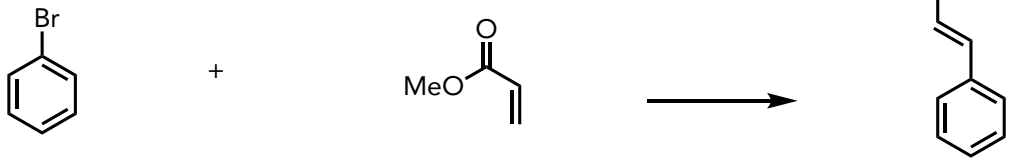
HTE reaction planning

Before getting started:

- Select the file that is appropriate for your experimental design
  - Direct calibration curves and ee will require “ee_noIS”
  - LCAP and >12 of something that isn’t preplated will require “lcap_yield_IS_notpreplated”
  - Everything else (most things!) will require “lcap_yield_IS”
- Complete list of available ligands can be found by going to: https://docs.google.com/spreadsheets/d/1AVvjK4NImj9yk8R7Be-ScvP-55ZgTwZerEuQbeGQft4/edit?usp=sharing

The underlying logic to the spreadsheet

- All experiments are described with sufficient detail to make troubleshooting and reproduction relatively easy
- All experiments are described such that translation of datasets into databases is relatively easy
- The basic version of this description is:



Role: substrate
Role ID: 1
Name: bromobenzene
SMILES: BrC1=CC=CC=C1
Source: as found
Loading in µmol: 10
Stock solution vol: 50
Stock concentration: 0.2
Order of addition: 3

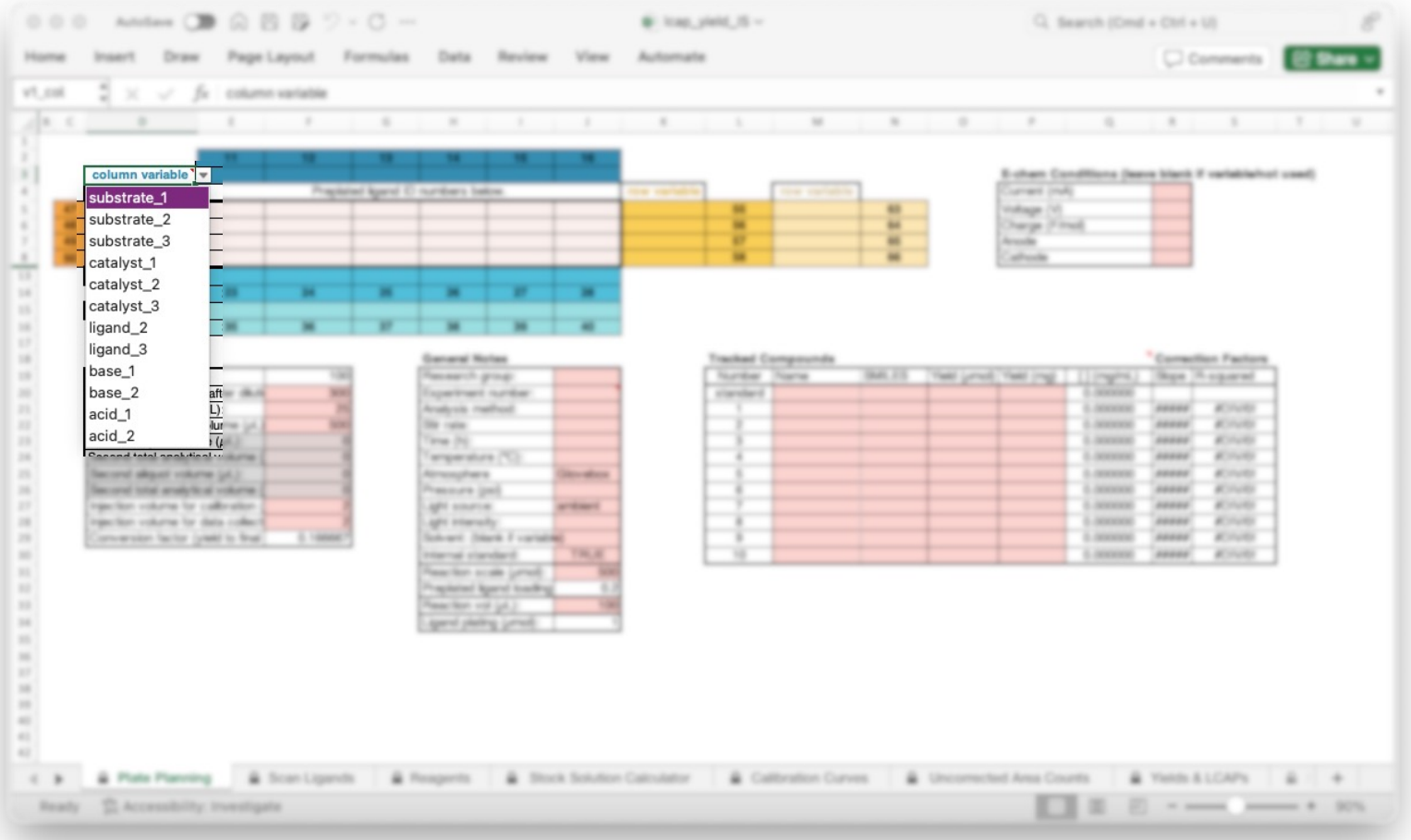
Role: substrate
Role ID: 2
Name: methyl acrylate
SMILES: C=CC(OC)=O
Source: as found
Loading in µmol: 20
Stock solution vol: 50
Stock concentration: 0.4
Order of addition: 4

Role: product
Role ID: 1
Name: methyl cinnamate
SMILES: O=C(OC)/C=C/C1=CC=CC=C1
Max yield: 10
Analysis: GC-FID
Yield method: IS ratio
Area count:
IS ratio:
Yield:
Selectivity:

- Because inputting all of that information is challenging, the spreadsheet aims to streamline all of that

