Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Electronic supplementary information

C−F Bond Arylation of Fluoroarenes Catalyzed by Pd^0 Phosphine Complexes: Theoretical Insight into Regioselectivity, Reactivity, and Prediction of Ligand

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1. Benchmark calculations to select DFT functionals and basis sets for geometry optimization

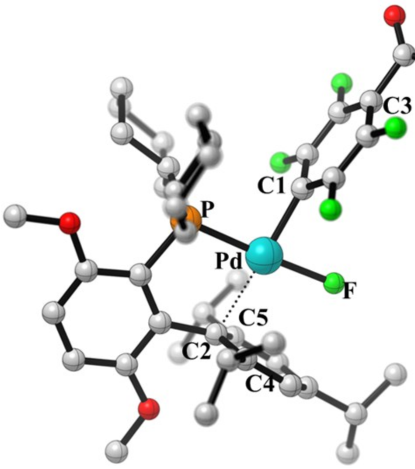


Figure S1. Crystal structure of Pd^{II}(Brettphos)(2,3,5,6-tetrafluoro-4-methylbenzoate)(F) [1].

Hydrogen atoms are omitted for clarity.

Table S1. Benchmark of functionals and basis sets for geometry optimization.

	Experiment	ωB97XD BS-I [a]	B3LYP-D3 BS-I	B3PW91-D3 BS-I	ωB97XD BS-III	B3LYP-D3 BS-III	B3PW91-D3 BS-III
$R_{Pd\text{-}C1}$	2.011	1.989	1.999	1.987	1.986	1.997	1.985
$R_{Pd\text{-}C2}$	2.386	2.409	2.477	2.381	2.426	2.489	2.401
$R_{Pd\text{-}C4}$	2.731	2.725	2.848	2.773	2.778	2.842	2.778
$R_{Pd\text{-}C5}$	2.879	2.855	2.908	2.832	2.852	2.907	2.836
$R_{Pd\text{-}P}$	2.238	2.288	2.290	2.269	2.307	2.311	2.288
$R_{Pd\text{-}F}$	2.014	1.977	1.984	1.975	1.971	1.979	1.971
RMSE		0.030	0.067	0.034	0.044	0.071	0.039

Angstrom unit was used.

[a] BS-I: SDD for Pd, 6-31G(d) for other atoms; BS-III: LANL2DZ for Pd, 6-31G(d) for other atoms.

The crystal structure of Pd^{II}(Brettphos)(2,3,5,6-tetrafluoro-4-methylbenzoate)(F) was obtained by experiment,[1] as shown in Figure S1. Several combinations of functionals and basis sets (See Table S1) have been tested for the geometry optimization and optimized geometrical parameters are compared with the experimental results. The Pd−C1, Pd−C2, Pd−C4, Pd−C5, Pd−P, and Pd−F bond distances have been used in this test. As listed in Table S1, the results of ωB97XD functional with BS-I show that this is the best combination to reproduce the important bond distances. In this work, all geometry optimizations were performed by the density functional theory (DFT) with the ωB97XD functional using the BS-I basis set system.

Reference

(1) Luo, Z.-J.; Zhao, H.-Y.; Zhang, X. *Highly Selective Pd-Catalyzed Direct C–F Bond Arylation of Polyfluoroarenes Org. lett.* **2018**, *20*, 2543.

