

Solid dosing in High-Throughput Experimentation: generalization of mass enhancer technologies for submilligram scale

Taline Kerackian,^{1,2§} Geraud Chacktas,^{1,3§} Didier Durand,³ Eugénie Romero*¹

§Contributed equally

1. Université Paris Saclay, CEA, INRAE, Département Médicaments et Technologies pour la Santé (DMTS), SCBM, 91191 Gif-sur-Yvette, France
2. CEA, DAM, Le Ripault, F-37260 Monts, France
3. Pole of Activity Drug Design Small Molecules Unit, Institut de Recherche Servier, 91191 Gif-sur-Yvette, France

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S1 – General information

All chemical products and glass beads commercially available were purchased from Sigma-Aldrich, Acros and Fluka and used without further purification. Anhydrous solvents: 1,2-dichloroethane, acetonitrile, DMF, DMSO were purchased in anhydrous form and used without further purification. THF was dried from sodium/benzophenone under nitrogen. Dichloromethane was distilled from calcium hydride under nitrogen.

^1H NMR (400 MHz), ^{13}C NMR (100 MHz), ^{19}F (376 MHz) were measured on a Bruker Avance 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from residual solvent peaks and coupling constants are reported as Hertz (Hz). Splitting patterns are designated as singlet (s), broad singlet (br. s), doublet (d), triplet (t), quartet (q), quintet (quint), heptuplet (hept), multiplet (m). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m).

Electrospray mass spectra were obtained using an ESI-Quadripole autopurify, Waters (pump: 2545, mass: ZQ2000) mass Spectrometer. High resolution mass spectroscopy of final compounds were determined using a Xevo[®] G2-XS QToF.

GC-MS analyses were performed using Thermo Scientific Trace 1300 Gas Chromatograph coupled to a ISQ LT Single Quadrupole Mass Spectrometer using helium as the carrier gas at a flow rate of 10 mL/min and an initial oven temperature of 50 °C. The column used was a Thermo TG-5MS (30 m length, 0.25 mm diameter and 0.25 μm thickness). The injector temperature was 200 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 50 °C, temperature was increased with a 15 °C/min ramp after 50 °C hold for 1 min to a final temperature of 280 °C, then hold at 280 °C for 4 min (split mode of injection, total run time of 20 min).

Flash chromatographies were performed using silica gel 60 Å (40-63 μm). Preparative chromatographies were performed using PLC plates of silica gel 60 F254 of 20x20 cm and 2 mm thickness. TLC analyses were carried out on pre-coated Glass TLC Silica gel plates 60 F254 from Merck. The plates were visualized using a 254 nm ultraviolet lamp.

Electrochemical experiments were conducted using an ElectraSyn 2.0. Information and details can be found at <https://www.ika.com/en/Products-Lab-Eq/Electrochemistry-Kit-csp-516/ElectraSyn-20-Package-cpdt20008980/>. All the electrodes (zinc and nickel foam) were purchased on the IKA website (<https://www.ika.com/en/Products-Lab-Eq/Electrochemistry-KitAccessories-cspacc-516/>).

For blue light irradiation, one Kessil PR160-456 nm lamps (19 V DC 40 W Max) were placed 2cm away from glass tubes and reactions were kept at room temperature using fans.

As an important note, we visually observed that BINAP seemed to be adhering to the glass vial (see SI), and this has been confirmed by the characterization.

Precision balance used: Sartorius Lab Quintix 125D-15

S2 – General procedure for Chembeads and ChemCarriers preparation

A. General protocol for the preparation of Chembeads

CB have been prepared by laying the powders (previously grinded with a mortar) between two slices of glass beads in a glass vial, followed by a 5 min hand mixing of the vial. This technique previously described [1, 2] is reproducible with most compounds as ligands or catalysts (as a note, Copper based salts/complexes require longer time of grinding), but does not work very well with inorganic bases. It explains why inorganic bases have not been considered on mixed CB systems, as our lab is not equipped with a Resodyn® type instrument.

For mixture coating, the mixture of compounds was previously prepared in the appropriate proportion in a glass vial by hand mixing during 2 min and then vortex mixing for 3 additional min (bench mini vortex). See examples of before/after hand mixing. Different size of CB were used (from left to right : size 1 is 106 μm , size 2 is 150-212 μm , size 3 is 212-300 μm , size 4 is 425-600 μm) with the same coating charge (5% w/w in Pd_2dba_3).



Figure S1: Preparation of Chembeads of four different sizes before and after mixing

B. General protocol for the preparation of Silica and Celite® ChemCarriers

Silica and Celite® ChemCarriers have been prepared by laying the powders (previously grinded as thin as possible with a mortar) between two slices of silica (60 Å porosity, 250 μm thickness) or Celite® (particle size 0.02-0.1 mm) in a glass vial, followed by a 5 min hand mixing of the vial. For mixture coating, the mixture of compounds was previously prepared in the appropriate proportion in a glass vial by hand mixing during 2 min and then vortex mixing for 3 additional min (bench mini vortex).

C. Double weight procedure for coating charge evaluation

For the coating charge evaluation, the double-weight procedure has been used. UV calibration dosing was not possible for CB coated with metals or mixture of ligands/metals. In addition, the laboratory is not equipped with ICP-MS.

After preparation of Chembeads or ChemCarriers in a tared vial (vial A), the CB or CC are transferred to a new vial (vial B), and the excess mass of solid remaining coated on the vial B is reported. Based on this excess, the real charge coated is calculated.

Table S1: Measured masses of supported compounds and calculated charges with error evaluation

Chemicals	Support	First support weight (mg)	Chemical 1 weight (mg)	Chemical 2 weight (mg)	Chemical 3 weight (mg)	Final weight (mg)	Vial empty (mg)	Vial coated (mg)	Targeted charge in chemical 1	Measured charge in %	Mass difference (mg)	Corrected charge in chemical 1	Error %
Ru(bpy) ₃ Cl ₂	CB #3	126.9	12.5			250.11	6046.31	6052.51	5	5.00	6.2	2.52	49.6
Phenanthroline	CB #3	126.1	12.56			252.06	6059.64	6060.23	5	4.98	0.59	4.75	4.7
Ni(OTf) ₂	CB #3	125.5	12			249.96	6031.77	6034.15	5	4.80	2.38	3.85	19.8
Ni(OAc) ₂	CB #3	125.7	13.18			249.6	6034.28	6040.01	5	5.28	5.73	2.98	43.5
bpy	CB #3	125.5	13.3			250.22	6123.13	6123.87	5	5.32	0.74	5.02	5.6
Ni(OTf) ₂ + Phen + Ru(bpy) ₃ Cl ₂	CB #3	124.6	2.72	6.28	12.1	250.09	6065.22	6066.37	5	1.09	1.15	0.63	42.3
Ni(OAc) ₂ + bpy	CB #3	126.9	9.53	15.96		250.59	8756.74	8759.57	5	6.37	2.83	5.24	17.7
Ni(OAc) ₂ + bpy	Silica	126.3	9.83	15.82		250.78	8668.56	8669.89	5	6.31	1.33	5.78	8.4
Ni(OAc) ₂ + bpy	Celite®	128	10.27	16.65		249.5	8795.14	8796.07	5	6.67	0.93	6.30	5.6
Pd ₂ dba ₃	CB #1	120.5	12.77			250.91	4685.37	4691.02	5	5.09	5.65	2.84	44.2
Pd ₂ dba ₃	CB #2	125	13.46			250.53	4728.35	4732.83	5	5.37	4.48	3.58	33.3
Pd ₂ dba ₃	CB #3	130.2	13.81			253.05	4797.49	4802.07	5	5.46	4.58	3.65	33.2
Pd ₂ dba ₃	CB #4	127.2	12.52			525.35	4912.19	4917.55	5	2.38	5.36	1.36	42.8
Xantphos	CB #1	130.2	15.51			251.59	4722.4	4722.97	6.31	6.16	0.57	5.94	3.7
Xantphos	CB #2	132.7	17.64			252.25	4854.49	4860.96	6.31	6.99	6.47	4.43	36.7
Xantphos	CB #3	125.7	15.66			252.7	4865.86	4870.05	6.31	6.20	4.19	4.54	26.8
Xantphos	CB #4	125.8	16.32			251.2	4884.04	4889.08	6.31	6.50	5.04	4.49	30.9
Xantphos	Silica	120.8	12.31			250.3	4782.12	4782.42	5	4.92	0.3	4.80	2.4
Xantphos	Celite®	123.9	12.42			251.1	4830.23	4830.7	5	4.95	0.47	4.76	3.8
Pd ₂ dba ₃ + Xantphos	CB #1	126.2	12.53			250.9	4841.5	4846.15	5	4.99	4.65	3.14	37.1
Pd ₂ dba ₃ + Xantphos	CB #2	130.1	12.49			251.6	4850.31	4855.33	5	4.96	5.02	2.97	40.2
Pd ₂ dba ₃ + Xantphos	CB #3	124.6	12.51			249.2	4798.37	4802.64	5	5.02	4.27	3.31	34.1
Pd ₂ dba ₃ + Xantphos	CB #4	124.3	12.39			250.9	4820.64	4825.27	5	4.94	4.63	3.09	37.4
Pd ₂ dba ₃ + Ruphos	CB #3	121.3	12.45			251	4844.32	4848	5	4.96	3.68	3.49	29.6
Pd ₂ dba ₃ + Sphos	CB #3	125.7	12.52			250.4	4795.33	4797.72	5	5.00	2.39	4.05	19.1
Pd ₂ dba ₃ + BINAP	CB #3	125.5	12.54			250.2	4882.65	4886.01	5	5.01	3.36	3.67	26.8
Pd(PPh ₃) ₂ Cl ₂	CB #3	121.3	12.66			250.08	4695.71	4697.91	5	5.06	2.2	4.18	17.4
CuI	CB #3	123.7	15.69			311.5	4724.25	4727.63	5	5.04	3.38	3.95	21.5
Pd(PPh ₃) ₂ Cl ₂ +CuI	CB #3	124.1	7.19	12.46		251.37	4746.27	4749.29	5	2.86	3.02	1.66	42.0
Pd(PPh ₃) ₂ Cl ₂	Silica	129.7	12.15			250.12	4721.45	4721.69	5	4.86	0.24	4.76	2.0
Pd(PPh ₃) ₂ Cl ₂	Celite®	120.4	12.14			250.21	4706.08	4707.34	5	4.85	1.26	4.35	10.4

S3 – Procedures for HTE experiments

A. General procedures

The screening of conditions and scope evaluations were performed in a 96 well plate format using 1 mL vials (8x30 mm vials number 884001 from Analytical Sales and Services) in a Paradox reactor (96973 from Analytical Sales and Services). The homogeneous stirring was controlled thanks to Stainless Steel, Parylene C Coated stirring elements and a tumble stirrer (VP 711D-1 and VP 710 Series from V&P Scientific). The liquid dispensing was performed using calibrated manual pipettes and multipipettes (Fisher/Eppendorf). The heating control was performed thanks to a heating block from V&P scientific (VP 741DCE). The HTE experiments were designed using an in-house software called HTDesign[®], and developed by the GIPSI team at CEA Paris-Saclay (DRF/Joliot).