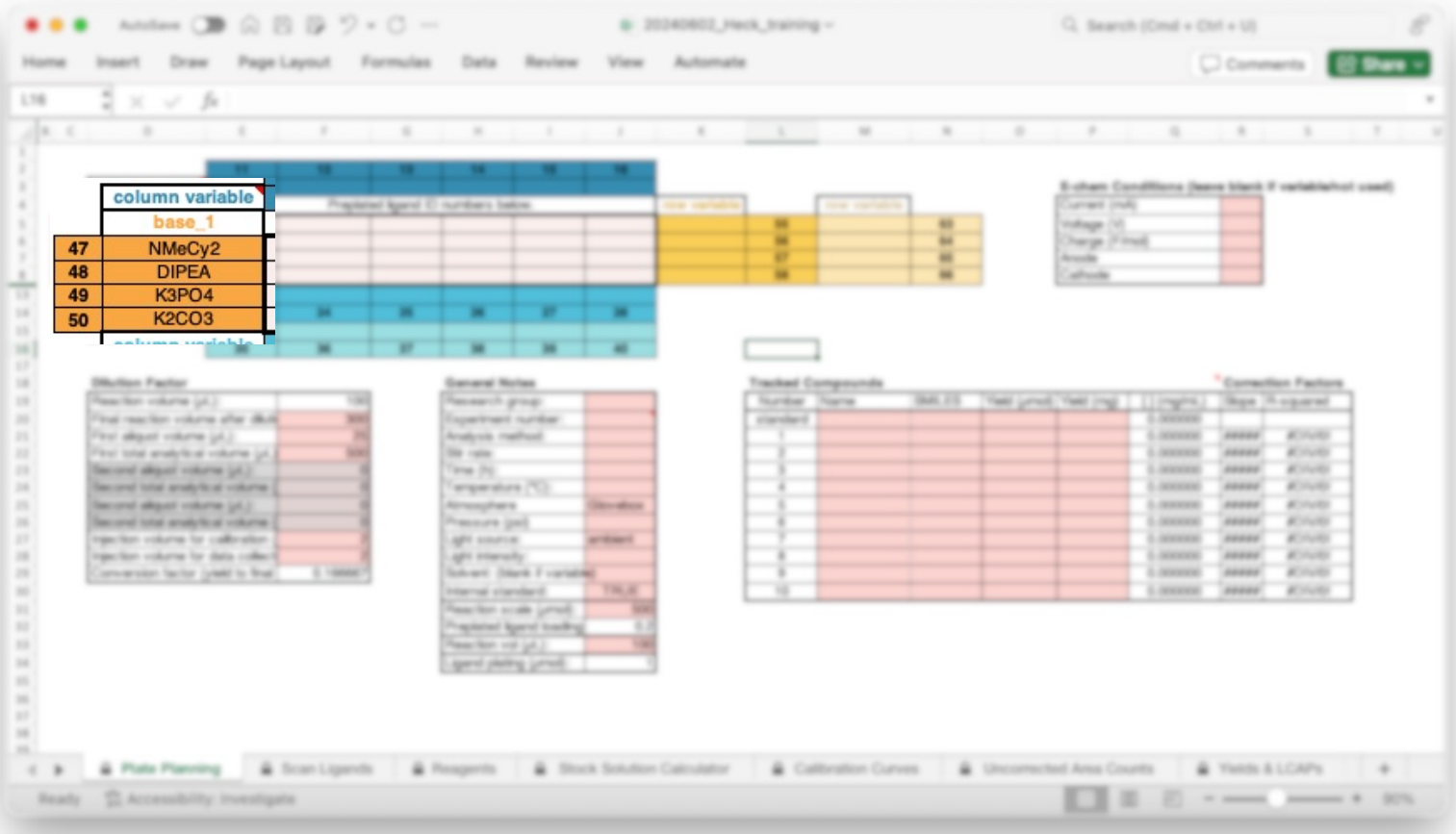
1. Adding Reaction Inputs: variable values

- All chemical and electrochemical inputs need to be added to the sheet, but that is split up between adding things to the plate on the “Plate Planning” sheet and on the “Reagents” tab
- Any input type where you are adding multiple variations should go on “Plate Planning”
- To enter the values, first select the role/role id for that column or row



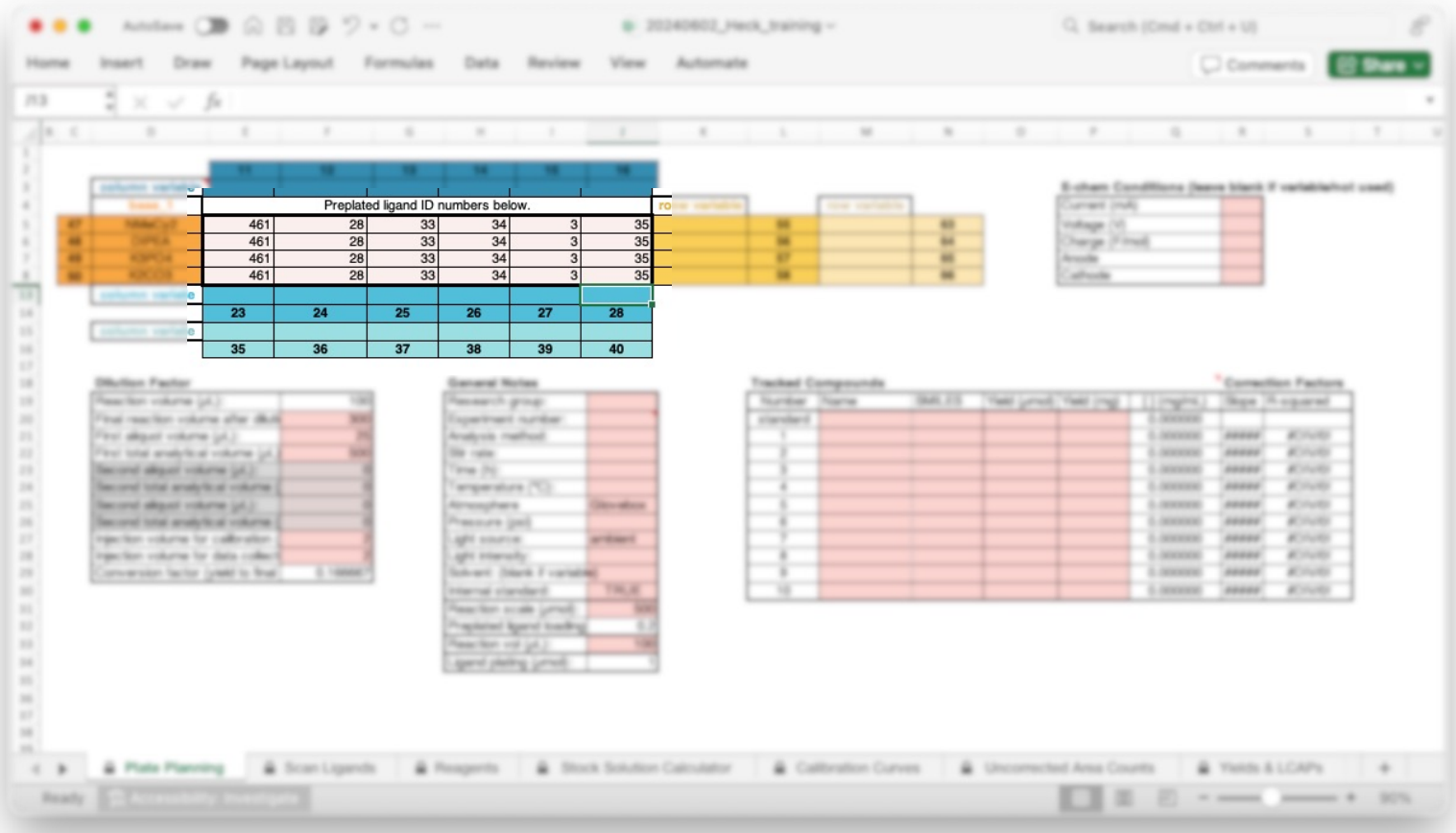
1. Adding Reaction Inputs: variable values

- Once a role has been assigned, go ahead and add what the values are that you will be testing. This name can be as formal or informal as you'd like. If you are testing multiple concentrations or loadings and it's helpful to have that be explicitly in the label, then you should include it. These labels should be helpful to **you**