2. Benchmark calculations to select DFT functionals and basis sets for energy evaluation

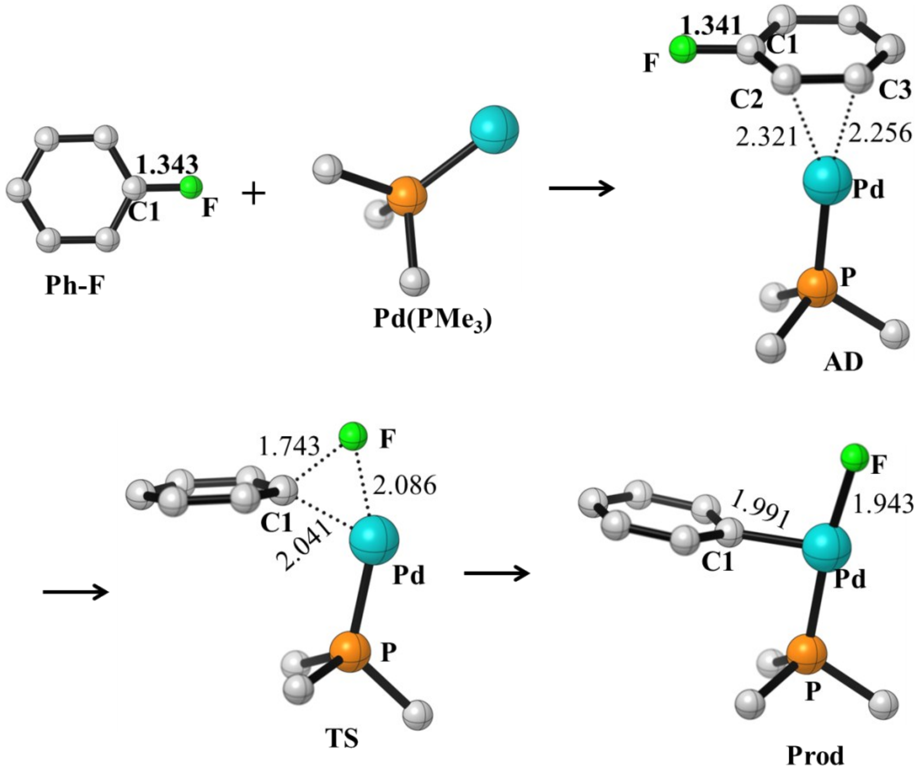


Figure S2. Oxidative addition reaction of fluorobenzene to Pd^0(PMe$_3$) (hydrogen atoms are omitted for clarity).

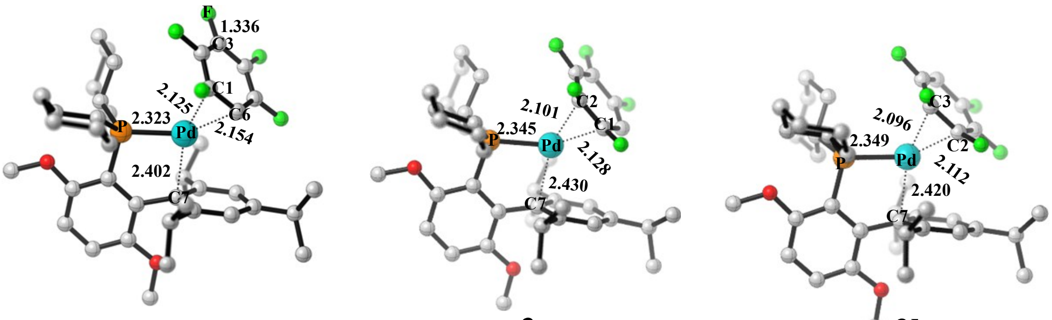
Table S2. Benchmark of functionals for potential energy change.

	BE	E_a	ΔE	RMSE
CCSD(T)	-23.5[a]	34.0	0.1	
B3PW91-D3	-21.2	28.5	-4.4	4.4
B3LYP-D3	-17.8	27.2	-5.5	6.1
M06	-20.6	35.8	7.3	4.6
M06-L	-20.1	25.4	-3.3	5.7
M06-HF	-17.7	36.5	-6.7	5.3
ωB97XD	-20.0	32.3	-2.2	2.6

[a] *BE* represents the binding energy, which is the potential energy difference between adduct and the sum of reactants (see Figure S2); E_a represents the activation barrier, which is the potential energy difference between transition state transition state and adduct; ΔE represents the reaction energy, which is the potential energy difference between product and adduct.

