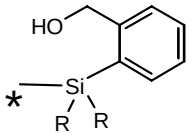
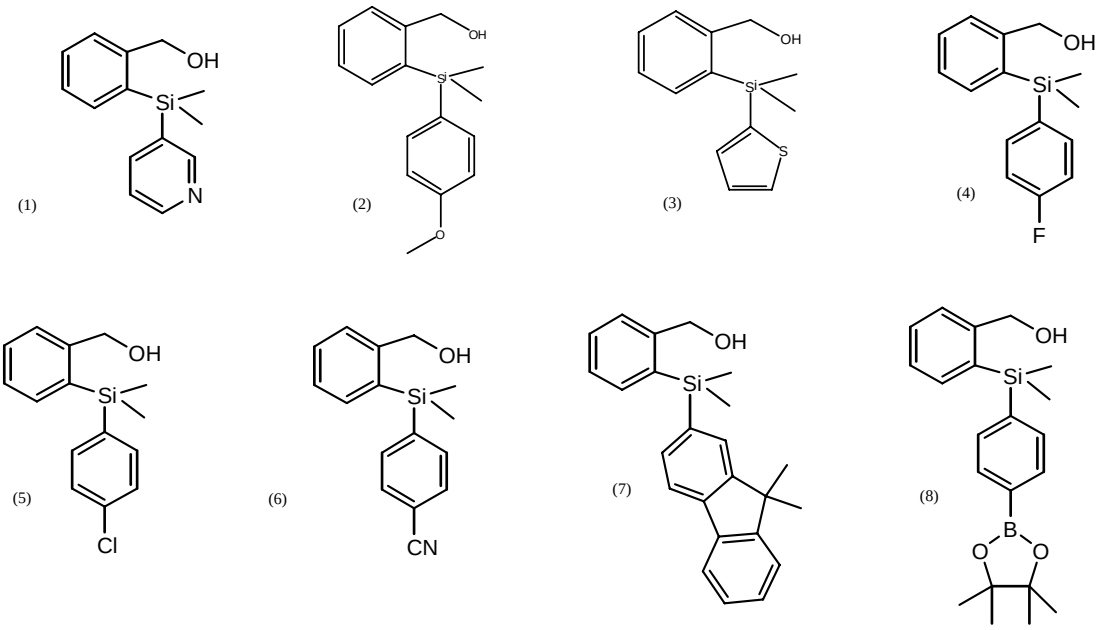
HOMSi® REAGENTS FOR HIYAMA CROSS-COUPLING REACTIONS

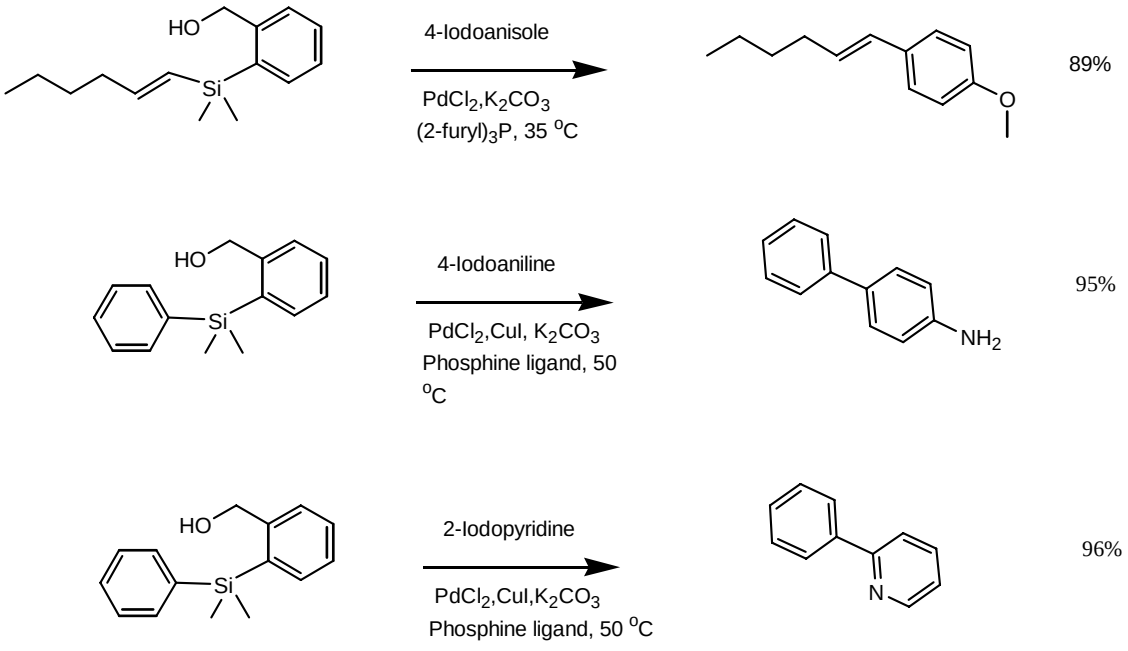
In 2008 AMT released a range of HOMSi® reagents developed by Professor Hiyama, Assistant Professor Nakao and co-workers.[1-9] We have grown this range to over 80 products over the past three years.
A selection of HOMSi® reagents are shown below:



= HOMSi®



Silicon substituted HOMSi ((2-hydroxymethylphenyl)dimethylsilanes) reagents are excellent cross-coupling partners which can provide the desired coupled products under mild conditions and in high yields.[2]



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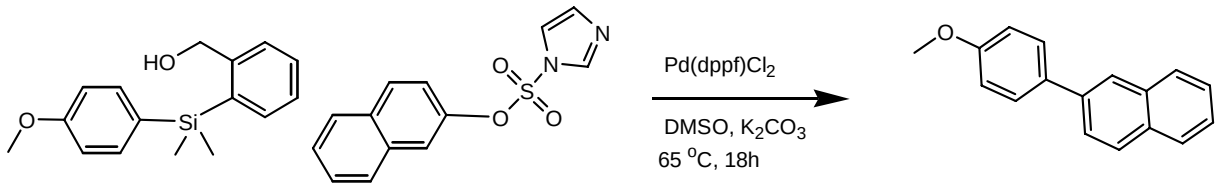
Recently HOMSi® reagents have been shown to cross couple with aryl imidazol-1-ylsulfonates which are alternative cross coupling partners to aryl halides. It is interesting to note that no copper iodide was required using these reagents.[10]

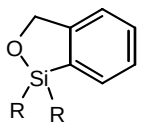


99%

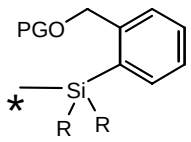
The cross-coupling reactions using HOMSi® reagents have the following characteristics:

1. High functional group compatibility (amino, cyano, hydroxy, ester, ketone, nitro etc.)
2. React with a variety of halide coupling partners including iodides, bromides and chlorides
3. A relatively mild base such as potassium carbonate is generally used
4. Can be performed under fluoride-free conditions
5. Mild reaction conditions (RT to 75 °C)
6. Organosilicon "by-product" can be recycled if required
7. The cross-coupling reactions can be turned "OFF" by the use of suitable protecting groups on the 2-hydroxymethyl group[6]

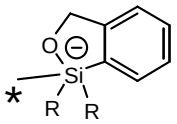
Protected HOMSi® Reagents



Organosilicon "by-product"

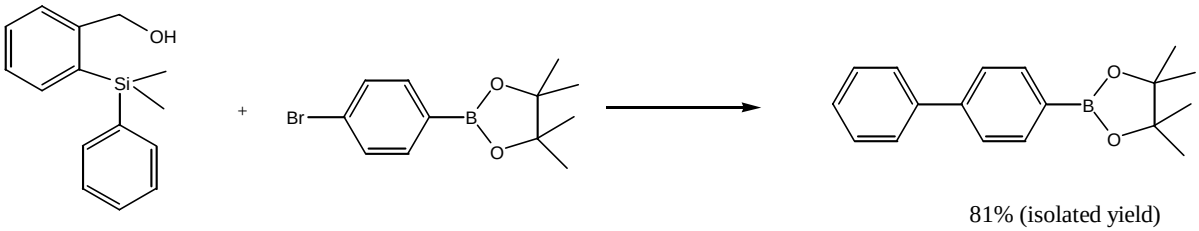


"OFF" position



"ON" position

Another key advantage of the HOMSi reagents is that the cross-coupling reactions can be conducted in the presence of pinacol esters of aryl boronates as shown below.



81% (isolated yield)

The HOMSi® reagents have been reported to undergo a number of other organic transformations.[5,7,8]

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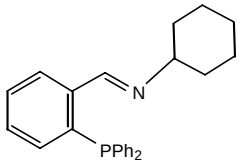
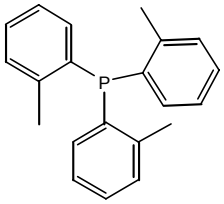
The phosphine ligands that have been reported to work well in the cross coupling reactions include N-[2-(Diphenylphosphino)benzylidene] cyclohexylamine[1-4,6,7] and tri(o-tolyl)phosphine.[11,12] Both phosphines are available commercially from various suppliers.



N-[2-(Diphenylphosphino)benzylidene] cyclohexylamine



tri(o-Tolyl)phosphine

References

(1) Y. Nakao et al. *J. Am. Chem. Soc.* **2005**, *127*, 6952-6953
(2) Y. Nakao et al. *Pure Appl. Chem.* **2006**, *78(2)*, 435-440
(3) Y. Nakao et al. *Sci. Tech. Adv. Mat.* **2006**, *7*, 536-543.
(4) Y. Nakao et al. *Chem. Lett.* **2007**, *36(5)*, 606-607
(5) Y. Nakao et al. *J. Am. Chem. Soc.* **2007**, *129 (29)*, 9137-9143
(6) Y. Nakao et al. *J. Am. Chem. Soc.* **2007**, *129*, 11694-11695
(7) Y. Nakao et al. *J. Organometallic Chem.* **2007**, *692*, 585-603
(8) Y. Nakao et al. *Chem. Lett.* **2008**, *37(3)*, 290-291
(9) Y. Nakao et al. *SynLett.* **2008**, *5*, 774-776
(10) S. Shirbin et al. Tetrahedron letters, **2010**, 51, 2979
(11) S. Marcuccio et al. Intersect 09, Melbourne Australia
(12) S. Marcuccio et al. Tetrahedron letters, **2011**, 52, 7178

For a full listing of reagents for Hiyama cross-couplings, visit www.amtechpl.com.

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