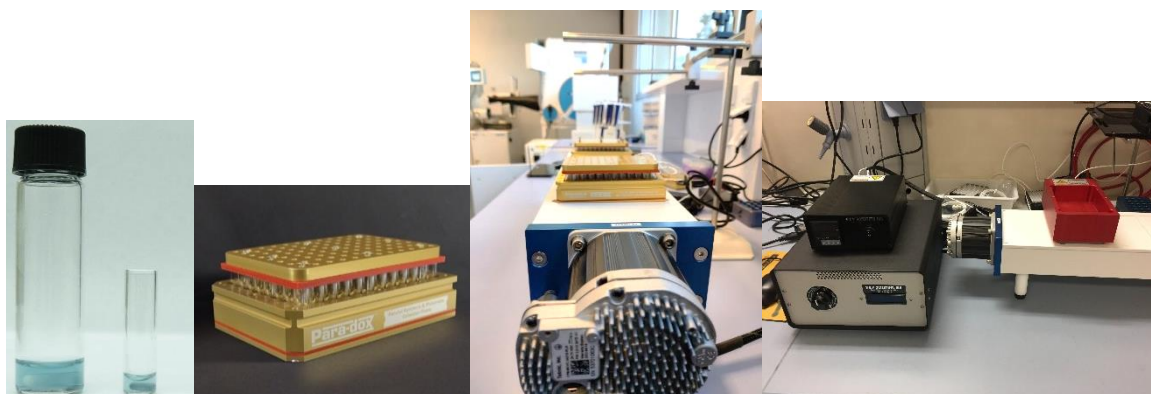
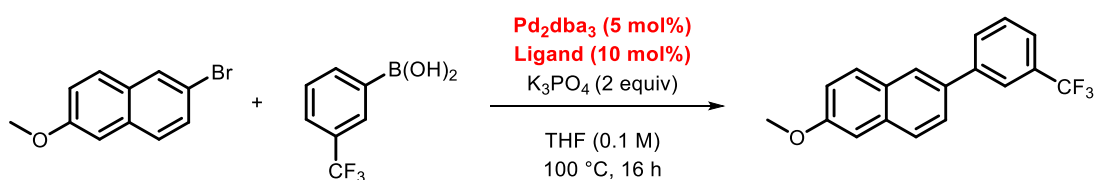


Figure S2: HTE set-up description

B. Suzuki-Miyaura cross-coupling



Experiment #1:

	Pd ₂ dba ₃ + Xantphos	Pd ₂ dba ₃ on ChemB + Xantphos on ChemBeads	Mixture (Pd ₂ dba ₃ + Xantphos) on ChemBeads									
Ø1												
Ø2												
Ø3												
Ø4												
	Quadruplicate #1			Quadruplicate #2			Quadruplicate #3			Quadruplicate #4		

Plate preparation: In a glovebox, base is added in stock solution (in acetone) as a slurry mixture and then evaporated, palladium source and Xantphos were added in stock solution (in acetone) then evaporated, both coupling partners were added in stock solution (in acetone) then evaporated,

Chembeads were weighed one by one with a precision balance, finally solvent was added. Reaction block was sealed and stirred at 300 rpm for 3h at 80°C.

HTDesign® protocol:

Solutions Mères

1 Solution «Aryl Bromide»:	ajouter 142,260 mg de Aryl Bromide dans	6,00 ml de solvant acetone
2 Solution «Boronic Acid»:	ajouter 171,036 mg de Boronic Acid dans	6,00 ml de solvant acetone
3 Solution «Potassium phosphate tribasic»:	ajouter 254,724 mg de Potassium phosphate tribasic dans	6,00 ml de solvant water
4 Solution «tetrahydrofuran (THF)»:	SOLVANT	
5 Solution «Pd2dba3»:	ajouter 9,157 mg de Pd2dba3 dans	2,00 ml de solvant acetone
6 Solution «Xantphos»:	ajouter 115,724 mg de Xantphos dans	2,00 ml de solvant acetone
7 Solution «Pd2dba3 on Chembeads 5% w/w»:	ajouter 7,326 mg de Pd2dba3 on Chembeads 5% w/w dans	1,60 ml de solvant acetone
8 Solution «Xantphos on Chembeads 6,31% w/w»:	ajouter 9,258 mg de Xantphos on Chembeads 6,31% w/w dans	1,60 ml de solvant acetone
9 Solution «Pd2dba3 5% + Xantphos 6,31% on Chembeads»:	ajouter 16,607 mg de Pd2dba3 5% + Xantphos 6,31% on Chembeads dans	1,60 ml de solvant acetone

Plaques

Etape 1: ajouter 100,00 µl de la solution «Aryl Bromide» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	●	●	●	●	●	●	●	●	●	●
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

Etape 2: ajouter 100,00 µl de la solution «Boronic Acid» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	●	●	●	●	●	●	●	●	●	●
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

Etape 3: ajouter 100,00 µl de la solution «Potassium phosphate tribasic» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	●	●	●	●	●	●	●	●	●	●
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

Etape 4: ajouter 100,00 µl de la solution «tetrahydrofuran (THF)» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	●	●	●	●	●	●	●	●	●	●
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

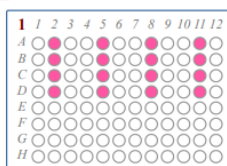
Etape 5: ajouter 100,00 µl de la solution «Pd2dba3» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	○	○	○	○	○	○	○	○	○	○	○
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

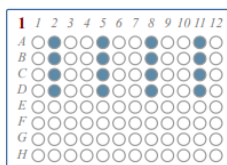
Etape 6: ajouter 100,00 µl de la solution «Xantphos» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	○	○	○	○	○	○	○	○	○	○	○
B	○	○	○	○	○	○	○	○	○	○	○	○
C	○	○	○	○	○	○	○	○	○	○	○	○
D	○	○	○	○	○	○	○	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

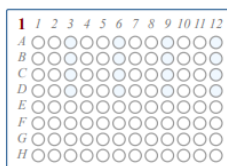
Etape 7: ajouter 100,00 µl de la solution «Pd2dba3 on Chembeads 5% w/w» dans les puits:



Etape 8: ajouter 100,00 µl de la solution «Xantphos on Chembeads 6,31% w/w» dans les puits:



Etape 9: ajouter 100,00 µl de la solution «Pd2dba3 5% + Xantphos 6,31% on Chembeads» dans les puits:



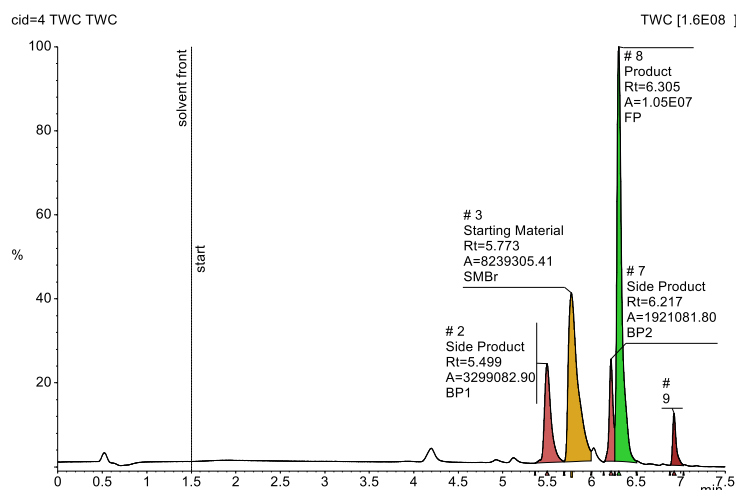
HTE analytical method: The plate was prepared as mentioned above with respect of the HTDesign[®] protocol (see above). The plate was sealed and stirred 3h at 80°C. After this time each sample was diluted with a MeCN solution containing 1 µmol of biphenyl (500 µL, 0.002 M). 50 µL aliquots were sampled into a 1 mL deep 96 well plate containing 600 µL MeCN. Ratios of Area Under Curve of starting material, products and side products were tabulated as well as areas for peaks of interest.

Analytical assay: 7.30 min Assay with Waters UPLC-UV-MS: CSH Phenyl-Hexyl 50*2,1 in 1,7 µm; 4 µL injection; 50 mm x 2.1 mm; 0.4 mL/min; H₂O/MeCN; gradient: 95% MeCN to 0% in 6.00 min; QDA ESI 110-1200 pos/neg; nebulizer: 700 L/hr; cone gas: 30 L/hr; source 150 °C; desolvation 450 °C.

Retention times – Major peaks 7.30 min assay:

Peak Label	Retention Time (in min)
Final Product (FP)	6.30
Aryl Bromide (SM1)	5.77
Byproduct (BP1)	5.49
Byproduct (BP2)	6.21
IS	6.96

TWC Chromatogram example: vial D7



Results:

col	Catalytic system name	Chembeads name	Solvent Name	Temp °C	Time h	% Conv.	Pdt/IS	SM/IS	BP1/IS	BP2/IS
1	Pd ₂ dba ₃ /XantPhos	#1	THF	100	3.0	38%	11.0	8.81	6.66	2.26
2	Pd ₂ dba ₃ on beads/XantPhos on beads	#1	THF	100	3.0	49%	10.6	7.89	1.22	1.81
3	(Pd ₂ dba ₃ +XantPhos) on beads	#1	THF	100	3.0	40%	9.9	7.96	4.89	2.19
4	Pd ₂ dba ₃ /XantPhos	#1	THF	100	3.0	45%	11.5	8.58	3.48	1.99
5	Pd ₂ dba ₃ on beads/XantPhos on beads	#1	THF	100	3.0	52%	11.1	7.29	1.32	1.73
6	(Pd ₂ dba ₃ +XantPhos) on beads	#1	THF	100	3.0	45%	10.2	7.81	2.81	2.06
7	Pd ₂ dba ₃ /XantPhos	#1	THF	100	3.0	48%	12.0	7.94	3.28	1.87
8	Pd ₂ dba ₃ on beads/XantPhos on beads	#1	THF	100	3.0	49%	10.5	7.70	1.62	1.83
9	(Pd ₂ dba ₃ +XantPhos) on beads	#1	THF	100	3.0	43%	10.8	7.22	5.23	2.11
10	Pd ₂ dba ₃ /XantPhos	#1	THF	100	3.0	44%	11.3	8.81	3.59	1.99
11	Pd ₂ dba ₃ on beads/XantPhos on beads	#1	THF	100	3.0	49%	10.2	7.50	1.38	1.90
12	(Pd ₂ dba ₃ +XantPhos) on beads	#1	THF	100	3.0	48%	11.0	7.01	2.89	1.99
1	Pd ₂ dba ₃ /XantPhos	#2	THF	100	3.0	39%	10.1	9.48	4.25	2.13
2	Pd ₂ dba ₃ on beads/XantPhos on beads	#2	THF	100	3.0	47%	10.1	7.91	1.41	1.94
3	(Pd ₂ dba ₃ +XantPhos) on beads	#2	THF	100	3.0	43%	10.4	7.63	4.15	2.16
4	Pd ₂ dba ₃ /XantPhos	#2	THF	100	3.0	41%	10.3	9.48	3.50	2.09
5	Pd ₂ dba ₃ on beads/XantPhos on beads	#2	THF	100	3.0	49%	10.5	7.90	1.10	1.84
6	(Pd ₂ dba ₃ +XantPhos) on beads	#2	THF	100	3.0	46%	11.1	7.60	3.23	1.98
7	Pd ₂ dba ₃ /XantPhos	#2	THF	100	3.0	42%	10.7	9.05	3.52	2.04
8	Pd ₂ dba ₃ on beads/XantPhos on beads	#2	THF	100	3.0	50%	10.8	7.84	1.16	1.91
9	(Pd ₂ dba ₃ +XantPhos) on beads	#2	THF	100	3.0	50%	12.1	7.18	3.19	1.89
10	Pd ₂ dba ₃ /XantPhos	#2	THF	100	3.0	42%	10.9	9.34	3.82	2.05
11	Pd ₂ dba ₃ on beads/XantPhos on beads	#2	THF	100	3.0	51%	10.9	7.39	1.07	1.95
12	(Pd ₂ dba ₃ +XantPhos) on beads	#2	THF	100	3.0	48%	12.0	7.34	3.52	1.95
1	Pd ₂ dba ₃ /XantPhos	#3	THF	100	3.0	47%	11.8	8.24	3.26	2.02
2	Pd ₂ dba ₃ on beads/XantPhos on beads	#3	THF	100	3.0	48%	10.4	7.97	1.52	1.95
3	(Pd ₂ dba ₃ +XantPhos) on beads	#3	THF	100	3.0	44%	10.6	7.87	3.58	2.18
4	Pd ₂ dba ₃ /XantPhos	#3	THF	100	3.0	42%	10.8	9.25	3.48	2.06
5	Pd ₂ dba ₃ on beads/XantPhos on beads	#3	THF	100	3.0	53%	11.4	7.49	0.97	1.77
6	(Pd ₂ dba ₃ +XantPhos) on beads	#3	THF	100	3.0	46%	10.8	7.59	2.83	2.12
7	Pd ₂ dba ₃ /XantPhos	#3	THF	100	3.0	43%	10.7	8.88	3.47	2.00
8	Pd ₂ dba ₃ on beads/XantPhos on beads	#3	THF	100	3.0	45%	10.1	8.08	2.10	2.26
9	(Pd ₂ dba ₃ +XantPhos) on beads	#3	THF	100	3.0	45%	10.7	7.69	3.31	2.18
10	Pd ₂ dba ₃ /XantPhos	#3	THF	100	3.0	43%	11.4	8.70	4.19	2.03
11	Pd ₂ dba ₃ on beads/XantPhos on beads	#3	THF	100	3.0	45%	10.2	8.52	1.79	1.96
12	(Pd ₂ dba ₃ +XantPhos) on beads	#3	THF	100	3.0	47%	11.3	7.55	3.13	2.09
1	Pd ₂ dba ₃ /XantPhos	#4	THF	100	3.0	42%	11.0	9.56	3.47	2.07
2	Pd ₂ dba ₃ on beads/XantPhos on beads	#4	THF	100	3.0	47%	10.1	8.31	1.21	1.95
3	(Pd ₂ dba ₃ +XantPhos) on beads	#4	THF	100	3.0	45%	10.3	8.40	2.13	2.01
4	Pd ₂ dba ₃ /XantPhos	#4	THF	100	3.0	44%	11.2	9.04	3.43	2.05
5	Pd ₂ dba ₃ on beads/XantPhos on beads	#4	THF	100	3.0	47%	10.2	8.13	1.25	1.97
6	(Pd ₂ dba ₃ +XantPhos) on beads	#4	THF	100	3.0	45%	10.8	8.27	2.91	1.96
7	Pd ₂ dba ₃ /XantPhos	#4	THF	100	3.0	44%	11.2	8.74	3.50	2.04
8	Pd ₂ dba ₃ on beads/XantPhos on beads	#4	THF	100	3.0	48%	10.4	8.36	1.14	1.82
9	(Pd ₂ dba ₃ +XantPhos) on beads	#4	THF	100	3.0	55%	13.4	6.66	2.46	1.81
10	Pd ₂ dba ₃ /XantPhos	#4	THF	100	3.0	47%	13.0	7.91	4.75	1.99
11	Pd ₂ dba ₃ on beads/XantPhos on beads	#4	THF	100	3.0	48%	10.6	8.38	1.29	1.98
12	(Pd ₂ dba ₃ +XantPhos) on beads	#4	THF	100	3.0	67%	6.4	1.88	0.46	0.81