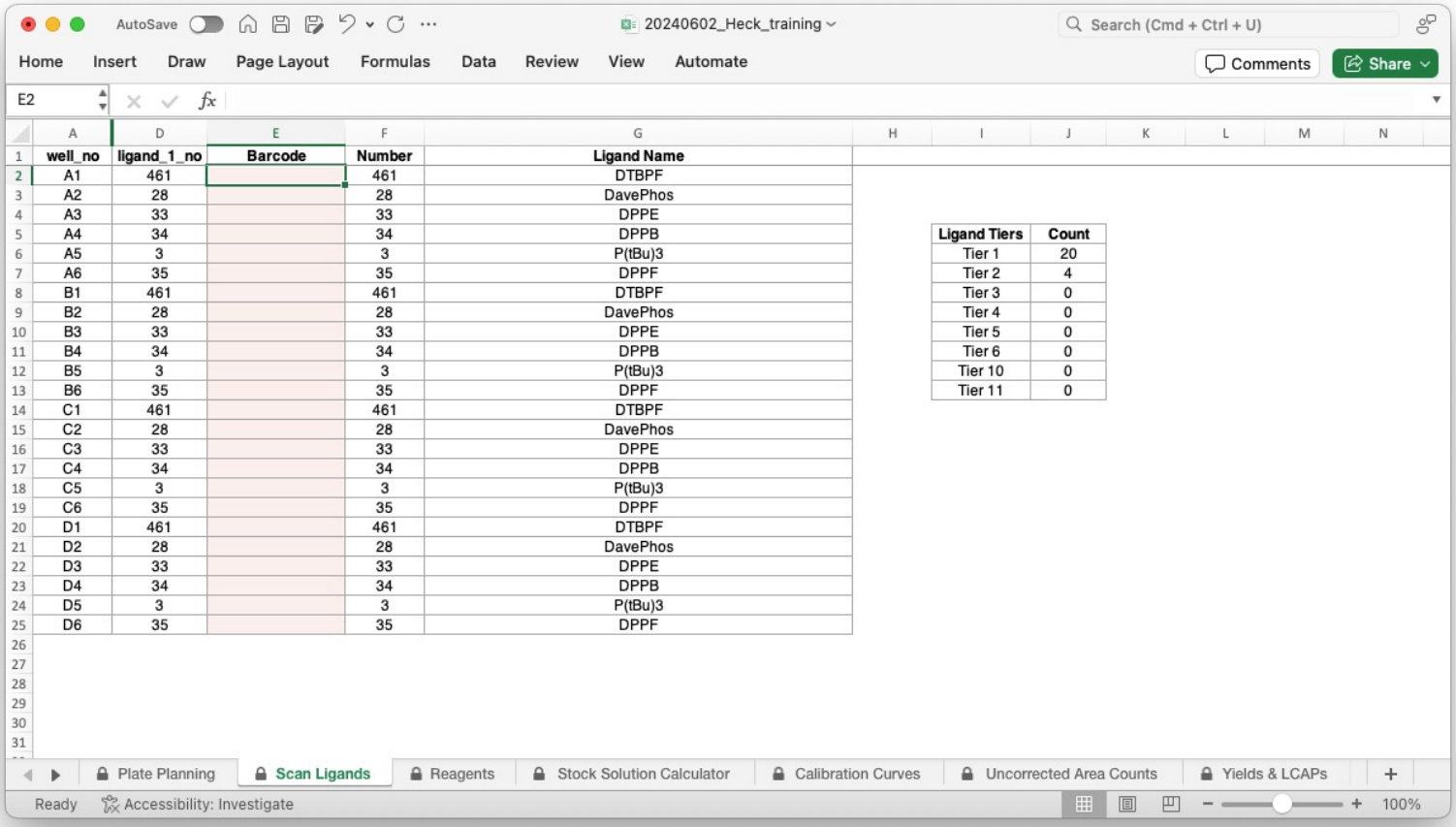
2. Adding Reaction Inputs: preplated ligands

- The ID numbers of any preplated materials can be found in the inventory linked on the first slide
- You can enter those ID numbers in the center of the plate as shown below



2. Adding Reaction Inputs: preplated ligands

- To confirm that the correct ligands have been added, you can check their names by going to the “Scan Ligands” tab
- It is recommended (but not required!) that you scan the barcodes on each tray as you are adding ligands, as confirmation that the correct one has been selected

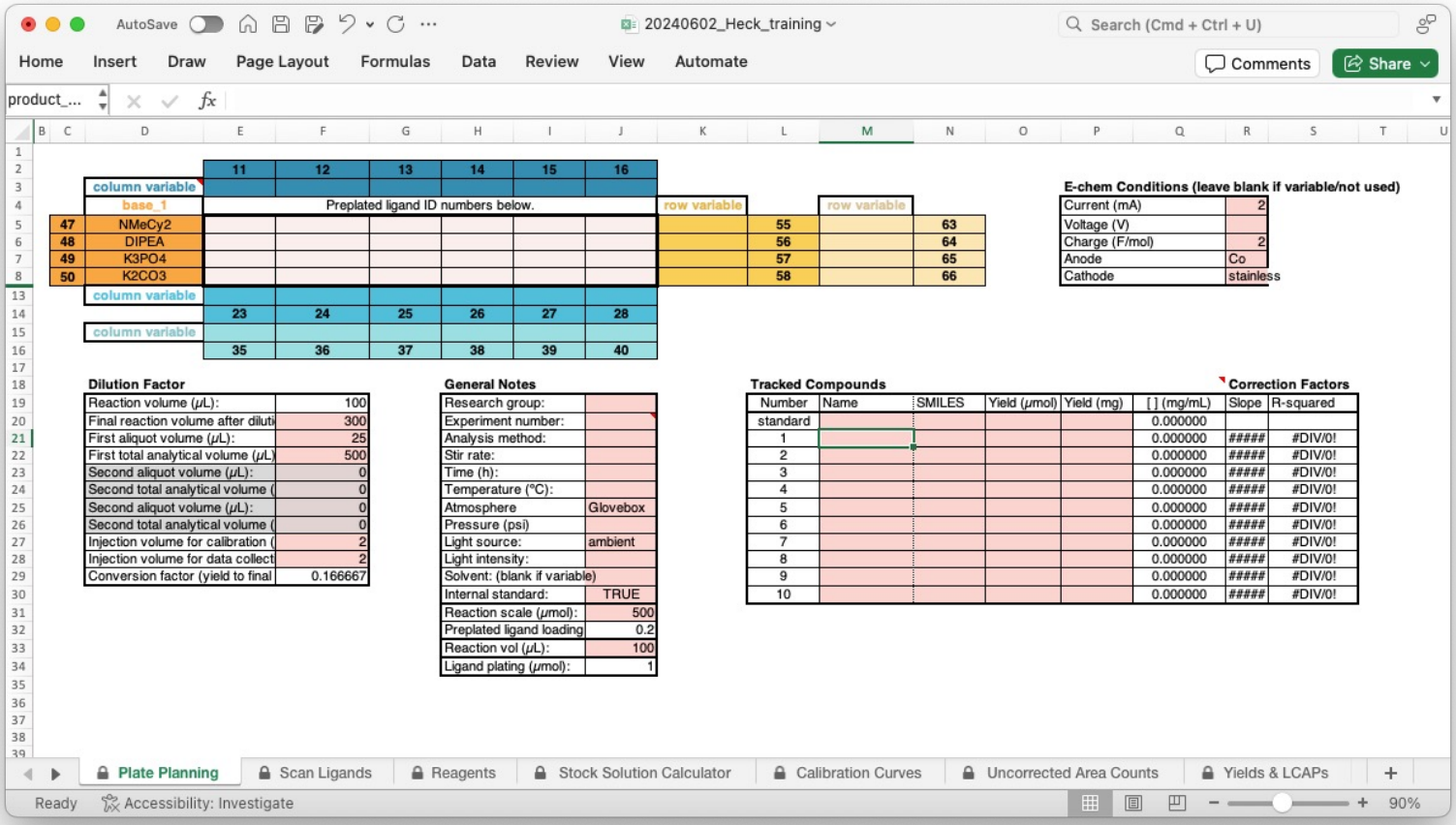


well_no	ligand_1_no	Barcode	Number	Ligand Name
A1	461		461	DTBPF
A2	28		28	DavePhos
A3	33		33	DPPE
A4	34		34	DPPB
A5	3		3	P(tBu)3
A6	35		35	DPPF
B1	461		461	DTBPF
B2	28		28	DavePhos
B3	33		33	DPPE
B4	34		34	DPPB
B5	3		3	P(tBu)3
B6	35		35	DPPF
C1	461		461	DTBPF
C2	28		28	DavePhos
C3	33		33	DPPE
C4	34		34	DPPB
C5	3		3	P(tBu)3
C6	35		35	DPPF
D1	461		461	DTBPF
D2	28		28	DavePhos
D3	33		33	DPPE
D4	34		34	DPPB
D5	3		3	P(tBu)3
D6	35		35	DPPF

Ligand Tiers	Count
Tier 1	20
Tier 2	4
Tier 3	0
Tier 4	0
Tier 5	0
Tier 6	0
Tier 10	0
Tier 11	0

