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Bimetallic Cu/Pd Catalysts with Bridging Aminopyrimidinyl Phosphines for Decarboxylative Cross-Coupling Reactions at Moderate Temperature

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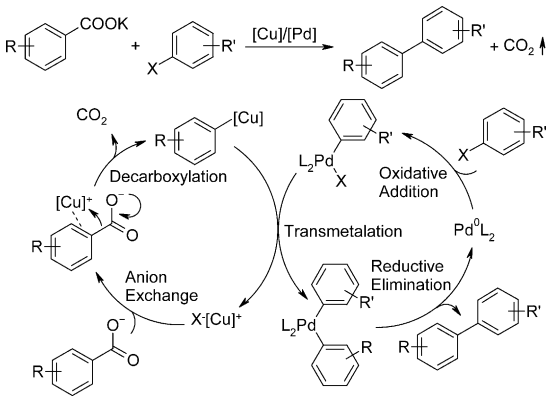
A bimetallic catalyst system is presented that enables the decarboxylative cross-coupling of triflates with carboxylate salts at only 100 °C, which is 70 °C lower than with previous Cu/Pd-based systems. The new protocol allows the coupling of a broad range of aryl triflates with various substituted 2-nitrobenzoates in good to excellent yields. The key feature of the catalyst system is a bidentate P,N-ligand designed to bridge the Pd and Cu centres and thereby facilitating the rate-determining transmetalation step. Mass spectrometry (ESI-MS) studies support the ability of the aminopyrimidinyl phosphine to simultaneously coordinate copper and palladium.

Introduction

In the last decades, decarboxylative cross-coupling reactions have been established as a powerful methodology for the regioselective formation of C–C and C–heteroatom bonds.[1] The advantage of this reaction type is that it draws on stable and readily available carboxylic acids as the coupling partners. Decarboxylative Heck-type reactions,[2] allylations,[3] redox-neutral cross-couplings,[4] oxidative couplings,[5] homo-couplings,[6] C–H arylations,[7] as well as Chan–Evans–Lam-type reactions[8] have recently been disclosed.

Our key contribution to this rapidly expanding field was the development of redox-neutral decarboxylative cross-coupling reactions mediated by Cu/Pd bimetallic catalyst systems.[4a] Within the coordination sphere of a Cu-based decarboxylation catalyst, the carbon nucleophile is generated by extrusion of CO_2 from the carboxylate and is then transferred to the Pd centre, where coupling with the carbon electrophile takes place (Scheme 1). Bimetallic Cu/Pd systems proved to have a particularly broad substrate scope and high functional-group tolerance for both coupling partners.[9] However, their practical applicability is still limited by the relatively high reaction temperatures, which usually exceed 150 °C.



Scheme 1. Mechanism of decarboxylative cross-coupling reactions.

Over the last years, some progress has been achieved in lowering the reaction temperature of decarboxylative cross-coupling reactions. Cahiez et al. reported that with tetramethylethylenediamine (TMEDA) as the copper ligand and *N*,*N*′-dimethylpropyleneurea (DMPU) as the reaction solvent, pre-formed caesium 2-nitrobenzoates can be coupled with aryl bromides at 120–140 °C.[10] Similarly activated aromatic carboxylates were coupled with alkenyl bromides and chlorides at 130 °C.[11] At the same temperature, particularly reactive polyfluoroben-

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zoates can be decarboxylatively coupled with monometallic copper or palladium catalysts.[12]

DFT calculations have guided the discovery of a silver-based catalyst system that promotes the protodecarboxylation of *ortho*-substituted benzoates at only 120 °C.[13] Consequently, Ag/Pd catalyst systems allow decarboxylative cross-coupling of these carboxylates with aryl triflates at 130 °C.[14]

Up to that point, the decarboxylation had been considered to be the sole rate-determining step; therefore, all efforts were directed at optimising the decarboxylation catalyst. Recent, extensive DFT calculations of Cu/Pd-catalysed decarboxylative cross-coupling reactions revealed, however, that the transmetalation step may also become rate-determining.[15] The electronic activation energy of the transmetalation step is much lower than that of the decarboxylation step, but the free-energy loss during the Cu/Pd adduct formation preceding the actual aryl-group transfer is so high that the transmetalation step becomes strongly endergonic. For certain *ortho*-substituted substrates, the transmetalation will be rate-determining.

This leads to a paradigm shift in the development of decarboxylative coupling catalysts. Now, the most promising approach to lower the reaction temperature of decarboxylative couplings consists of facilitating Pd/Cu adduct formation by employing bidentate ligands designed to bridge the two metals and bring them into close spatial proximity.

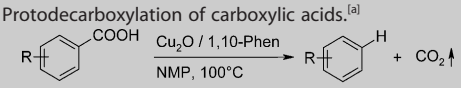
Results and Discussion

To probe the effect of bridging ligands on the transmetalation step, a test reaction needed to be identified in which this step alone was rate-determining.

Thus, a series of protodecarboxylation experiments were performed aimed at identifying substrates that decarboxylate so easily at 100 °C that the decarboxylation step will not be rate-determining in a decarboxylative coupling. Various benzoic acids **1** were heated to 100 °C in the presence of a catalyst system consisting of 5 mol% Cu_2O and 10 mol% 1,10-phenanthroline (1,10-Phen) (Table 1). As expected, most carboxylic acids tested were inert at such low temperatures with this standard decarboxylation catalyst (entries 2–7). However, 2-nitrobenzoic acid (**1a**) and 2,6-difluorobenzoic acid (**1e**) decarboxylated smoothly to give the corresponding arenes (entries 10, 11) and even for the heterocyclic carboxylic acid **1f** reasonable protodecarboxylation could be achieved.

The decarboxylative coupling of potassium 2-nitrobenzoate (**3a**) with 4-chlorophenyl triflate (**4a**) was investigated next (Table 2). Triflates had previously been shown to give the best performance in coupling reactions at moderate temperatures.[14] However, the state-of-the-art catalyst system (2 mol% PdI_2, 6 mol% P(*p*-Tol_3), 5 mol% Cu_2O, 10 mol% 1,10-Phen), which gave high yields of the desired 4-chloro-2′-nitrobiphenyl product (**5aa**) at 170 °C,[9c] was almost ineffective at 100 °C (Table 2, entries 1, 2). Variation of the phosphine ligand confirmed P(*p*-Tol_3) to be the optimal monodentate ligand. Even with high-performance ligands, such as John-Phos and X-Phos, no conversion was obtained.

Table 1. Protodecarboxylation of carboxylic acids.[a]

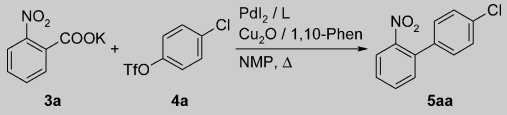


1 2

Entry	Carboxylic acid	R	*t* [h]	Product	Yield [%]
1	**1a**	2-NO_2	6	**2a**	64
2	**1a′**	4-NO_2	6	**2a**	0
3	**1b**	2-F	6	**2b**	3
4	**1b′**	4-F	6	**2b**	0
5	**1c**	2-OMe	6	**2c**	0
6	**1c′**	4-OMe	6	**2c**	0
7	**1d**	2,6-OMe	6	**2d**	0
8	**1e**	2,6-F	6	**2e**	57
9[b]	**1f**	–	6	**2f**	7
10	**1a**	2-NO_2	24	**2a**	99
11	**1e**	2,6-F	24	**2e**	96
12[b]	**1f**	–	24	**2f**	24

[a] Reaction conditions: 0.5 mmol carboxylic acid, 5 mol% Cu_2O, 10 mol% 1,10-Phen, 2 mL NMP, 100 °C. GC yields with *n*-tetradecane as internal standard. 1,10-Phen = 1,10-phenanthroline; NMP = *N*-methyl-2-pyrrolidone. [b] **1f** = 3-Chloro-benzo[b]thiophene-2-carboxylic acid, **2f** = benzo[b]thiophene.