Experiment #2:

	Pd ₂ dba ₃ + Ligand	Mixture (Pd ₂ dba ₃ + Ligand) on ChemBeads					
XantPhos							
RuPhos							
BINAP							
SPhos							
		TriPLICATE #1		TriPLICATE #2		TriPLICATE #3	

Plate preparation: In a glovebox, base was added in stock solution (in acetone) as a slurry mixture then evaporated, Palladium and Ligands (Xantphos, Ruphos, Sphos and BINAP) were added in stock solution (in acetone) then evaporated, coupling partners were added in stock solution (in acetone) then evaporated, Chembeads (size 3, 212-300µm) were weighed one by one with a precision balance, finally solvent was added. Reaction block was sealed and stirred at 300 rpm for 16 h at 80 °C.

HTDesign® protocol:

Solutions Mères

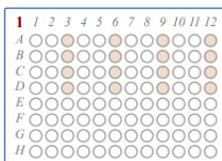
1	Solution «Aryl Bromide»:	ajouter 94,840 mg de Aryl Bromide dans	4,00 ml de solvant acetone
2	Solution «Boronic Acid»:	ajouter 114,024 mg de Boronic Acid dans	4,00 ml de solvant acetone
3	Solution «Potassium phosphate tribasic»:	ajouter 101,890 mg de Potassium phosphate tribasic dans	2,40 ml de solvant water
4	Solution «tetrahydrofuran (THF)»:		
5	Solution «Pd2dba3»:	ajouter 4,579 mg de Pd2dba3 dans	1,00 ml de solvant acetone
6	Solution «Xantphos»:	ajouter 5,786 mg de Xantphos dans	1,00 ml de solvant acetone
7	Solution «RuPhos»:	ajouter 4,666 mg de RuPhos dans	1,00 ml de solvant acetone
8	Solution «BINAP»:	ajouter 6,227 mg de BINAP dans	1,00 ml de solvant acetone
9	Solution «SPhos»:	ajouter 4,105 mg de SPhos dans	1,00 ml de solvant acetone
10	Solution «Pd2dba3 5% + Xantphos 6.31% on Chembeads»:	ajouter 16,607 mg de Pd2dba3 5% + Xantphos 6.31% on Chembeads dans	1,60 ml de solvant acetone
11	Solution «Pd2dba3 5% w/w RuPhos 6.31% w/w on Chembeads»:	ajouter 2,773 mg de Pd2dba3 5% w/w RuPhos 6.31% w/w on Chembeads dans	0,30 ml de solvant acetone
12	Solution «Pd2dba3 5% w/w + BINAP 6.31% w/w on Chembeads»:	ajouter 3,242 mg de Pd2dba3 5% w/w + BINAP 6.31% w/w on Chembeads dans	0,30 ml de solvant acetone
13	Solution «Pd2dba3 5% w/w + SPhos 6.31% w/w on Chembeads»:	ajouter 2,605 mg de Pd2dba3 5% w/w + SPhos 6.31% w/w on Chembeads dans	0,30 ml de solvant acetone

Plaques

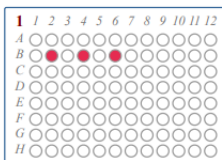
Etape 1: ajouter 100,00 µl de la solution «Aryl Bromide» dans les puits:

1	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	●	●	●	●	●	○	○	○	○	○
B	●	●	●	●	●	●	●	○	○	○	○	○
C	●	●	●	●	●	●	●	○	○	○	○	○
D	●	●	●	●	●	●	●	○	○	○	○	○
E	○	○	○	○	○	○	○	○	○	○	○	○
F	○	○	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

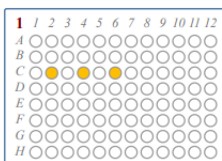
Etape 10: ajouter 100,00 µl de la solution «Pd2dba3 5% + Xantphos 6.31% on Chembeads» dans les puits:



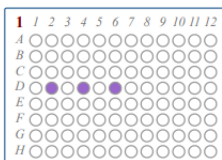
Etape 11: ajouter 100,00 µl de la solution «Pd2dba3 5% w/w RuPhos 6.31% w/w on Chembeads» dans les puits:



Etape 12: ajouter 100,00 µl de la solution «Pd2dba3 5% w/w + BINAP 6.31% w/w on Chembeads» dans les puits:



Etape 13: ajouter 100,00 µl de la solution «Pd2dba3 5% w/w + SPhos 6.31% w/w on Chembeads» dans les puits:



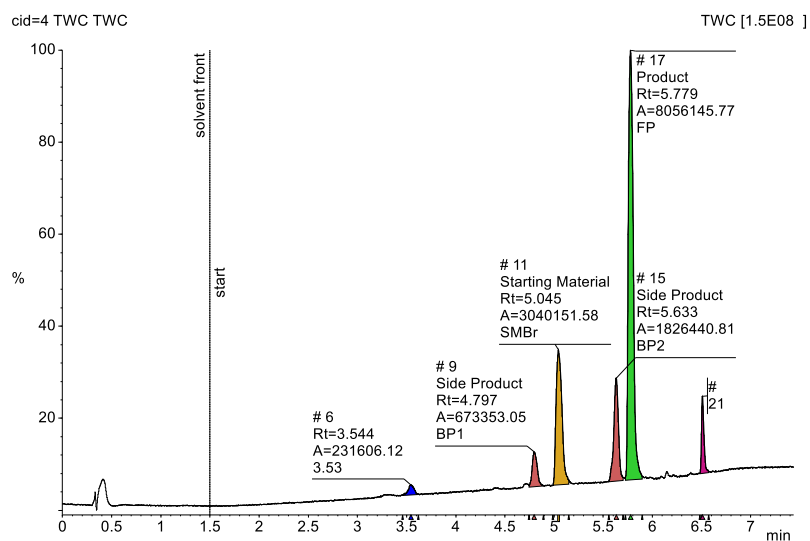
HTE analytical method: The plate was prepared as mentioned above with respect of the HTDesign protocol (see above). The plate was sealed and stirred 16 h at 80 °C. After this time each sample was diluted with a MeCN solution containing 1 µmol of biphenyl (500 µL, 0.002 M). 50 µL aliquots were sampled into a 1 mL deep 96 well plate containing 600 µL MeCN. Ratios of Area Under Curve of starting material, products and side products were tabulated as well as areas for peaks of interest.

Analytical assay: 7.30 min Assay with Waters UPLC-UV-MS: CSH Phenyl-Hexyl 50*2,1 in 1,7 µm; 4 µL injection; 50 mm x 2.1 mm; 0.4 mL/min; H₂O/MeCN; gradient: 95% MeCN to 0% in 6.00 min; QDA ESI 110-1200 pos/neg; nebulizer: 700 L/hr; cone gas: 30 L/hr; source 150 °C; desolvation 450 °C.

Retention times – Major peaks 7.30 min assay:

Peak Label	Retention Time (in min)
Final Product (FP)	6.30
Aryl Bromide (SM1)	5.77
Byproduct (BP1)	4.79
Byproduct (BP2)	5.63
IS	6.96

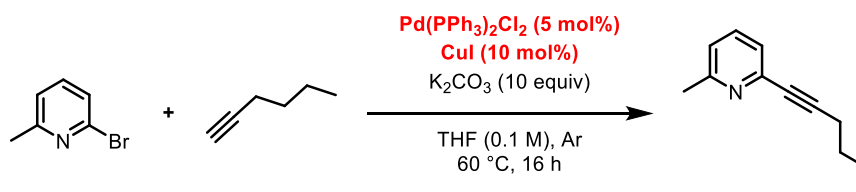
TWC Chromatogram example: vial B4



Results:

