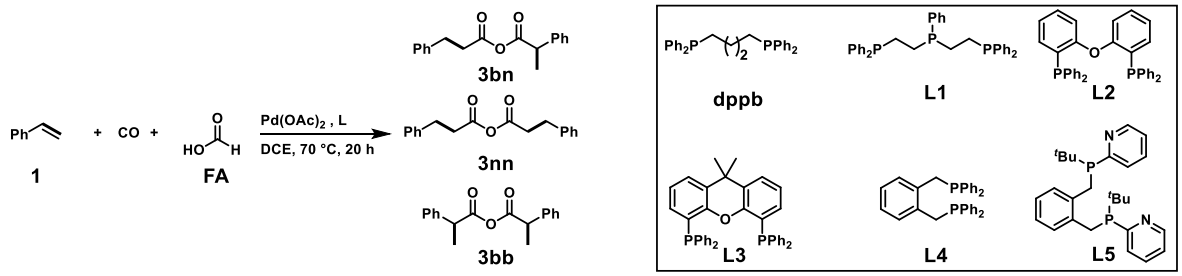
Figure AII.1. Relative CO pressure drop when **1**:FA is 15:5 mmol (left graph, Table AII.1, entry 4) and 5:5 mmol (right graph, Table AII.1, entry 2).

AII.4.2. Ligand screening

a. Procedure same as GP

b. Mass Balance:

Table AII.2. Mass Balance: Influence of ligands on synthesis of anhydrides from alkenes.



Ligand	1[a] (mmol)	2n[b] (mmol)	2b[b] (mmol)	3nn[b] (mmol)	3bn[b] (mmol)	3bb[b] (mmol)	Linearity %	Yield% of 4/ (4n:4b)[a]	Mass Balance %
dppb[c]	4.2	0.8	0.2	2.5	1.6	0.2	77	84 (86:14)	93
L1	8.3	0	0	0	0	0	-	0	56
L2	4.5	0.8	0.1	2.5	1.4	0.2	78	82 (86:14)	91
L3[d]	5.1	1.9	0.3	2.0	1.3	0.3	76	72 (86:14)	97
L4[e]	3.7	0.3	0.2	0.4	0.3	0	79	22 (73:27)	75
L5[e]	5.2	1.0	0.5	0.2	0.2	0	74		93

Reaction conditions: **1** (15 mmol), formic acid (5 mmol), CO (50 bar), $Pd(OAc)_2$ (0.05 mmol), ligand (0.1 mmol), 70 °C, DCE (6 mL), 20 h. Yield% based on FA. Linearity%: **3nn**% + (0.5×**3bn**%). [a] Determined by GC analysis using undecane as internal standard. [b] Determined by NMR analysis using dibromomethane as internal standard. [c] t = 15 h instead of 20 h. [d] 85 °C instead of 70 °C. [e] **1** (7.5 mmol), formic acid (2.5 mmol), CO (50 bar), $Pd(OAc)_2$ (0.025 mmol), ligand (0.0375 mmol), 70 °C, DCE (6 mL), 20 h.

AII.5. General procedure for substrate scope

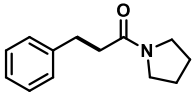
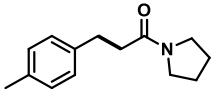
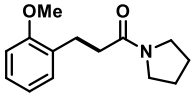
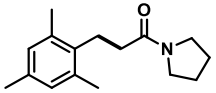
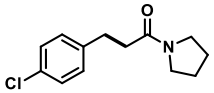
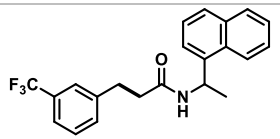
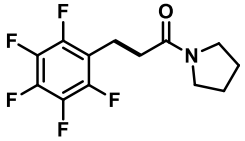
Palladium acetate (1.0 mol%) and 1,4-bis(diphenylphosphanyl)butane, dppb, (2.0 mol%) were weighed into a clean and dried glass liner containing an oven−dried stirring bar. The glass liner was fitted inside a 100 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. A freeze-pump-thawed solution of formic acid (1.0 equiv.) in dried DCE (6.0 mL) was added using standard Schlenk techniques and the mixture was stirred for 30 mins. Then the required volume of degassed and dried alkene (3.0 equiv.) was added using standard Schlenk procedures and the autoclave was closed and disconnected from the Schlenk line. The autoclave was transferred to a HEL PB4 polyblock and connected to the gas lines. The lines connecting the autoclave was flushed with nitrogen (N_2) (3 × 30 bar). The autoclave was flushed with carbon monoxide (CO) (1 × 30 bar) and then was charged with CO to 50 bar. The autoclave was stirred at 350 rpm and heated for 20 to 36 h at 70 °C. At the end of the reaction time, the autoclave was brought to room temperature, cooled further for 30 minutes using an ice-bath and then was slowly depressurized. After 30 minutes of thawing, the contents of the glass liner were transferred to a 10 mL volumetric flask (**A**) and the total volume was adjusted to 10 mL using dichloromethane (DCM).

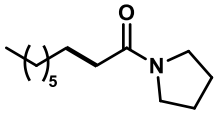
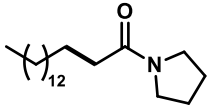
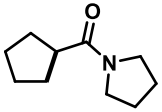
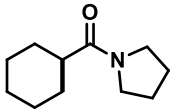
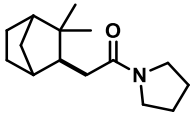
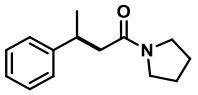
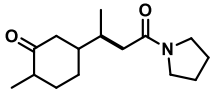
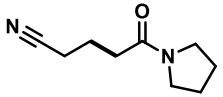
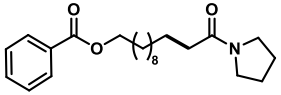
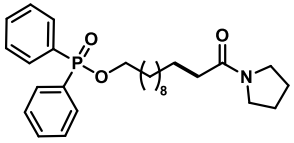
a. *Derivatization procedure with pyrrolidine*: In a capped microwave vial, 5.0 mL of the reaction mixture from flask **A** was added under N_2 to a cooled solution of pyrrolidine (0.5 mL; 6.1 mmol) and triethylamine (1.0 mL; 7.3 mmol). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 35 °C for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (20 to 50%).
b. *Derivatization procedure with (1R)-(+)-1-naphthylethylamine:* In a capped microwave vial, 5.0 mL of the reaction mixture from flask **A** was added under N_2 to a cooled solution of *(1R)-(+)-1-naphthylethylamine* (222.6 mg; 1.30 mmol), DMAP (6.1 mg ; 0.05 mmol) and triethylamine (278 µL; 2.0 mmol). The reaction mixture was stirred for 5 mins in an ice-bath

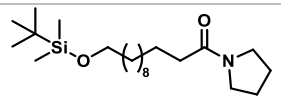
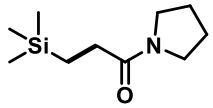
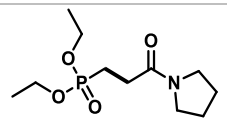
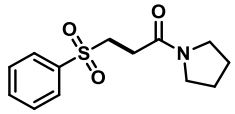
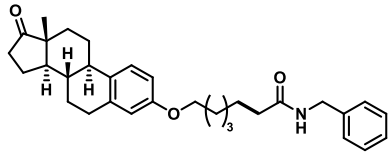
and then heated to 50 °C for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using diethyl ether/pentane mixture (20%). The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 30%).

c. *Derivatization procedure with benzylamine:* In a capped microwave vial, 5.0 mL of the reaction mixture from flask **A** was added under N_2 to a cooled solution of benzylamine (82 µL; 0.75 mmol), DMAP (6.1 mg ; 0.05 mmol) and triethylamine (139 µL; 1.0 mmol). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 50 °C for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 30%).

Table AII.3. Substrate scope: Synthesis of symmetric acid anhydrides from alkenes.

Entry	**Structure of derivatized product**	**Scale based on FA of catalytic reaction (mmol)**	**NMR Yield% of anhydride before der^{n}.**[a]	**Regio-selectivity of anhydride formed before der^{n}.** [a] **nn:bn:bb**	**Scale of der^{n}. (mmol)**	**Isolated yield of pure linear product**	**Isolated yield % of linear product**	**Physical Properties**
4[b]		5.0	86	58:37:5	2.5	374 mg	74%	Pale yellow oil
5		5.0	90	58:37:5	2.5	434 mg	80%	Pale yellow oil
6		2.5	89	74:21:5	1.25	245 mg	84%	Pale yellow oil
7[c]		2.5	65	>99:-:-	1.25	164 mg	54%	Pale yellow oil – turns waxy on freezing
8		5.0	98	59:38:3	2.5	511 mg	86%	Off-white solid
9[d]		2.5	68	66:34:trace	1.25	270 mg	58%	White solid
10[c]		2.5	52	89:11:trace	1.25	159 mg	43%	White solid

11		5.0	>99	84:16:trace	2.5	491 mg	93%	Pale yellow oil
12		2.5	n.d	n.d.	1.25	351 mg	91%	White solid
13		5.0	77	>99	2.5	319 mg	76%	Pale yellow oil
14[e]		10.0	82	>99	2.5	365 mg	81%	White solid
15[c]		2.5	n.d.	n.d.	1.25	115 mg	39% (endo:exo 2:1)	Yellow oil turns solid on freezing
16		5.0	70	>99:trace:-	2.5	337 mg	62%	Pale yellow oil
17[c]		2.5	57	>99: -	1.25	151 mg	48%	Yellow solid (wax)
18		2.5	72	>99:-	1.25	143 mg	69%	Yellow oil
19		5.0	n.d.	n.d.	1.25	391 mg	84%	Pale yellow oil
20[c]		2.5	n.d.	n.d.	1.25	380 mg	65%	Pale yellow oil

21		5.0	n.d.	n.d.	1.25	226 mg	47%	Pale yellow oil
22		5.0	43	>99:-	2.5	171 mg	34%	Colourless oil
23		2.5	<10	-	-	-	-	Did not isolate
24		2.5	0	-	-	-	-	-
25[f]		1.0	n.d.	n.d.	0.5	181 mg	74%	White solid

Reaction conditions: Scale based on formic acid (5.0 mmol): Alkene (15.0 mmol), formic acid (5.0 mmol), CO (50 bar), $Pd(OAc)_2$ (0.05 mmol), ligand (0.1 mmol), 70 °C, DCE (6 mL), 20 h. Scale based on formic acid (2.5 mmol): Alkene (7.5 mmol), formic acid (2.5 mmol), CO (50 bar), $Pd(OAc)_2$ (0.025 mmol), ligand (0.05 mmol), 70 °C, DCE (6 mL), 20 h. Procedure AII.5a followed for derivatization of reaction mixtures unless specified. [a] Determined by NMR analysis using dibromomethane as internal standard. [b] t = 15 h instead of 20 h. [c] t = 36 h instead of 20 h. [d] Procedure AII.5b followed for derivatization. [e] Alkene (30 mmol), formic acid (10 mmol), CO (50 bar), $Pd(OAc)_2$ (0.05 mmol), ligand (0.1 mmol), 70 °C, DCE (6 mL), 24 h. [f] Alkene (2.0 mmol), formic acid (1.0 mmol), CO (50 bar), $Pd(OAc)_2$ (0.025 mmol), ligand (0.05 mmol), 70 °C, DCE (6 mL), 20 h, Procedure AII.5c followed for derivatization. Abbreviation: der^n.: derivatization, n.d.: not determined.

AII.6. Procedure of derivatizations for applications

a. Reaction with ammonia: In a capped microwave vial, 0.5 mL of the reaction mixture (maximum anhydride yield 0.25 mmol) from flask **A** was added under N_2 to a cooled solution of 7N ammonia in methanol (47.2 µL; 0.5 mmol). The reaction mixture was stirred for 5 mins in an ice-bath and then at room temperature for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using MeOH/DCM (0 to 10%).

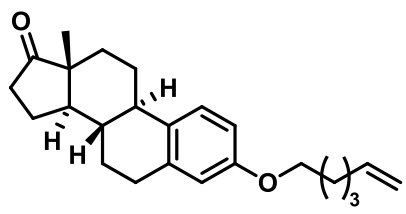
b. Reaction with β-naphthol: In a capped microwave vial, 0.5 mL of the reaction mixture (maximum anhydride yield 0.25 mmol) from flask **A** was added under N_2 to a cooled solution of β-naphthol (43.3 mg; 0.3 mmol), DMAP (3.1 mg ; 0.025 mmol) and triethylamine (69.6 µL; 0.5 mmol). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 50 °C for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 20%).

c. Reaction with tert-butyl thiol: In a capped microwave vial, 0.5 mL of the reaction mixture (maximum anhydride yield 0.25 mmol) from flask **A** was added under N_2 to a cooled solution of *tert*-butyl thiol (34 µL; 0.3 mmol), DMAP (3.1 mg ; 0.025 mmol) and triethylamine (69.6 µL; 0.5 mmol). The reaction mixture was stirred for 5 mins in an ice-bath and then heated to 50 °C for 15 h in an aluminium block. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 5%).

d. Friedel-Craft's acylation: In a capped microwave vial, 0.5 mL of the reaction mixture from flask **A** was taken. To the solution anisole (27.2 µL, 0.25 mmol) and $SnCl_4$ (29 uL, 0.25 mmol) were added under N_2. The mixture was stirred overnight at room temperature. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 10%).

e. Suzuki coupling: 0.5 mL of the reaction mixture from flask **A** was dried *in vacuo*, the concentrate was dissolved in 0.5 mL dry toluene and transferred into a microwave vial under N_2. $Pd(PPh_3)_2Cl_2$ (2 mol%, 0.005 mmol, 3.5 mg), K_2CO_3 (103.7 mg, 0.75 mmol, 3.0 eq.) and phenylboronic acid (36.6 mg, 0.3 mmol, 1.2 eq.) were added sequentially under N_2. The mixture was stirred overnight at 80 °C. The reaction mixture was subjected to column chromatography using ethyl acetate/pentane mixture (0 to 10%).