To evaluate the DFT functionals for energy evaluation, we employed here the oxidative addition of fluorobenzene to $Pd^0(PMe_3)$ as a model reaction (see Figure S2). Three important energies relative to adduct, transition state, and product of this reaction were examined. The binding energy (*BE*) is energy difference between adduct and the sum of fluorobenzene and $Pd^0(PMe_3)$. E_a is energy difference between transition state and adduct, which corresponds to the energy barriers of C−F activation. ΔE represents the reaction energy, which is the energy difference between product and adduct. CCSD(T) calculations were carried out to present reference values. Six different functionals such as B3LYP-D3, B3PW91-D3, ωB97XD, M06, M06-HF and M06-2X were tested. As listed in Table S2, the Root Mean Squared Error (RMSE) of the ωB97XD calculation is the smallest. Thus, the ωB97XD functional was used for energy evaluation and NBO population analysis, using a better basis set system (BSII) described in the main text.

3. Isomers of Pd^0(BrettPhos)(pentafluorobenzene)



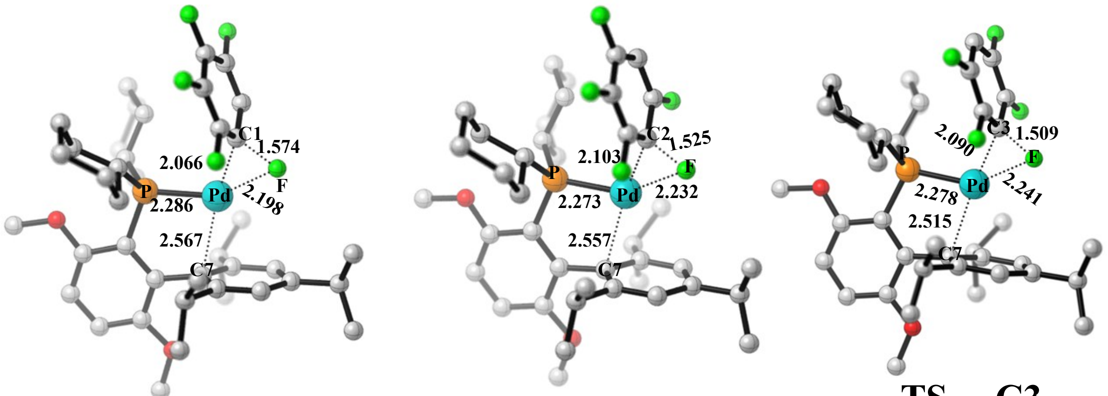
3
-23.9

3a
-20.9

3b
-22.1

Figure S3. Geometrical parameters and relative Gibbs energy of three isomers of η^2-coordinated adducts Pd^0(BrettPhos)(pentafluorobenzene).

4. Three transition states for oxidative addition of pentafluorobenzene to Pd^0(BrettPhos) complex.



$TS_{3/4}$-C1
1.5

$TS_{3/4}$-C2
1.2

$TS_{3/4}$-C3
-1.6

Figure S4. Geometrical parameters and relative Gibbs energy of three transition states for oxidative addition of pentafluorobenzene to Pd^0(BrettPhos) complex.