HPLC	row	col	Catalytic system name	Solvent Name	Temp °C	Time h	% Conv.	Pdt/IS	SM/IS	BP1/IS	BP2/IS
1	A	1	Pd ₂ dba ₃ /XantPhos	THF	100	3.0	65%	2.68E+1	6.22	3.73	4.18
2	A	2	(Pd ₂ dba ₃ /XantPhos) on beads	THF	100	3.0	83%	5.60E+1	6.15	1.79	3.28
3	A	3	Pd ₂ dba ₃ /XantPhos	THF	100	3.0	46%	1.43E+1	5.86	6.99	3.88
4	A	4	(Pd ₂ dba ₃ /XantPhos) on beads	THF	100	3.0	84%	5.92E+1	5.39	1.69	3.81
5	A	5	Pd ₂ dba ₃ /XantPhos	THF	100	3.0	65%	2.43E+1	5.36	4.11	3.57
6	A	6	(Pd ₂ dba ₃ /XantPhos) on beads	THF	100	3.0	80%	4.55E+1	5.78	2.20	3.62
7	B	1	Pd ₂ dba ₃ /RuPhos	THF	100	3.0	74%	2.78E+1	3.06	3.59	3.29
8	B	2	(Pd ₂ dba ₃ /RuPhos) on beads	THF	100	3.0	93%	1.11E+2	4.26	0.90	2.78
9	B	3	Pd ₂ dba ₃ /RuPhos	THF	100	3.0	45%	1.40E+1	4.75	7.14	5.50
10	B	4	(Pd ₂ dba ₃ /RuPhos) on beads	THF	100	3.0	93%	1.07E+2	4.23	0.94	2.54
11	B	5	Pd ₂ dba ₃ /RuPhos	THF	100	3.0	83%	4.01E+1	2.78	2.49	2.85
12	B	6	(Pd ₂ dba ₃ /RuPhos) on beads	THF	100	3.0	93%	1.00E+2	4.11	1.00	2.64
13	C	1	Pd ₂ dba ₃ /BINAP	THF	100	3.0	81%	3.34E+1	1.96	2.99	2.75
14	C	2	(Pd ₂ dba ₃ /BINAP) on beads	THF	100	3.0	94%	8.25E+1	2.03	1.21	2.45
15	C	3	Pd ₂ dba ₃ /BINAP	THF	100	3.0	65%	1.93E+1	2.43	5.17	2.89
16	C	4	(Pd ₂ dba ₃ /BINAP) on beads	THF	100	3.0	94%	7.91E+1	1.66	1.26	2.32
17	C	5	Pd ₂ dba ₃ /BINAP	THF	100	3.0	82%	3.36E+1	1.78	2.98	2.51
18	C	6	(Pd ₂ dba ₃ /BINAP) on beads	THF	100	3.0	95%	7.19E+1	0.19	1.39	2.12
19	D	1	Pd ₂ dba ₃ /SPhos	THF	100	3.0	80%	3.85E+1	3.43	2.60	3.40
20	D	2	(Pd ₂ dba ₃ /SPhos) on beads	THF	100	3.0	97%	1.86E+2	3.28	0.54	2.07
21	D	3	Pd ₂ dba ₃ /SPhos	THF	100	3.0	83%	3.95E+1	2.89	2.53	2.82
22	D	4	(Pd ₂ dba ₃ /SPhos) on beads	THF	100	3.0	97%	1.75E+2	2.74	0.57	2.07
23	D	5	Pd ₂ dba ₃ /SPhos	THF	100	3.0	81%	3.67E+1	2.91	2.72	2.95
24	D	6	(Pd ₂ dba ₃ /SPhos) on beads	THF	100	3.0	97%	1.67E+2	2.55	0.60	2.02

C. Sonogashira cross-coupling

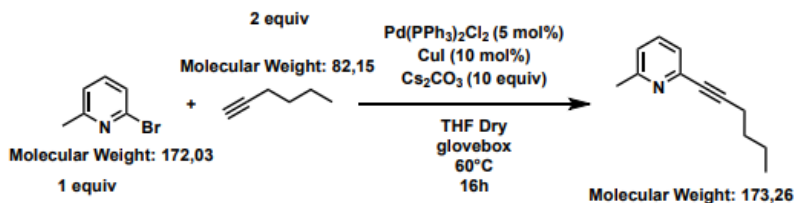


Experiment #3:

	Triplicate 1	Triplicate 2	Triplicate 3
No support			
Pd(PPh ₃) ₂ Cl ₂ on CB			
CuI on CB			
Mixed CB			
Pd(PPh ₃) ₂ Cl ₂ on Silica CC			
Pd(PPh ₃) ₂ Cl ₂ on Celite® CC			

Plate preparation: In a glovebox, base was added in stock solution (in acetone) as slurry mixture then evaporated, copper iodide and palladium complex were added in stock solution (in acetone) then evaporated, coupling partners were added in stock solution (in acetone) then evaporated, Chembeads Chembeads (size 3, 212-300µm) were weighed one by one with a precision balance, finally solvent was added. Reaction block was sealed and stirred at 300 rpm for 3 h at 60 °C.

HTDesign® protocol:



Solutions Mères

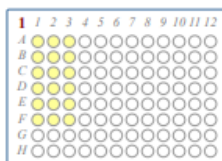
1 Solution «2-Bromo-6-methylpyridine»:	ajouter 30,964 mg / 20,48 µl de 2-Bromo-6-methylpyridine dans	1,80 ml de solvant acetone
2 Solution «Hex-1-yne»:	ajouter 118,282 mg / 165,43 µl de Hex-1-yne dans	1,80 ml de solvant acetone
3 Solution «Bis(triphenylphosphine)palladium(II) dichloride»:	ajouter 7,019 mg de Bis(triphenylphosphine)palladium(II) dichloride dans	2,00 ml de solvant acetone
4 Solution «Copper(I) iodide»:	ajouter 3,809 mg de Copper(I) iodide dans	2,00 ml de solvant acetone
5 Solution «cesium carbonate»:	ajouter 651,640 mg de cesium carbonate dans	2,00 ml de solvant water

Plaques

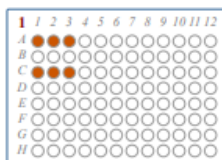
Etape 1: ajouter 100,00 µl de la solution «2-Bromo-6-methylpyridine» dans les puits:

	1	2	3	4	5	6	7	8	9	10	11	12
A	●	●	○	○	○	○	○	○	○	○	○	○
B	●	●	○	○	○	○	○	○	○	○	○	○
C	●	●	○	○	○	○	○	○	○	○	○	○
D	●	●	○	○	○	○	○	○	○	○	○	○
E	●	●	○	○	○	○	○	○	○	○	○	○
F	●	●	○	○	○	○	○	○	○	○	○	○
G	○	○	○	○	○	○	○	○	○	○	○	○
H	○	○	○	○	○	○	○	○	○	○	○	○

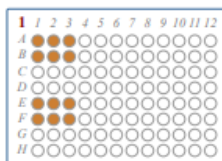
Etape 2: ajouter 100,00 µl de la solution «Hex-1-yne» dans les puits:



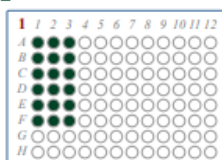
Etape 3: ajouter 100,00 µl de la solution «Bis(triphenylphosphine)palladium(II) dichloride» dans les puits:



Etape 4: ajouter 100,00 µl de la solution «Copper(I) iodide» dans les puits:



Etape 5: ajouter 100,00 µl de la solution «cesium carbonate» dans les puits:



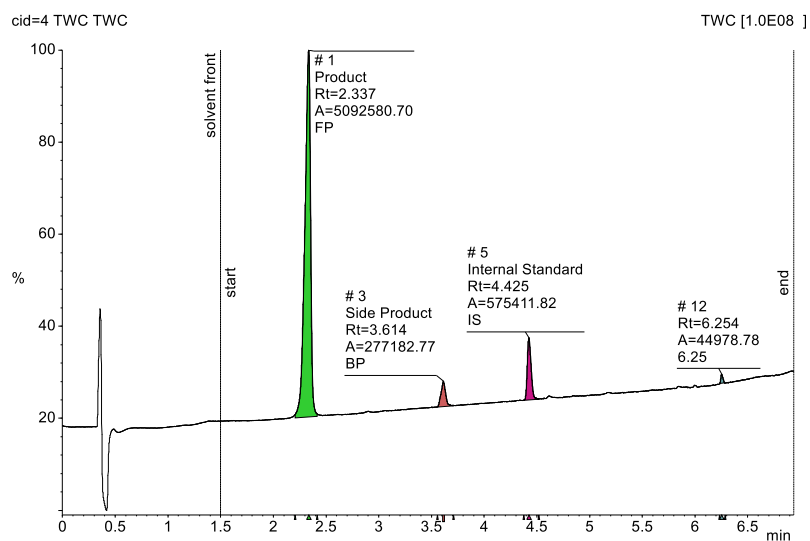
HTE analytical method: The plate was prepared as mentioned above with respect of the HTDesign protocol (see above). The plate was sealed and stirred 3 h at 60 °C. After this time each sample was diluted with a MeCN solution containing 1 µmol of biphenyl (500 µL, 0.002 M). 50 µL aliquots were sampled into a 1 mL deep 96 well plate containing 600 µL MeCN. Ratios of Area Under Curve of starting material, products and side products were tabulated as well as areas for peaks of interest.

Analytical assay: 7.00 min assay with Waters UPLC-UV-MS: CSH Phenyl-Hexyl 50*2,1 in 1,7 µm; 4 µL injection; 50 mm x 2.1 mm; 0.4 mL/min; H₂O/MeCN; gradient: 95% MeCN to 0% in 6.00 min; QDA ESI 110-1200 pos/neg; nebulizer: 700 L/hr; cone gas: 30 L/hr; source 150 °C; desolvation 450 °C.

Retention times – Major peaks 7.00 min assay:

Peak Label	Retention Time
Final Product (FP)	2.34
Starting Material (SM)	N/A
Byproduct (BP)	3.62
IS	4.42

TWC Chromatogram example: vial D3

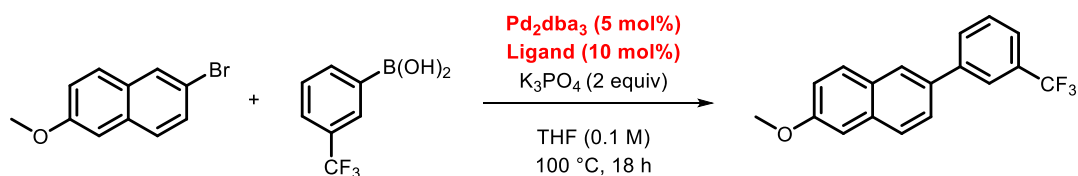


Results:

row	col	% Conv.	Pdt/IS	SM/IS	Carrier System	Test
A	1	100%	7.8	0.00	No carrier	#1
A	2	100%	8.3	0.00	No carrier	#2
A	3	100%	8.5	0.00	No carrier	#3
B	1	100%	7.7	0.00	Pd(PPh ₃) ₂ Cl ₂ on Chembeads	#1
B	2	100%	8.3	0.00	Pd(PPh ₃) ₂ Cl ₂ on Chembeads	#2
B	3	100%	8.7	0.00	Pd(PPh ₃) ₂ Cl ₂ on Chembeads	#3
C	1	100%	7.5	0.00	Cul on Chembeads	#1
C	2	100%	8.1	0.00	Cul on Chembeads	#2
C	3	100%	8.1	0.00	Cul on Chembeads	#3
D	1	100%	8.4	0.00	Mixed Chembeads	#1
D	2	100%	8.3	0.00	Mixed Chembeads	#2
D	3	100%	8.9	0.00	Mixed Chembeads	#3
E	1	100%	8.8	0.00	Pd(PPh ₃) ₂ Cl ₂ on SiO ₂	#1
E	2	100%	8.9	0.00	Pd(PPh ₃) ₂ Cl ₂ on SiO ₂	#2
E	3	100%	8.9	0.00	Pd(PPh ₃) ₂ Cl ₂ on SiO ₂	#3
F	1	100%	8.3	0.00	Pd(PPh ₃) ₂ Cl ₂ on Celite	#1
F	2	100%	8.3	0.00	Pd(PPh ₃) ₂ Cl ₂ on Celite	#2
F	3	100%	8.7	0.00	Pd(PPh ₃) ₂ Cl ₂ on Celite	#3

S4 – Procedures for batch experiments

A. Suzuki-Miyaura cross-coupling

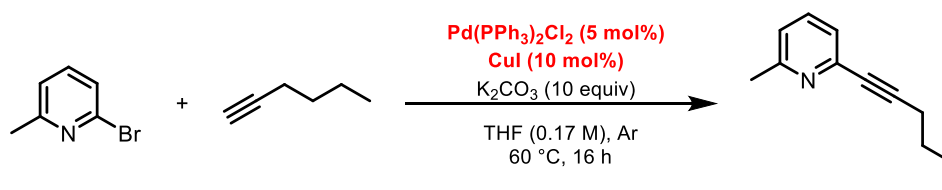


General procedure: A 5 mL microwave tube equipped with a magnetic stirbar was charged with 2-bromo-6-methoxynaphthalene (1 equiv, 0.1 mmol, 24 mg), 3-(trifluoromethyl)phenylboronic acid (1.5 equiv, 0.15 mmol, 28 mg), tris(dibenzylidèneacétone)dipalladium(0) (5 mol%, 0.005 mmol, 5 mg), Xantphos (10 mol%; 0.01 mmol, 6 mg) supported (Chembeads size 3: 212-300 μm) or not and potassium phosphate (2 equiv; 0.2 mmol; 42 mg) in THF (1 mL). The vial was sealed and the reaction mixture was stirred at 100 °C for 18 h.