3. Adding Reaction Inputs: electrochemical

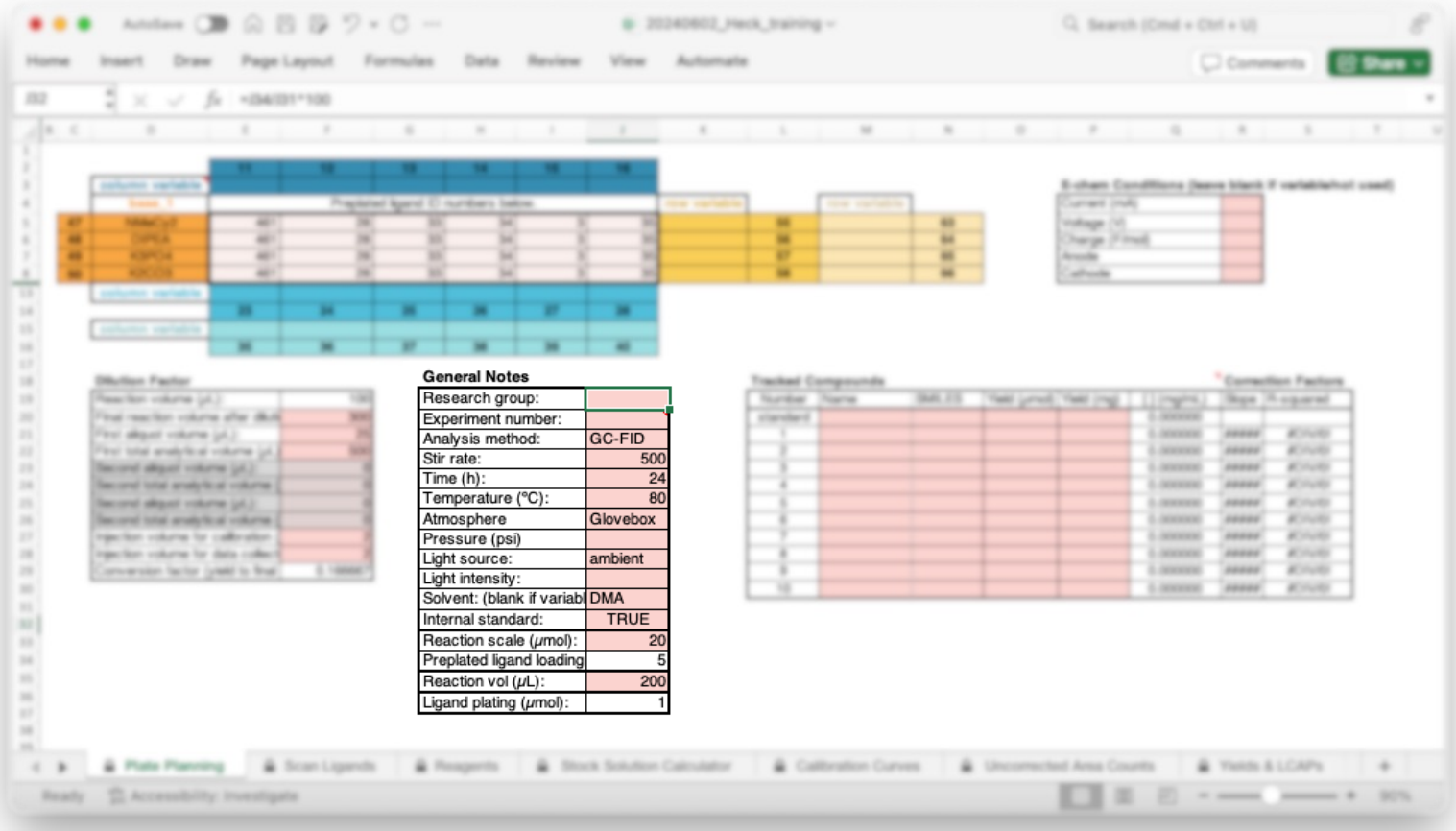
- If you are testing multiple electrochemical conditions then can be entered in the same way
- If you are testing at one condition, then you should complete this section (24 well versions only)



- If you are not running an electrochemical reaction then leave these fields blank

4. Adding Reaction Inputs: non-chemical inputs

- There are many contributors to reaction to success beyond just chemical inputs and those are documented in the central column below the plate
- These inputs include stir rate, time, temperature, atmosphere, light source



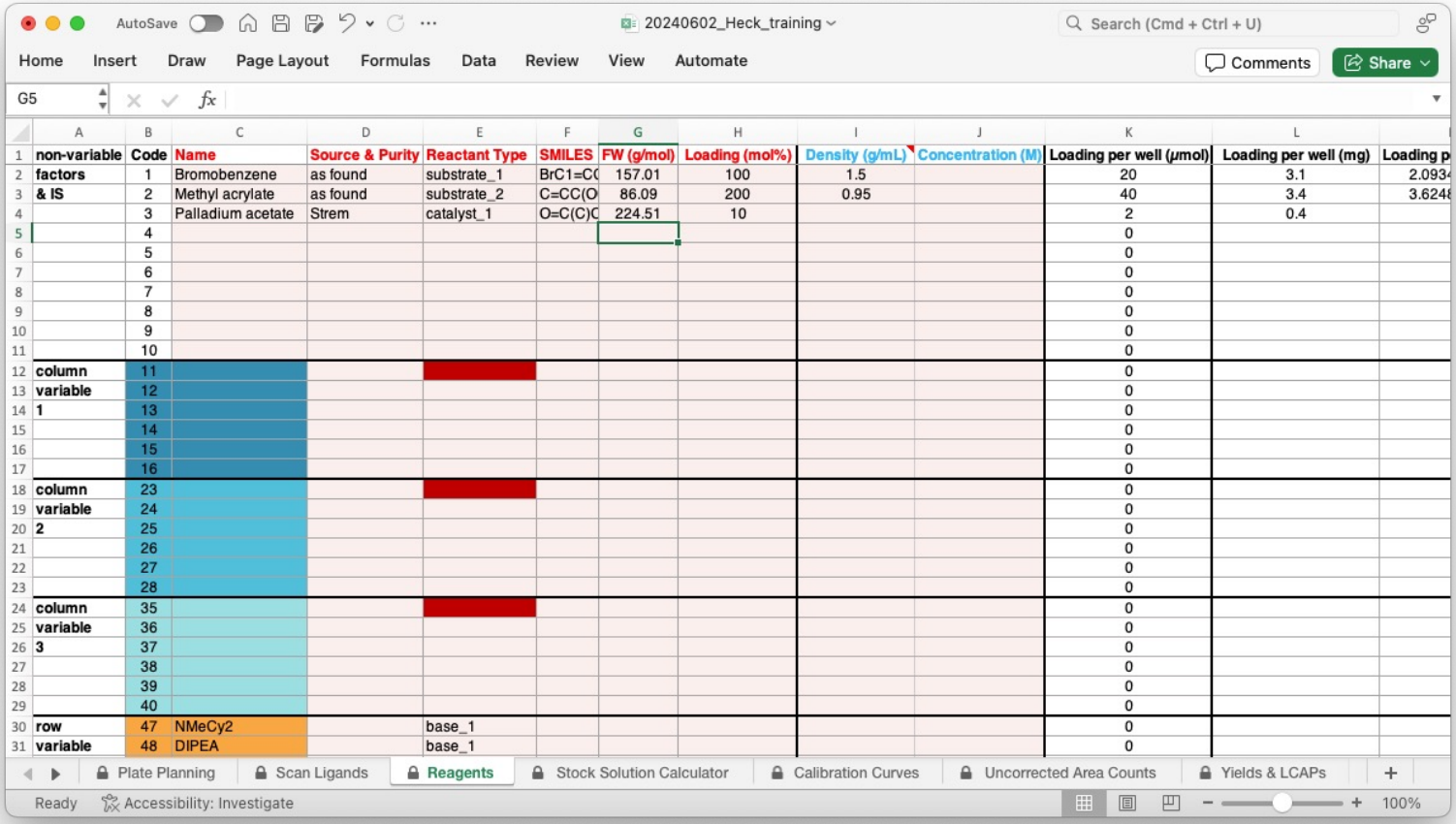
General Notes

Research group:	
Experiment number:	
Analysis method:	GC-FID
Stir rate:	500
Time (h):	24
Temperature (°C):	80
Atmosphere	Glovebox
Pressure (psi)	
Light source:	ambient
Light intensity:	
Solvent: (blank if variab	DMA
Internal standard:	TRUE
Reaction scale (μmol):	20
Preplated ligand loading	5
Reaction vol (μL):	200
Ligand plating (μmol):	1