5. Effect of CsF

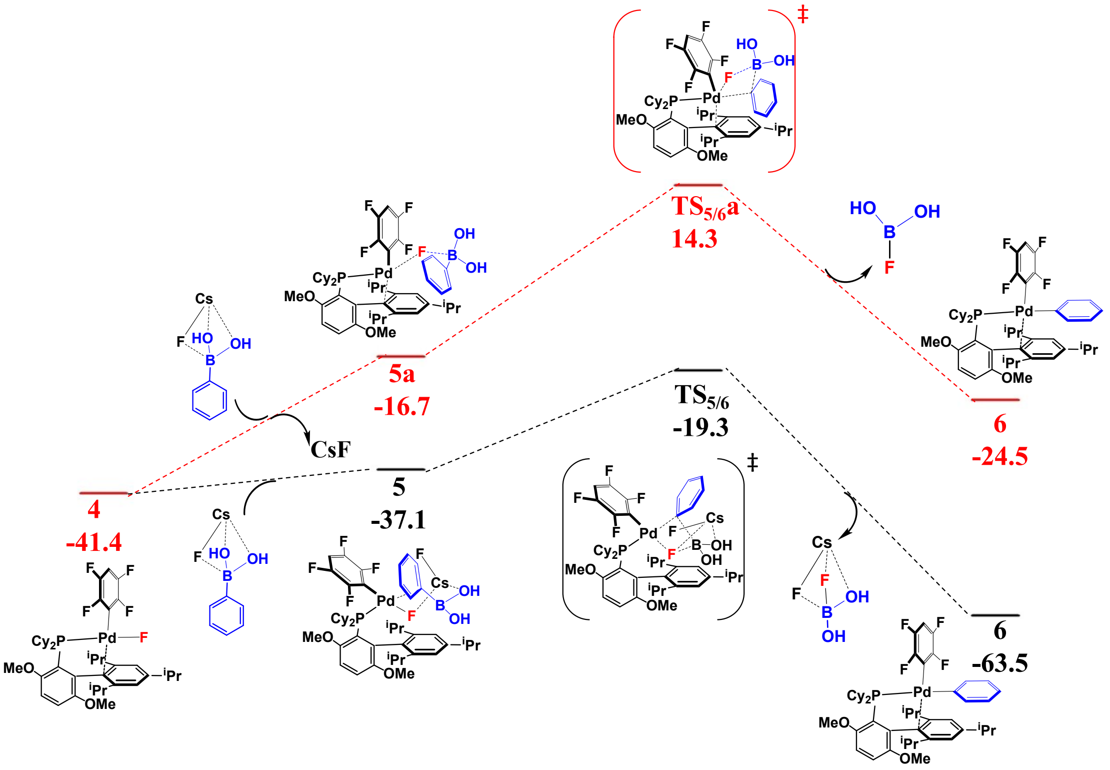


Figure S5. Energy profile for transmetalation step in the present of CsF and the absence of CsF.

According to experimental results, base is also important for the reaction. The base should play an important role in the transmetalation step. Here, CsF was employed as a base instead of Cs_2CO_3 because CsF was also effective for this cross-coupling reaction. Our propose is to reveal the role of base in the transmetalation step by comparing the activation barrier with CsF and without any base. As shown in Figure S5 of supporting information, the TS of transmetalation is stabilized by the CsF and so that the barrier is decreased.

6. Detail about deformation/interaction analysis

Table S3. The C−F distance and activation barrier (E_a) of the real transition state and those of approximate transition state which has the C−F distance almost the same.

substrate		*Real TS*		*Approximate TS*	
		R(C−F)	E_a	R(C−F)	E_a
Pentafluorobenzene	$TS_{3/4}$-C1	1.574	-4.5	1.614	-5.0
	$TS_{3/4}$-C2	1.525	-5.7	1.606	-7.0
	$TS_{3/4}$-C3	1.509	-8.9	1.605	-10.3
fluorobenzene	$TS_{3/4}$	1.668	4.9	1.627	4.6

The deformation/interaction analysis can provide clear results when we compare two transition states at the similar reaction coordinate. If the comparison is made between late and early transition states, the late transition state exhibits larger deformation energy and larger interaction energy than the early transition state and clear conclusion cannot be obtained. Here, we took the C−F distance as an approximate reaction coordinate because this is the oxidative addition of the C−F bond. We obtained such approximate transition state geometry by IRC calculation, where the C−F distance of 1.600 Å was taken as reference; in other words, the geometry which has the C−F distance almost the same as 1.600 Å was taken as approximate transition state, and the comparison was made using the approximate transition state geometry. The activation barrier differs little between the real transition state and the approximated one, as shown in Table S3. This result is not surprising because the potential energy surface is flat around the transition state. Thus, the comparison can be made in a reasonable way using approximate transition state geometry.

As shown in the above section and main text, in the transition state of C−F bond oxidative addition to the Pd^0(BrettPhos) complex, the substrate distorted to decrease σ* orbital energy of C−F bond, which is favorable for charge transfer from dπ Pd orbital to σ* orbital to stabilize the transition state. In this distortion, the C−F distance elongates to about 1.600 Å and the C1-C-F angle bends to about 145°. The LUMO energy of the model structure shown in Figure S6 is very close to that in TS and also the difference of distortion energy is also very small as shown in Table S4. Therefore, the LUMO energy of the model shown in Figure S6 is a reasonable parameter to evaluate the reactivity of C−F bond for the oxidative addition reaction as discussed in the above section.