Analytical method: An internal standard was then added (biphenyl, 0.1 mmol, 15 mg) and the mixture was analyzed by GC-MS giving the ratio between the product area and the internal standard area.

Isolation procedure: A 5 mL microwave tube equipped with a magnetic stir bar was charged with 2-bromo-6-methoxynaphthalene (1 equiv, 0.2 mmol, 47.2 mg), 3-(trifluoromethyl)phenylboronic acid (1.5 equiv, 0.3 mmol, 58.9 mg), tris(dibenzylidèneacétone)dipalladium(0) (5 mol%, 0.005 mmol, 10 mg), Xantphos (10 mol%; 0.01 mmol, 12 mg) supported or not and potassium phosphate (2 equiv; 0.4 mmol; 88.7 mg) in THF (2 mL). The vial was sealed and the reaction mixture was stirred at 100 °C for 18 h. The crude was filtered through celite pad and concentrated in vacuo. The product was purified by column chromatography (eluent: cyclohexane/EtOAc) and preparative TLC (eluent: cyclohexane/EtOAc).

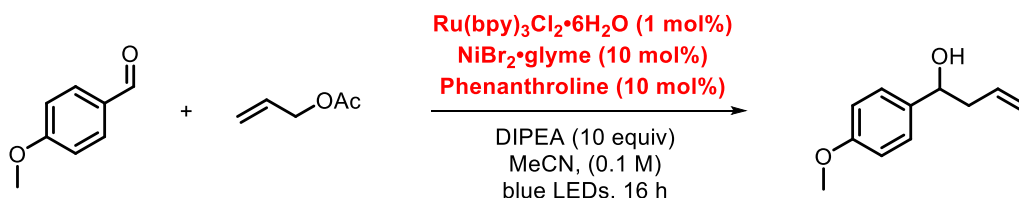
B. Sonogashira coupling



General procedure: Under argon atmosphere, a 15 mL #15 Ace-Threds pressure tube equipped with a magnetic stir bar was charged with bis(triphenylphosphine)palladium(II) dichloride (5 mol%, 0.030 mmol, 21.1 mg), copper iodide (10 mol%, 0.061 mmol, 11 mg) followed by 2-bromo-6-methylpyridine (1 equiv, 0.61 mmol, 104.9 mg, 69.4 μL) and 1-hexyne (10 equiv, 6.1 mmol, 501.05 mg, 700 μL). Freshly distilled THF (3.6 mL) was added followed by the addition of potassium carbonate (10 equiv, 6.1 mmol, 806.5 mg). The tube was closed with a back seal PTFE screw cap and the reaction mixture was stirred at 60 °C for 16 h.

Isolation procedure: The mixture was filtered through celite pad and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel (eluent: cyclohexane/EtOAc).

C. Allylation reaction via a photoredox dual catalysis



General procedure: An 8 mL scintillation vial equipped with a magnetic stirbar was charged with tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate (1 mol%, 0.001 mmol, 0.75 mg), nickel(II) trifluoromethanesulfonate (10 mol%, 0.01 mmol, 4 mg), 1,10-phenanthroline (10 mol%, 0.01 mmol, 3 mg) supported (Chembeads size 3: 212-300 μm) or not, MeCN (1 mL) was added, followed by DIPEA (10 equiv, 1 mmol, 174 μL), allyl acetate (10 equiv, 1 mmol, 108 μL) and p-anisaldehyde (1 equiv; 0.1 mmol, 12 μL). The vial was capped, and the reaction mixture was stirred at room temperature under the irradiation of a 40 W blue LED Kessil[®] lamp (A160WE Tuna Blue 455 nm) used at 100% color and light intensity and placed 2-3 cm away from the reaction vessel with an external cooling fan that maintains the temperature below 35°C, during 48h.

Analytical method: An internal standard was then added (biphenyl, 0.1 mmol, 15 mg) and the mixture was analyzed by GC-MS giving the ratio between the product area and the internal standard area.

Isolation procedure: An 8 mL scintillation vial equipped with a magnetic stirbar was charged with tris(2,2'-bipyridyl)dichlororuthenium(II) hexahydrate (1 mol%, 0.005 mmol, 3 mg), nickel(II) trifluoromethanesulfonate (10 mol%, 0.05 mmol, 18 mg), 1,10-phenanthroline (10 mol%, 0.05 mmol, 9 mg) supported on Chembeads (212-300 μm), MeCN (5 mL) was added, followed by DIPEA (10 equiv, 1 mmol, 646 μL), allyl acetate (10 equiv, 1 mmol, 539 μL) and p-anisaldehyde (1 equiv; 0.1 mmol, 61 μL). The vial was capped, and the reaction mixture was stirred at room temperature under the irradiation of a of a 40 W blue LED Kessil[®] lamp (A160WE Tuna Blue 455 nm) used at 100% color and light intensity, and placed 2-3 cm away from the reaction vessel with an external cooling fan that maintains the temperature below 35°C, during 48h. The mixture was concentrated in vacuo, and the crude residue was subjected to column chromatography on silica gel (eluent: cyclohexane/EtOAc).

D. Cross electrophile coupling via electrosynthesis



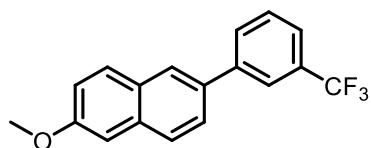
General procedure: A 5 mL ElectraSyn vial equipped with a magnetic stir bar was charged first with solids, N-cyclohexylsuccinimide (1 equiv; 0.25 mmol, 52 mg), $\text{Ni(OAc)}_2 \cdot 4\text{H}_2\text{O}$ (10 mol%; 0.025 mmol;

6 mg), 2,2'-bipyridine (10 mol%, 0.025 mmol; 4 mg) supported (Chembeads size 3: 212-300 μm) or not and KPF_6 (2 equiv; 0.5 mmol; 92 mg). The ElectraSyn vial was then sealed with a cap equipped with sacrificial anode (zinc) and cathode (Ni foam). The vial was put under argon atmosphere and an argon balloon was kept on the reaction. Dry DMF (3.5 mL) was then added, followed by 1-bromo-3-phenylpropane (1.5 equiv; 0.375 mmol, 57 μL). The reaction mixture was electrolyzed under a constant current of 8 mA until 4 $\text{F}\cdot\text{mol}^{-1}$ were delivered. An internal standard was then added (biphenyl, 0.25 mmol, 39 mg) and the mixture was analyzed by GC-MS giving the ratio between the product area and the internal standard area.

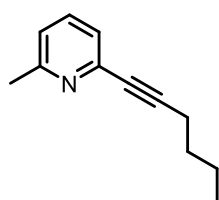
Analytical method: An internal standard was then added (biphenyl, 0.25 mmol, 39 mg) and the mixture was analyzed by GC-MS giving the ratio between the product area and the internal standard.

Isolation procedure: The mixture was then filtered through Celite[®] using dichloromethane as eluent to remove solid residues, concentrated in vacuo, and the crude residue was subjected to column chromatography on silica gel (eluent: cyclohexane/EtOAc) to give the title compound.

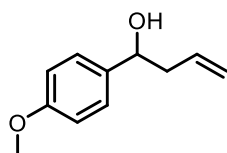
S5 – Characterisation of products



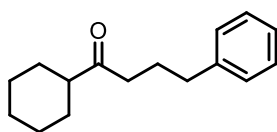
2-methoxy-6-(3-(trifluoromethyl)phenyl)naphthalene: Known compound [3], prepared according to general conditions of the Suzuki-Miyaura cross-coupling reaction and purified by column chromatography (cyclohexane/EtOAc, gradient 100:0 to 90:10) followed by a preparative TLC (cyclohexane/EtOAc, 95:5) to give white solid (40.5 mg; 54%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.99 (d, $J = 1.16$ Hz, 1H), 7.95-7.94 (m, 1H), 7.89 – 7.86 (m, 1H), 7.83 (t, $J = 9.12$ Hz, 2H), 7.70 (dd, $J = 8.49, 1.97$ Hz, 1H), 7.64 – 7.54 (m, 2H), 7.23 – 7.16 (m, 2H), 3.96 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 158.2, 142.1, 134.9, 134.3, 131.3 (q, $J = 32.13$ Hz), 130.6 (d, $J = 1.45$ Hz), 129.9, 129.4, 129.2, 127.7, 126.1, 125.7, 124.4 (q, $J = 272.31$ Hz), 124.0 (q, $J = 3.76$ Hz), 123.8 (q, $J = 3.83$ Hz), 119.6, 105.7, 55.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -62.48.



2-(hex-1-yn-1-yl)-6-methylpyridine: Prepared according to general conditions of the Sonogashira coupling reaction and purified by column chromatography (cyclohexane/EtOAc, gradient 100:0 to 50:50) to give brown oil (73.7 mg; 70%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.49 (t, $J = 7.74$ Hz, 1H), 7.18 (d, $J = 7.68$ Hz, 1H), 7.04 (d, $J = 7.73$ Hz, 1H), 2.53 (s, 3H), 2.43 (t, $J = 7.14$ Hz, 2H), 1.65 – 1.57 (m, 2H), 1.52 – 1.44 (m, 2H), 0.93 (t, $J = 7.29$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 158.7, 143.2, 136.3, 123.9, 122.0, 90.7, 80.5, 30.5, 24.6, 22.1, 19.1, 13.7. **HRMS** (ESI/Q-TOF) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{16}\text{N}$ 174.1284; Found 174.1283.