Table 2. Decarboxylative cross-coupling with monodentate and P,N-ligands.[a]



3a 4a 5aa

Entry	L	*T* [°C]	Yield [%]
1	P(*p*-Tol_3)	170	84 (91)[b,9c]
2	P(*p*-Tol_3)	100	9[c]
3	John-Phos	100	0[c]
4	X-Phos	100	0[c]
5	**L1**	100	50
6	**L2**	100	37
7	**L3**	100	48
8	**L4**	100	49
9	**L5**	100	45
10	**L6**	100	29
11	**L7**	100	28
12	**L8**	100	65
13	**L9**	100	60

[a] Reaction conditions: 0.3 mmol scale, **3a**/**4a** = 1.5:1, 2 mol% PdI_2, 6 mol% L, 5 mol% Cu_2O, 10 mol% 1,10-Phen, 2 mL NMP, 100 °C, 24 h. GC yields with *n*-tetradecane as internal standard. [b] 1 mmol scale, **3a**/**4a** = 1:2, 5 mol% Cu_2O, 10 mol% 1,10-Phen, 2 mol% PdI_2, 6 mol% P(*p*-Tol_3), 4 mL NMP, 170 °C, 1 h. GC yield with *n*-tetradecane as internal standard, isolated yield in parentheses. [c] 0.5 mmol scale, **3a**/**4a** = 1:2.

Next, it was investigated whether ligands able to bring copper and palladium into close spatial proximity, and thereby facilitate the transmetalation, would be superior to the above monodentate ligands. An overview of the ligands investigated in this context is provided in Figure 1. The modular synthesis of pyrimidine-based bidentate ligands **L1**–**L9** allows the simple and broad variation of their molecular structures. In preceding investigations, ligands carrying a pyrimidin-4-yl unit have proved to have pronounced effects on the catalytic activity de-

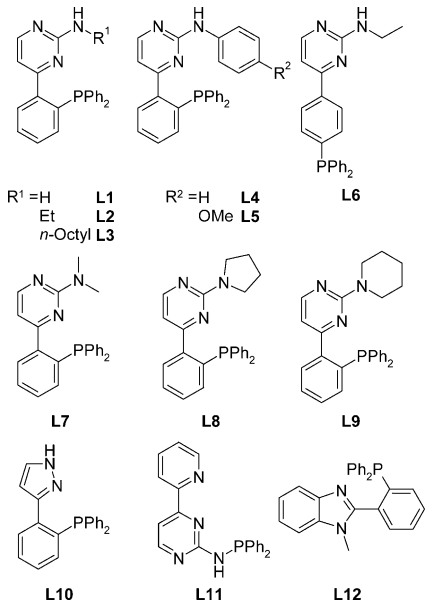
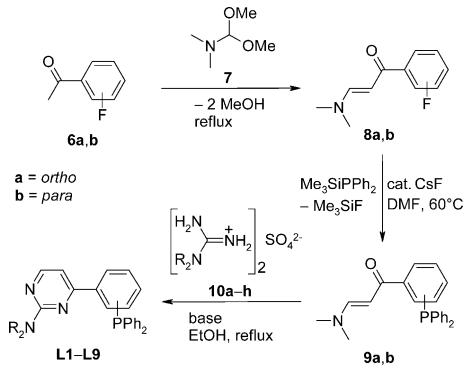


Figure 1. P,N-Ligands for the decarboxylative cross-coupling reaction.

pending on the nature of the amino group in the 2-position. This may be attributed to a C–H activation process in the 5-position of the pyrimidine ring, leading to ligands with a carbanionic nature.[16]

The ligands were prepared starting from the fluoride-functionalised acetophenones **6a**,**b**, which underwent condensation with *N*,*N*-dimethylformamide dimethyl acetal **7** to yield the corresponding aminopropenones **8a**,**b**.[17] These aminopropenones were then converted to the phosphine-functionalised aminopropenones **9a**,**b** in high yields by a fluoride-catalysed P–C coupling reaction.[18] Further condensation of **9a**,**b** with the guanidinium salts **10a**–**h** in ethanol under basic conditions led to ligands **L1**–**L9** in good to excellent yields (Scheme 2). Cyclisation of **9a** with hydrazine provides the pyrazole-functionalised ligand **L10**.[19]

Ligand **L11** was synthesised from 2-(2-aminopyrimidin-4-yl)-pyridine by reaction with Ph_2PCl in the presence of a base.[20] The benzimidazolyl phosphine ligand **L12** was synthesised through a sequence of cyclisation, alkylation and phosphonation reactions starting from 2-bromobenzoic acid and 1,2-phenylenediamine.[9f] The P,N-ligands were evaluated in the test reaction between potassium 2-nitrobenzoate (**3a**) and 4-chlorophenyl triflate (**4a**) at 100 °C. Most of the aminopyrimidinyl phosphines **L1**–**L9** showed higher catalytic activity than the optimal monodentate ligand P(*p*-Tol)$_3$ (Table 2), whereas ligands with a different backbone (**L10**–**L12**) were ineffective.[15] Among the aminopyrimidinyl phosphines tested, **L1**, which bears a primary amino group, was more active than ligands substituted with secondary amino groups (**L2**–**L6**). Among the latter, electron-rich residues on the secondary amino nitrogen (**L2**, **L3**, **L5**) were beneficial. Ligand **L6**, in which the PPh_2 group is *para* to the pyrimidinyl ring, is less effective than the corresponding *ortho*-substituted derivative **L2**. Tertiary amino groups with acyclic amino groups (**L7**) led to moderate yields, but ligands with cyclic amine substituents (**L8** and **L9**), particularly **L8**, featuring a pyrrolidine group, showed the highest catalytic activity overall.

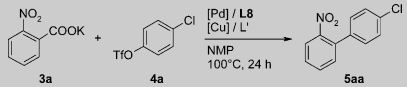


Scheme 2. Synthesis of the aminopyrimidinyl phosphine ligands.

The reaction conditions were systematically optimised with the most effective bridging ligand **L8** (Table 3). Slightly increasing the amount of palladium from 2 to 3 mol% led to a decisive increase in the yields (entry 1). Among the palladium sources tested, $Pd(acac)_2$ (acac = acetylacetonate) was the most effective, resulting in an 88% yield of the desired product (entries 2–7). Further experiments showed that although Cu_2O is the most effective copper pre-catalyst, several other copper salts may also be used (entries 8–10).

1,10-Phenanthroline has the optimal properties as a copper-stabilising ligand. The use of phenanthrolines substituted with either electron-donating or -withdrawing substituents reduced the yields (entries 11, 12). In the absence of a stabilising ligand,

Table 3. Optimisation of decarboxylative cross-coupling at moderate temperatures.[a]



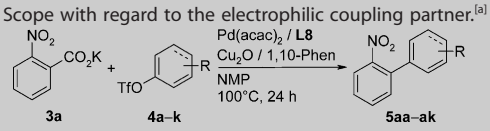
Entry	[Pd]	[Cu]	L′	Yield [%]
1	PdI_2	Cu_2O	1,10-Phen	84
2	$Pd(acac)_2$	Cu_2O	1,10-Phen	88
3	$Pd(F_6\text{-acac})_2$	Cu_2O	1,10-Phen	70
4	$PdBr_2$	Cu_2O	1,10-Phen	72
5	$Pd(OAc)_2$	Cu_2O	1,10-Phen	80
6	$[AllylPdCl]_2$	Cu_2O	1,10-Phen	77
7[c]	[Pd(**L8**)(vs)]	Cu_2O	1,10-Phen	73
8	$Pd(acac)_2$	CuBr[b]	1,10-Phen	80
9	$Pd(acac)_2$	CuCl[b]	1,10-Phen	82
10	$Pd(acac)_2$	$[Cu(MeCN)_4]BF_4$[b]	1,10-Phen	74
11	$Pd(acac)_2$	Cu_2O	NO_2-Phen	9
12	$Pd(acac)_2$	Cu_2O	Me_4-Phen	66
13	$Pd(acac)_2$	Cu_2O	–	16
14	$Pd(acac)_2$	–	–	0
15	–	Cu_2O	1,10-Phen	0
16[d]	$Pd(acac)_2$	Cu_2O	1,10-Phen	23

[a] Reaction conditions: 0.3 mmol scale, **3a**/**4a** = 1.5:1, 3 mol% [Pd], 6 mol% **L8**, 5 mol% [Cu], 10 mol% L′, 2 mL NMP, 100 °C, 24 h. GC yields with *n*-tetradecane as internal standard. NO_2-Phen = 5-nitro-1,10-phenanthroline; Me_4-Phen = 3,4,7,8-tetramethyl-1,10-phenanthroline. [b] 10 mol% [Cu]. [c] No additional amount of **L8** was added. vs = 1,3-divinyl-1,1,3,3-tetramethyldisiloxane. [d] 90 °C.