AII.7. Synthesis of substrates



(8R,9S,13S,14S)-3-(hex-5-en-1-yloxy)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one,

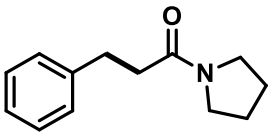
(ether derivative of estrone)

Estrone (810 mg; 3.0 mmol,) was dissolved in DMF (10 mL) and cesium carbonate (1.27 g; 3.9 mmol) was added followed by the addition of 6-bromo-1-hexene (481 µL; 3.6 mmol) and tetrabutylammonium iodide (110.8 mg; 0.3 mmol). The reaction mixture was heated to 50 °C for 16 h. The reaction was worked up using water (50 mL) and diethyl ether (50 mL), and the organic layer was washed with dilute NaOH solution, water, and brine (each 50 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The resulting residue was purified by column chromatography using ethyl

acetate/pentane (0. to 20%) to afford the corresponding pure product, a white solid. 820 mg (78%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.19 (dd, *J* = 8.7, 1.1 Hz, 1H), 6.71 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.64 (d, *J* = 2.6 Hz, 1H), 5.88 – 5.96 (m, 1H), 5.05 – 4.95 (m, 2H), 3.94 (t, *J* = 6.5 Hz, 2H), 2.92 – 2.88 (m, 2H), 2.54 – 2.47 (m, 1H), 2.41 – 2.37 (m, 1H), 2.29– 1.94 (m, 7H), 1.82 – 1.75 (m, 2H), 1.66 – 1.41 (m, 9H), 0.91 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 221.05, 157.09, 138.59, 137.70, 131.85, 126.30, 114.70, 114.51, 112.08, 67.64, 50.39, 48.02, 43.98, 38.37, 35.89, 33.44, 31.57, 29.66, 28.77, 26.56, 25.92, 25.33, 21.59, 13.85. The NMR spectra are in agreement with the literature.[1]

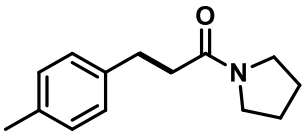
The synthesis of *undec-10-en-1-yl benzoate, tert-butyldimethyl-(undec-10-en-1-yloxy)-silane* and *undec-10-en-1-yl diphenylphosphinate* are described in AI.5 (Appendix I).

AII.8. Experimental data characterization of products (substrate scope and applications)



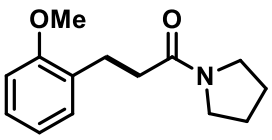
4n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 – 7.18 (m, 5H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.29 (t, *J* = 6.6 Hz, 2H), 3.01 – 2.97 (m, 2H), 2.58 – 2.54 (m, 2H), 1.90 – 1.80 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.73, 141.55, 128.46, 128.43, 126.06, 46.54, 45.64, 36.79, 31.21, 26.07, 24.39. NMR spectra are in agreement with the literature.[2]



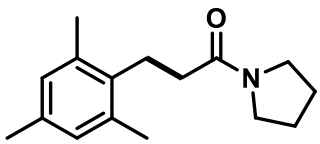
5n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.13 – 7.08 (m, 4H), 3.46 (t, *J* = 6.7 Hz, 2H), 3.30 (t, *J* = 6.6 Hz, 2H), 2.96 – 2.92 (m, 2H), 2.56 – 2.52 (m, 2H), 2.32 (s, 3H), 1.96 – 1.79 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.82, 138.46, 135.53, 129.10, 128.32, 46.53, 45.62, 36.96, 30.74, 26.07, 24.40, 21.01. NMR spectra are in agreement with the literature.[3]



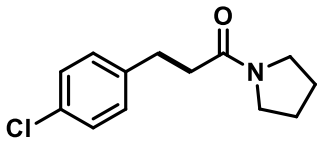
6n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.21 – 7.18 (m, 2H), 6.90 – 6.83 (m, 2H), 3.82 (s, 3H), 3.46 (t, *J* = 6.8 Hz, 2H), 3.32 (t, *J* = 6.7 Hz, 2H), 2.99 – 2.95 (m, 2H), 2.55 – 2.51 (m, 2H), 1.90 – 1.80 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.44, 157.54, 130.26, 129.82, 127.47, 120.54, 110.22, 55.26, 46.55, 45.63, 35.13, 26.40, 26.17, 24.49. **HRMS**: $[M + H]^+$ calculated for $C_{14}H_{20}NO_2^+$ 234.14886; Found 234.1487.



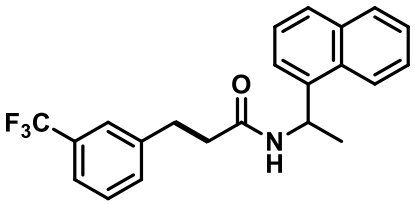
7n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.85 (s, 2H), 3.49 (t, *J* = 6.7 Hz, 2H), 3.30 (t, *J* = 6.6 Hz, 2H), 2.99 – 2.95 (m, 2H), 2.40 – 2.36 (m, 2H), 2.30 (s, 6H), 2.25 (s, 3H), 1.93 – 1.83 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.00, 136.16, 135.40, 135.00, 128.95, 46.48, 45.70, 34.01, 26.13, 24.58, 24.40, 20.79, 19.73. **HRMS**: $[M + H]^+$ calculated for $C_{16}H_{24}NO^+$ 286.1852; Found 286.1852.



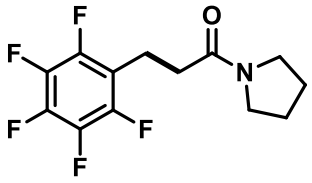
8n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.26 – 7.23 (m, 2H), 7.17 – 7.15 (m, 2H), 3.46 (t, *J* = 6.8 Hz, 2H), 3.30 (t, *J* = 6.7 Hz, 2H), 2.98 – 2.94 (m, 2H), 2.55 – 2.51 (m, 2H), 1.94 – 1.79 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.34, 140.06, 131.79, 129.89, 128.51, 46.56, 45.68, 36.49, 30.42, 26.08, 24.40. **HRMS**: $[M + H]^+$ calculated for $C_{13}H_{17}ClNO^+$ 238.0993; Found 238.0992.



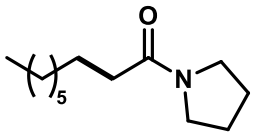
9n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 – 8.00 (m, 1H), 7.88 – 7.83 (m, 1H), 7.81 – 7.76 (m, 1H), 7.51 – 7.49 (m, 2H), 7.45 – 7.39 (m, 4H), 7.35 – 7.30 (m, 2H), 5.93 – 5.86 (m, 1H), 5.63 – 5.61 (m, 1H), 3.09 – 2.96 (m, 2H), 2.47 – 2.42 (m, 2H), 1.59 (d, *J* = 6.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.26, 141.69, 137.95, 133.89, 131.96, 131.03, 128.89, 128.79, 128.43, 126.59, 125.90, 125.15, 125.02, 124.98, 123.31, 123.13, 123.09, 122.51, 44.61, 38.01, 31.29, 20.51. **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -62.80. NMR spectra are in agreement with the literature.[4]



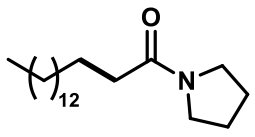
10n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.47 (t, *J* = 6.9 Hz, 2H), 3.37 (t, *J* = 6.8 Hz, 2H), 3.08 – 3.04 (m, 2H), 2.58 – 2.54 (m, 2H), 2.00 – 1.93 (m, 2H), 1.90 – 1.83 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.19, 46.45, 45.77, 33.57, 26.10, 24.38, 17.87. **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -143.61, -157.64, -162.81. **HRMS**: $[M + H]^+$ calculated for $C_{13}H_{13}F_5NO^+$ 294.0911; Found 294.0911.



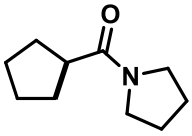
11n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.24 (m, 2H), 1.98 – 1.91 (m, 2H), 1.88 – 1.81 (m, 2H), 1.68 – 1.61 (m, 2H), 1.31 – 1.27 (m, 10H), 0.88 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.99, 46.65, 45.60, 34.88, 31.86, 29.56, 29.44, 29.21, 26.14, 24.98, 24.43, 22.67, 14.12. NMR spectra are in agreement with the literature.[5]



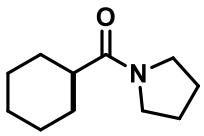
12n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.25 (t, *J* = 7.7 Hz, 2H), 1.98 – 1.83 (m, 4H), 1.67 – 1.60 (m, 2H), 1.25 (s, 25H), 0.88 (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.89, 46.62, 45.57, 34.90, 31.94, 29.71, 29.68, 29.65, 29.57, 29.55, 29.49, 29.38, 26.16, 24.98, 24.44, 22.71, 14.14. **HRMS**: $[M + H]^+$ calculated for $C_{20}H_{40}NO^+$ 310.3104; Found 310.3102.



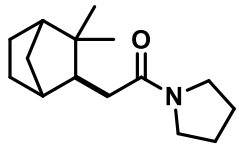
13n

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.49 – 3.44 m, 4H), 2.81 – 2.73 (m, 1H), 2.00 – 1.91 (m, 2H), 1.90 – 1.69 (m, 8H), 1.65 – 1.52 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.93, 46.46, 45.78, 43.10, 29.85, 26.17, 26.12, 24.36. NMR spectra are in agreement with the literature.[6]



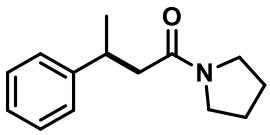
14n

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.48 – 3.43 (m, 4H), 2.37 – 2.29 (m, 1H), 1.98 – 1.89 (m, 2H), 1.88 – 1.62 (m, 7H), 1.58 – 1.44 (m, 2H), 1.33 – 1.19 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.78, 46.27, 45.64, 42.94, 28.90, 26.19, 25.90, 25.82, 24.30. NMR spectra are in agreement with the literature. [7]



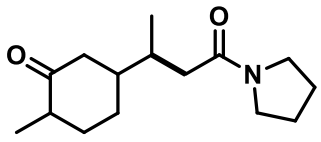
15n
Mixture of endo and exo products

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.49 – 3.39 (m, 6H), 2.35 – 2.16 (m, 4H), 2.15 – 1.97 (m, 2H), 1.95 – 1.92 (m, 3H), 1.88 – 1.81 (m, 3H), 1.81 – 1.65 (m, 7H), 1.59 – 1.49 (m, 2H), 1.37 – 1.21 (m, 5H), 1.17 – 1.15 (m, 1H), 1.10 – 1.07 (m, 1H), 1.04 (s, 1.5 H(~2H), *exo* -CH_3), 1.02 (s, 3H, *endo* -CH_3), 0.86 (s, 1.5 H(~2H), *exo* -CH_3), 0.80 (s, 3H, *endo* -CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.85, 54.55, 49.72, 49.48, 49.02, 46.68, 46.60, 46.16, 45.65, 45.63, 43.74, 42.11, 40.15, 37.06, 36.88, 36.38, 35.71, 32.22, 31.91, 29.57, 27.66, 26.18, 26.16, 25.07, 24.68, 24.42, 24.39, 24.13, 23.48, 21.62, 20.82. **HRMS**: $[M + H]^+$ calculated for $C_{15}H_{26}NO^+$ 236.2008; Found 236.2010. Note: The NMR of the derivatized products were compared with their parent carboxylic acids as reported by Kulkarni and co-workers[8] and Alper and co-workers[9] and ratio of *endo*:*exo* was determined.



