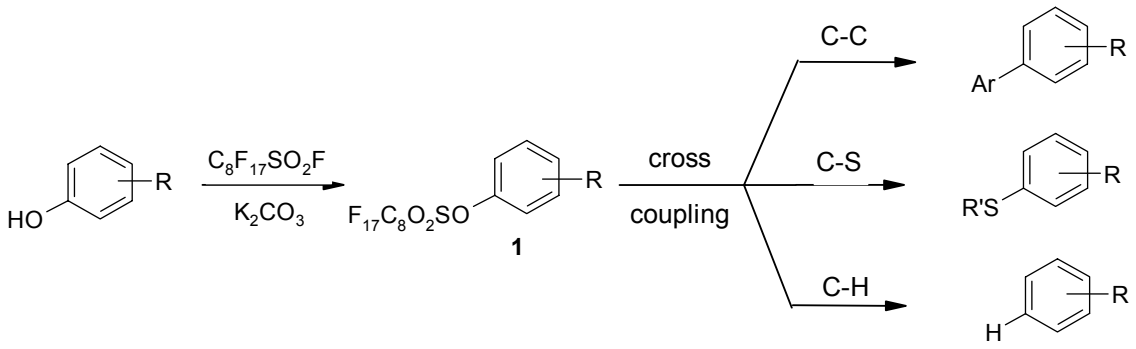
$C_8F_{17}SO_2F$

Perfluoro-1-octanesulfonyl fluoride

Chemical Formula:	$C_8F_{18}O_2S$
Formula Weight:	502.12
Description:	Protecting Group & Tag
CAS Number:	307-35-7
Appearance:	Clear liquid
Soluble in:	Dichloromethane, chloroform, THF, ether, toluene and most other typical organic solvents
Stability:	Moisture sensitive

DESCRIPTION AND USES:

- Perfluorooctanesulfonyl fluoride is used to react with phenols to form perfluorooctanesulfonates.
- The perfluoroalkanesulfonyl tag has three functions:
  - A phenol protecting group
  - A phase tag for reaction mixture purification
  - A hydroxy activating group for the cross-coupling reaction
- Compounds bearing the tag can be manipulated in multi step synthesis. Detagging can be achieved by cross-coupling reactions to introduce additional diversity point or by traceless manner.[2-5]
- The intermediates can also be purified by fluorous SPE[1] or other methods such as flash column chromatography.

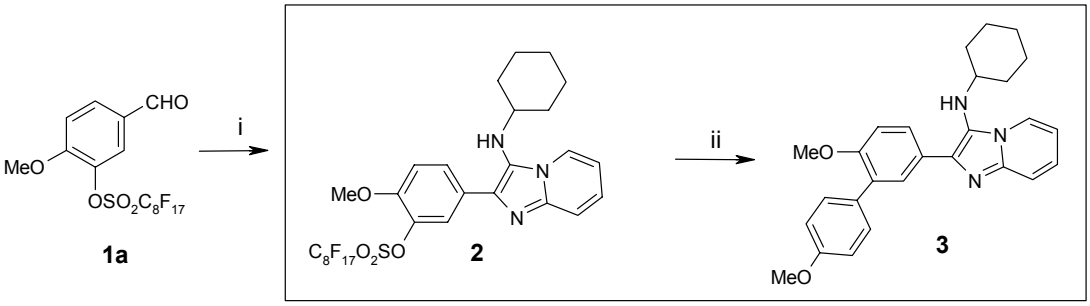


TYPICAL TAGGING PROCEDURE:[2]

To a solution of a hydroxybenzaldehyde (11 mmol) in DMF (5 mL) was added K_2CO_3 powder (14 mmol) at room temperature. The reaction mixture was stirred for 10 minutes before the addition of perfluorooctanesulfonyl fluoride (9 mmol). The mixture was heated at 70°C for 2 hours. The purification of crude product can be conducted by F-SPE[1], precipitation, or flash chromatography on normal silica gel.

TYPICAL PROCEDURE FOR SUZUKI COUPLING:[2,3]

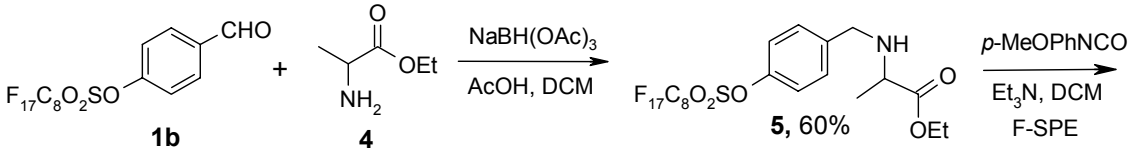
A mixture of **2** (0.2 mmol), boronic acid (0.19 mmol), K_2CO_3 (0.4 mmol), $Pd(dppf)Cl_2$ (10 mol%) in 4:4:1 acetone/toluene/H_2O (1 mL) was heated at 130°C for 20 min under microwave irradiation (see figure below). The mixture was loaded onto a 5g Fluoro*Flash*® SPE cartridge and then eluted with 80:20 MeOH/H_2O (10 mL). The MeOH/H_2O fraction was concentrated to afford the desired product **3**. The fluorous component on the cartridge can be washed out by acetone (2x10 mL).