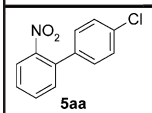
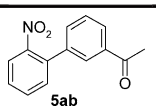
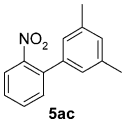
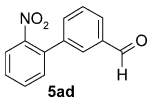
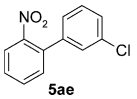
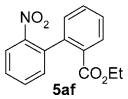
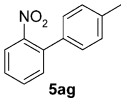
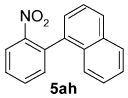
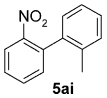
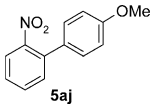
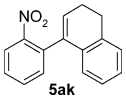
the transformation still led to 16% yield (entry 13). Further control experiments confirmed that the decarboxylative coupling requires both copper and palladium to proceed (entries 14, 15). Furthermore, the catalyst is still active even at 90 °C (entry 16). A solvent screening revealed that *N*-methyl-2-pyrrolidone (NMP) is the best solvent for the reaction. Mixtures of NMP with other polar solvents such as dimethylformamide (DMF), dimethyl sulfoxide (DMSO) or 2-methoxyethyl ether (diglyme) or in quinoline resulted in lower yields. Mesitylene was ineffective, probably because of the poor solubility of the benzoate in this non-polar solvent (see the Supporting Information).

Having found an effective reaction protocol, the scope of the reaction with regard to the electrophilic coupling partner was investigated. As can be seen from the examples in Table 4,

Table 4. Scope with regard to the electrophilic coupling partner.[a]



3a 4a–k 5aa–ak

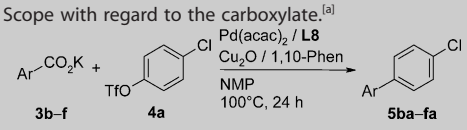
Product	Yield [%]	Product	Yield [%]
 5aa	80 14[b] 34[b,c]	 5ab	66
 5ac	58 90[c]	 5ad	66
 5ae	54[c]	 5af	68[c]
 5ag	92[c]	 5ah	75[c]
 5ai	70[c]	 5aj	80[c]
 5ak	81[c]		

[a] Reaction conditions: 0.75 mmol **3a**, 0.50 mmol **4**, 3 mol% $Pd(acac)_2$, 6 mol% **L8**, 5 mol% Cu_2O, 10 mol% 1,10-Phen, 4 mL NMP, 100 °C, 24 h. Isolated yields from two identical runs. [b] 1-bromo-4-chlorobenzene was used as electrophile, GC yield with *n*-tetradecane as internal standard. [c] 120 °C.

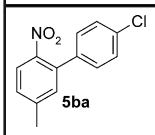
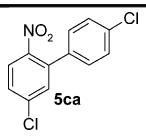
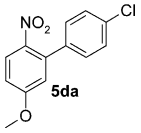
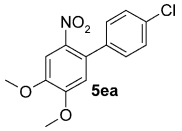
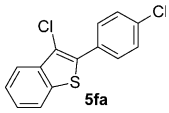
various aryl triflates **4** with alkyl, halide, acyl or keto substituents were coupled in reasonable yields with potassium 2-nitrobenzoate (**3a**). After increasing the reaction temperature to 120 °C, less reactive substrates bearing, for example, ester or ether groups were converted in high yields; the same transformations at 100 °C did not proceed well. Beside aromatic triflates, vinyl triflate **4k** was also smoothly converted into the corresponding product **5ak** at 120 °C. Moreover, 1-bromo-4-chlorobenzene was converted into the corresponding biaryl **5aa**, albeit in low yield.

The scope of the reaction with regard to the carboxylate coupling partner was investigated by using 4-chlorophenyl triflate (**4a**) as the electrophile. As illustrated in Table 5, various

Table 5. Scope with regard to the carboxylate.[a]



3b–f 4a 5ba–fa

Product	Yield [%]	Product	Yield [%]
 5ba	73	 5ca	59
 5da	70	 5ea	75
 5fa	31[b]		

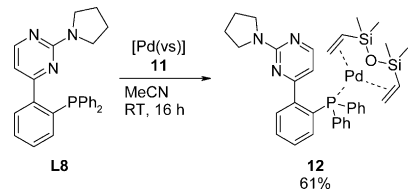
[a] Reaction conditions: 0.75 mmol **3**, 0.50 mmol **4a**, 3 mol% $Pd(acac)_2$, 6 mol% **L8**, 5 mol% Cu_2O, 10 mol% 1,10-Phen, 4 mL NMP, 100 °C, 24 h. Isolated yields from two identical runs. [b] 120 °C.

substituted 2-nitrobenzoates **3** were successfully converted into the corresponding biaryls in high yields at 100 °C. The coupling of the heterocyclic carboxylate **3f** took place only when the temperature was increased to 120 °C. Potassium 2,6-difluorobenzoate gave only small amounts of the desired biaryl, presumably as a result of the low solubility of this substrate in NMP at 100 °C.

As expected, only activated benzoates were successfully converted because these are the only substrates to decarboxylate sufficiently at the given temperature to make the transmetalation step rate-determining. In contrast, no conversion was observed in the coupling of 2-fluoro-, penta-fluoro-, 2-trifluoromethyl-, 2-methoxy-, 2-cyano- and 2,6-dimethoxy-substituted benzoates with 4-chlorophenyl triflate (**4a**).

Mechanistic studies were performed to elucidate the nature of the catalytic species and to investigate whether the ligand is indeed able to coordinate to both Pd and Cu. Based on previous mechanistic studies, it can be assumed that Pd enters the catalytic cycle as a Pd^0–phosphine complex. To obtain structural information on this species, we added the olefin-stabilised Pd^0 complex 1,3-divinyl-1,1,3,3-tetramethyldisiloxane palladium(0) ([Pd(vs)]) (**11**) in 2,4,6,8-tetramethyl-cyclotetrasiloxane (TMCTS) to ligand **L8** in acetonitrile and crystallised the resulting complex, which proved to be active in the decarboxylative cross-coupling reaction (Table 3, entry 7), from diethyl ether/acetonitrile at −20 °C (Scheme 3).

Single crystals suitable for X-ray structural analysis were obtained. The palladium atom is coordinated by the phosphorous



Scheme 3. Synthesis of palladium complex **12**.

atom and the two C=C bonds of the vs ligand in a trigonal-planar coordination mode. The Pd–P bond length (2.320 Å) and the Pd–D bond lengths (D = mid points of the C=C bonds; 2.062 and 2.065 Å) are in the typical range for other reported structures.[21] The C=C bonds lie exactly in the coordination plane. The bond lengths are slightly lengthened (1.394 and 1.397 Å) compared with an uncoordinated C=C bond length (1.34 Å), indicating a weak back-bonding for the Pd atom. The three bond angles D1-Pd-D2: 132.53°, D1-Pd-P: 114.00° and D2-Pd-P: 113.42° show that the trigonal-planar geometry is highly distorted. The five-membered ring in the backbone of **L8** adapts two slightly different conformations with the same probability as depicted in Figure 2.