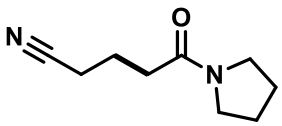
16n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 – 7.24 (m, 4H), 7.21 – 7.17 (m, 1H), 3.48 – 3.29 (m, 4H), 3.15 – 3.09 (m, 1H), 2.56 – 2.44 (m, 2H), 1.86 – 1.74 (m, 4H), 1.35 (d, *J* = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.32, 146.53, 128.38, 126.89, 126.21, 46.64, 45.54, 43.62, 36.38, 26.03, 24.34, 21.39. NMR spectra are in agreement with the literature.[10]



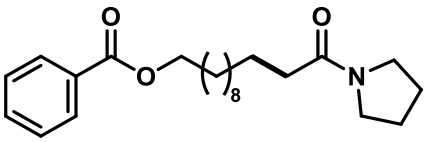
17n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.48 – 3.39 (m, 4H), 2.40 – 2.21 (m, 3H), 2.15 – 2.05 (m, 4H), 1.99 – 1.92 (m, 2H), 1.89 – 1.84 (m, 3H), 1.77 – 1.66 (m, 2H), 1.62 – 1.44 (m, 1H), 1.39 – 1.25 (m, 1H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.97 – 0.93 (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 213.46, 213.11, 170.72, 170.62, 54.19, 46.75, 46.72, 45.95, 45.71, 45.69, 45.11, 44.90, 44.75, 43.97, 39.30, 39.14, 34.90, 34.85, 34.41, 34.09, 29.83, 28.16, 26.14, 26.12, 24.38, 23.39, 16.75, 15.79, 14.35, 14.33. **HRMS**: $[M + H]^+$ calculated for $C_{15}H_{26}NO_2^+$ 252.1958; Found 252.1958. Note: The NMR of the derivatized products were compared with their parent carboxylic acids as reported by Beller and co-workers.[11]



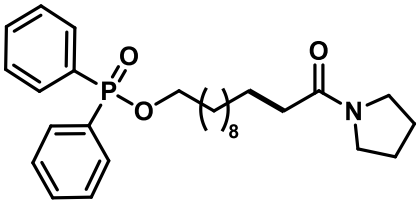
18n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.48 – 3.41 (m, 4H), 2.53 (t, *J* = 6.9 Hz, 2H), 2.44 (t, *J* = 6.8 Hz, 2H), 2.05 – 1.91 (m, 4H), 1.89 – 1.84 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 169.40, 119.71, 46.52, 45.73, 32.25, 26.04, 24.35, 20.52, 16.68. **HRMS**: $[M + H]^+$ calculated for $C_9H_{15}N_2O^+$ 167.1178; Found 167.1179.



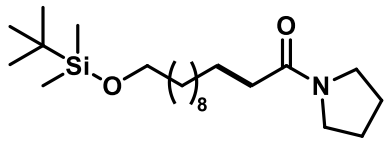
19n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 – 8.04 (m, 2H), 7.58 – 7.53 (m, 1H), 7.46 – 7.42 (m, 2H), 4.31 (t, *J* = 6.7 Hz, 2H), 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 -1.91 (m, 2H), 1.88 – 1.73 (m, 4H), 1.68 – 1.60 (m, 2H), 1.47 – 1.25 (m, 15H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.85, 166.71, 132.79, 130.52, 129.53, 128.32, 65.14, 46.61, 45.56, 34.87, 29.55, 29.53, 29.50, 29.48, 29.46, 29.28, 28.71, 26.14, 26.04, 24.96, 24.43. **HRMS**: $[M + H]^+$ calculated for $C_{23}H_{36}NO_3^+$ 374.2689; Found 374.2684, $[M + Na]^+$ calculated for $C_{23}H_{35}NO_3Na^+$ 396.2509; Found 396.2505.



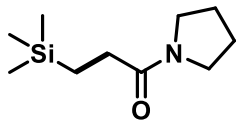
20
l:b 79:21

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 – 7.79 (m, 5H), 7.54 – 7.43 (m, 8H), 4.02 (q, *J* = 6.7 Hz, 3H), 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 – 1.91 (m, 2H), 1.86 – 1.82 (m, 2H), 1.73 – 1.62 (d, *J* = 7.1 Hz, 6H), 1.30 – 1.25 (m, 18H), 1.10 (d, *J* = 6.7 Hz, 0.81 H, *branched product* -CH_3). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.95, 132.27, 132.15, 132.12, 132.09, 131.68, 131.58, 130.90, 128.58, 128.45, 65.10, 65.04, 46.64, 45.60, 34.86, 30.56, 30.49, 29.53, 29.50, 29.45, 29.13, 26.12, 25.59, 24.95, 24.42. **^{31}P NMR** (162 MHz, $CDCl_3$) δ: 31.88. **HRMS**: $[M + H]^+$ calculated for $C_{28}H_{41}NO_3P^+$ 470.2819; Found 470.2818.



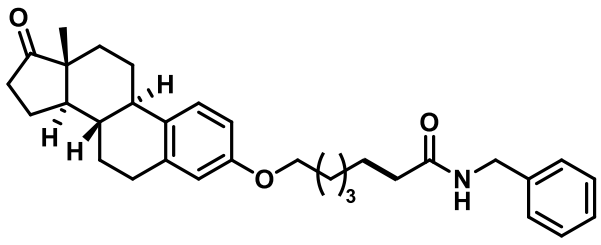
21n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.59 (t, *J* = 6.6 Hz, 2H), 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.27 – 2.23 (m, 2H), 1.98 – 1.91 (m, 2H), 1.88 – 1.79 (m, 2H), 1.68 – 1.60 (m, 2H), 1.55 – 1.47 (m, 2H), 1.30 – 1.25 (m, 16H), 0.89 (s, 9H), 0.05 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.87, 63.36, 46.61, 45.56, 34.89, 32.89, 29.63, 29.58, 29.56, 29.52, 29.48, 29.45, 26.15, 26.00, 25.80, 24.97, 24.43, 18.39, -5.25. **HRMS**: $[M + H]^+$ calculated for $C_{22}H_{46}NO_2Si^+$ 384.3292; Found 384.3291.



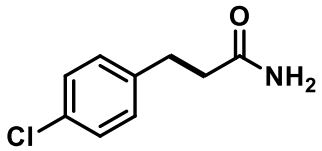
22n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.46 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.24 – 2.20 (m, 2H), 1.99 – 1.92 (m, 2H), 1.88 – 1.81 (m, 2H), 0.87 – 0.83 (m, 2H), 0.01 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 172.98, 46.48, 45.77, 29.20, 26.18, 24.42, 11.45, -1.84. **HRMS**: $[M + H]^+$ calculated for $C_{10}H_{22}NOSi^+$ 200.1465; Found 200.1466.



25n

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.36 – 7.28 (m, 4H), 7.20 – 7.17 (m, 1H), 6.71 – 6.69 (m, 1H), 6.64 – 6.63 (m, 1H), 5.72 (s, 1H), 4.44 (d, *J* = 5.7 Hz, 2H), 3.92 (t, *J* = 6.5 Hz, 2H), 2.91 – 2.87 (m, 2H), 2.54 – 2.47 (m, 1H), 2.40 – 2.37 (m, 1H), 2.24 – 1.93 (m, 7H), 1.78 – 1.51 (m, 9H), 1.49 – 1.35 (m, 5H), 1.28 – 1.17 (m, 1H), 0.90 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 221.10, 172.80, 157.06, 138.36, 137.71, 131.87, 128.73, 127.84, 127.53, 126.30, 114.51, 112.09, 67.67, 50.38, 48.03, 43.97, 43.60, 38.36, 36.66, 35.89, 31.56, 29.65, 29.14, 28.99, 26.56, 25.91, 25.80, 25.64, 21.58, 13.85. **HRMS**: $[M + H]^+$ calculated for $C_{32}H_{42}NO_3^+$ 488.3159; Found 488.3159.



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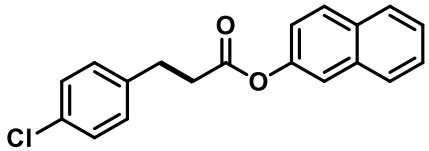
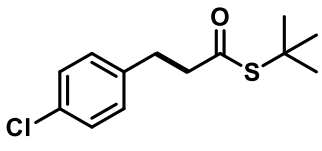
l:b 79:21

Followed procedure AII.6a. White solid, 32 mg, 83%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.33 – 7.31 (m, 0.50H, *branched amide phenyl H*) 7.27 – 7.24 (m, 2.7H, *2H belongs to linear amide phenyl + ~ 0.7H belongs to branched amide phenyl H*), 7.16 – 7.13 (m, 2H), 5.54 (d, *J* = 100.6 Hz, 2.5H; *2H belongs to linear amide* -NH + *0.5H belongs to branched amide* -NH), 3.58 (q, *J* = 7.2 Hz, 0.26 H, *belongs to branched amide* -CH *of tertiary* C), 2.94 (t, *J* = 7.6 Hz, 2H), 2.50 (t, *J* = 8.4 Hz, 2H), 1.50 (d, J = 7.2 Hz, 0.80 H, *belongs to branched amide* -CH_3 group present *on tertiary* C). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 174.17, 139.13, 132.05, 129.72, 128.65, 37.28, 30.61. δ (branched amide) : 176.13, 139.66, 133.22, 129.08, 128.93, 45.98, 18.48. NMR spectra are in agreement with the literature.[12]



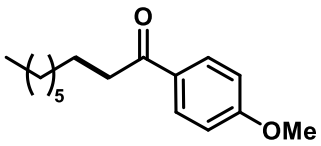
27n

Followed procedure AII.6b. White solid, 58 mg, 92%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.85 – 7.77 (m, 3H), 7.51 – 7.44 (m, 3H), 7.32 – 7.29 (m, 2H), 7.25 – 7.21 (m, 2H), 7.15 – 7.13 (m, 1H), 3.07 (t, *J* = 7.5 Hz, 2H), 2.92 (t, *J* = 7.5, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.32, 148.17, 138.56, 133.69, 132.27, 131.45, 129.84, 129.44, 128.73, 127.76, 127.63, 126.59, 125.75, 120.99, 118.45, 35.86, 30.27. **HRMS**: $[M + NH_4]^+$ calculated for $C_{19}H_{19}ClO_2N_1^+$ 328.1099; Found 328.1111.



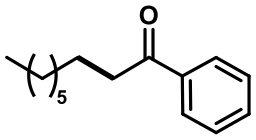
28
l:b 85:15

Followed procedure AII.6c. Colourless oil, 59 mg, 92%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.30 – 7.28 (m, 0.37 H, *branched thioester phenyl H)*, 7.26 – 7.23 (m, 2.34H, *2H belongs to linear thioester phenyl + ~ 0.34H belongs to branched thioester phenyl H*), 7.13 – 7.08 (m, 2H), 3.75 (q, *J* = 7.2 Hz, 0.18H, *belongs to branched thioester* -CH *of tertiary* C), 2.93 – 2.89 (m, 2H), 2.75 – 2.70 (m, 2H), 1.44 (s, 9H), 1.41 (s, 1.65H, *belongs to branched thioester* -CH_3 *group on tertiary* C). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (*mixture with branched thioester*): 201.25, 199.20, 138.69, 132.00, 129.75, 129.10, 128.75, 128.56, 53.84, 48.14, 45.70, 30.74, 29.77, 29.71. **GC-MS** (EI, 70 eV): m/z = 256, 200, 167, 138, 131, 125, 111, 103, 89, 77, 57.



29n

Followed procedure AII.6d. Off-white solid, 60 mg, 97%. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 2.93 – 2.89 (m, 2H), 1.75 – 1.68 (m, 2H), 1.38 – 1.24 (m, 11H), 0.88 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 199.32, 163.29, 130.33, 130.19, 113.65, 55.45, 38.34, 31.85, 29.47, 29.46, 29.19, 24.65, 22.67, 14.12. NMR spectra are in agreement with the literature.[13]



30
l:b 92:8

Followed procedure AII.6e. Colourless oil, 46 mg, 84%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 – 7.93 (m, 2H), 7.59 – 7.52 (m, 1H), 7.48 – 7.44 (m, 2H), 3.45 (q, *J* = 6.8 Hz, 0.09H, *belongs to branched ketone* -CH *of tertiary* C), 2.98 – 2.94 (m, 2H), 1.77 – 1.70 (m, 2H), 1.43 – 1.18 (m, 13H), 1.19 (d, *J* = 6.9 Hz, 0.34H, *belongs to branched ketone* -CH_3 *group on tertiary* C), 0.90 – 0.86 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 200.66, 137.08, 132.87, 128.55, 128.06, 38.65, 31.85, 29.46, 29.39, 29.19, 24.39, 22.67, 14.12. δ (branched ketone) : 204.63, 132.79, 128.60, 128.24, 40.58, 33.74, 31.70, 29.71, 27.38, 22.59, 17.23, 14.07. NMR spectra are in agreement with the literature.[13]

AII.9. References

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Appendix III

Supporting Information for Chapter 4

Regioselectivity in Carbonylation of Pentenoic Acid to Synthesize Cyclic Anhydrides