- This is additionally where you can set the scale of the reaction with the variable that says “Reaction scale (μmol)”
- If you are using multiple main solvents then the Solvent field should be empty

5. Adding Reaction Inputs: everything else

- Once plate planning is complete, advance to the “Reagents” tab
- Any reagent that will be added to every well on a plate should be added to rows 1-10 as shown below
  - Concentration (M) should be used if the stock solution is not being prepared for the reaction in particular (i.e. a commercial solution, etc.)



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	A	B	C	D	E	F	G	H	I	J	K	L
1	non-variable	Code	Name	Source & Purity	Reactant Type	SMILES	FW (g/mol)	Loading (mol%)	Density (g/mL)	Concentration (M)	Loading per well (µmol)	Loading per well (mg)
2	factors	1	Bromobenzene	as found	substrate_1	BrC1=CC	157.01	100	1.5		20	3.1
3	& IS	2	Methyl acrylate	as found	substrate_2	C=CC(O	86.09	200	0.95		40	3.4
4		3	Palladium acetate	Strem	catalyst_1	O=C(C)C	224.51	10			2	0.4
5		4									0	
6		5									0	
7		6									0	
8		7									0	
9		8									0	
10		9									0	
11		10									0	
12	column	11									0	
13	variable	12									0	
14	1	13									0	
15		14									0	
16		15									0	
17		16									0	
18	column	23									0	
19	variable	24									0	
20	2	25									0	
21		26									0	
22		27									0	
23		28									0	
24	column	35									0	
25	variable	36									0	
26	3	37									0	
27		38									0	
28		39									0	
29		40									0	
30	row	47	NMeCy2		base_1						0	
31	variable	48	DIPEA		base_1						0	

Plate Planning Scan Ligands Reagents Stock Solution Calculator Calibration Curves Uncorrected Area Counts Yields & LCAPs

Ready Accessibility: Investigate 100%

5. Adding Reaction Inputs: everything else

- Columns C-H are essential for every reagent including the variable ones entered on the previous sheet
- You will not be able to change any names of variable inputs here, but will need to switch back to “Plate Planning” to reassign those values
- Every reagent will need to have a unique label+id number. If they do not, then the cell will show an error

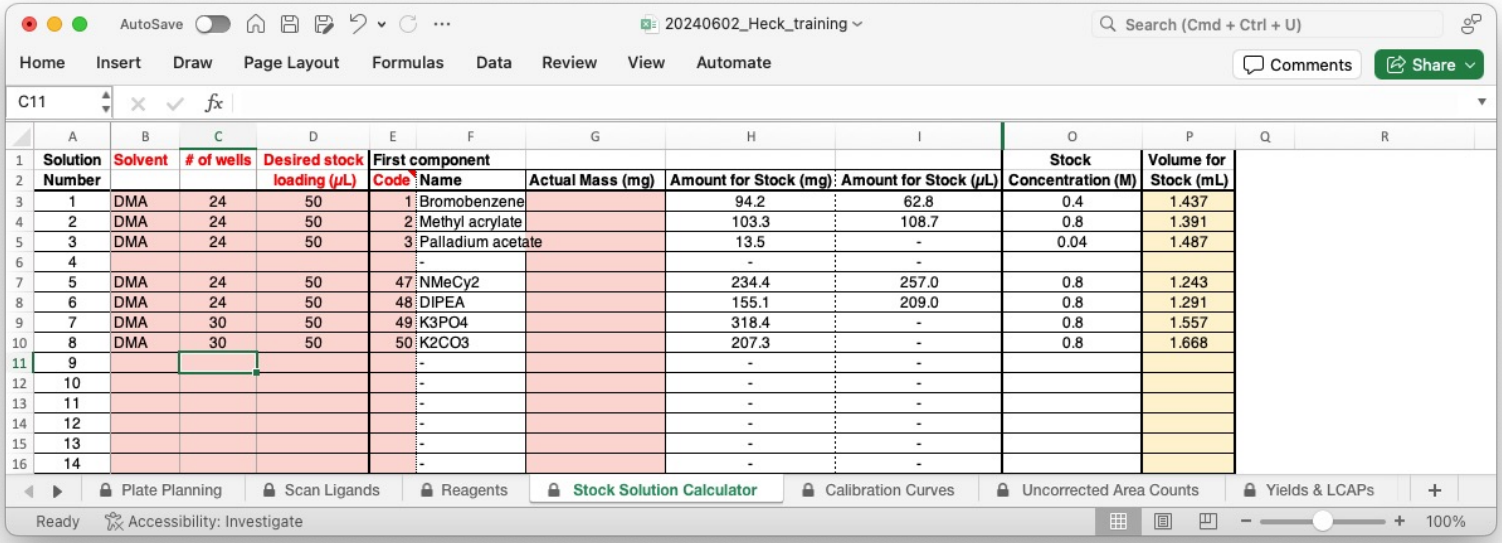
Code	Name	Source & Purity	Reactant Type	SMILES
1	Bromobenzene	as found	substrate_1	BrC1=CC
2	Methyl acrylate	as found	substrate_1	C=CC(O
3	Palladium acetate	Strem	catalyst_1	O=C(C)C

6. Figuring out stock solutions

- Most reagents will be added to the plate using stock solutions in the reaction solvent – this is the most straightforward and least error prone way of doing plate setup
- This means that for each well, the sum of the stock solution volumes should be equal to the desired reaction volume
- In general, you should aim to minimize the concentrations of stock solutions as much as possible as that will increase the accuracy
- In other words:
  - for a reaction run at 20 µmol at 0.1 M, the total volume will be 200 µL
  - In this particular case, the stock solutions that need adding are:
    - $Pd(OAc)_2$ – 2 µmol
    - Bromobenzene – 20 µmol
    - Methyl acrylate – 40 µmol
    - Base – 40 µmol
  - The 200 µL can be divided evenly but if you have more than 4 stock solutions, then it is preferable to make the volumes of the higher loading components larger (i.e. more dilute)

6. Figuring out stock solutions

- To actually plan this out, go to the “Stock Solution Calculator” and enter the solvent, the number of wells the stock solution needs to go for, the desired stock loading, and the code for each reagent
  - The code is listed next to each name on “Reagents”
- This will automatically calculate how much you need to weigh out, the resulting concentration, and the amount of solvent you need to add
- If you need to do a slurry loading of a particular component then it is recommended to increase the number of wells to around 1.25x as many as are actually needed
- You do not need to be precise when weighing things out – if you list the actual mass weighed out then the sheet will account for that in the volume of solvent you need to add