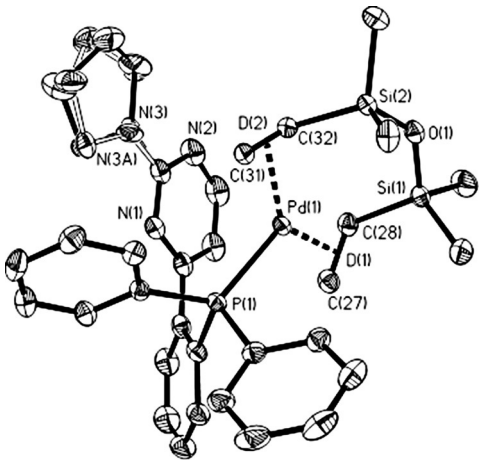


Figure 2. Perspective view of complex **12** showing 50% thermal ellipsoids. Hydrogen atoms are omitted for the purpose of clarity. Relevant distances [Å] and angles [°]: Pd(1)–P(1) 2.3203(4), Pd(1)–D1 2.062(6), Pd(1)–D2 2.065(6), C(27)–C(28) 1.394(2), C(31)–C(32) 1.397(2), P(1)-Pd(1)-D1 113.42 (0.20), P(1)-Pd(1)-D2 114.00(0.20), D1-Pd1-D2 132.53(0.29).

Upon addition of $[Cu(MeCN)_4]BF_4$ **13** to an acetonitrile solution of complex **12**, a yellowish solution formed. However, all attempts to crystallise a bimetallic complex from this solution failed. The non-polar palladium complex **12** crystallised from polar solvents, whereas the polar copper complex **13** precipitated from non-polar solvents, both crystallisation processes shifting the equilibrium to monometallic species. We thus investigated an equimolar mixture of ligand **L8**, [Pd(vs)] (**11**), and $[Cu(MeCN)_4]BF_4$ (**13**) in acetonitrile by ESI-MS.

The resulting mass spectra exhibit an intense peak at approximately 472 *m/z* (most abundant mass), which was assigned to a $[Cu^I(\mathbf{L8})]^+$ complex (Figure 3 and Figure S1 a). The high abundance of this complex provides evidence for the

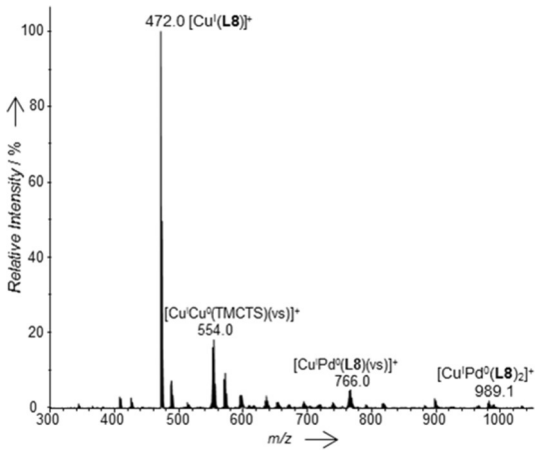


Figure 3. Mass spectrum of a solution of ligand **L8**, [Pd(vs)] (**11**) and $[Cu(MeCN)_4]BF_4$ (**13**) in acetonitrile (see Figure S1 for details and simulations of isotopic distributions).

ability of the ligand to bind copper ions in solution. Several smaller signals could also be assigned to bimetallic species by comparing their mass and isotopic distribution with simulated patterns. Most interesting are the signals at approximately 766 and 989 *m/z*, which correspond to the heterobimetallic Cu/Pd species $[Cu^IPd^0(\mathbf{L8})(vs)]^+$ and $[Cu^IPd^0(\mathbf{L8})_2]^+$ (Figure S1 c, d). The isotope signals corresponding to the latter complex are partially overlaid by a second mass signal at approximately 981 *m/z* with an unknown composition. The peak at approximately 554 *m/z* was assigned to the bimetallic copper complex $[Cu^ICu^0(TMCTS)(vs)]^+$ (Figure S1 b).

Equimolar amounts of nitrogen donor ligands were then added to a mixture of ligand **L8**, [Pd(vs)] (**11**) and $[Cu(MeCN)_4]BF_4$ (**13**) in acetonitrile to investigate their influence on the abundance of heterobimetallic complexes. We had expected to see bimetallic complexes with additionally coordinated nitrogen ligands. However, no such species were detected when adding either pyridine or triethylamine. Instead, the mass spectral intensity of the peaks at approximately *m/z* = 766 for $[Cu^IPd^0(\mathbf{L8})(vs)]^+$, and 989 for $[Cu^IPd^0(\mathbf{L8})_2]^+$ strongly increased. The latter was no longer overlaid by the unassigned signal at approximately 981 *m/z*. Additional peaks detected at approximately 881 and 580 *m/z* are likely to represent $[Cu^I(\mathbf{L8})_2]^+$ and the bimetallic complex $[Cu^IPd^0(\mathbf{L8})]^+$, respectively (Figure 4 and Figure S2 b, d). Thus, the presence of nitrogen donor ligands has a critical effect on the composition of the species detected in the mass spectrum.

We assume that the influence of these additives results from the basicity of the molecules. The fact that the composition of the solution has such a strong influence on the detected signals suggests that bimetallic adducts are already present in solution, rather than that their detection is a consequence of the spray process. However, a detailed understanding on the observed effect remains to be achieved.

Added 1,10-phenanthroline, the optimal ligand for decarboxylative couplings, also affects the composition of the solution of **L8**, [Pd(vs)] (**11**) and $[Cu(MeCN)_4]BF_4$ (**13**) in acetonitrile, but in a different way (Figure 5).

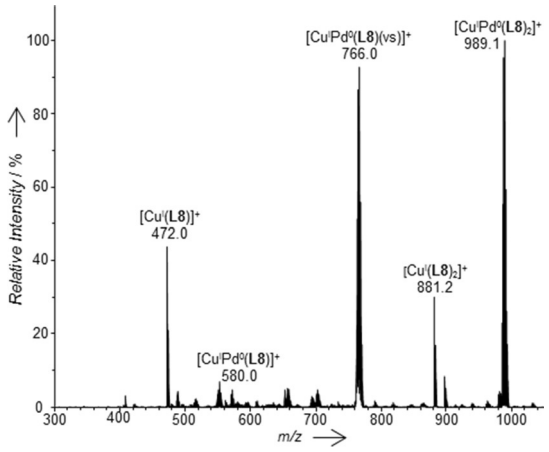


Figure 4. Mass spectrum of a solution of ligand **L8**, [Pd(vs)] (**11**), $[Cu(MeCN)_4]BF_4$ (**13**) and pyridine in acetonitrile (see Figure S2 for details and simulations of isotopic distributions).

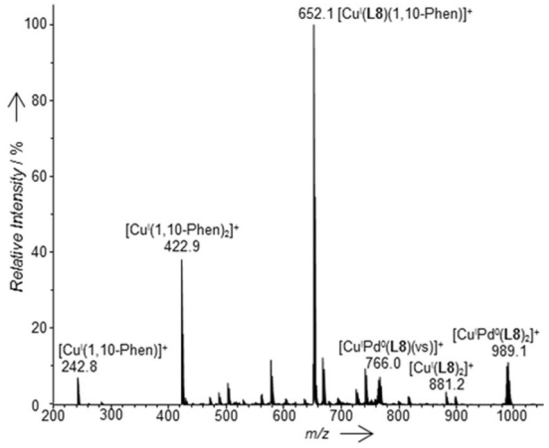


Figure 5. Mass spectrum of a solution of ligand **L8**, [Pd(vs)] (**11**), $[Cu(MeCN)_4]BF_4$ (**13**) and 1,10-phenanthroline in acetonitrile (see Figure S3 for details and simulations of isotopic distributions).