AIII.1. General experiment details and materials

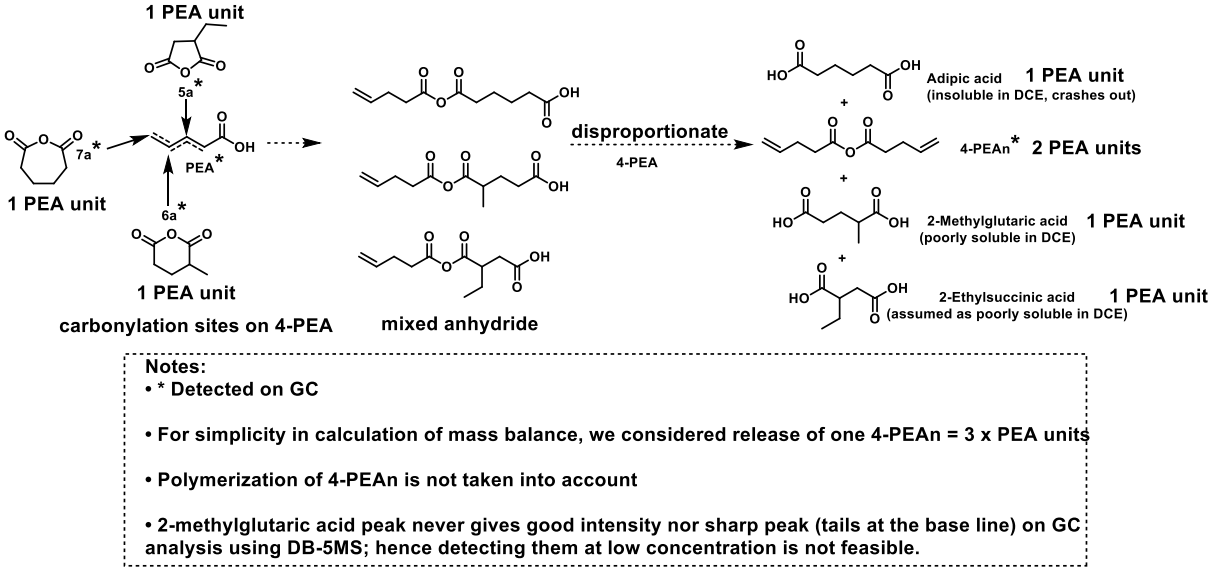
Reactions and chemicals related: All reactions and operations involving air- or moisture-sensitive compounds were performed using standard Schlenk techniques in heated and vacuum dried glassware or in N_2-filled glove box. 4-pentenoic acid and 4-pentenoic anhydride were purchased from Sigma-Aldrich and used without further purification. 2-Ethylsuccinic anhydride (**5a**) was purchased from Enamine Ltd. Anhydrous 1,2-dichloroethane (DCE) was purchased from Biosolve and dried over flame dried 4Å molecular sieves. Solvents were freeze-pump-thawed (FPT) before all catalytic reactions. All ligands were purchased from Sigma-Aldrich, Strem Chemicals and BLD pharm except 1,4-bis(*p*-chlorophenylphosphanyl)butane (**L16**),1,2-bis(diphenylphosphanylmethyl)benzene (**L5**) and o-bpax (**L6**). which were synthesized in-house. 1,2-bis((tert-butyl(pyridine-2-yl)phosphanyl)methyl)benzene (py^{t}bpx) (**L12**) was generously provided by Prof. Dr. Matthias Beller from LIKAT, Rostock, Germany.

a. Autoclaves: 75 mL stainless steel Parr autoclaves equipped with temperature probe and pressure adapter were used. For heating and stirring, Parr Multi Reactor System 5000 was used.

b. GC Analysis: Gas chromatography (GC) was measured on Shimadzu GC-2010, equipped with DB5MS (60 m) column, coupled to Flame Ionization Detector (FID). Gas chromatography-mass spectrometry (GC-MS) was measured on Agilent Technologies 7820A equipped with DB5MS (30 m) column and coupled to mass detector MSD 5975.

c. NMR Spectroscopy: ^{1}H NMR and ^{13}C NMR were recorded on Bruker Avance 400 (400MHz) NMR spectrometers. Multiplets were assigned as s (singlet), d (doublet), t (triplet), dd (doublet of doublet), and m (multiplet). All measurements were carried out at room temperature. NMR yields were calculated using dibromomethane as internal standard.

AIII.2. General reaction scheme showing all possible products of catalysis



Scheme AIII.1. Reaction scheme depicting the possible products formed in a catalytic reaction, calculation of PEA units and compounds that can be detected and quantified by GC analysis.

AIII.2.1. Calculations

a. Mass Balance

The mass balance was calculated in terms of "number of **PEA units**" present in the reaction mixture after catalysis as follows:

$$\frac{(unreacted\ 4PEA\ and\ isomers) + (cyclic\ anhydrides) + (4PEAn\ and\ related\ disproportionation\ products)}{Initial\ 4PEA\ concentration} \times 100$$

Where,

PEA units of 4-PEA = mmol of unreacted 4-PEA

PEA units of PEA isomers = mmol of PEA isomers

PEA units of cyclic anhydrides (**7a** or **6a** or **5a**) = mmol of **7a** or **6a** or **5a**

PEA units of 4-PEAn (along with disproportionated products) = 3 × mmol of 4-PEAn

An error margin of ±10% is considered to be acceptable for the mass balance.

b. Total yield % of cyclic anhydrides

$$\frac{\boldsymbol{7a} + \boldsymbol{6a} + \boldsymbol{5a}}{initial\ mmol\ of\ 4PEA} \times 100$$

c. Regioselectivity:

7a:**6a**:**5a** was calculated as follows:

$$\frac{\boldsymbol{7a}\ or\ \boldsymbol{6a}\ or\ \boldsymbol{5a}}{\boldsymbol{7a} + \boldsymbol{6a} + \boldsymbol{5a}} \times 100$$

d. Conversion %

Conversion % with respect to PEA was calculated as follows

$$\left[1 - \frac{Unreacted\ 4PEA + isomers\ of\ PEA}{initial\ mmol\ of\ 4PEA}\right] \times 100$$

An error margin of ±5% is considered to be acceptable for the conversion.

AIII.3. General catalytic procedure (GP) and analysis

Palladium acetate (0.05 mmol; 11.2 mg), ligand (0.10 mmol) and additive (0.125 mmol) were weighed into a clean and dried glass liner, in air, containing an oven−dried stirring bar. The glass liner was fitted inside a 75 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas.

For air-sensitive phosphine ligands, palladium acetate and ligand were weighed in the glove-box and dissolved in a fixed volume of dried and degassed 1,2-dichloroethane (DCE) in a Schlenk flask. Any additive to be added was weighed separately in air into the glass liner directly. The glass liner was fitted inside a 75 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. The catalyst solution prepared in the glove-box was added to the autoclave using standard Schlenk techniques.

Degassed solution of 4-pentenoic acid (4-PEA) (1.0 mmol; 102.2 µL) in dried DCE was added using standard Schlenk techniques The autoclave was transferred to Parr MRS5000 heating block and connected to the gas lines. The lines connecting the autoclave was flushed with nitrogen (N_2) (3 × 30 bars). The autoclave was flushed with carbon monoxide (CO) (1 × 30 bars) and subsequently charged with CO to 50 bar. The autoclave was stirred at 500 rpm and heated for 15 h at the desired temperature. At the end of the reaction time, the autoclave was brought to room temperature. The contents of the glass liner were transferred to a 10 mL volumetric flask, 0.3 mL undecane (internal standard for GC analysis) was added and the total volume was adjusted to 10 mL using DCE. The resulting solution was then analyzed using GC.

GC Analysis: Quantification of compounds: 4-PEA, **7a**, **6a**, **5a** and 4-PEAn present in the GC sample were determined using calibration lines with undecane as the internal standard. Calibration line of 4-PEA was applied for the quantification of PEA isomers. A 60 m × 0.250 mm ; 1.0 µm thickness DB-5MS GC column was used for analysis. 3.0 µL of each sample was injected and the following temperature program was used: injector at 300 °C, FID at 350 °C, oven at 50 °C for 3 min, increasing to 300 °C at 5 °C/min, then increasing to 325 °C at 15 °C/min and hold at 325 °C for 5 min.

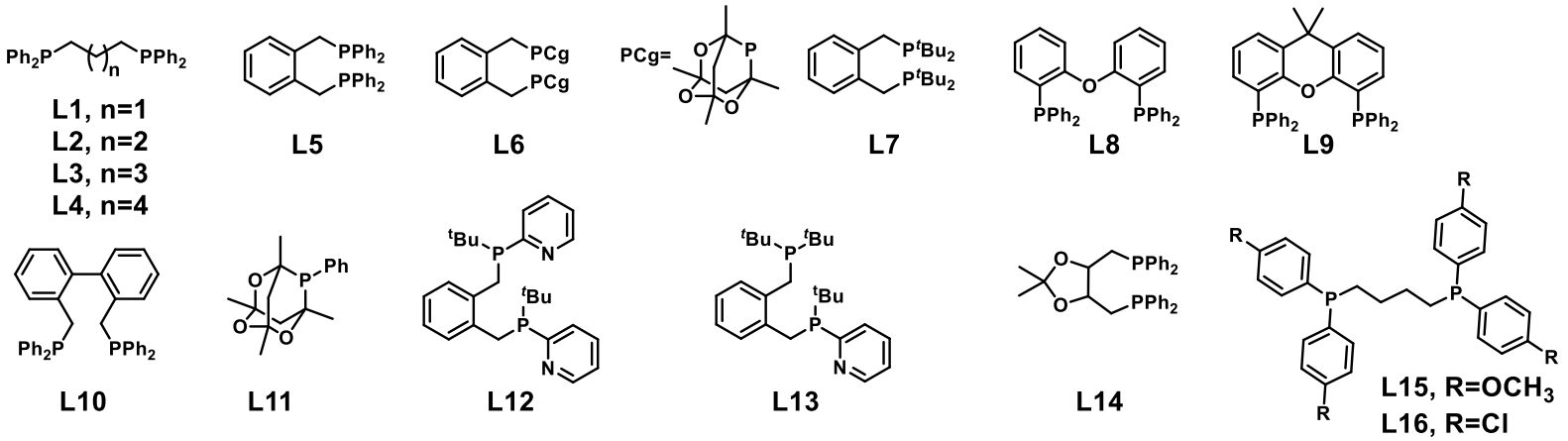
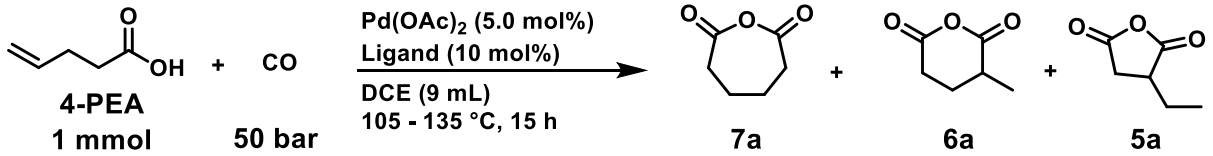


Figure AIII.1. Structures of phosphine ligands tested for cyclocarbonylation of 4-PEA.

AIII.4. Results of ligand screening

GP followed with one deviation: no additive was added

Table AIII.1. Cyclocarbonylation of 4-PEA: Study of influence of ligands on regioselectivity.



Entry	*L*	*T* (°C)	Unreacted 4-PEA mmol	PEA isomers mmol	4-PEAn mmol	7a mmol	6a mmol	5a mmol	Conversion %	Total Yield %	Selectivity 7a:6a:5a	Mass balance %
1	**L1**	105	0.29	0.03	0.07	0.12	0.09	0	68	21	57 : 43 : --	73
2[a]	**L2**	105	0.08	0	0.02	0.58	0.15	0	92	73	79: 21 : --	87
3	**L3**	105	0.24	0.05	0.03	0.38	0.11	0	71	49	78 : 22 : --	87
4	**L4**	105	0.80	0	0.05	0	0	0	20	0	--	96
5[b]	**L5**	120	0.27	0.03	0.04	0.35	0.07	0	70	42	88 : 12 : --	84

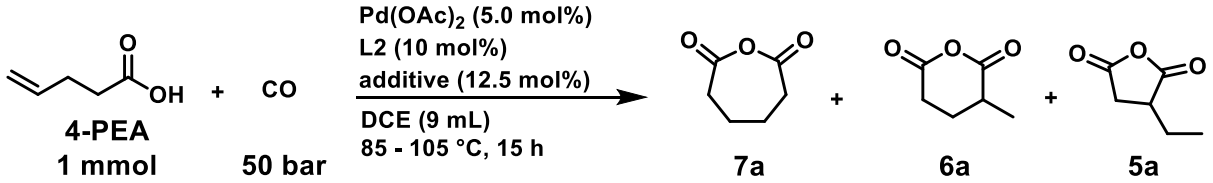
6[b]	**L6**	120	0.33	0.08	0.03	0.17	0	0	59	17	>99 : -- : --	68
7[b]	**L6**	135	0.13	0.43	0	0.06	0.02	0	44	8	75 : 25 : --	64
8[b]	**L7**	120	0.78	0.11	0	0	0	0	11	0	--	89
9	**L8**	120	0.24	0	0.04	0.31	0.09	0	76	40	78 : 22 : --	75
10	**L8**	135	0.12	0.03	0	0.39	0.10	0	85	49	79 : 21 : --	65
11	**L9**	120	0.29	0	0.04	0.10	0.18	0	71	28	36 : 64 : --	69
12[b]	**L10**	120	0.52	0	0.05	0.01	0.08	0	48	9	11 : 89 : --	76
13[c]	**L11**	105	0.24	0.48	0	0	0.28	Trace	28	28	-- : >99 : --	100
14[b]	**L12**	120	0.31	0.09	0.05	Trace	0.04	0	60	4	-- : >99 : --	59
15	**L14**	105	0.39	0	0.06	0.15	0.09	0	61	24	64 : 36 : --	81
16	**L15**	105	0.24	0.07	0.02	Trace	0.15	0.05	69	20	-- : 74 : 26	58
17	**L16**	105	0.33	0.04	0.05	0.22	0.06	0	63	28	79 : 21 : --	81

Reaction conditions: 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), *L* : diphosphine ligand (0.1 mmol) or monophosphine ligand (0.20 mmol), additive (0.125 mmol), CO (50 bar), *T* °C DCE (9 mL), 15 h. Quantification of compounds, conversion %, total yield % and regioselectivity were determined by GC using undecane as internal standard. [a] Adipic acid was found to be 8% (0.08 mmol) by NMR analysis; Mass Balance becomes 93%. [b] ligand 0.075 mmol used instead of 0.10 mmol. [c] ligand 0.20 mmol used instead of 0.10 mmol.