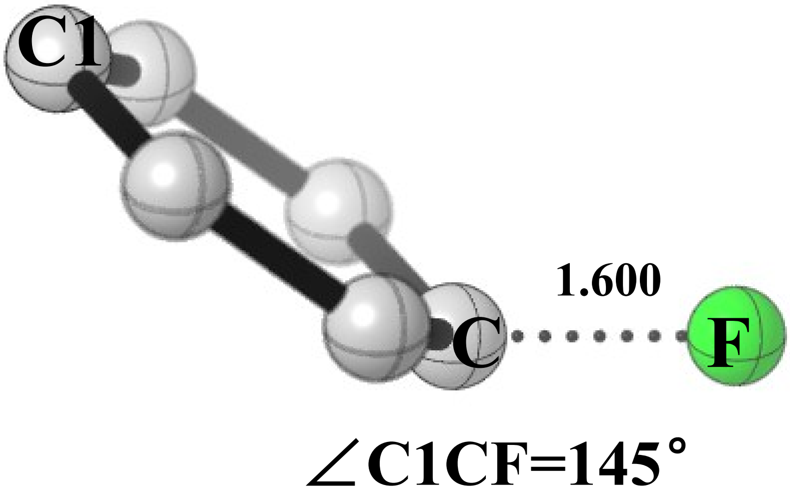


Figure S6. Model structure for calculating LUMO energy.

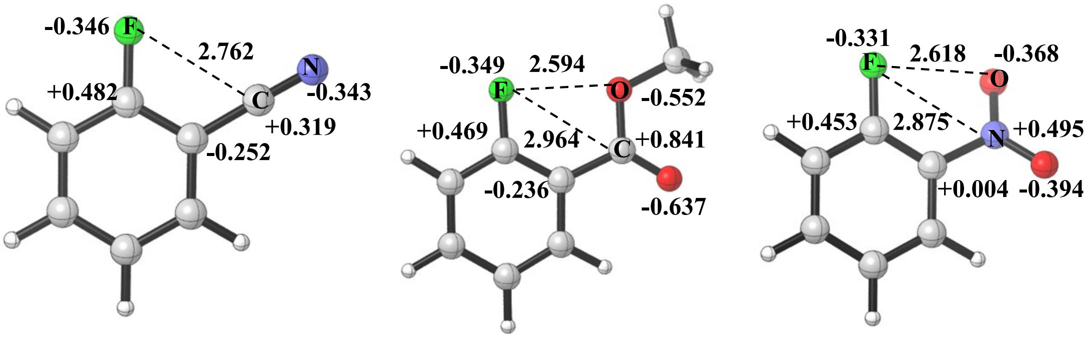
Table S4. The LUMO energy (eV), deformation energy (E_{def} kcal mol^{-1}) of distorted difluorobenzene and fluorobenzene when the C−F distance elongates to 1.600 Å and the C1-C-F angle bends to 145° and bond dissociation energy (BDE, kcal mol^{-1}) of C−F bond.

	difluorobenzene			fluorobenzene
	o	*m*	*p*	
LUMO	-0.33	-0.22	-0.03	0.09
E_{def}	31.5	31.8	31.0	30.7
BDE	124.8	126.4	126.6	126.9
C-F	1.600	1.600	1.600	1.600
C1-C-F	145°	145°	145°	145°

Discussion on the lower σ* orbital of C3−F bond in the pentafluorobenzene

As discussed in the main text, the σ* orbital of distorted C−F bond is decreased by *o*-substitution (0.42 eV) > *m*-substitution (0.31 eV) > *p*-substitution (0.12 eV) of another F atom. In pentafluorobenzene, for the C3−F bond, there are two *o*-substitution and two *m*-substitution F atoms. As results, the σ* orbital of C3−F bond is approximatively decreased by 1.46 eV compared to that of fluorobenzene; For the C2−F bond, there are two *o*-substitution, one *m*-substitution, and one *p*-substitution F atoms; As results, the σ* orbital of C2−F bond is approximatively decreased by 1.27 eV compared to that of fluorobenzene; For the C1−F bond in the pentafluorobenzene, there are one *o*-substitution, two *m*-substitution F atoms, and one *p*-substitution F atoms. As results, the σ* orbital of C2−F bond is approximatively decreased by 1.16 eV compared to that of fluorobenzene. This is consistent with the order of σ* orbital energy, -1.78 **(**C3−F**)** < -1.54 **(**C2−F**)** < -1.42 **(**C1−F**)** eV. It should be concluded that, the σ* orbital of C3−F bond in the pentafluorobenzene is lower than C1−F and C2−F ones mainly because σ* orbital energy of C−F bond is decreased by the substitution of another F atom in the order of: *o*-substitution > *m*-substitution > *p*-substitution.