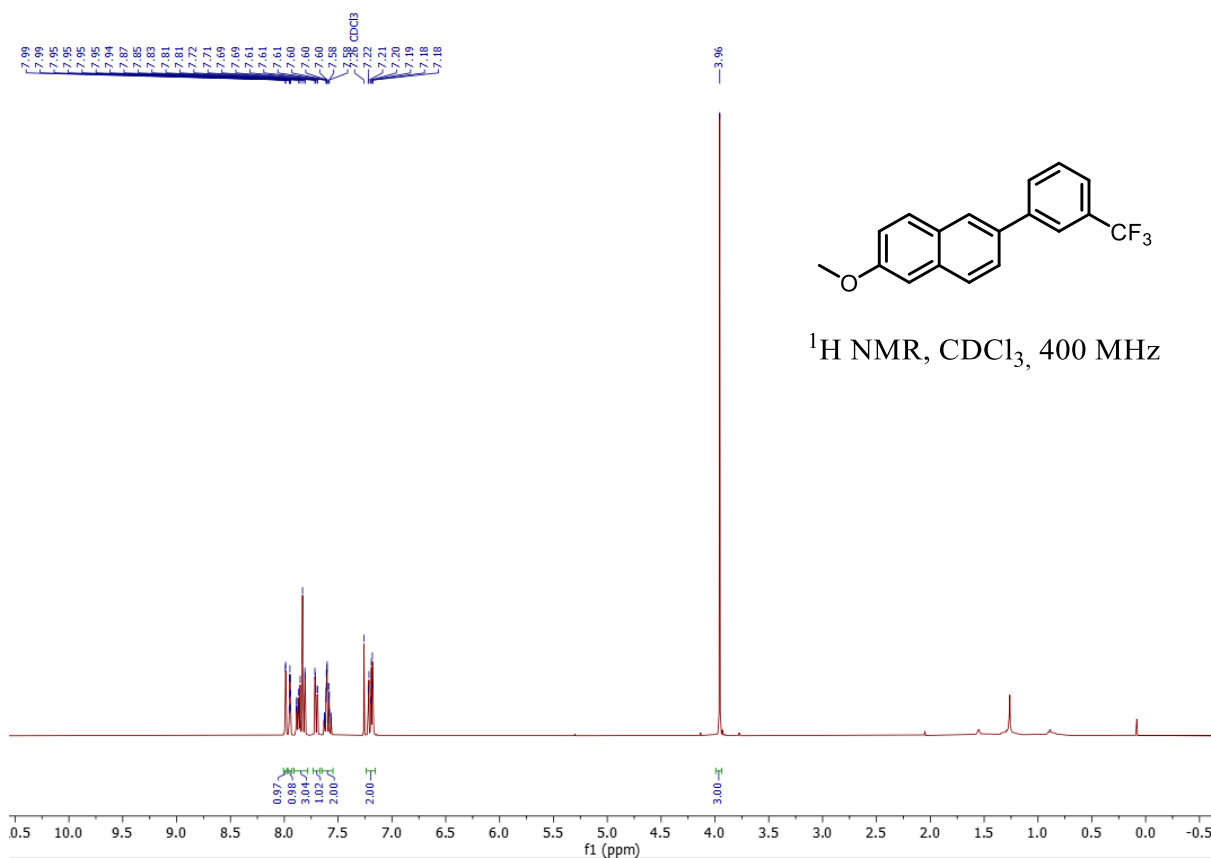


1-(4-Methoxyphenyl)but-3-en-1-ol: Known compound [4] prepared according to general conditions of allylation reaction via photoredox dual catalysis and purified by flash chromatography (cyclohexane/ethyl acetate, gradient 100:0 to 85:15) to give a brown oil (0.037 g; 42%). $^1\text{H NMR}$ (400MHz, CDCl_3) δ 7.30-7.27 (m, 2H), 6.90-6.87 (m, 2H), 5.85–5.75 (m, 1H), 5.18–5.11 (m, 2H), 4.69 (t, $J = 6.6$ Hz, 1H), 3.81 (s, 3H), 2.52-2.48 (m, 2H), 1.73 (br s, 1H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 159.1, 136.2, 134.7, 127.2, 118.2, 113.9, 73.1, 55.3, 43.8.

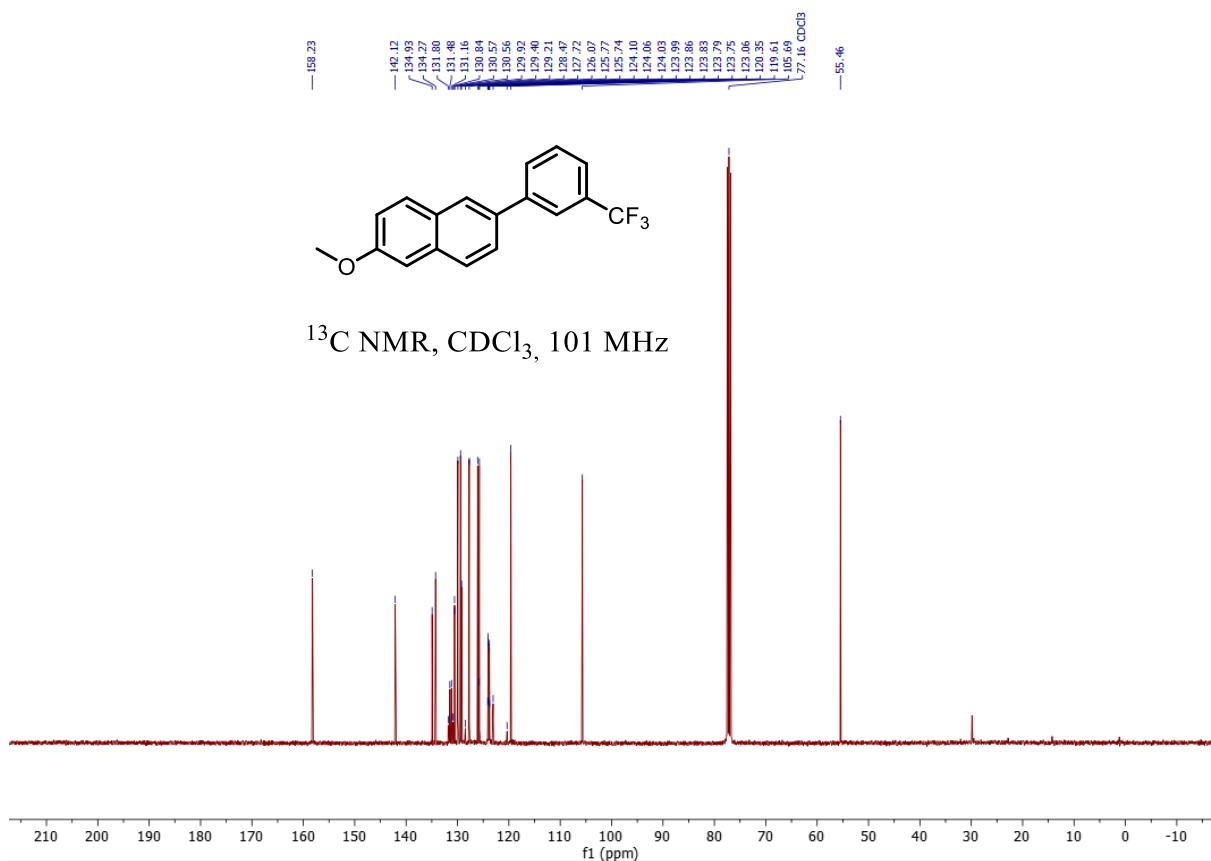


1-Cyclohexyl-4-phenylbutan-1-one: Known compound [5], prepared according to general conditions of cross electrophile coupling via electrocatalysis and purified by flash chromatography (cyclohexane/ethyl acetate, gradient 100:0 to 95:5) to give a colorless oil (0.024 g; 42%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.30- 7.26 (m, 2H), 7.20-7.16 (m, 3H), 2.61 (t, $J = 7.32$ Hz, 2H), 2.44 (t, $J = 7.32$ Hz, 2H), 2.33-2.27 (m, 1H), 1.89 (q, $J = 7.56$ Hz, 2H), 1.81-1.76 (m, 4H), 1.67-1.65 (m, 1H), 1.33-1.19 (m, 5H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 214.1, 141.9, 128.6, 128.4, 126.0, 50.9, 39.9, 35.3, 28.6, 26.0, 25.8, 25.2.

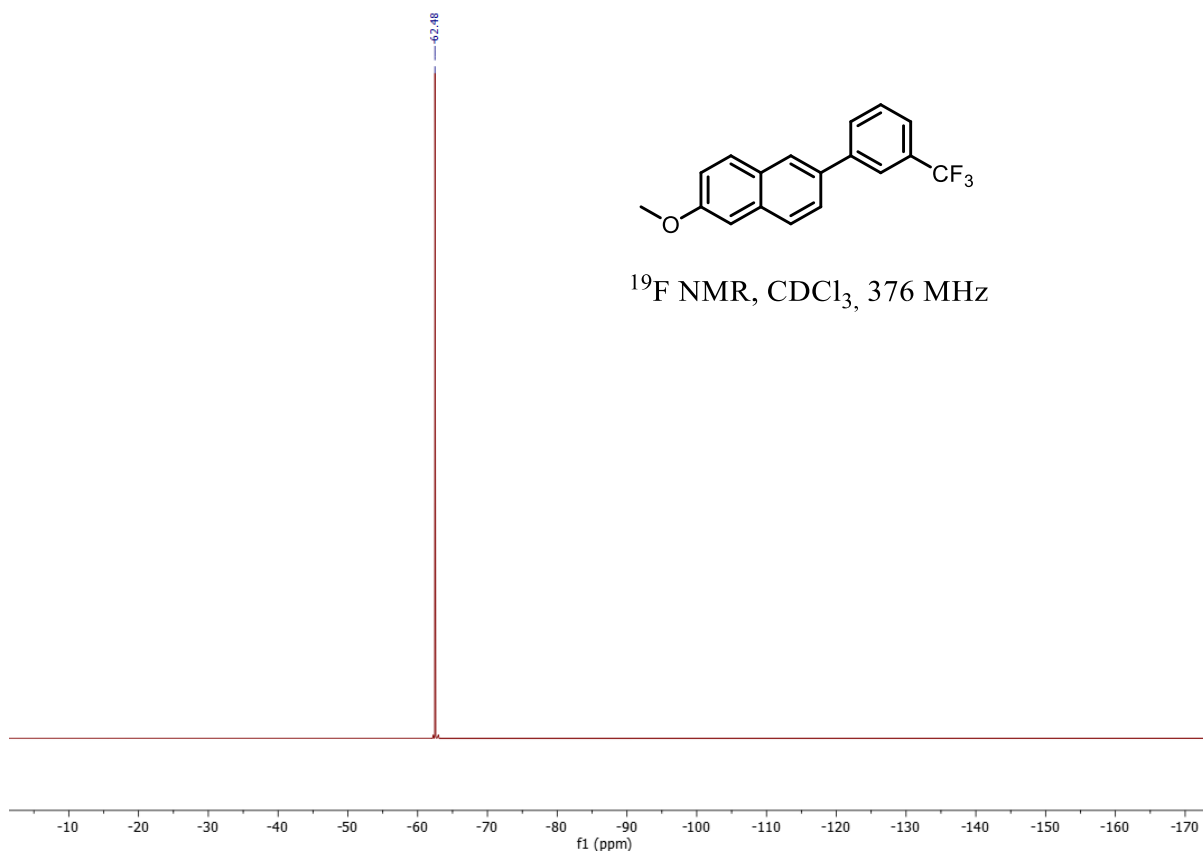
¹H NMR of 2-methoxy-6-(3-(trifluoromethyl)phenyl)naphthalene, CDCl₃, 400MHz



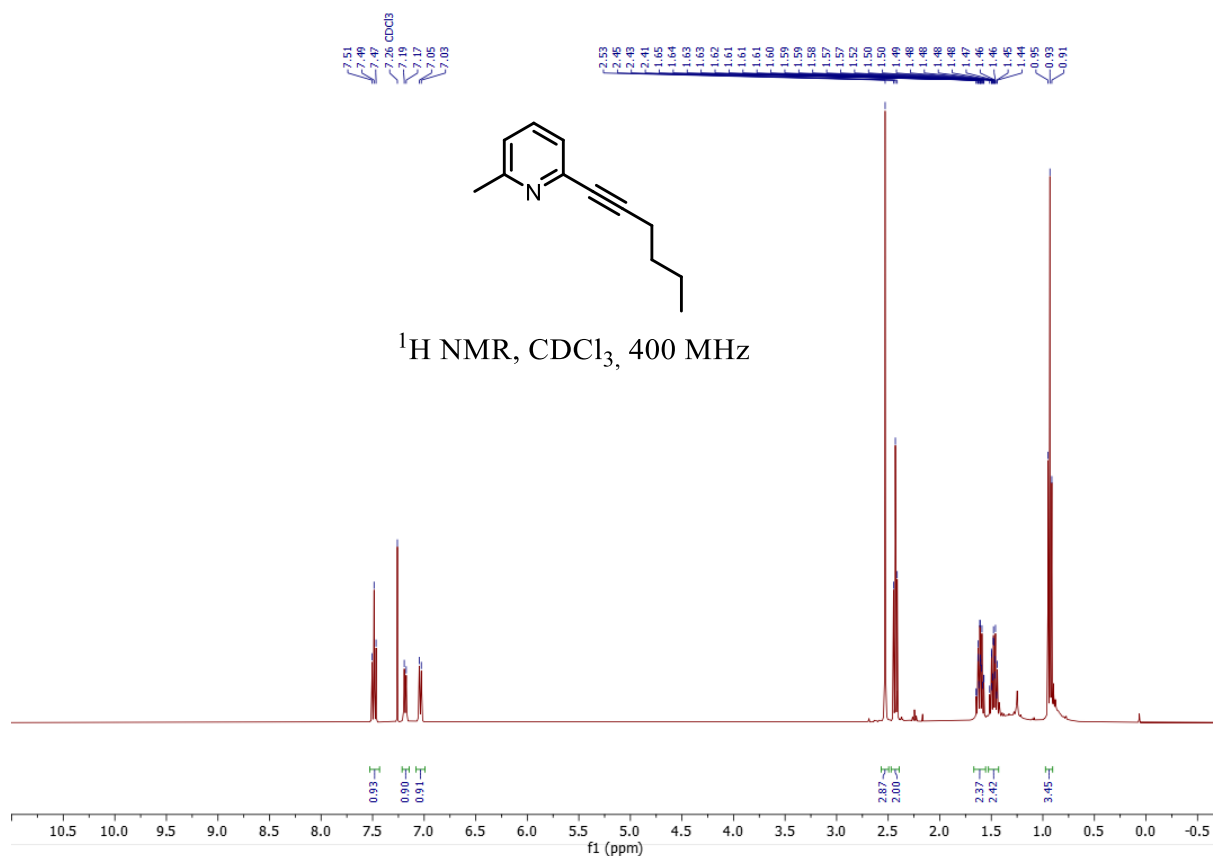
¹³C NMR of 2-methoxy-6-(3-(trifluoromethyl)phenyl)naphthalene, CDCl₃, 100MHz