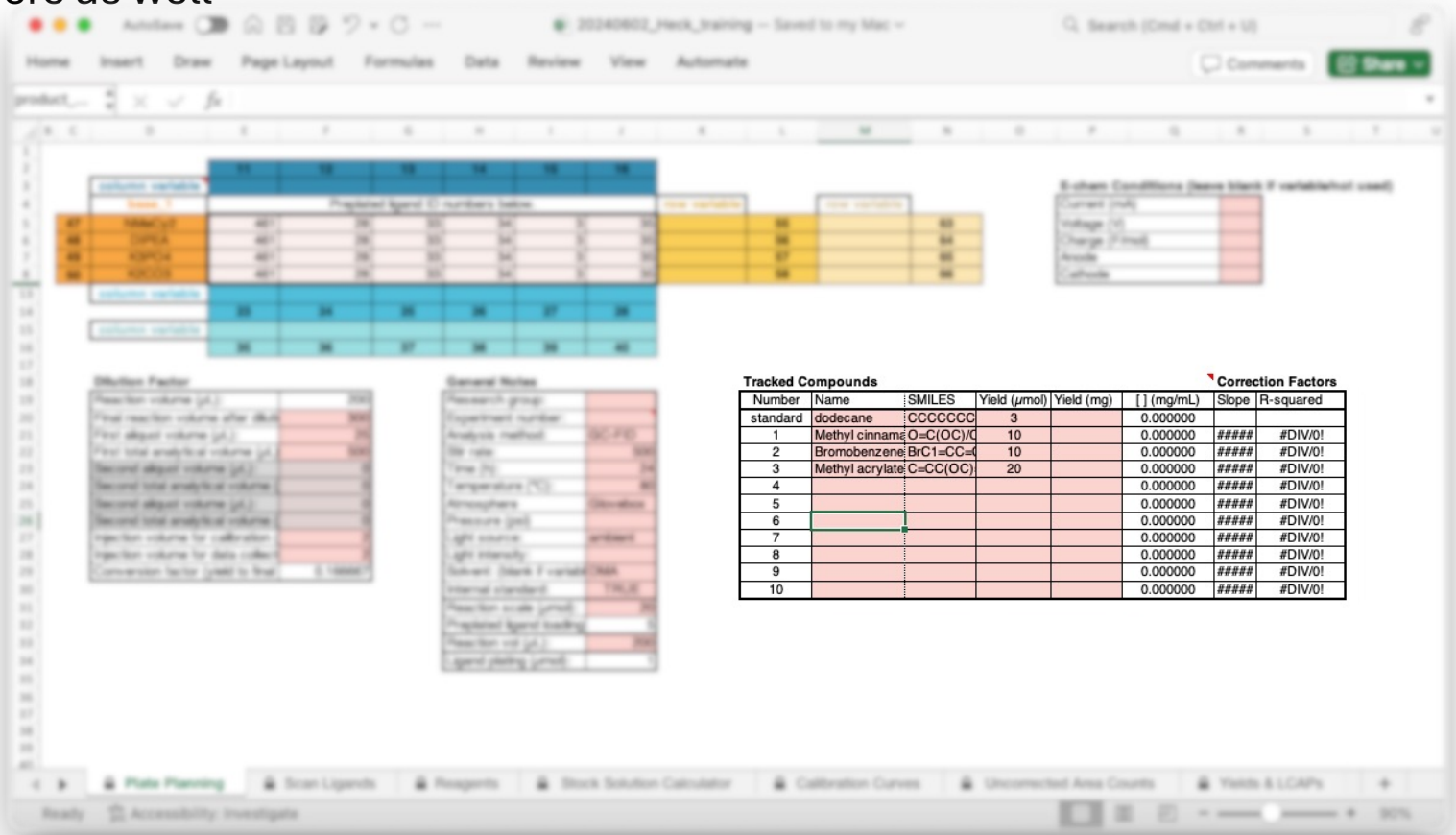
Solution Number	Solvent	# of wells	Desired stock loading (µL)	First component Code	First component Name	First component Actual Mass (mg)	First component Amount for Stock (mg)	First component Amount for Stock (µL)	Stock Concentration (M)	Volume for Stock (mL)
1	DMA	24	50	1	Bromobenzene		94.2	62.8	0.4	1.437
2	DMA	24	50	2	Methyl acrylate		103.3	108.7	0.8	1.391
3	DMA	24	50	3	Palladium acetate		13.5	-	0.04	1.487
4					-		-	-		
5	DMA	24	50	47	NMeCy2		234.4	257.0	0.8	1.243
6	DMA	24	50	48	DIPEA		155.1	209.0	0.8	1.291
7	DMA	30	50	49	K3PO4		318.4	-	0.8	1.557
8	DMA	30	50	50	K2CO3		207.3	-	0.8	1.668
9					-		-	-		
10					-		-	-		
11					-		-	-		
12					-		-	-		
13					-		-	-		
14					-		-	-		

7. Running the experiment

- At this point you have entered all the plate inputs!
  - Hooray!!
- If you are on the 96-well version of the spreadsheet then there is a sheet that will color code wells according to how much of each reagent needs to be added

8. Analyzing the data

- Once you have finished running the experiment then the workbook will help you additionally figure out the dilutions required for your analytics and calculate yields
- To get started, go back to “Plate Planning” and complete the “Tracked Compounds” table with the names, SMILES, and yield in µmol of any compound present in your reaction mixture that you want to quantify
- If you have a correction factor for that reaction component then you can add it here as well