AIII.5. Influence of additives

Procedure same as GP

Table AIII.2. Cyclocarbonylation of 4-PEA: Study of additives on regioselectivity.



Entry	*L*	*T* (°C)	Additive	Unreacted 4-PEA mmol	PEA isomers mmol	4-PEAn mmol	7a mmol	6a mmol	5a mmol	Conv. %	Total Yield %	Selectivity 7a:6a:5a	Mass balance %
1[a]	**L2**	105	none	0.08	0	0.02	0.58	0.15	0	92	73	79: 21 : --	87

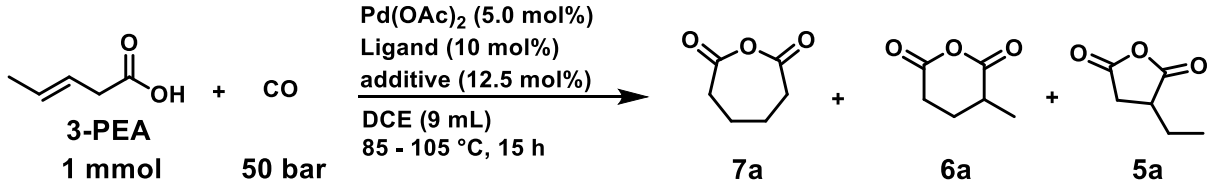
2[b]	**L2**	105	none	0	0	0	0.08	0.39	0.23	>99	70	12 : 55 : 33	70
3[c]	**L2**	105	none	0.83	0	0	0	0	0	17	0	-- : -- : --	83
4	**L2**	105	Formic acid	0.14	0.03	0.02	0.39	0.14	0.05	83	58	67 : 24 : 9	84
5	**L2**	105	2,4,6-trimethylbenzoic acid	0.28	0	0.06	0.20	0.07	0.05	72	32	61 : 23 : 16	80
6	**L2**	85	PPA	0.04	0	0	0.08	0.42	0.26	96	76	10 : 56 : 34	80
7	**L2**	85	HOTs.H_2O	0.05	0.07	0	0	0	0.69	88	69	-- : -- : >99	81
8	**L2**	85	HOMs	0	0	0	0	0	0.83	>99	83	-- : -- : >99	83
9	**L2**	85	10-CSA	0	0	0	0	0.22	0.63	>99	85	-- : 26 : 74	85
10	**L2**	85	$SnCl_2$	0	0	0	0	0.08	0.80	>99	92	-- : 10 : 90	88
11	**L2**	85	$Sn(OAc)_2$	0.13	0	0	0.49	0.09	0.15	87	73	67 : 13 : 20	86
12[c]	**L2**	85	$SnCl_2$	0	0.54	0	0	0	0.24	46	24	-- : -- : >99	78
13	**L2**	85	LiOAc	0.23	0.03	0.04	0.33	0.10	0.04	74	47	70 : 21 : 9	86
14	**L2**	85	LiCl	0.72	0	0.04	0	0.05	0	28	5	-- : >99 : --	88
15	**L2**	85	$Al(^iOPr)_3$	0.28	0	0.07	0.08	0.06	0.04	>72	18	46 : 32 : 22	67
16	**L2**	85	2,4,6-trimethylphenol	0.41	0.03	0.08	0.10	0.04	0.04	56	18	56 : 22 : 22	85
17	**L2**	85	2,6-diisopropylphenol	0.29	0	0.06	0.32	0.08	0	71	40	80 : 20 : --	88
18	**L2**	105	2,6-diisopropylphenol	0.12	0.03	0	0.48	0.12	0.04	85	64	76 : 18 : 6	79
19	**L2**	85	HFIP	0.24	0.03	0.04	0.24	0.07	0.07	73	37	63 : 18 : 18	77
20	**L2**	85	2-napthol	0.07	0.05	0	0.25	0.15	0.07	88	46	54 : 31 : 15	59
21[d]	**L5**	85	HOTs.H_2O	0	0	0	0	0	0.75	>99	75	-- : -- : >99	75
22[e]	**L6**	85	HOTs.H_2O	0	0	0	0	0.06	0.90	>99	96	-- : 6 : 94	96
23[f]	**L7**	120	HOMs	0	0.60	Trace	Trace	0.04	0	36	4	-- : >99 : --	64
24	**L8**	85	HOTs.H_2O	0	0	0	0	0	0.89	>99	89	-- : -- : >99	89
25[d]	**L9**	85	HOTs.H_2O	0	0	0	0.11	0.40	0.14	>99	65	17 : 62 : 21	65
26[d]	**L9**	85	$SnCl_2$	0	0	0	0	0.78	0.18	>99	96	-- : 81 : 19	96
27[f]	**L10**	85	HOTs.H_2O	0	0	0	0	0.47	0.21	>99	68	-- : 69 : 31	68
28[f]	**L10**	85	$SnCl_2$	0	0	0	0	0.74	0.17	>99	91	-- : 81 : 19	91
29[g]	**L12**	85	HOTs.H_2O	0.34	0.11	0	Trace	0.24	0	55	24	-- : >99 : --	69
30[h]	**L12**	120	HOTs.H_2O	0.12	0.50	0	Trace	0.06	0	38	6	-- : >99 : --	65
31[g]	**L13**	85	HOTs.H_2O	0.61	0.17	0	0	0	0	22	0	--	78

Reaction conditions: 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), *L* (0.1 mmol), additive (0.125 mmol), CO (50 bar), *T* °C, DCE (9 mL), 15 h. Quantification of compounds, conversion %, total yield % and regioselectivity were determined by GC using undecane as internal standard. [a] Adipic acid was found to be 8% (0.08 mmol) by NMR analysis; Mass Balance becomes 93%. [b] $Pd(TFA)_2$ instead of $Pd(OAc)_2$. [c] $PdCl_2$ instead of $Pd(OAc)_2$. [d] 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), *L* (0.05 mmol), additive (0.0625 mmol), CO (50 bar), *T* °C, DCE (9 mL), 15 h. [e] 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), *L* (0.0375 mmol), additive (0.0625 mmol), CO (50 bar), *T* °C, toluene (9 mL), 15 h. [f] 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.025 mmol), *L* (0.0375 mmol), additive (0.0625 mmol), CO (50 bar), *T* °C, DCE (9 mL), 15 h. [g] 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.01 mmol), *L* (0.015 mmol), additive (0.025 mmol), CO (50 bar), *T* °C, DCE (9 mL), 15 h. [h] 4-PEA (1.0 mmol), $Pd(OAc)_2$ (0.01 mmol), *L* (0.02 mmol), additive (0.04 mmol), CO (50 bar), *T* °C, toluene (9 mL), 15 h. Abbreviations: PPA: Phenylphosphonic acid, 10-CSA: Camphorsulfonic acid, $HOTs.H_2O$: *p*-Toluenesulfonic acid monohydrate, HOMs: Methanesulfonic acid, HFIP: 1,1,1,3,3,3-Hexafluoroisopropanol.

AIII.6. Study of certain reaction conditions on 3-PEA

GP followed with a deviation: 3-PEA used instead of 4-PEA

Table AIII.3. Cyclocarbonylation of 3-PEA: Testing of various conditions to observe regioselectivity of products.



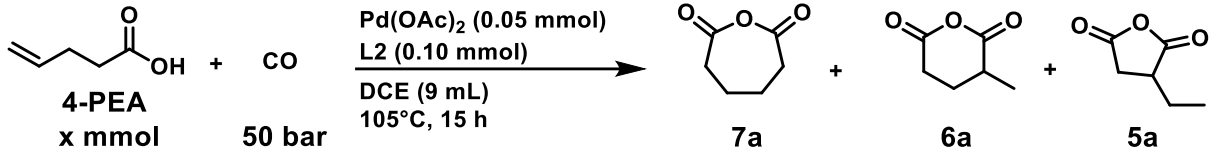
Entry	*L*	*T* (°C)	Additive	Unreacted 3-PEA mmol	PEA isomers mmol	4-PEAn	7a mmol	6a mmol	5a mmol	Conversion %	Total Yield %	Selectivity 7a:6a:5a	Mass balance%
1	**L2**	105	-	0.16	0	0	0	0.25	0.36	84	61	-- : 41 : 59	78
2[a]	**L2**	90	$HOTs.H_2O$	0.6	0	0	0	0	7.1	94	71	-- : -- : >99	77
3	**L9**	85	$HOTs.H_2O$	0	0	0	0	0.26	0.57	>99	83	-- : 31 : 69	83
4	**L9**	85	$SnCl_2$	0	0	0	0	0.34	0.56	>99	90	-- : 38 : 62	90

Reaction conditions: 3-PEA (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), *L* (0.1 mmol), additive (0.125 mmol), CO (50 bar), DCE (9 mL), *T* °C, 15 h. Quantification of compounds, conversion %, total yield % and regioselectivity were determined by GC using undecane as internal standard. [a] 3-PEA (10 mmol), $Pd(OAc)_2$ (0.08 mmol), diphosphine ligand (0.24 mmol), additive (0.80 mmol), CO (40 bar), Anisole (8 mL), 5 h.

AIII.7. Study of substrate:[Pd] ratio and dilution effect on formation of 7a, 4-PEAn and mass balance

GP followed with a deviation: mmol of 4-PEA used as mentioned in Table AIII.4

Table AIII.4. Cyclocarbonylation of 4-PEA: Study of [substrate]:[Pd] ratio and dilution factor to observe changes in **7a** selectivity and mass balance.



Entry	Scale (mmol)	Ligand	Additive	Temperature (°C)	Unreacted 4-PEA mmol	PEA isomers mmol	4-PEAn mmol	Adipic acid mmol[a]	7a mmol	6a mmol	5a mmol	Conversion %	Total Yield %	Selectivity 7a:6a:5a	Mass balance%
1	5	**L2**	-	105	0.75	0.10	0.45	0.95	0.45	0.30	Trace	83	16	63 : 37 : --	69
2	2.5	**L2**	-	105	0.45	0.10	0.13	0.40	0.78	0.25	Trace	78	45	76 : 24 : -	90
3[b]	2.5	**L2**	-	105	0.35	0.10	0.23	0.48	0.40	0.18	0.10	82	27	59 : 27 : 14	83
4	1	**L2**	-	105	0.08	0	0.02	0.08	0.58	0.15	0	92	73	79 : 21 : -	93
5[c]	10	**L10**	$SnCl_2$	85	0	0	0	0	0.4	7.4	1.5	>99	93	4 : 80 : 16	93
6	10	**L2**	$HOTs.H_2O$	90	0.6	0	0	0	0	0	5.8	94	58	-- : -- : >99	62

Reaction conditions: 4-PEA (x mmol), $Pd(OAc)_2$ (0.05 mmol), **L2** (0.10 mmol), additive (0.125 mmol), CO (50 bar), *T* °C, DCE (9 mL), 15 h. [a] determined by NMR using dibromomethane as internal standard. [b] $Pd(OAc)_2$ 0.025 mmol used instead of 0.05 mmol, **L2** 0.05 mmol used instead of 0.10 mmol. [c] **L10** 0.0625 mmol used instead of 0.10 mmol.

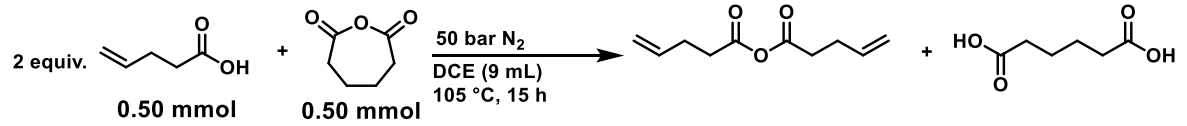
AIII.8. Control experiments for reaction insights

AIII.8.1. Reaction of 4-PEA and 7a in absence of catalyst

4-PEA (0.50 mmol; 51.2 µL) and **7a** (0.50 mmol; 64.1 mg) were weighed in a Schlenk flask, dissolved in dried DCE and transferred into an autoclave fitted with a glass liner containing an oven-dried magnetic stirring bar. The autoclave was transferred to Parr MRS5000 heating block and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (3× 30 bars). The autoclave was flushed with N_2 (1× 30 bars) and subsequently charged with N_2 to 50 bar. The autoclave was stirred at 500 rpm and heated for 15 h at 105 °C. At the end of the reaction time, the autoclave was brought to room temperature and slowly depressurized. The contents of the glass liner were transferred to a 10 mL volumetric flask. 0.3 mL undecane (internal standard for GC analysis) was added to the volumetric flask and the total volume was adjusted to 10 mL using DCE. The resulting solution was then analyzed using GC. Following observations were noted:

i. GC analysis indicated the formation of 4-PEAn majorly along with several small unknown peaks
ii. A white precipitate formed in the reaction mixture was analyzed by NMR and identified as adipic acid (9% ; 0.05 mmol).

Table AIII.5. Mass balance of reaction between 4-PEA and **7a** under N_2.