The intensities of the signals at approximately 989, 881 and 766 *m/z* are low, and the signal at 472 *m/z* corresponding to $[Cu^{I}(\mathbf{L8})]^{+}$ is missing altogether. Instead, a strong signal at 652 *m/z* was recorded that can be assigned to a $[Cu^{I}(\mathbf{L8})(1,10\text{-Phen})]^{+}$ complex (Figure S3 c). Two additional signals were detected at 243 and 423 *m/z*, and assigned to the monometallic 1,10-phenanthroline copper species $[Cu^{I}(1,10\text{-Phen})]^{+}$ and $[Cu^{I}(1,10\text{-Phen})_2]^{+}$ (Figure S3 a,b). The large abundance of these three Cu/phenanthroline-containing complexes shows that phenanthroline coordinates more strongly to Cu than ligand **L8**. Unfortunately, no signals were detected resulting from a bimetallic Cu/Pd species bearing both ligands (Figure 2, and Figure 3). It is unclear whether such complexes are not present in solution, or whether they decompose during the spray process.

On the basis of these ESI-MS experiments, it appears likely that bimetallic Pd^0/Cu^I complexes with ligand **L8** are present in solution, but especially in the presence of phenanthroline, they are unlikely to form exclusively. Instead, they appear to be present in low quantities, along with monometallic Pd/phosphine and Cu/phenanthroline complexes. This would be in agreement with the proposed mechanism in which the temporary formation of Pd/Cu adducts is facilitated, but the two metals do not stay together throughout the catalytic cycle.

It would certainly be possible to design P,N-ligands with a nitrogen subunit that coordinates so strongly to copper that Cu/Pd complexes would prevail in solution. However, we expect that such rigid coordination of both metals would hamper the individual catalytic cycles of each metal owing to steric crowding. Therefore, a P,N-ligand that coordinates to Pd throughout, and is able to facilitate temporary Pd/Cu adduct formation by reversibly coordinating to the copper centre with its nitrogen binding site, might be the optimal design for efficient catalytic turnover. Further experimental studies with a broader range of P,N-ligands are clearly needed to elucidate this aspect.

Conclusions

The use of a potentially bridging aminopyrimidinyl phosphine ligand with a bimetallic Cu/Pd-based catalyst system allows decarboxylative cross-coupling of aryl triflates with aromatic carboxylate salts to be performed at only 100 °C.

The P,N-ligand, which is able to simultaneously coordinate Cu and Pd, lowers the reaction temperature by more than 50 °C in comparison with monodentate phosphine ligands. This is an important milestone in the evolution of decarboxylative cross-coupling reactions as a synthetic alternative to traditional coupling reactions.

DFT studies have previously revealed that for activated carboxylic acids, the transmetalation rather than the decarboxylation step should be rate-determining. The potential bridging ligand should facilitate the formation of adducts between the two metals and, thus, facilitate the transmetalation step. However, it is unlikely to strongly affect other reaction steps. The decisive effect of the rationally designed P,N-ligand on the reaction temperatures, thus, confirms the predictions by the DFT calculations.

In combination with high-performance decarboxylation catalysts, the use of such bridging P,N-ligands could soon allow inexpensive decarboxylative couplings to be performed at the low temperature of traditional couplings of preformed organometallic reagents.

Experimental Section

General methods

Chemicals and solvents were either purchased (puriss p.a.) from commercial suppliers or purified by standard procedures prior to use.[22] Reactions were performed in oven-dried glassware, under a nitrogen atmosphere, containing a Teflon-coated stirrer bar and dry septum. Triflates were saturated with argon to exclude atmospheric oxygen and solvents were degassed by three freeze-pump-thaw cycles. All reactions were monitored by GC using *n*-tetradecane as an internal standard. Response factors of the products with regard to *n*-tetradecane were obtained experimentally by analysing known quantities of the substances. GC analyses were per-

formed by using an HP-5 capillary column (phenyl methyl siloxane, 30 m×320×0.25, 100/2.3–30–300/3, 2 min at 60 °C, heating rate 30 °C min^{-1}, 3 min at 300 °C). Column chromatography was performed by using a Combi Flash Companion Chromatography System and Reveleris packed columns (12 g). NMR spectra were recorded on Bruker Avance 600, Avance 400 or Avance 200 at ambient temperature using $CDCl_3$, CD_3OD, [D_6]DMSO or D_2O as solvent, with proton, carbon, and phosphorus resonances at 600/400/200, 151/101/50, and 243/162 MHz respectively. Mass spectral data were acquired on a Varian GC-MS Saturn 2100 T. ESI-MS data were acquired on a Bruker Esquire 6000. Sample solutions at concentrations of approximately 1×10^{-4} M were continuously infused into the ESI chamber at a flow rate of 2 μL min^{-1} by using a syringe pump. Nitrogen was used as the drying gas at a flow rate of 3.0 to 4.0 L min^{-1} at 300 °C and the solutions were sprayed at a nebuliser pressure of 4 psi with the electrospray needle held at 4.5 kV. CHN elemental analysis was performed with a Hanau Elemental Analyzer vario Micro cube. Melting points were measured on a Mettler FP 61 and infrared spectra on a PerkinElmer Spectrum 100 ATR-FTIR. The X-ray crystallographic data was collected on a Gemini S Ultra single crystal CCD diffractometer from Agilent equipped with a CryojetHT-temperature system.

General procedure for the protodecarboxylation experiments

An oven-dried vessel was charged with the carboxylic acid **1a–f** (0.50 mmol), copper(I) oxide (3.61 mg, 25.0 μmol) and 1,10-phenanthroline (9.10 mg, 50.0 μmol). The vessel was flushed with three alternating vacuum and nitrogen purge cycles and degassed NMP (2 mL) was added through a syringe. The resulting mixture was stirred at 100 °C for the given time. The reaction mixture was then allowed to cool to RT, *n*-tetradecane (50 μL) was added through a syringe and the mixture was diluted with ethyl acetate (4 mL). A sample of the reaction mixture (0.25 mL) was dissolved in ethyl acetate (2 mL), washed with a saturated solution of bicarbonate (2 mL), dried over $MgSO_4$ and analysed by GC.

Published synthesis of precursors and ligands

The precursors **9a**,**b**[18] and the ligands **L1**, **L2**, **L7**, **L8** and **L9**[16a] as well as **L10**,[19] **L11**[20] and **L12**[9f] were synthesised according to procedures published in the literature. The analytical data matched those reported in the literature.

Ligand synthesis

4-(1-Diphenylphosphinophenyl)-2-octylaminopyrimidine (L3): Aminopropenone **9a** (2.35 g, 6.50 mmol) and *N*-octylguanidinium sulfate **10c** (2.73 g, 13.00 mmol) were suspended in dry EtOH (80 mL). After addition of KOH (0.67 g, 13.0 mmol), the mixture was heated at reflux for 48 h. After removal of the solvent under reduced pressure, the residue was dissolved in a mixture of water and CH_2Cl_2. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. Recrystallisation of the crude material from ethanol afforded **L3** (2.37 g, 5.07 mmol, 78%). M.p. 78–79 °C; ^{1}H NMR ([D_6]DMSO, 400 MHz): δ = 0.82 (brs, 3H), 1.00–1.50 (brs, 14H), 2.61–3.00 (brs, 2H), signal not observed: NH, 6.66 (d, $^3J_{HH}$ = 4.9 Hz, 1H), 6.98 (dd, $^3J_{HH}$ = 7.0, 3.9 Hz, 1H), 7.12–7.23 (m, 4H), 7.30–7.35 (m, 6H), 7.37 (t, $^3J_{HH}$ = 7.6 Hz, 1H), 7.48 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.60 (m, 1H), 8.20 ppm (d, $^3J_{HH}$ = 5.0 Hz, 1H); ^{13}C NMR ([D_6]DMSO, 101 MHz): δ = 13.9, 22.0, 26.3, 28.7, 28.8, 28.9, 31.2, 40.2, 108.9, 128.35, 128.41, 129.0 (d, $^3J_{CP}$ = 16.8 Hz, 129.09, 129.13, 133.2 (d, $^2J_{CP}$ = 19.9 Hz), 134.5, 135.5 (d, $^1J_{CP}$ = 20.3 Hz), 138.2 (d, $^1J_{CP}$ = 12.3 Hz), 144.5, 157.9, 161.5, 166.1 ppm; ^{31}P NMR ([D_6]DMSO, 162 MHz): δ = −12.0 ppm; elemental analysis: calcd (%) for $C_{30}H_{34}N_3P$ (467.59): C 77.06, H 7.33, N 8.99; found C 77.08, H 7.71, N 8.74.