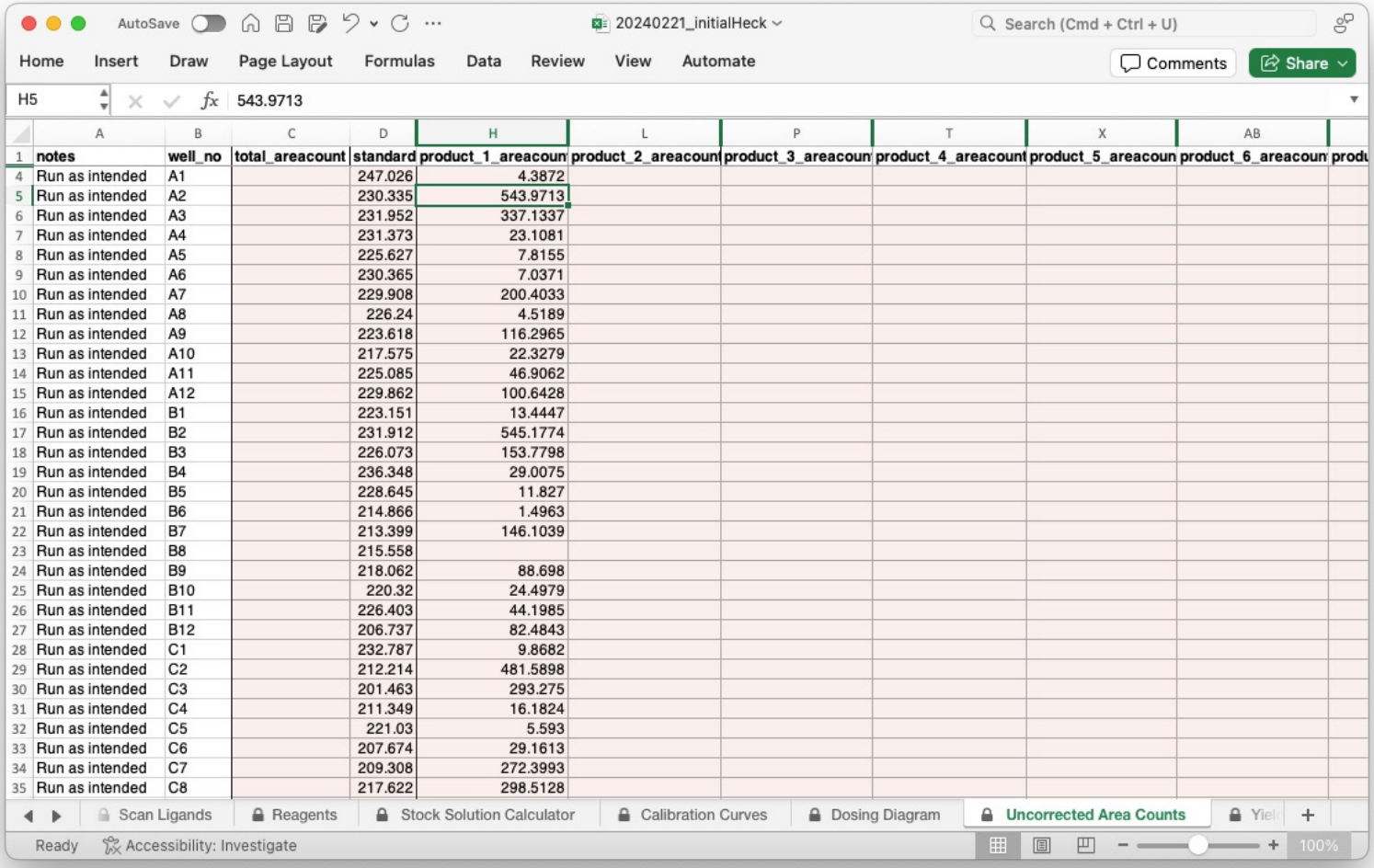


Tracked Compounds — **Correction Factors**

Number	Name	SMILES	Yield (µmol)	Yield (mg)	[ ] (mg/mL)	Slope	R-squared
standard	dodecane	CCCCCCC	3		0.000000		
1	Methyl cinnama	O=C(OC)/C	10		0.000000	#####	#DIV/0!
2	Bromobenzene	BrC1=CC=C	10		0.000000	#####	#DIV/0!
3	Methyl acrylate	C=CC(OC)	20		0.000000	#####	#DIV/0!
4					0.000000	#####	#DIV/0!
5					0.000000	#####	#DIV/0!
6					0.000000	#####	#DIV/0!
7					0.000000	#####	#DIV/0!
8					0.000000	#####	#DIV/0!
9					0.000000	#####	#DIV/0!
10					0.000000	#####	#DIV/0!

8. Analyzing the data

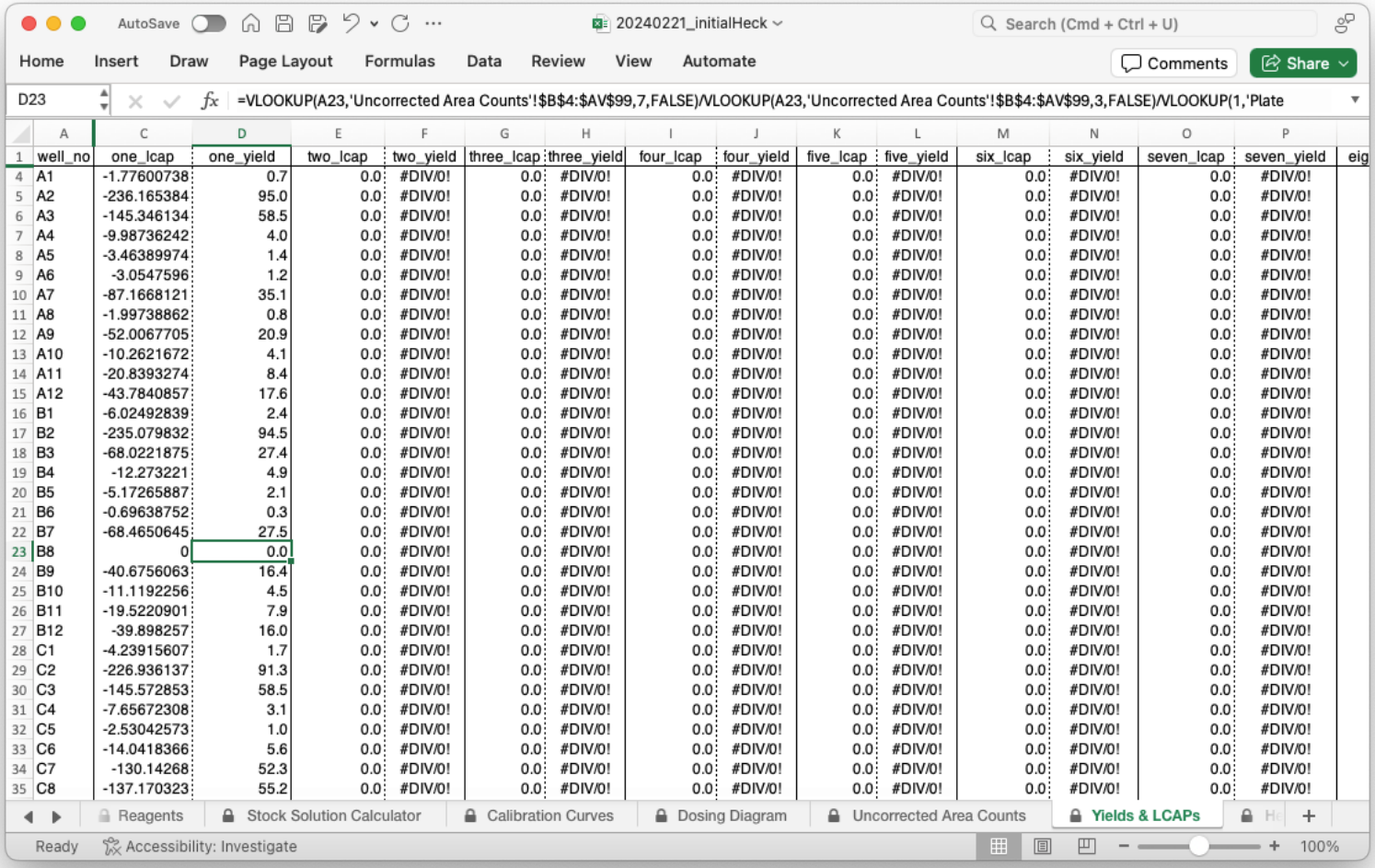
- Area counts can then be pasted into the “Uncorrected Area Counts” sheet but be sure to make sure that they are in the column with the heating correspond to the ID number listed on the “Plate Planning Sheet”
- In the 96-well version of the spreadsheet you will also see a notes column – if any well was not run as intended or not run, then this should be indicated here



	A	B	C	D	H	L	P	T	X	AB
1	notes	well_no	total_areacount	standard	product_1_areacoun	product_2_areacoun	product_3_areacoun	product_4_areacount	product_5_areacoun	product_6_areacoun
4	Run as intended	A1		247.026	4.3872					
5	Run as intended	A2		230.335	543.9713					
6	Run as intended	A3		231.952	337.1337					
7	Run as intended	A4		231.373	23.1081					
8	Run as intended	A5		225.627	7.8155					
9	Run as intended	A6		230.365	7.0371					
10	Run as intended	A7		229.908	200.4033					
11	Run as intended	A8		226.24	4.5189					
12	Run as intended	A9		223.618	116.2965					
13	Run as intended	A10		217.575	22.3279					
14	Run as intended	A11		225.085	46.9062					
15	Run as intended	A12		229.862	100.6428					
16	Run as intended	B1		223.151	13.4447					
17	Run as intended	B2		231.912	545.1774					
18	Run as intended	B3		226.073	153.7798					
19	Run as intended	B4		236.348	29.0075					
20	Run as intended	B5		228.645	11.827					
21	Run as intended	B6		214.866	1.4963					
22	Run as intended	B7		213.399	146.1039					
23	Run as intended	B8		215.558						
24	Run as intended	B9		218.062	88.698					
25	Run as intended	B10		220.32	24.4979					
26	Run as intended	B11		226.403	44.1985					
27	Run as intended	B12		206.737	82.4843					
28	Run as intended	C1		232.787	9.8682					
29	Run as intended	C2		212.214	481.5898					
30	Run as intended	C3		201.463	293.275					
31	Run as intended	C4		211.349	16.1824					
32	Run as intended	C5		221.03	5.593					
33	Run as intended	C6		207.674	29.1613					
34	Run as intended	C7		209.308	272.3993					
35	Run as intended	C8		217.622	298.5128					

