



Optimize Your Cross-Coupling

The Phosphine Predictor: A new digital solution recommending phosphine ligands for C-C or C-N cross coupling reactions.

The Phosphine Predictor, developed in collaboration with Prof. Matthew S. Sigman and Dr. Tobias Gensch, suggests which commercially available monodentate phosphine ligands might be optimal for your particular C-C or C-N cross-coupling reaction. By using this digital tool, screening a handful of phosphine ligands (and recording their yields, good or bad) is tantamount to screening hundreds of phosphines in pursuit of the optimal ligand. Notably, the structures and conditions of your reaction need not be shared for the predictor to produce a suggested list of ligands to try; the information needed is fully contained in the yields attributed to the phosphines you screened.

Select Reactions

Enter Yields

Review Results

Reactions

Please select the type of reaction you performed experiments on.

Suzuki Coupling

Buchwald-Hartwig Amination

In the next step we will ask you to provide yield values for each ligand in the test set.

Next

About the Phosphine Predictor Portal

The Phosphine Predictor is hosted on a password-protected portal accessible at sigmaaldrich.com/phosphinepredictorportal. Access and use of the Portal is sold as a single-use (919845-1EA) password, or package of five single-use passwords (919845-5EA). The passwords are shipped to you as a physical document (and received as you would other orders from your sigmaaldrich.com account) for security and ease of use. The required screening ligands can be purchased separately; see sigmaaldrich.com/phosphinepredictor.

How Does the Predictor Work?

Over 600 commercially available monophosphine ligands have been parameterized according to a methodology developed by the Sigman group. In essence, each phosphine ligand is converted into a multi-variable mathematical equation that represents their most relevant steric and electronic properties. From the hundreds, a set of 32 ligands was identified that can be used to represent the larger group of phosphines; the yields recorded from each help to identify the ideal combination of parameters, and through use of an algorithm, the ideal ligand itself.

What Do I Need to Do?

1. Obtain your desired number of Phosphine Predictor portal passwords at sigmaaldrich.com/phosphinepredictor (Product number [919845](#)).
2. Acquire the 32 Universal Training Set ligands, or as many as possible. List is below, and available with more information at sigmaaldrich.com/phosphinepredictor.
3. Run screening reactions with each of the UTS ligands under currently optimized reaction conditions and record yield. Analytical yields (GC, HPLC, etc.) acceptable so long as they are consistent.
4. Access the Phosphine Predictor portal at sigmaaldrich.com/phosphinepredictorportal.
5. Click "Sign up for an account" and follow the instructions, including adding the one-time use password when requested.

Sign in

Enter email

Next

OR



Google

Can't log in?

[Sign up for an account](#)

6. Select the type of cross-coupling reaction.

Select Reactions Enter Yields Review Results

Reactions

Please select the type of reaction you performed experiments on.

Suzuki Coupling

Buchwald-Hartwig Amination

In the next step we will ask you to provide yield values for each ligand in the test set.

Next

7. Once selected, the password entered will be consumed. Enter the yields obtained for each of the ligands screened.

Suzuki Coupling

Please enter the yield values for the Suzuki Coupling and press **Save** at the bottom of the list.

ID	Ligand	Yield
3	SPhos CAS 657408-07-6, 1356823-31-8 (15)	86.90
15	P(2OMePh)3 CAS 4731-65-1	15.34
650	P(OBn)2NEt2 CAS 67746-43-4	3.59

Save

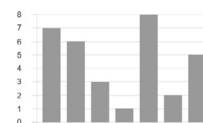
8. A new window will appear; click Next to go to the results page.

Suzuki Coupling

32 results entered.

0 missing.

Predictive power of the provided input is OK.



Edit

In the next step we will provide a preliminary analysis of the quality of the provided values.

Back

Next

9. Results will be emailed to the account given at sign in. Click the link in the email to receive the ligand recommendations (account log in will be required). Results will remain saved in your account for future viewing.

Results

Please allow several minutes for the model training and the suggested ligands to be returned.

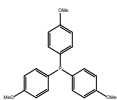
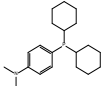
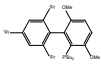
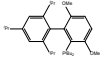
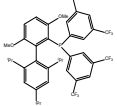
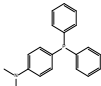
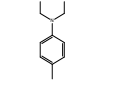
We will email the results to [redacted].

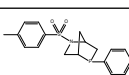
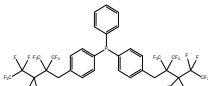
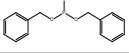
Job IDs

Each reaction is assigned its own unique job ID.

Suzuki Coupling: 00609e7d82ee15bf6c8948eba95f

Universal Training Set (UTS) Ligands Required for the Portal (Sold Separately)

Portal ID	Ligand	Structure	CAS Number	Product Number
3	SPhos		657408-07-6	638072
15	P(2-OMePh) ₃		4731-65-1	710563
30	PtBu ₂ Cy		436865-11-1	ATE456786846
62	P(4-OMePh) ₃		855-38-9	395102
68	PCy ₂ Ph		6476-37-5	288284
69	Dicyclohexyl(4-(<i>N,N</i> -dimethylamino)phenyl)phosphine		40438-64-0	692689
79	P(<i>i</i> Pr) ₃		6476-36-4	377309
84	PallylPh ₂		2741-38-0	336874
89	<i>t</i> BuBrettPhos		1160861-53-9	730998
102	BrettPhos		1070663-78-3	718742
104	JackiePhos		1160861-60-8	731013
116	4-(Dimethylamino)phenyldiphenylphosphine		739-58-2	395021
130	PPh ₂ (2-OMe-Ph)		53111-20-9	287865
139	P(OEt)Ph ₂		719-80-2	149489
148	P(OEt) ₃		122-52-1	T61204
217	1,3-Di- <i>p</i> -tolyl-5-phenyl-1,3,5-diazaphosphorinane		72897-07-5	917990
239	P(<i>n</i> Oct) ₃		4731-53-7	718165
251	P(Allyl) ₃		16523-89-0	336939

Portal ID	Ligand	Structure	CAS Number	Product Number
280	tBuMePhos		255837-19-5	695211
327	Cy-BippyPhos		1021176-69-1	738611
329	CM-Phos		1067883-58-2	752231
338	PAd ₂ (2-piperidyl-Ph)		1237588-13-4	759198
340	AdBippypHos		1239478-87-5	740845
351	4-(Diethylphosphino)-N,N-dimethylaniline		17005-57-1	747270
401	Exo-Phenyl Kwon [2.2.1] Bicyclic Phosphine		1621906-60-2	798371
449	P(NEt ₂) ₃		2283-11-6	253189
458	PPh ₂ (1-Isochinolin-2-Nap)		149245-03-4	779911
487	Bis[4-(3,3,4,4,5,5,5-heptafluoro-2,2-bis(trifluoromethyl) pentyl)phenyl] phenylphosphine		322647-83-6	50476
640	PNEt ₂ -Benzodioxaphosphepine		82372-35-8	393835
644	POPh_5,5-dimethyldioxaphosphinane		3057-08-7	916234
648	P(OtBu) ₂ N(iPr) ₂		137348-86-8	419362
650	P(Obn) ₂ NEt ₂		67746-43-4	362883

Reference

1. Zhao, S.; Gensch, T.; Murray, B.; Niemeyer, Z. L.; Sigman, M. S.; Biscoe, M. R. "Enantiodivergent Pd-catalyzed C–C bond formation enabled through ligand parameterization" *Science*, **2018**, 362, 670

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