Unreacted 4-PEA (mmol)	PEA isomers (mmol)	4-PEAn (mmol)	Adipic acid (mmol)	7a (mmol)	6a (mmol)	5a (mmol)	Mass balance %
0.24	0	0.06	0.05	0.31	0	0	72

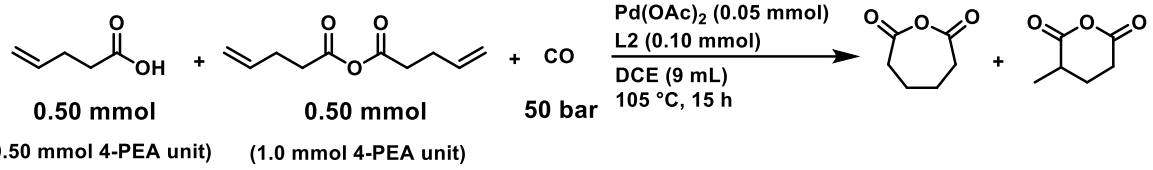
Reaction conditions: 4-PEA (0.50 mmol), **7a** (0.50 mmol), N_2 (50 bar), 105 °C, DCE (9 mL), 15 h.

AIII.8.2. Reaction of 4-PEA and 4-PEAn under catalytic conditions

Palladium acetate (0.05 mmol; 11.2 mg) and **L2** (0.10 mmol; 42.6 mg) weighed into a clean and dried glass liner, in open air, containing an oven−dried stirring bar. The glass liner was fitted inside a 75 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed solution of 4-PEA (0.50 mmol; 51.2 µL) and 4-PEAn (0.50 mmol; 92.0 µL) in dried DCE was added using standard Schlenk techniques. The autoclave was transferred to Parr MRS5000 heating block and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (3 × 30 bars). The autoclave was flushed with CO (1 × 30 bars) and subsequently charged with CO to 50 bar. The autoclave was stirred at 500 rpm and heated for 15 h at 105 °C. At the end of the reaction time, the autoclave was brought to room temperature. The contents of the glass liner were transferred to a 10 mL volumetric flask, 0.3 mL undecane (internal standard for GC analysis) was added and the total volume was adjusted to 10 mL using DCE. The resulting solution was then analyzed using GC. Following observations were noted:

i. Reaction mixture was turbid indicating formation of adipic acid (17%; 0.09 mmol)
ii. Increase in 4-PEA concentration than expected by 0.17 mmol
iii. Decrease in 4-PEAn concentration by 0.32 mmol

Table AIII. 6. Mass balance of reaction between 4-PEA and 4-PEAn under catalytic conditions.



Unreacted 4-PEA (mmol)	PEA isomers (mmol)	4-PEAn (mmol)	Adipic acid (mmol)	7a (mmol)	6a (mmol)	5a (mmol)	Mass balance %
0.36	0	0.18	0.09	0.19	0.12	0	75

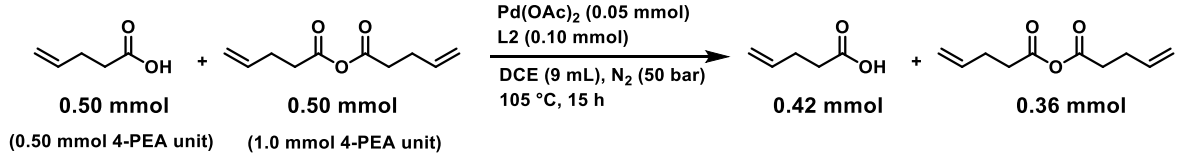
Reaction conditions: 4-PEA (0.50 mmol), 4-PEAn (0.50 mmol), $Pd(OAc)_2$ (0.05 mmol), **L2** (0.10 mmol), CO (50 bar), 105 °C, DCE (9 mL), 15 h.

AIII.8.3. Reaction of 4-PEA and 4-PEAn under catalytic conditions in absence of CO

Palladium acetate (0.05 mmol; 11.2 mg) and **L2** (0.10 mmol; 42.6 mg) weighed into a clean and dried glass liner, in open air, containing an oven−dried stirring bar. The glass liner was fitted inside a 75 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed solution of 4-PEA (0.50 mmol; 51.2 µL) and 4-PEAn (0.50 mmol; 92.0 µL) in dried DCE was added using standard Schlenk techniques. The autoclave was transferred to Parr MRS5000 heating block and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (3 × 30 bars). The autoclave was flushed with N_2 (1 × 30 bars) and subsequently charged with N_2 to 50 bar. The autoclave was stirred at 500 rpm and heated for 15 h at 105 °C. At the end of the reaction time, the autoclave was brought to room temperature. The contents of the glass liner were transferred to a 10 mL volumetric flask, 0.3 mL undecane (internal standard for GC analysis) was added and the total volume was adjusted to 10 mL using DCE. The resulting solution was then analyzed using GC. Following observations were noted:

i. Clear reaction mixture: no formation of adipic acid
ii. Loss of 4-PEAn is lesser than in presence of CO

Table AIII.7. Mass balance of reaction between 4-PEA and 4-PEAn under catalytic conditions but in absence of CO.



Unreacted 4-PEA (mmol)	PEA isomers (mmol)	4-PEAn (mmol)	7a (mmol)	6a (mmol)	5a (mmol)	Mass balance %
0.42	0	0.36	0	0	0	76

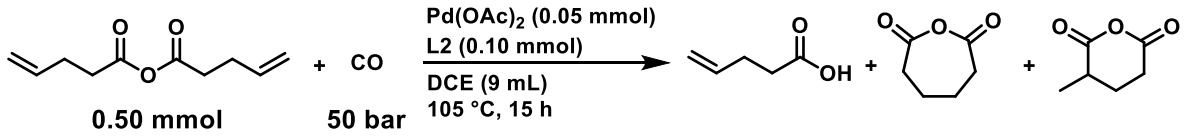
Reaction conditions: 4-PEA (0.50 mmol), 4-PEAn (0.50 mmol), $Pd(OAc)_2$ (0.05 mmol), **L2** (0.10 mmol), N_2 (50 bar), 105 °C, DCE (9 mL), 15 h.

AIII.8.4. Reaction of 4-PEAn under catalytic conditions

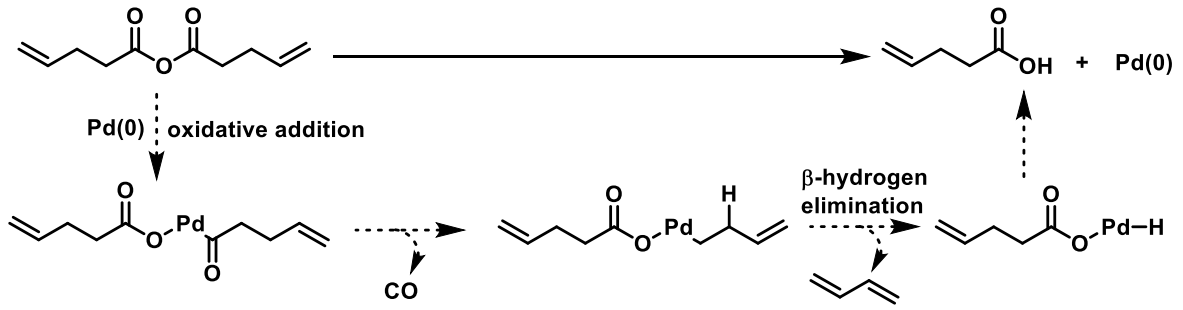
Palladium acetate (0.05 mmol; 11.2 mg) and **L2** (0.10 mmol; 42.6 mg) weighed into a clean and dried glass liner, in open air, containing an oven−dried stirring bar. The glass liner was fitted inside a 75 mL stainless steel Parr autoclave and the autoclave was closed. The autoclave was connected to a Schlenk line and subjected to five cycles of evacuation and refilling with nitrogen gas. Degassed solution of 4-PEAn (0.50 mmol; 92.0 µL) in dried DCE was added using standard Schlenk techniques. The autoclave was transferred to Parr MRS5000 heating block and connected to the gas lines. The lines connecting the autoclave was flushed with N_2 (3 × 30 bars). The autoclave was flushed with N_2 (1 × 30 bars) and subsequently charged with CO to 50 bar. The autoclave was stirred at 500 rpm and heated for 15 h at 105 °C. At the end of the reaction time, the autoclave was brought to room temperature. The contents of the glass liner were transferred to a 10 mL volumetric flask, 0.3 mL undecane (internal standard for GC analysis) was added and the total volume was adjusted to 10 mL using DCE. The resulting solution was then analyzed using GC. Following observations were noted:

i. 4-PEA formation observed along with traces of **7a** and **6a**

Table AIII. 8. Mass balance of reaction of 4-PEAn under catalytic conditions.

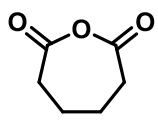


4-PEA formed (mmol)	PEA isomers (mmol)	4-PEAn (mmol)	7a (mmol)	6a (mmol)	5a (mmol)	Mass balance %
0.06	0	0.31	Trace	Trace	0	74



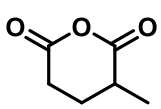
Scheme AIII.2. Possible mechanism of 4-PEA formation from 4-PEAn.

AIII.9. Synthesis of GC standards



Adipic anhydride (**7a**)

Adipic acid (2.0 g) was weighed in a 2-necked round bottom flask fitted with a reflux condenser at one end. 8.0 mL acetic anhydride was charged into the flask and the reaction mixture was refluxed overnight (~18 h). The reaction mixture was cooled to room temperature. Acetic anhydride was distilled out under vacuum to leave an oily residue. The oily residue was subjected to repeated vacuum distillations with toluene (10 mL × 3) followed by trituration with diethyl ether (10 mL) till solid appears. The suspension was filtered and the off-white precipitate collected was dried under high vacuum. The yield of the solid obtained was 1.02 g, 58% (97% purity), off-white to beige colour in appearance. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.56 – 2.48 (m, 4H), 1.82 – 1.70 (m, 4H). Peak observed at δ: 2.23 (0.22H) belongs to acetic anhydride.**^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.87, 34.73, 23.27. The NMR spectra are in agreement with the literature.[1]



2-Methylglutaric anhydride (**6a**)

2-Methylglutaric acid (2.0 g) was weighed in a 2-necked round bottom flask fitted with a reflux condenser at one end. 8.0 mL acetic anhydride was charged into the flask and the reaction mixture was refluxed overnight (~18 h). The reaction mixture was cooled to room temperature. Acetic anhydride was distilled out under vacuum to leave an oily residue. The oily residue was subjected to repeated vacuum distillations with toluene (10 mL × 3). The oil was completely solubilized in diethyl ether and cooled to -20 °C to obtain a white precipitate. The suspension was quickly filtered cold and the solid collected was immediately dried under high vacuum. The yield of the solid obtained was 594 mg, 34% and white colour in appearance. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.93 (ddd, J = 18.1, 5.1, 3.5 Hz, 1H), 2.79 – 2.61 (m, 2H), 2.07 (dddd, J = 13.8, 6.0, 5.3, 3.5 Hz, 1H), 1.79 (ddd, J = 13.8, 12.1, 5.1 Hz, 1H), 1.39 (d, J = 6.9 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 169.67, 166.80, 35.80, 30.19, 24.38, 15.73. The NMR spectra are in agreement with the literature.[2]

AIII.10. Typical GC chromatograms, NMR of precipitate in attempted catalysis to synthesize 7a

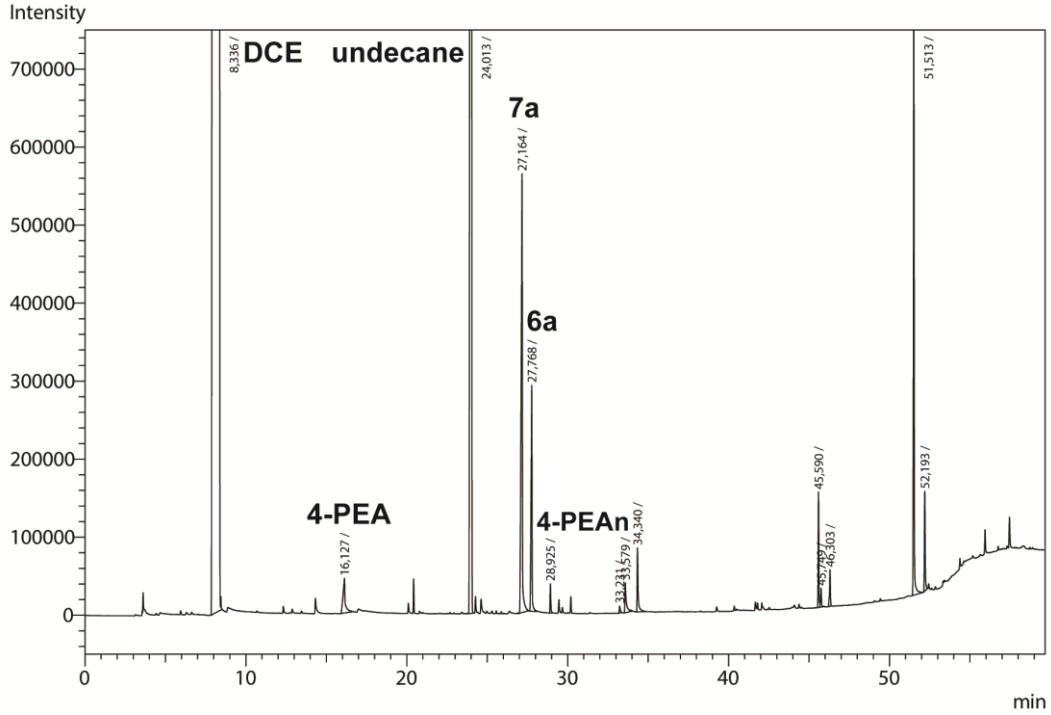


Figure AIII.2. Typical GC-FID chromatogram of catalytic reaction mixture with selectivity towards **7a** (Table AIII.1, entry 2). Peaks >30 mins could not be identified.