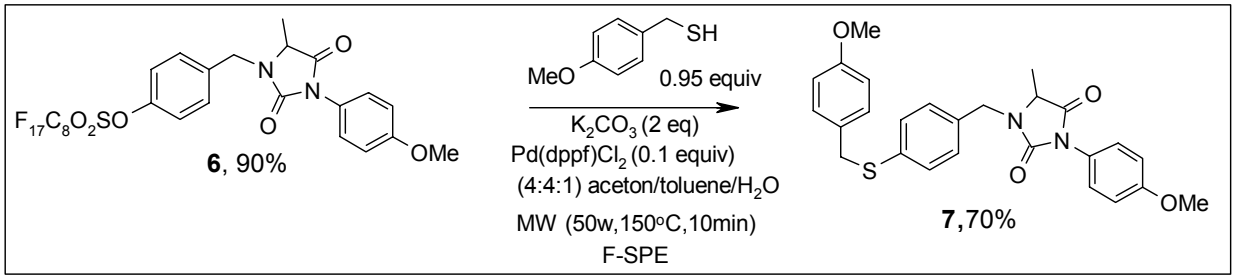


i) 2-aminopyridine (1.1 equiv), cyclohexylisonitrile (1.2 equiv), Sc(OTf)3 (0.05 equiv), 3:1 DCM/MeOH, microwave (150 w, 150 °C, 10 min), 76%;
ii) 4-methoxyboronic acid (0.95 equiv), Pd(pddf)Cl_2 (0.1 equiv), K_2CO_3 (2.0 equiv), 4:4:1 acetone/toluene/H_2O, microwave (150 w, 130 °C, 20 min), 75%

TYPICAL PROCEDURE FOR THIOL COUPLING:[2,4]

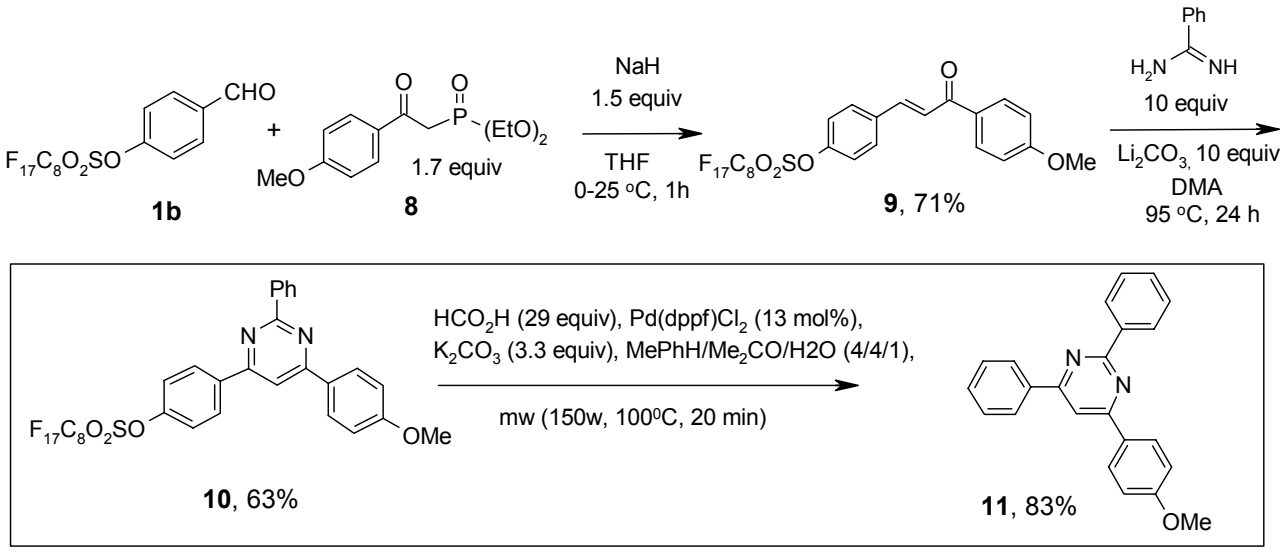
A mixture of **6** (0.2 mmol), thiol (0.19 mmol), K_2CO_3 (0.4 mmol), Pd(dppf)Cl_2 (10 mol%) in 4:4:1acetone/toluene/H_2O (1 mL) was heated at 150°C for 10 min under microwave irradiation (see figure below). The mixture was loaded onto a 5g Fluoro*Flash*® SPE cartridge and then eluted with 80:20 MeOH/H_2O (15 mL). The MeOH/H_2O fraction was concentrated to afford the desired product **7**.





TYPICAL PROCEDURE FOR TRACELESS DETAGGING:[5]

A mixture of **10** (0.2 mmol), HCOOH (5.8 mmol), K_2CO_3 (0.66 mmol), Pd(dppf)Cl_2 (13 mol%) in 4:4:1 acetone/toluene/H_2O (1 mL) was heated at 100°C for 20 min under microwave irradiation (see figure below). The mixture was loaded onto a 5g Fluoro*Flash*® SPE cartridge and then eluted with 80:20 MeOH/H_2O (15 mL). The MeOH/H_2O fraction was concentrated to afford the desired product **11**.



REFERENCES:

1) FTI Application Note "Fluorous Solid Phase Extraction"
2) Lu, Y., Zhang, W., *QSAR & Combinatorial Chemistry,* in press.
3) Zhang, W., Chen, C. H.-T., Lu, Y., Nagashima, T., *Org. Lett.,* 2004, 6 (9), 1473.
4) Zhang, W., Lu, Y., Chen, C. H.-T., *Molecular Diversity,* 2004, 7, 199.
5) Zhang, W., Nagashima, T., Lu, Y., Chen, C., H.-T., *Tetrahedron Lett.,* 2004, 45, 4611.