4-(1-Diphenylphosphinophenyl)-2-phenylaminopyrimidine (L4): Sodium ethoxide (0.98 g, 14.4 mmol), *N*-phenylguanidinium sulfate **10d** (2.65 g, 7.19 mmol) and aminopropenone **9a** (2.35 g, 6.54 mmol) were dissolved in dry EtOH (32 mL). The mixture was heated at reflux for 48 h. After removal of the solvent under reduced pressure the residue was dissolved in a mixture of water and dichloromethane. The layers were separated and the aqueous layer was extracted three times with dichloromethane (20 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was recrystallized from ethanol and then purified by column chromatography (dichloromethane/methanol gradient) to remove some of phosphine oxide, leading to a relatively high loss of yield. A second recrystallization from ethanol afforded **L4** (50.0 mg, 0.12 mmol, 2%). M.p. 149–150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 6.62 (s, 1H), 6.83–6.95 (m, 2H), 6.97–7.06 (m, 1H), 7.11–7.32 (m, 10H), 7.32–7.46 (m, 4H), 7.56–7.65 (m, 1H), 8.30 ppm (d, $^3J_{HH}$ = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 111.3, 119.1, 122.5, 128.6, 128.6, 128.7, 128.9, 129.1, 129.8, 133.9 (d, $^2J_{CP}$ = 20.0 Hz), 135.5, 136.9 (d, $^2J_{CP}$ = 20.0 Hz), 139.0 (d, $^1J_{CP}$ = 9.8 Hz), 143.0 ($^2J_{CP}$ = 22.1 Hz), 157.4, 158.6, 166.5 ppm, ^{31}P NMR ($CDCl_3$, 162 MHz): δ = −9.42 ppm; elemental analysis: calcd (%) for $C_{28}H_{22}N_3P$ (431.47): C 77.94, H 5.14, N 9.74; found: C 77.77, H 5.02, N 9.70.

4-(1-Diphenylphosphinophenyl)-2-(4-methoxyphenyl)aminopyrimidine (L5): Ligand **L5** was synthesised according to the procedure described for **L4** from *N*-(4-methoxyphenyl)guanidinium sulfate **10e**. Yield: 1.05 g, 2.27 mmol, 82 %. M.p. 122–123 °C; ^{1}H NMR ([D_6]DMSO, 400 MHz): δ = 3.69 (s, 3H), 6.71–6.79 (m, 3H), 7.04 (dd, $^3J_{HH}$ = 7.3, 3.9 Hz, 1H), 7.16–7.23 (m, 4H), 7.33–7.39 (m, 6H), 7.43 (t, $^3J_{HH}$ = 7.5 Hz, 1H), 7.51 (t, $^3J_{HH}$ = 7.4 Hz, 1H), 7.55–7.61 (m, 3H), 8.33 (d, $^3J_{HH}$ = 4.9 Hz, 1H), 9.13–9.26 ppm (brs, NH); ^{13}C NMR ([D_6]DMSO, 101 MHz): δ = 55.12, 111.9 (d, $^4J_{CP}$ = 5.1 Hz), 113.6, 120.5, 120.6, 128.7, 128.7, 128.8, 129.2 (d, $^3J_{CP}$ = 8.0 Hz), 129.4, 129.4, 133.3 (d, $^2J_{CP}$ = 20.1 Hz), 134.2, 135.2 (d, $^1J_{CP}$ = 18.9 Hz), 137.3 (d, $^1J_{CP}$ = 12.4 Hz), 144.4 (d, $^2J_{CP}$ = 25.8 Hz), 154.1, 157.6, 159.6, 166.6 ppm (d, $^3J_{CP}$ = 3.5 Hz); ^{31}P NMR ([D_6]DMSO, 162 MHz): δ = −13.0 ppm; elemental analysis: calcd (%) for $C_{29}H_{24}N_3OP$ (461.49): C 75.47, H 5.24, N 9.11; found: C 75.29, H 5.30, N 9.07.

4-(4-Diphenylphosphinophenyl)-2-ethylaminopyrimidine (L6): 1-Ethylguanidinium sulfate **10b** (2.35 g, 8.62 mmol) was added in one portion to a suspension of sodium methoxide (0.77 g, 14.2 mmol) in dry oxygen-free ethanol (25 mL) and the mixture was heated at reflux for 4 h. The aminopropenone **9b** (2.00 g, 5.56 mmol) was then added and the resulting mixture was heated at reflux for another 16 h. After cooling to RT, the mixture was stirred for 6 h and the solvent was removed under reduced pressure, producing an orange solid. This residue was dissolved in ether (30 mL) and the organic phase was extracted with water (3× 10 mL) until a pH of approximately 5.0–5.5 was reached. The aqueous layer was extracted with ether (2×10 mL) and the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure to give an orange solid (1.41 g, 3.66 mmol, 66%). The solid was purified by MPLC to give the desired product **L7** as a colourless solid (0.59 g, 1.56 mmol, 28%). M.p. 109–110 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.17 (t, 3H), 3.38–3.46 (m, 2H), 5.24

(brs, 1H, N-H), 6.84 (d, $^{3}J_{HH}=5.2$ Hz, 1H), 7.25–7.32 (m, 12H), 7.98 (d, $^{3}J_{HH}=7.7$ Hz, 2H), 8.23 ppm (d, $^{3}J_{HH}=5.2$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): $\delta=15.1$, 36.4, 106.4, 127.0 (d, $^{3}J_{CP}=6.7$ Hz), 128.7 (d, $^{3}J_{CP}=7.1$ Hz), 129.0, 133.8 (d, $^{2}J_{CP}=18.9$ Hz), 133.9 (d, $^{2}J_{CP}=22.4$ Hz), 137.0 (d, $^{1}J_{CP}=11.1$ Hz), 138.0, 140.5 (d, $^{1}J_{CP}=12.9$ Hz), 158.7, 162.9, 164.3 ppm; ^{31}P NMR ($CDCl_3$, 162 MHz): $\delta=-4.2$ ppm; IR: $\tilde{\nu}=3251$ (s), 3055 (m), 2972 (m), 1683 (w), 1578 (s), 1556 (s), 1433 (m), 1417 (s), 1340 (m), 1186 (w), 1154 (w), 1090 (m), 851 (w), 801 (s), 747 (s), 694 (s), 667 (s), 514 cm^{-1} (s); elemental analysis: calcd (%) for $C_{24}H_{22}N_3P$ (383.43): C 75.18, H 5.75, N 10.96; found: C 75.03, H 5.73, N 11.06.

General procedure for the biaryl synthesis

An oven-dried 20 mL vessel was charged with potassium carboxylate **3** (0.75 mmol), copper(I) oxide (3.61 mg, 25.0 μmol, 5 mol%), palladium(II) acetylacetonate (4.57 mg, 15.0 μmol, 3 mol%), ligand **L8** (12.3 mg, 30 μmol, 6 mol%) and 1,10-phenanthroline (9.10 mg, 50 μmol, 10 mol%) inside a glovebox. NMP (4 mL) and triflate **4** (0.5 mmol) were added inside the glovebox and the resulting mixture was stirred at the given temperature for 24 h outside of the glovebox under a dry atmosphere of nitrogen. After the reaction was complete, the mixture was allowed to cool to RT, diluted with aqueous HCl (1 N, 20 mL) and extracted with ethyl acetate (3× 20 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$, filtered and the volatiles were removed under reduced pressure. The residue was purified by column chromatography (SiO_2, ethyl acetate/hexane gradient) yielding the corresponding biaryl **5**. The isolated yield was determined by combining two identical 0.5 mmol scale reactions.