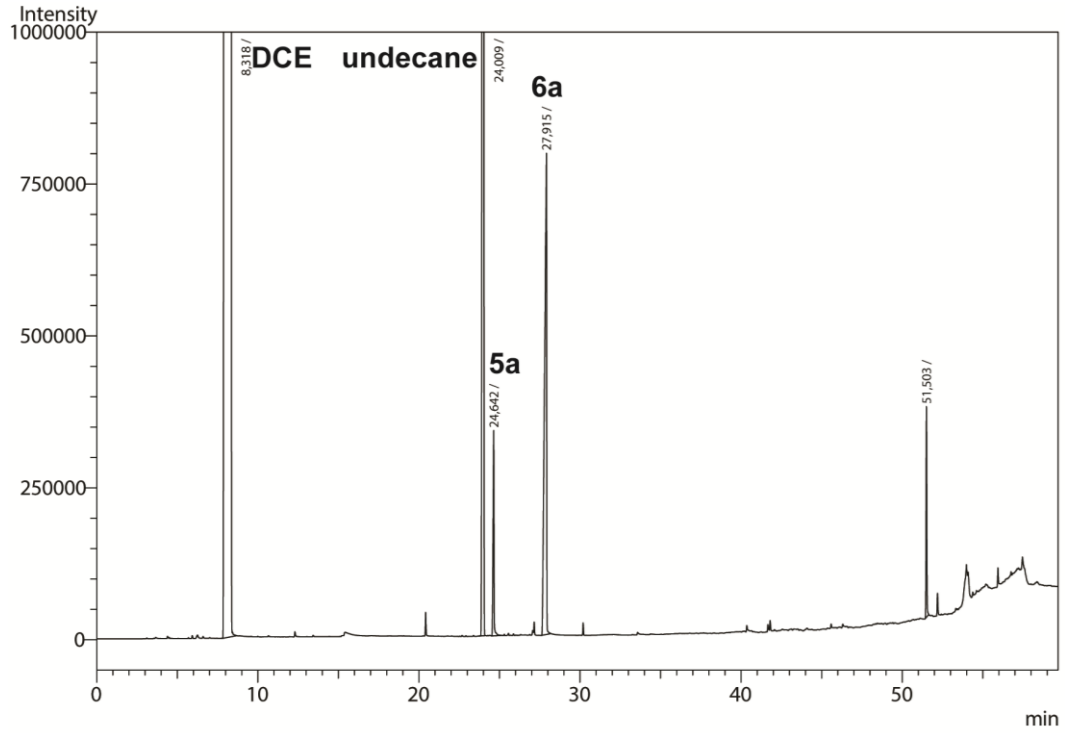


Figure AIII.3. Typical GC-FID chromatogram of catalytic reaction mixture with selectivity towards **6a** (Table AIII.2, entry 26). Peaks >30 mins could not be identified.

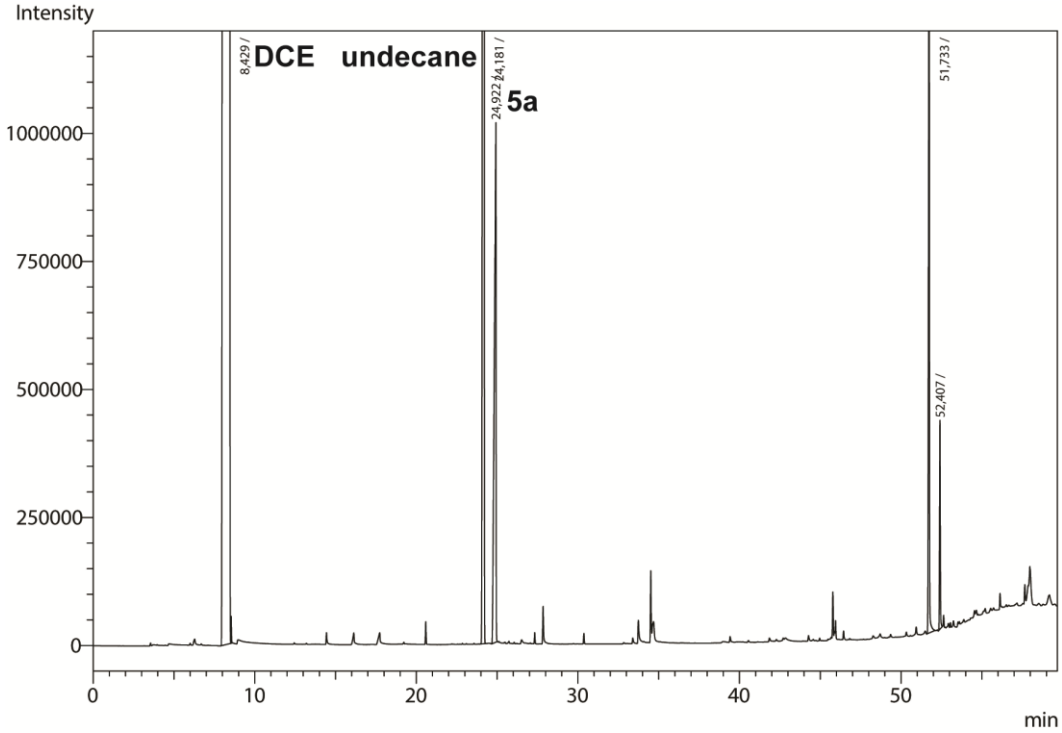


Figure AIII. 4. Typical GC-FID chromatogram of catalytic reaction mixture with selectivity towards **5a** (Table AIII.2, entry 8). Peaks >30 mins could not be identified.

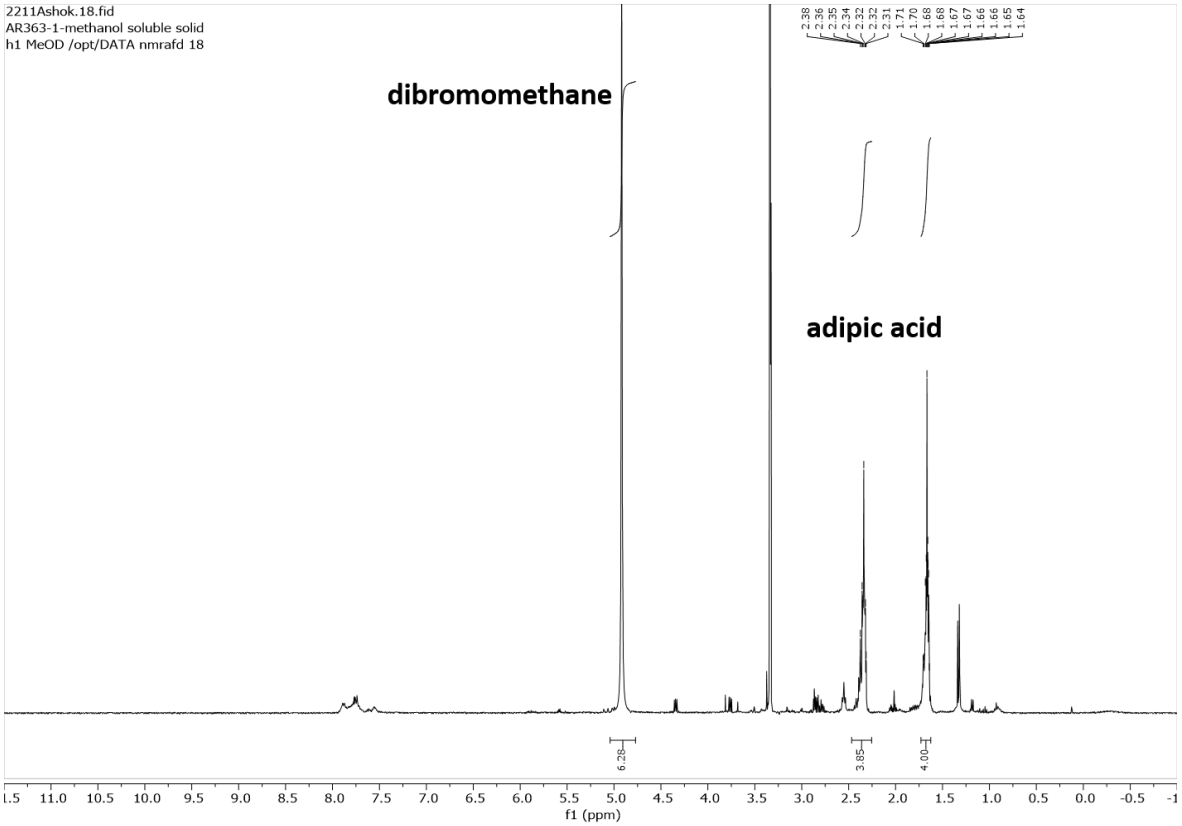


Figure AIII.5. ^{1}H NMR of precipitate formed in the catalytic reaction of Table AIII.1, entry 2.

AIII.11. ESI-MS spectra of methanolic solution of $SnCl_2$ and 4-PEA (0.125 : 1.0 mmol $SnCl_2$:4-PEA)