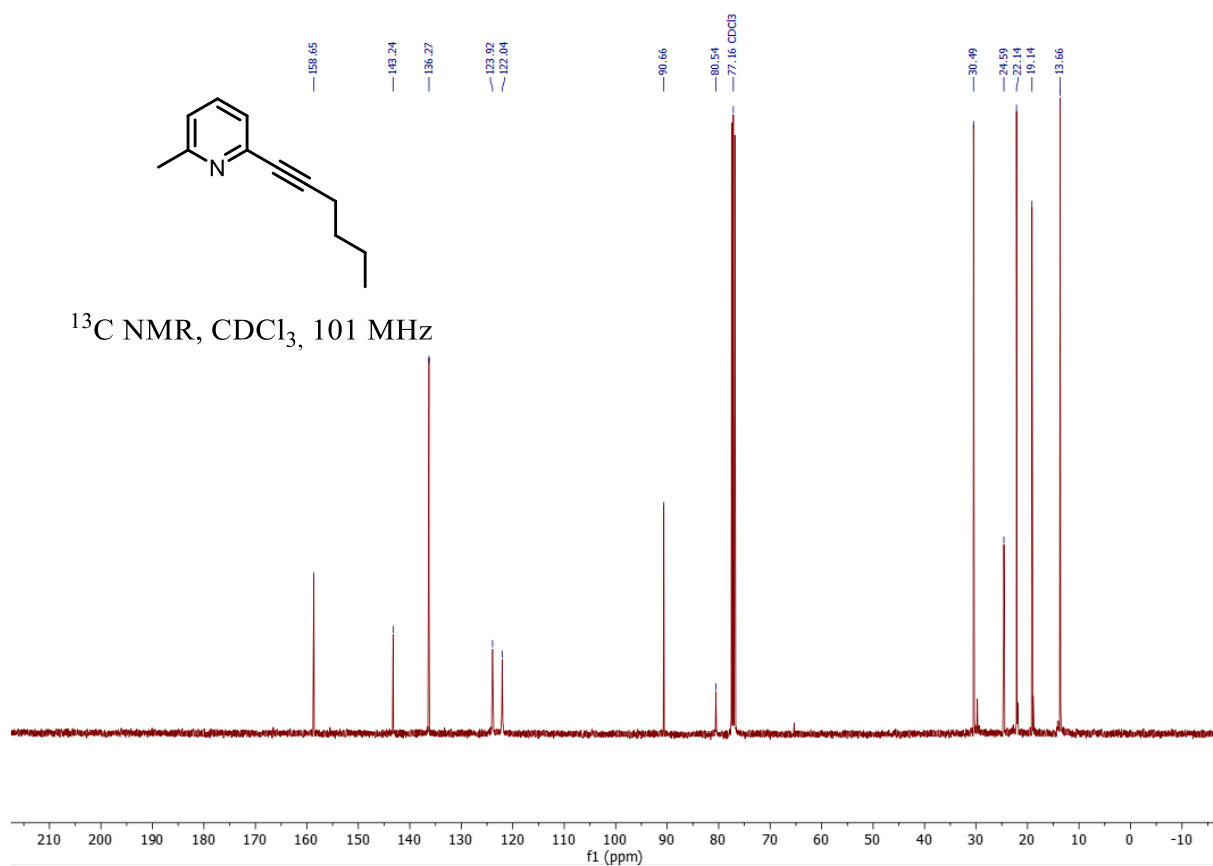
^{19}F NMR of 2-methoxy-6-(3-(trifluoromethyl)phenyl)naphthalene, CDCl_3 , 376MHz



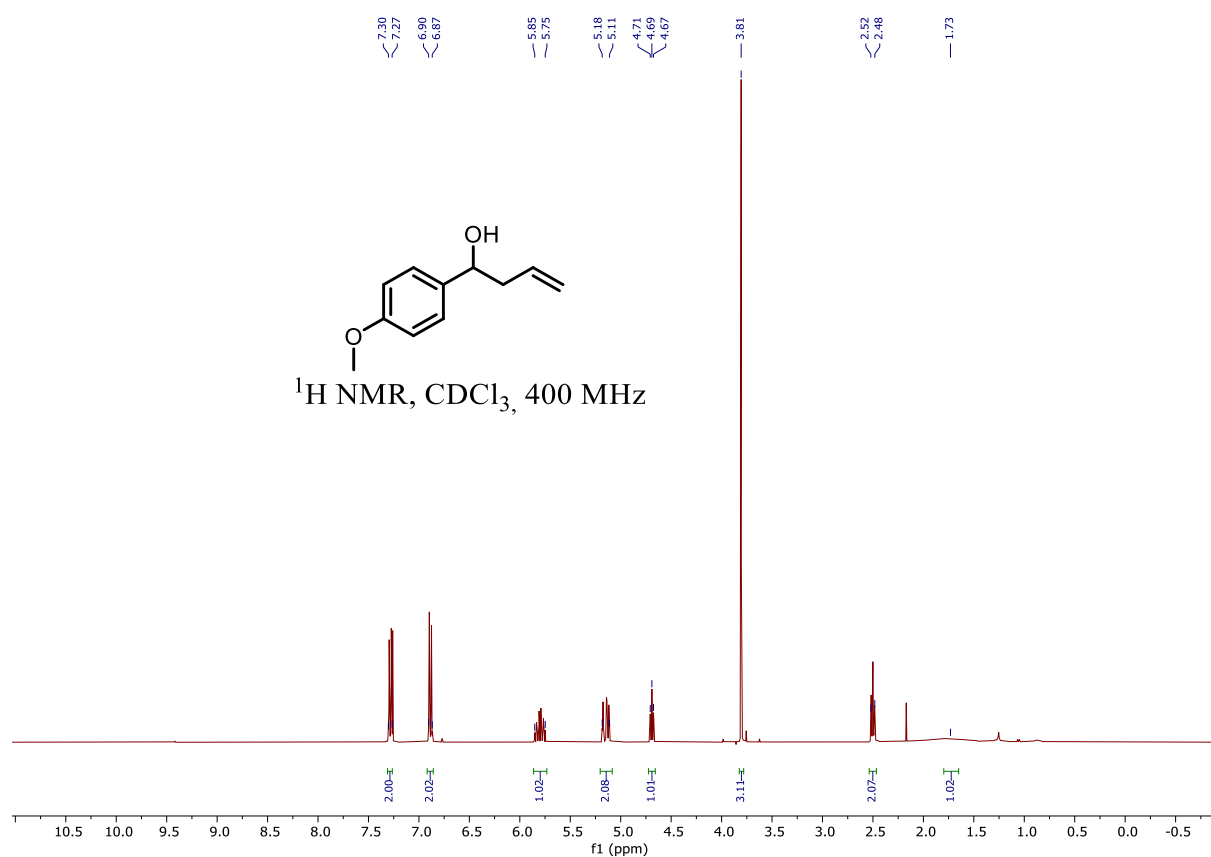
¹H NMR of 2-(hex-1-yn-1-yl)-6-methylpyridine, CDCl₃, 400MHz



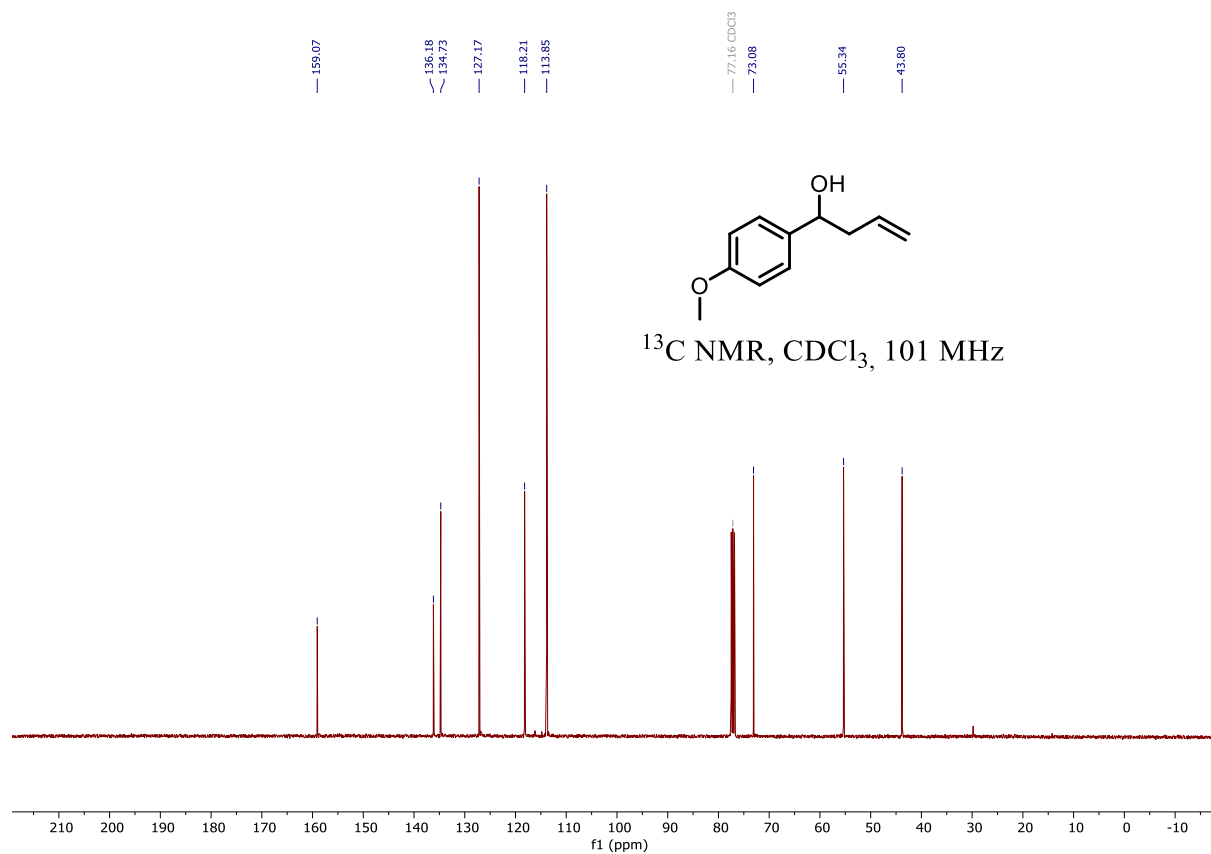
¹³C NMR of 2-(hex-1-yn-1-yl)-6-methylpyridine, CDCl₃, 100MHz