4-Chloro-2′-nitrobiphenyl (5aa): Compound **5aa** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4a**) (130 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5aa** was isolated as a yellow oil (186 mg, 80%). The analytical data (NMR, GC-MS) matched those reported in the literature[9d, 23] [CAS: 6271-80-3].

3-Acetyl-2′-nitrobiphenyl (5ab): Compound **5ab** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 3-acetylphenyl triflate (**4b**) (134 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ab** was isolated as a colourless solid (158 mg, 66%; M.p. 103–104 °C). The analytical data (NMR, GC-MS) matched those reported in the literature[9d] [CAS: 1195761-01-3].

3,5-Dimethyl-2′-nitrobiphenyl (5ac): Compound **5ac** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 3,5-dimethylphenyl triflate (**4c**) (127 mg, 0.5 mmol) at 100 °C and at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ac** was isolated as an orange oil (132 mg, 58% (100 °C); 204 mg, 90% (120 °C)). The analytical data (NMR, GC-MS) matched those reported in the literature[9d, 24] [CAS: 51839-09-9].

3-Formyl-2′-nitrobiphenyl (5ad): Compound **5ad** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 3-formylphenyl triflate (**4d**) (127 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ad** was isolated as a colourless solid (150 mg, 66%, M.p. 80–81 °C). The analytical data (NMR, GC-MS) matched those reported in the literature[9d] [CAS: 1181294-97-2].

3-Chloro-2′-nitrobiphenyl (5ae): Compound **5ae** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 3-chlorophenyl triflate (**4e**) (130 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ae** was isolated as a yellow oil (126 mg, 54%). The analytical data (NMR) matched those reported in the literature[14] [CAS: 951-22-4].

Ethyl 2′-nitrobiphenyl-2-carboxylate (5af): Compound **5af** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 2-trifluoromethylsulfonyloxy benzoic acid ethyl ester (**4f**) (149 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5af** was isolated as a yellow oil (184 mg, 68%). The analytical data (NMR) matched those reported in the literature[14] [CAS: 72256-33-8].

4-Methyl-2′-nitrobiphenyl (5ag): Compound **5ag** was prepared following the general procedure from potassium 2-nitrobenzoate (**2a**) (154 mg, 0.75 mmol) and 4-methylphenyl triflate (**4g**) (120 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ag** was isolated as an orange oil (197 mg, 92%). The analytical data (NMR, GC-MS) matched those reported in the literature[9d, 25] [CAS: 70680-21-6].

1-(2′-Nitrophenyl)naphthalene (5ah): Compound **5ah** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 1-naphthyl triflate (**4h**) (138 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ah** was isolated as an orange solid (188 mg, 75%) [CAS: 5415–59–8]. M.p. 93–94 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta=8.10$ (dd, $^{3}J_{HH}=8.0$, 1.5 Hz, 1H), 7.98–7.88 (m, 2H), 7.77–7.56 (m, 2H), 7.56–7.40 (m, 5H), 7.40–7.34 ppm (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta=149.8$, 135.5, 135.3, 133.4, 133.1, 132.5, 131.4, 128.6, 128.5, 128.5, 126.6, 126.0, 126.0, 125.2, 124.8, 124.2 ppm; IR: $\tilde{\nu}=3053$ (w), 2852 (w), 1612 (w), 1520 (vs), 1337 (s), 858 (w), 800 (m), 791 (w), 779 (vs), 750 (s), 715 (m), 697 (m), 663 cm^{-1} (w); MS, *m/z* (%): 249 (14) [M^+], 248 (100), 232 (25), 220 (10), 204 (17), 202 (10), 50 (6); elemental analysis: calcd (%) for $C_{16}H_{11}NO_2$ (265.31): C 77.10, H 4.45, N 5.62; found: C 77.06, H 4.61, N 5.61.

2-Methyl-2′-nitrobiphenyl (5ai): Compound **5ai** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 2-methylphenyl triflate (**4i**) (120 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ai** was isolated as an orange solid (150 mg, 70%, m.p. 63–64 °C). The analytical data (NMR, GC-MS) matched those reported in the literature[9d, 26] [CAS: 67992-12-5].

4-Methoxy-2′-nitrobiphenyl (5aj): Compound **5aj** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 4-methoxyphenyl triflate (**4j**) (128 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5aj** was isolated as an orange solid (184 mg, 80%, m.p. 58–59 °C). The analytical data (NMR, GC-MS) matched those reported in the literature[9d, 23] [CAS: 20013-55-2].

1-(2′-Nitrophenyl)-3,4-dihydronaphthalene (5ak): Compound **5ak** was prepared following the general procedure from potassium 2-nitrobenzoate (**3a**) (154 mg, 0.75 mmol) and 3,4-dihydronaphthalen-1-yl triflate (**4k**) (139 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5ak** was isolated as an yellow solid (204 mg, 81%). M.p. 83–84 °C;

^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.98$ (dd, $^3J_{HH} = 8.1$, 1.2 Hz, 1H), 7.71–7.58 (m, 1H), 7.53 (dd, $^3J_{HH} = 7.7$, 1.6 Hz, 1H), 7.49–7.39 (m,1H), 7.25–7.14 (m, 2H), 7.14–6.99 (m, 1H), 6.61 (d, $^3J_{HH} = 7.3$ Hz, 1H), 6.03 (t, $^3J_{HH} = 4.6$ Hz, 1H), 2.91 (brs, 2H), 2.54–2.35 ppm (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 149.2$, 136.6, 135.9, 135.7, 134.2, 132.9, 132.4, 128.3, 128.0, 127.7, 127.4, 126.4, 124.23, 123.6, 27.8, 23.4 ppm; IR: $\tilde{\nu} = 3072$ (w), 3022 (w), 2930 (w), 2853 (w), 1516 (vs), 1489 (m), 1346 (vs), 1270 (m), 1152 (w), 1041 (w), 848 (m), 787 (s), 768 (s), 753 (vs), 738 cm^{-1} (vs). MS, *m/z* (%): 250 (36) [M^+], 233 (31), 216 (19), 207 (19), 206 (100), 204 (17), 50 (17); elemental analysis: calcd (%) for $C_{16}H_{13}NO_2$ (251.29): C 76.48, H 5.21, N 5.57; found: C 76.30, H 5.35, N 5.69.

4-Chloro-5′-methyl-2′-nitrobiphenyl (5 ba): Compound **5 ba** was prepared following the general procedure from potassium 5-methyl-2-nitrobenzoate (**3 b**) (164 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4 a**) (130 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5 ba** was isolated as a yellow oil (180 mg, 73%). The analytical data (NMR) matched those reported in the literature[14] [CAS: 70690-00-5].

4,5′-Dichloro-2′-nitrobiphenyl (5 ca): Compound **5 ca** was prepared following the general procedure from potassium 5-chloro-2-nitrobenzoate (**3 c**) (180 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4 a**) (130 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5 ca** was isolated as a yellow solid (158 mg, 59%). M.p. 93–94 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.88$ (d, $^3J_{HH} = 8.8$ Hz, 1H), 7.49 (dd, $^3J_{HH} = 8.7$, 2.4 Hz, 1H), 7.45–7.40 (m, 3H), 7.27–7.23 ppm (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 147.2$, 138.7, 137.1, 135.0, 134.7, 131.8, 129.1, 129.1, 128.6, 125.8 ppm; IR: $\tilde{\nu} = 3084$ (w), 3053 (w), 2845 (w), 1605 (w), 1524 (s), 1509 (s), 1339 (vs), 1081 (m), 1012 (m), 859 (s), 829 (vs), 821 (vs), 799 (m), 756 cm^{-1} (s); MS, *m/z* (%): 268 (62) [M^+], 267 (19), 266 (100), 238 (25), 232 (31), 175 (29), 150 (20); elemental analysis: calcd (%) for $C_{12}H_7Cl_2NO_2$ (268.10): C 53.76, H 2.63, N 5.22; found: C 53.90, H 2.76, N 5.19.