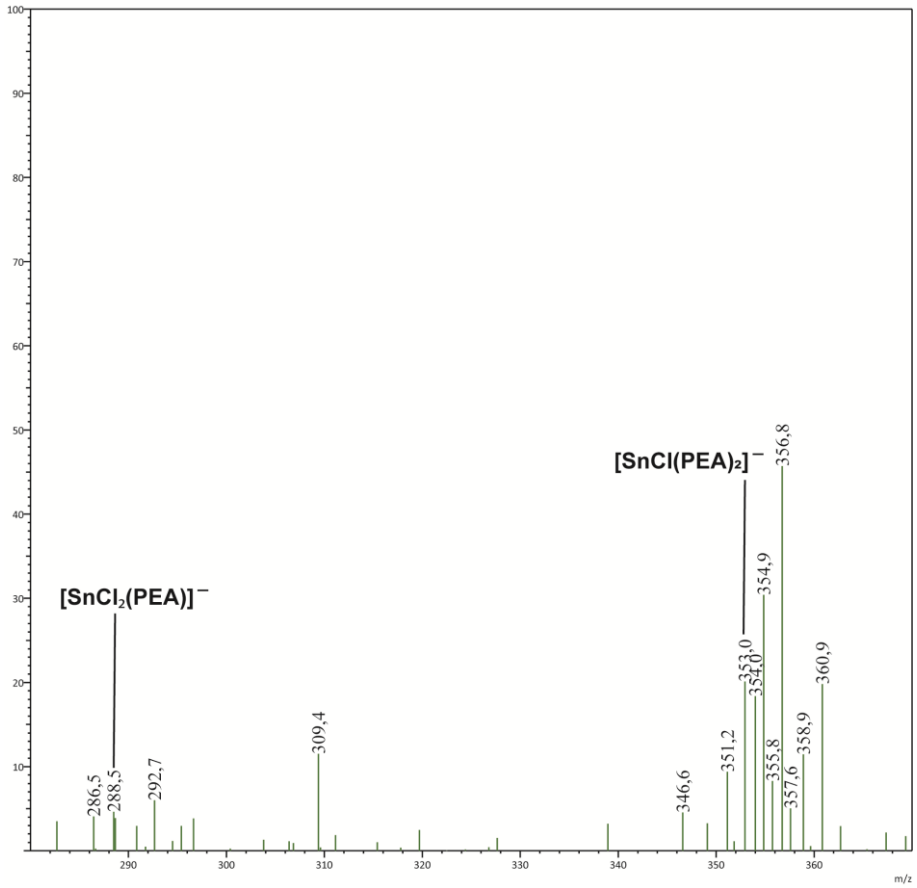


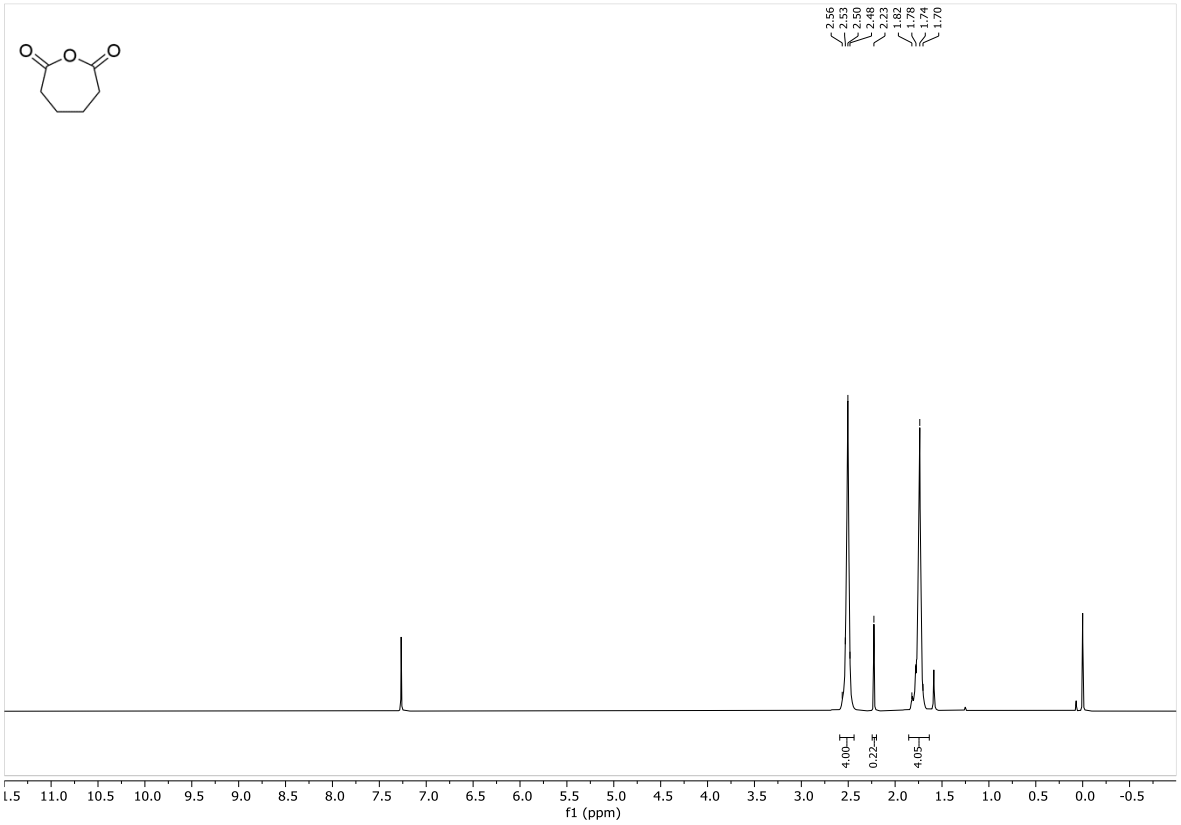
Figure AIII.6. ESI-MS (negative mode) of methanolic solution of $SnCl_2$ and 4-PEA; m/z calculated for $[SnCl_2(PEA)]^-$ is 288.9, found: 288.5; ; m/z calculated for $[SnCl(PEA)_2]^-$ is 352.96, found: 353.0.

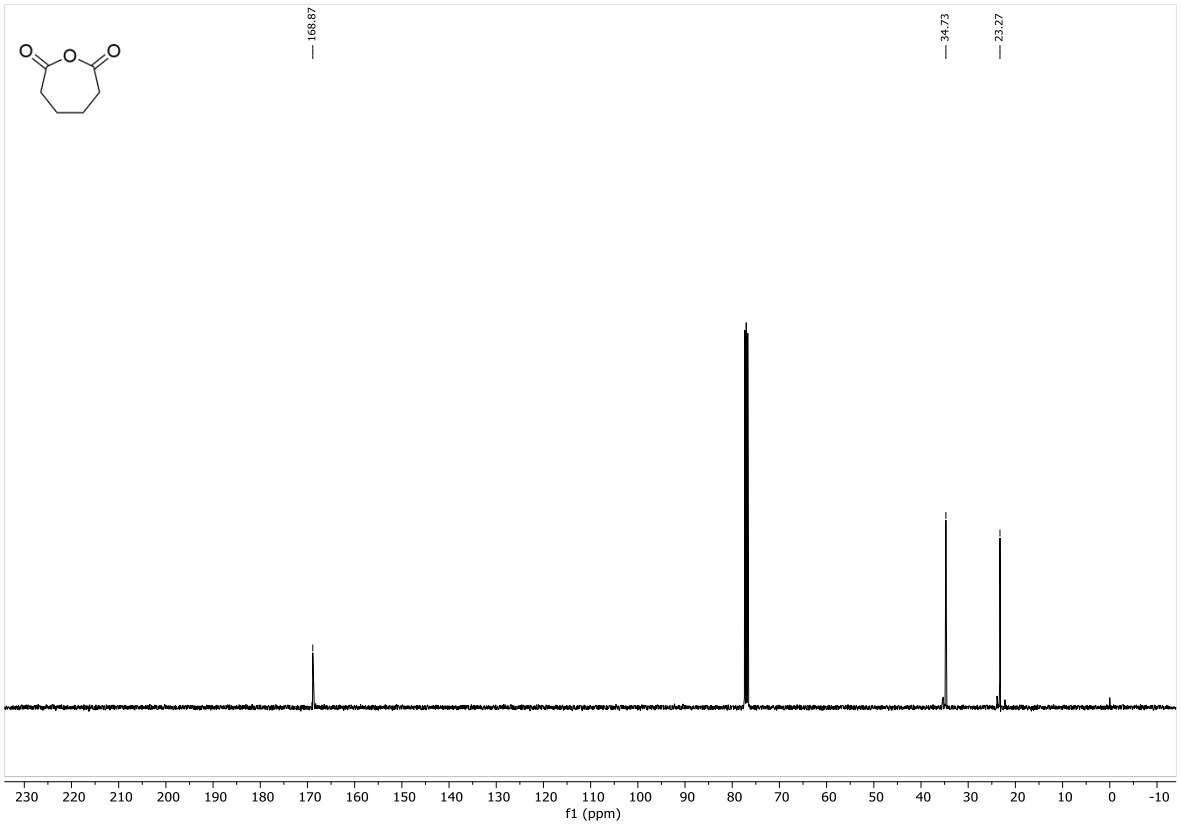
AIII.12. References

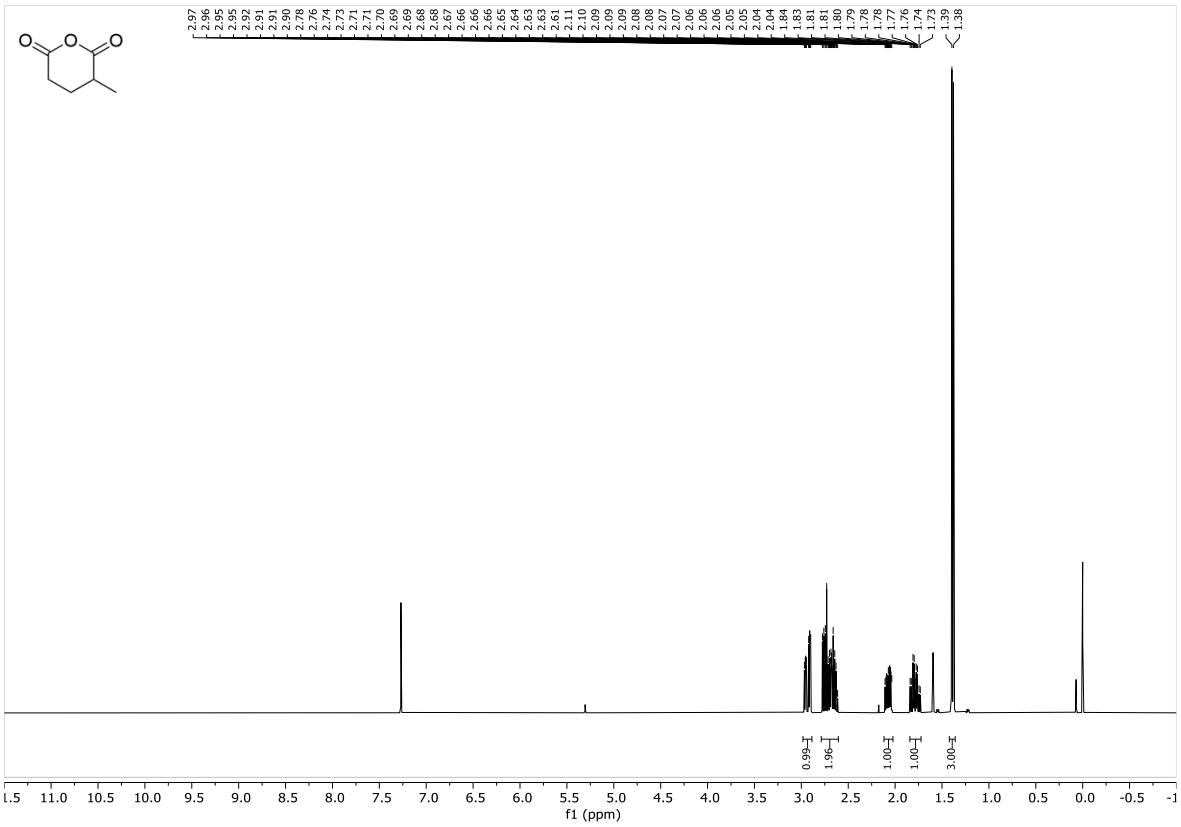
(1) Tarasenko, M.; Duderin, N.; Sharonova, T.; Baykov, S.; Shetnev, A.; Smirnov, A. V. Room-Temperature Synthesis of Pharmaceutically Important Carboxylic Acids Bearing the 1,2,4-Oxadiazole Moiety. *Tetrahedron Lett.* **2017**, *58* (37), 3672–3677.

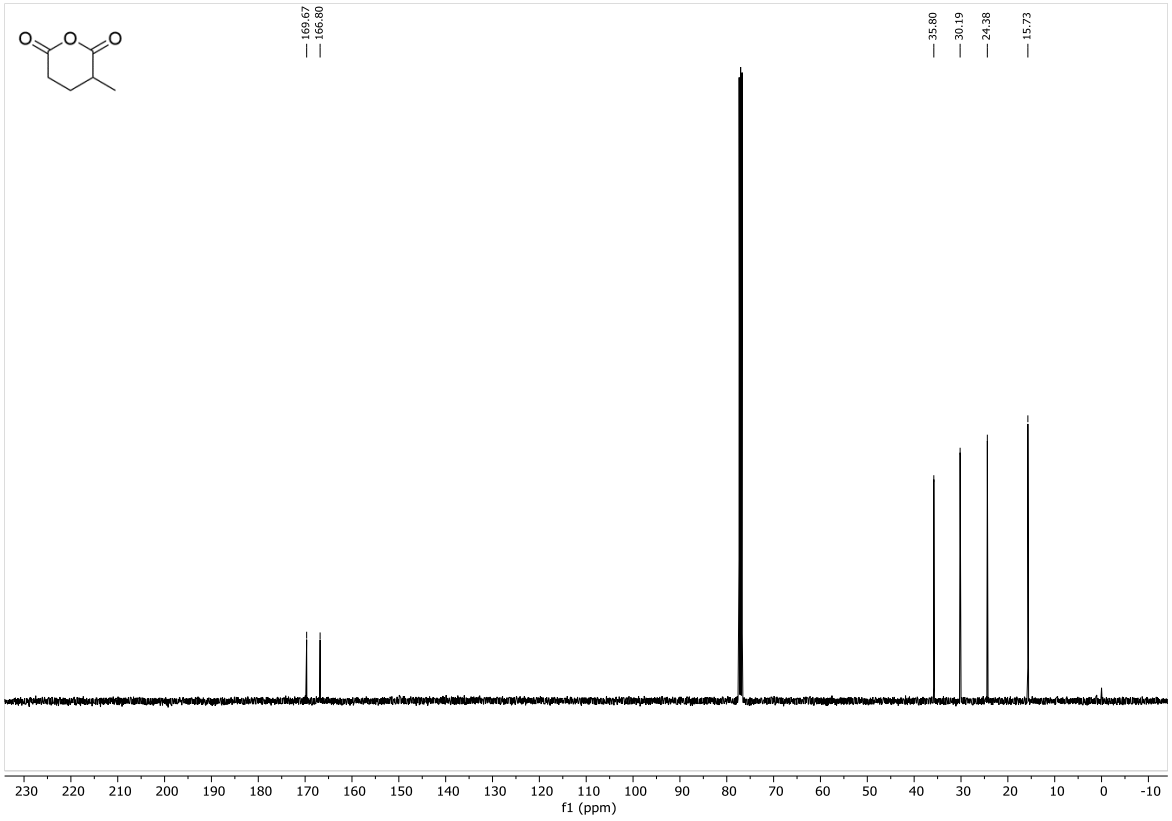
(2) Bennett, D. J.; Blake, A. J.; Cooke, P. A.; Godfrey, C. R. A.; Pickering, P. L.; Simpkins, N. S.; Walker, M. D.; Wilson, C. Stereoselectivity in Reactions of Atropisomeric Lactams and Imides. *Tetrahedron* **2004**, *60* (20), 4491–4511.

AIII.13. NMR spectra of standard compounds






2.97 2.96 2.95 2.95 2.92 2.91 2.91 2.90 2.78 2.76 2.74 2.73 2.71 2.71 2.70 2.69 2.69 2.68 2.68 2.67 2.66 2.66 2.66 2.65 2.64 2.63 2.63 2.61 2.11 2.10 2.09 2.09 2.09 2.08 2.08 2.07 2.07 2.06 2.06 2.06 2.05 2.05 2.04 2.04 2.04 1.84 1.83 1.81 1.81 1.80 1.79 1.78 1.78 1.77 1.76 1.74 1.73 1.39 1.38
0.99 1.96 1.00 1.00 3.00
11.5 11.0 10.5 10.0 9.5 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 -0.5
f1 (ppm)


169.67
166.80
35.80
30.19
24.38
15.73
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)