8. Analyzing the data

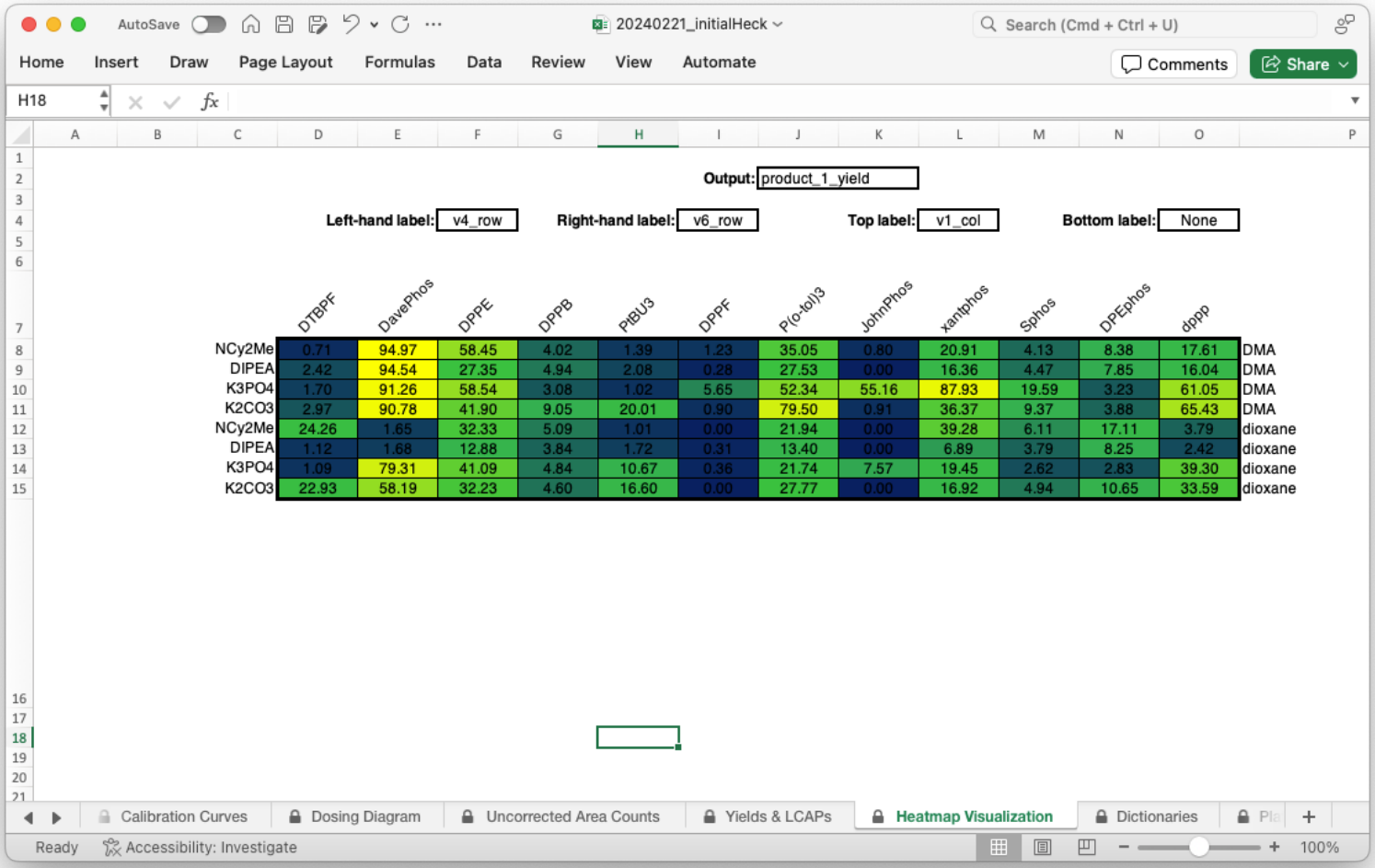
- If there is a correction factor and all yields are completed in “Plate Planning” then you should now see your yields in the “Yields and LCAP” tab



	A	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1	well_no	one_lcap	one_yield	two_lcap	two_yield	three_lcap	three_yield	four_lcap	four_yield	five_lcap	five_yield	six_lcap	six_yield	seven_lcap	seven_yield
4	A1	-1.77600738	0.7	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
5	A2	-236.165384	95.0	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
6	A3	-145.346134	58.5	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
7	A4	-9.98736242	4.0	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
8	A5	-3.46389974	1.4	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
9	A6	-3.0547596	1.2	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
10	A7	-87.1668121	35.1	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
11	A8	-1.99738862	0.8	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
12	A9	-52.0067705	20.9	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
13	A10	-10.2621672	4.1	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
14	A11	-20.8393274	8.4	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
15	A12	-43.7840857	17.6	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
16	B1	-6.02492839	2.4	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
17	B2	-235.079832	94.5	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
18	B3	-68.0221875	27.4	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
19	B4	-12.273221	4.9	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
20	B5	-5.17265887	2.1	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
21	B6	-0.69638752	0.3	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
22	B7	-68.4650645	27.5	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
23	B8	0	0.0	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
24	B9	-40.6756063	16.4	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
25	B10	-11.1192256	4.5	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
26	B11	-19.5220901	7.9	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
27	B12	-39.898257	16.0	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
28	C1	-4.23915607	1.7	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
29	C2	-226.936137	91.3	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
30	C3	-145.572853	58.5	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
31	C4	-7.65672308	3.1	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
32	C5	-2.53042573	1.0	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
33	C6	-14.0418366	5.6	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
34	C7	-130.14268	52.3	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!
35	C8	-137.170323	55.2	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!	0.0	#DIV/0!

9. Finishing up

- At this point your data can be visualized in notebook using the “Heatmap” tab, but you should also submit it to our visualization program to generate more complicated visualizations



AutoSave 20240221_initialHeck Search (Cmd + Ctrl + U)

Home Insert Draw Page Layout Formulas Data Review View Automate Comments Share

H18

Output: product_1_yield

Left-hand label: v4_row **Right-hand label:** v6_row **Top label:** v1_col **Bottom label:** None

	DTBPF	DavePhos	DPPE	DPPB	PtBU3	DPPF	P(o-tol)3	JohnPhos	xantphos	Sphos	DPEphos	dppp	
NCy2Me	0.71	94.97	58.45	4.02	1.39	1.23	35.05	0.80	20.91	4.13	8.38	17.61	DMA
DIPEA	2.42	94.54	27.35	4.94	2.08	0.28	27.53	0.00	16.36	4.47	7.85	16.04	DMA
K3PO4	1.70	91.26	58.54	3.08	1.02	5.65	52.34	55.16	87.93	19.59	3.23	61.05	DMA
K2CO3	2.97	90.78	41.90	9.05	20.01	0.90	79.50	0.91	36.37	9.37	3.88	65.43	DMA
NCy2Me	24.26	1.65	32.33	5.09	1.01	0.00	21.94	0.00	39.28	6.11	17.11	3.79	dioxane
DIPEA	1.12	1.68	12.88	3.84	1.72	0.31	13.40	0.00	6.89	3.79	8.25	2.42	dioxane
K3PO4	1.09	79.31	41.09	4.84	10.67	0.36	21.74	7.57	19.45	2.62	2.83	39.30	dioxane
K2CO3	22.93	58.19	32.23	4.60	16.60	0.00	27.77	0.00	16.92	4.94	10.65	33.59	dioxane

Calibration Curves | Dosing Diagram | Uncorrected Area Counts | Yields & LCAPs | Heatmap Visualization | Dictionaries

Ready Accessibility: Investigate 100%