^1H NMR of 1-(4-Methoxyphenyl)but-3-en-1-ol, CDCl_3 , 400MHz



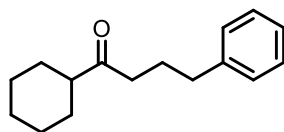
^{13}C NMR of 1-(4-Methoxyphenyl)but-3-en-1-ol, CDCl_3 , 100MHz



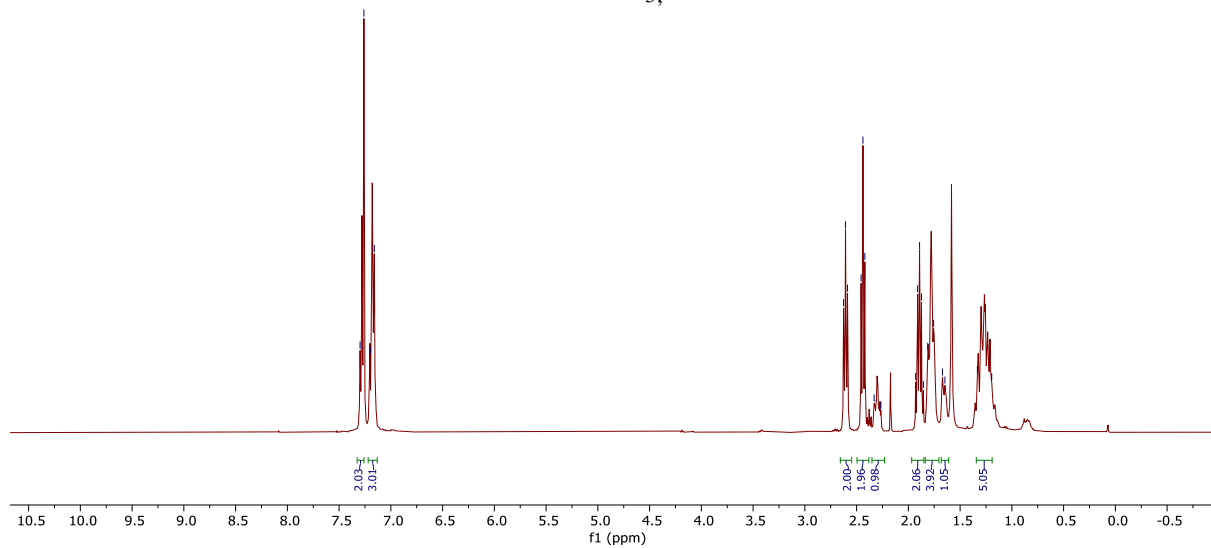
¹H NMR of 1-Cyclohexyl-4-phenylbutan-1-one, CDCl₃, 400MHz

7.30
7.26
7.20
7.16

2.63
2.60
2.56
2.46
2.44
2.42
2.33
2.27
1.93
1.89
1.87
1.85
1.81
1.76
1.65
1.33
1.19



¹H NMR, CDCl₃, 400 MHz



¹³C NMR of 1-Cyclohexyl-4-phenylbutan-1-one, CDCl₃, 100MHz

214.09

141.86

128.57
128.44
125.96

50.93

39.85

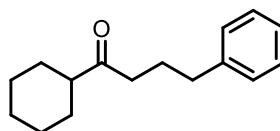
35.27

28.60

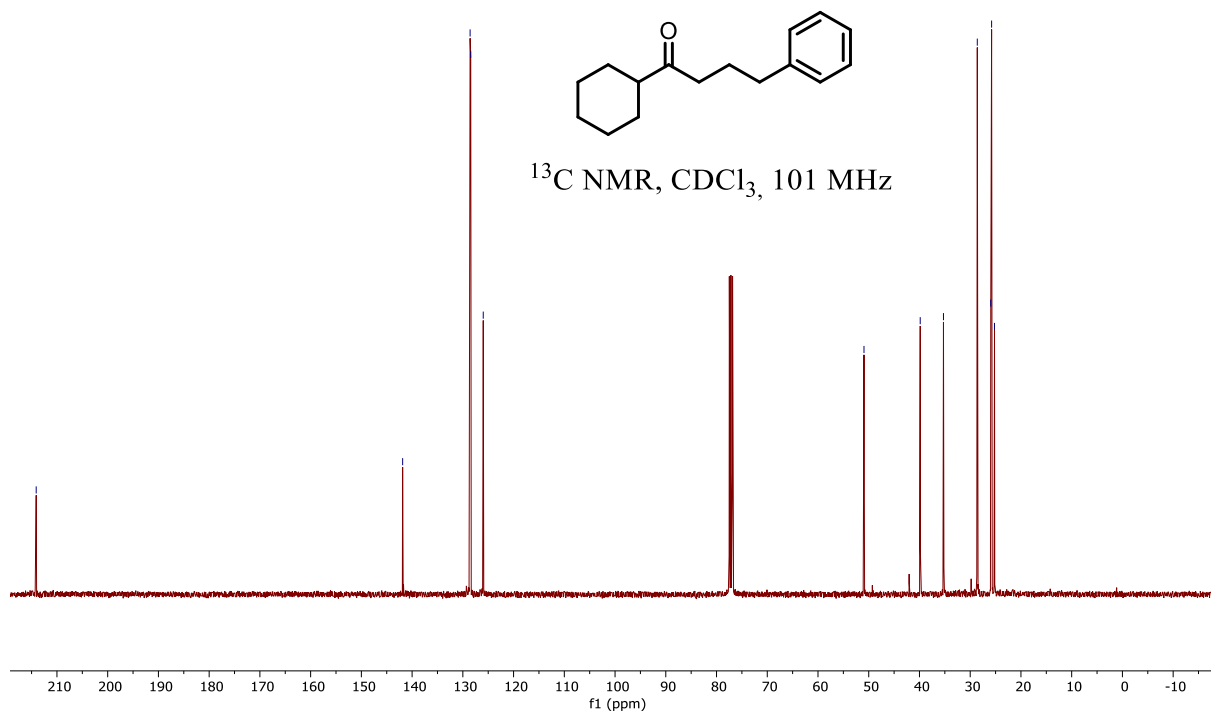
25.95

25.78

25.21



¹³C NMR, CDCl₃, 101 MHz



S6 – Evaluation of calibrated scoops



Figure S3: Commercial 3D printed scoops

Calibrated ChemBeads scoops allow you to weigh ChemBeads products volumetrically. These scoops have been designed to consistently deliver the calibrated amount of ChemBeads quickly and efficiently. The scoops are made of a chemical resistant plastic, acrylonitrile butadiene styrene, and can be reused multiple times, however they should not be cleaned with strong solvents.

The sizes are outlined below with Catalog Number and Calibrated Weight:

925470-1SET one of each scoop calibrated to deliver 5, 10, or 50 milligrams

Tables S2: Measured mass obtained from calibrated scoops depending on the Chembeads size

Chembeads size	5 mg	10 mg	50 mg
#1	6.04	10.64	44.35
#1	6.66	7.14	48.72
#1	5.2	9.08	46.31
#1	5.97	9.1	53.88
#1	5.06	10.21	55.25
#1	5.84		
#2	4.31	6.94	46.66
#2	5.55	10.46	49.06
#2	5.07	10.2	44.08
#2	4.64	8.1	43.24
#2	5.77	9.98	50.35
#2	4.55		
#3	5.06	9.48	50.36
#3	3.8	8.22	48.03
#3	7.1	12.34	43.94
#3	7	11.23	44.93
#3	5.47	8.58	53.22
#3	4.8		
#4	3.47	7.82	50.68
#4	5.11	5.9	48.1
#4	4.31	7.32	45.88
#4	4.02	8.74	45.55
#4	4.77	10.81	43.04
#4	4.75		

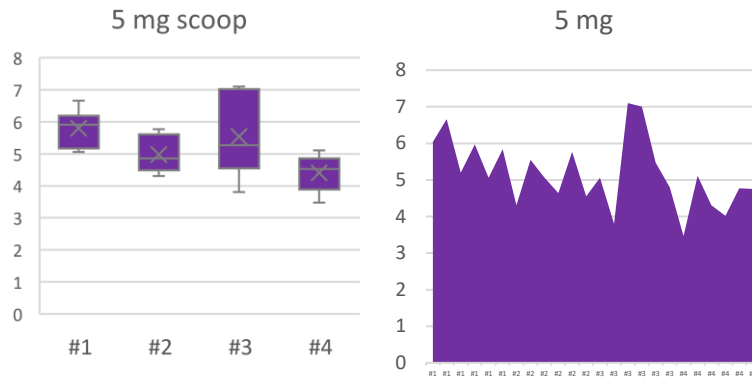


Figure S4: Mass variations obtained with 5 mg calibrated dosing scoops depending on the Chembeads size

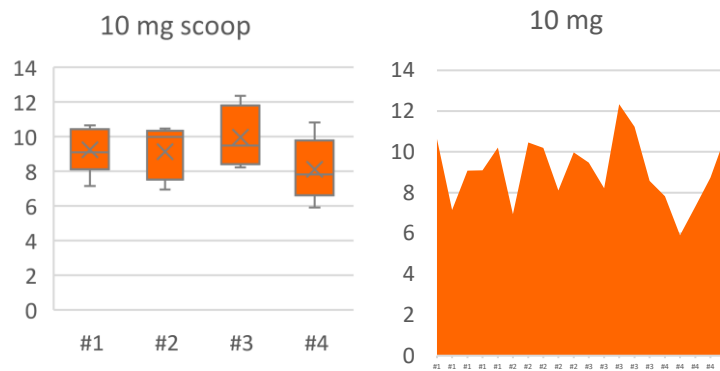


Figure S5: Mass variations obtained with 10 mg calibrated dosing scoops depending on the Chembeads size

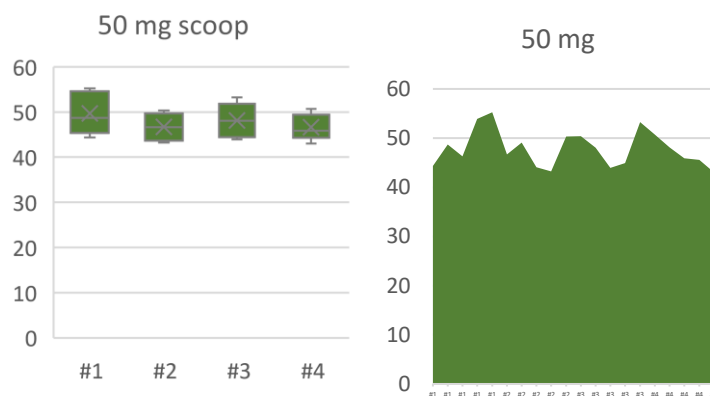


Figure S6: Mass variations obtained with 50 mg calibrated dosing scoops depending on the Chembeads size

References

- [1] Tu NP, Dombrowski AW, Goshu GM, Vasudevan A, Djuric SW, Wang Y (2019) *Angew Chem Int Ed* 58:7987–7991.
- [2] Martin MC, Goshu GM, Hartnell JR, Morris CD, Wang Y, Tu NP (2019) *Org Process Res Dev* 23:1900–1907.
- [3] Chen W, Shen Y, Li Z, Zhang M, Lu C, Shen Y (2014) *Eur J Med Chem* 86:782–796.
- [4] Gualandi A, Rodeghiero G, Faraone A, Patuzzo F, Marchini M, Calogero F, Perciaccan-te R, Jansen TP, Ceroni P, Cozzi PG (2019) *Chem Commun* 55:6838–6841.
- [5] Kerackian T, Bouyssi D, Pilet G, Médebielle M, Monteiro N, Vantourout JC, Amgoune A (2022) *ACS Catal* 12:12315–12325.