4-Chloro-5′-methoxy-2′-nitrobiphenyl (5 da): Compound **5 da** was prepared following the general procedure from potassium 5-methoxy-2-nitrobenzoate (**3 d**) (176 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4 a**) (130 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5 da** was isolated as a yellow solid (184 mg, 70%, m.p. 118–119 °C). The analytical data (NMR, GC-MS) matched those reported in the literature[4a] [CAS: 911217-07-7].

4-Chloro-4′,5′-dimethoxy-2′-nitrobiphenyl (5 ea): Compound **5 ea** was prepared following the general procedure from potassium 4,5-dimethoxy-2-nitrobenzoate (**3 e**) (199 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4 a**) (130 mg, 0.5 mmol) at 100 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5 ea** was isolated as a yellow solid (220 mg, 75%). M.p. 146–147 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.58$ (s, 1H), 7.43–7.38 (m, 2H), 7.25–7.20 (m, 2H), 6.74 (s, 1H), 4.00 (s, 3H), 3.96 ppm (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 152.4$, 148.3, 140.8, 136.8, 134.0, 130.2, 129.4, 128.7, 113.4, 107.9, 45.5 ppm; IR: $\tilde{\nu} = 3072$ (w), 2962 (w), 2833 (w), 1498 (s), 1488 (vs), 1332 (s), 1282 (vs), 1268 (s), 1220 (vs), 1089 (s), 1023 (s), 1013 (m), 844 (s), 822 (m), 791 (vs), 757 cm^{-1} (m); MS, *m/z* (%): 294 (31) [M^+], 293 (16), 292 (100), 258 (18), 197 (13), 125 (13), 43 (62); elemental analysis: calcd (%) for $C_{14}H_{12}ClNO_4$ (293.71): C 57.25, H 4.12, N 4.77; found: C 57.45, H 4.40, N 4.95.

3-Chloro-2-(4′-chlorophenyl)benzo[b]thiophene (5 fa): Compound **5 fa** was prepared following the general procedure from potassium 3-chlorobenzo[b]thiophene-2-carboxylate (**3 f**) (188 mg, 0.75 mmol) and 4-chlorophenyl triflate (**4 a**) (130 mg, 0.5 mmol) at 120 °C in 4 mL of NMP. After combining two identical 0.5 mmol scale reactions, compound **5 fa** was isolated as a colourless solid (86 mg, 31%). M.p. 97–98 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.89$ (d, $^3J_{HH} = 8.0$ Hz, 1H), 7.82 (d, $^3J_{HH} = 8.0$ Hz, 1H), 7.77–7.72 (m, 1H), 7.53–7.41 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 137.7$, 136.7, 134.9, 134.8, 130.8, 130.5, 128.9, 125.7, 125.2, 122.3, 117.1 ppm; IR: $\tilde{\nu} = 3058$ (w), 1522 (w), 1486 (w), 1434 (w), 1400 (w), 1301 (w), 1251 (w), 1098 (w), 1012 (w), 984 (w), 899 (m), 828 (m), 820 (s), 750 cm^{-1} (vs); MS, *m/z* (%): 281 (13), 279 (81) [M^+], 278 (100), 208 (19), 163 (8), 49 (6), 44 (6); elemental analysis: calcd (%) for $C_{14}H_8Cl_2S$ (279.19): C 60.23, H 2.89, S 11.49; found: C 60.19, H 3.10, S 11.19.

Synthesis of palladium(0) complex 12

1,3-divinyl-1,1,3,3-tetramethyldisiloxane palladium(0) (**11**) in 2,4,6,8-tetramethylcyclotetrasiloxane (1 M, 250 µL, 250 µmol) was added to a solution of **L8** (102 mg, 250 µmol) in MeCN (8 mL). The solution was stirred at RT for 16 h and a colourless solid formed. The solid was filtered off and washed with MeCN (2×1 mL). The complex was recrystallised from a solution of the crude product in Et_2O (0.5 mL) and MeCN (1.5 mL) at −20 °C yielding **12** as colourless crystals (107 mg, 61%). M.p. 293–294 °C (decomposed); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.07$ (d, $^3J_{HH} = 5.0$ Hz, 1H), 7.55 (dd, $^3J_{HH} = 7.2$, 4.3 Hz, 1H), 7.48 (t, $^3J_{HH} = 7.5$ Hz, 1H), 7.42 (t, $^3J_{HH} = 8.2$ Hz, 4H), 7.38–7.29 (m, 7H), 7.25 (t, $^3J_{HH} = 7.8$ Hz, 1H), 6.36 (d, $^3J_{HH} = 5.0$ Hz, 1H), 3.37 (brs, 2H), 3.14 (dd, $^3J_{HH} = 16.1$, 4.7 Hz, 2H), 2.84 (dd, $^3J_{HH} = 12.3$, 6.5 Hz, 2H), 2.62–2.54 (m, 2H), 2.43 (brs, 2H), 1.81 (brs, 2H), 1.59 (brs, 2H), 0.23 (s, 6H), −0.23 ppm (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 167.1$ (d, $^3J_{CP} = 3.6$ Hz), 159.1, 156.6, 144.4 (d, $^1J_{CP} = 17.3$ Hz), 138.6 (d, $^1J_{CP} = 28.2$ Hz), 134.9 (d. $^2J_{CP} = 21.8$ Hz), 134.8, 134.7, 132.9, 130.3 (d, $^2J_{CP} = 6.4$ Hz), 129.2, 128.8, 128.5 (d, $^3J_{CP} = 4.5$ Hz), 127.8, 127.7, 108.6, 68.6, 68.6, 66.8, 66.7, 45.9, 25.3, 1.4, −1.2 ppm; ^{31}P NMR (243 MHz, $CDCl_3$): $\delta = 25.3$ ppm; IR: $\tilde{\nu} = 3051$ (w), 3036 (w), 2957 (w), 2184 (w), 1569 (m), 1558 (m), 1543 (m), 1510 (m), 1478 (m), 1431 (w), 1339 (w), 1317 (m), 1247 (m), 1210 (w), 1090 (w), 998 (s), 837 (m), 781 (vs), 770 (vs), 740 cm^{-1} (s); ESI-MS, *m/z* (%): 702 [M+H]$^+$; elemental analysis: calcd (%) for $C_{34}H_{42}N_3OPPdSi_2$ (733.35): C 58.15, H 6.03, N 5.98, found: C 58.20, H 5.94, N 5.96. Crystal data for **12**: $C_{34}H_{42}N_3OPPdSi_2$; $M = 702.26$ gmol^{-1}; $T = 150(2)$ K; triclinic; $P\bar{1}$; $a = 10.5752(3)$ Å, $b = 10.9336(4)$ Å, $c = 15.6717(6)$ Å; $\alpha = 89.765(3)°$, $\beta = 88.537(3)°$, $\gamma = 68.120(3)°$; $V = 1680.94(10)$ Å^3; $Z = 2$; $\rho_{calcd} = 1.387$ mg m^{-1}; $\mu(MoK_\alpha) = 0.702$ mm^{-1} ($\lambda = 0.71023$ Å); 18112 reflections collected; independent reflections 9757; refinement converged to $R = 0.0324$, $wR2 = 0.0696$ ($I > 2\ \sigma(I)$), 429 Parameters and 12 restraints; min./max. residual electron density = +0.586 and −0.695 e Å^{-3}. CCDC 1033628 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre

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