7. Bond dissociation energy of C−F bond in 2-fluorobenzonitrile



2-fluorobenzonitrile
BDE$_{(C\text{-}F)}$=126.0

***o*-fluoronitrobenzene**
BDE$_{(C\text{-}F)}$=123.3

methyl 2-fluorobenzoate
BDE$_{(C\text{-}F)}$=121.6

Figure S7. The natural population analysis charge of important atoms, bond distance and bond dissociation energy of C−F bond (BDE$_{(C\text{-}F)}$) in 2-fluorobenzonitrile, *o*-fluoronitrobenzene, and methyl 2-fluorobenzoate.

Generally, the *ortho*-substitution of electron-withdrawing groups will stabilize the corresponding phenyl radical, suggesting that the BDE$_{(C−F)}$ would decrease with the increase of electron-withdrawing ability of the substituted group. As we know, the electron-withdrawing ability increases in the order: COOMe < CN < NO_2. However, according to our calculation the BDE of *ortho*-substituted C−F bond decrease in the order: CN > COOMe > NO_2. The order of CN and COOMe is out of our expectation. To find the reason(s), we summarized the natural population analysis charge of important atoms and important bond distance in Figure S7. From Figure S7, we can easily understand that the BDE$_{(C−F)}$ in 2-fluorobenzonitrile is larger mainly because the electrostatic attraction between negative charged F atom and positive charged C atom of CN group. On the other hand, in *o*-fluoronitrobenzene and methyl 2-fluorobenzoate, the electrostatic repulsion between negative charged F atom and negative charged O atom of NO_2 group or COOMe group is nonnegligible. Therefore, the BDE$_{(C−F)}$ in 2-fluorobenzonitrile is larger than that in methyl 2-fluorobenzoate could be understood by the intramolecular electrostatic interaction.

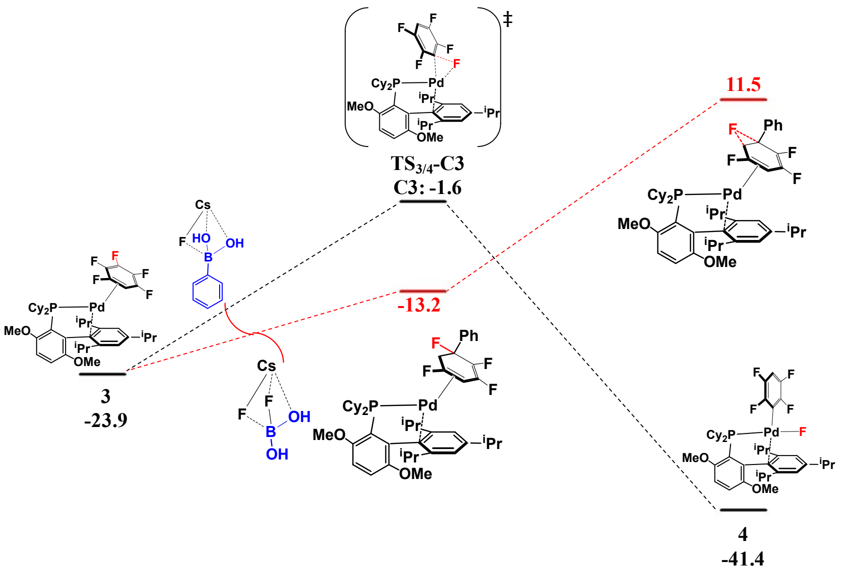


Figure S8. Comparison between one kind of SNAr type oxidative addition via a meisenheimer intermediate and concerted oxidative addition.