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CRITICAL REVIEW

Palladium-catalysed cross-coupling of organosilicon reagents

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The palladium catalysed cross-coupling of organosilicon reagents with organo halides and pseudo-halides has developed over the past 30 years into an efficient and attractive carbon–carbon bond forming strategy. Extensive research within this field to expand and diversify on the scope of the organosilicon coupling reaction will continue to promote its use in the synthesis of biologically and pharmaceutically important organic molecules. The recent advances made within this area are explored in this *critical review* (199 references).

1. Introduction

The synthesis of carbon–carbon bonds by transition metal catalysed cross-coupling has developed over the past 40 years into arguably one of the most useful and important classes of reactions in modern synthetic organic chemistry (Scheme 1).[1] Consequently, this vast array of reactions has found numerous applications in both academic and industrial settings in the synthesis of complex natural products and biologically active small molecules.[2]

In 1972, the independent discovery by Kumada and Corriu that Grignard reagents, when catalysed by nickel–phosphine complexes, could participate in cross-coupling reactions with alkenyl/aryl halides opened up a significant avenue of research.[3–5] Later in 1976, Negishi and co-workers developed the cross-coupling of organoaluminium, rapidly followed by organozinc and organozironium reagents, reducing the basicity of the organometallic species and accordingly improving the functional group tolerance of the coupling reaction.[6–11]

The coupling of organotin reagents was first reported in 1976, but it was Stille *et al*. who advanced this method with milder reaction conditions and improved yields.[12–16] The Stille reaction has evolved into a robust and reliable method as a consequence of the stability and wide functional group tolerance of the organotin reagent; however, the major drawback of this procedure remains the high toxicity of the tin by-products.[17–19]

Suzuki and Miyaura reported the base activated palladium catalysed reaction of aryl and vinyl halides with vinylboronates in 1979.[20,21] Today the Suzuki reaction is the most widely employed of the cross-coupling reactions, finding continual application in the synthesis of drug-like molecules within the pharmaceutical industry. The main advantages of the Suzuki reaction include: mild reaction conditions; ready availability of starting materials; retention of regio- and stereochemistry during coupling; excellent functional group tolerance; broad substrate scope; low toxicity and reliably high reaction yields.[22–26] Although the Suzuki reaction has seen widespread application

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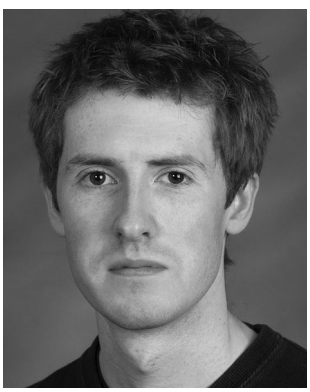
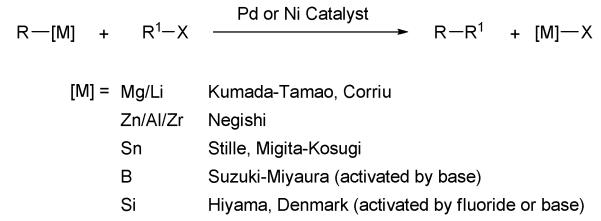
Hannah F. Sore

Hannah Sore attended the University of Durham for her undergraduate chemistry degree. After working as a medicinal chemist at Millennium Pharmaceuticals and Astex Therapeutics she started a PhD at the University of Cambridge under the supervision of Dr David Spring. Her studies focused on the development of new silicon-based cross-coupling methodologies. Hannah now works as a Research Analyst at Frost & Sullivan.



Warren R. J. D. Galloway

Warren Galloway was born in Dundee, Scotland and attended the University of Cambridge for his undergraduate chemistry degree. He stayed at Cambridge for his PhD studies under the supervision of Dr David Spring, where he worked on the development of strategies for diversity-oriented synthesis. Warren received his PhD in 2008 and is currently a postdoctoral research assistant for Dr David Spring, working on the design and synthesis of small molecule modulators of biological processes.



Scheme 1 Metal catalysed cross-coupling reactions.

some challenges with the procedure still remain these include; protodeborylation, loss of selectivity in cross-coupling, homocoupling of starting reagents and incorporation of the aryl group from the phosphorus ligand into the coupled product.[26] Consequently, further developments in transition metal catalysed cross-coupling reactions are necessary to expand upon the armoury of tools available to the synthetic organic chemist.

A decade later, the pioneering discovery by Hiyama that organosilanes can participate in cross-coupling reactions by activation with fluoride created another viable alternative to the existing array of organometallic cross-coupling reactions.[27] Extensive research over the past 30 years has established organosilicon reagents as an attractive organometallic species for palladium catalysed cross-coupling reactions with organic halides and pseudohalides. The development of new organosilanes and modified reaction conditions has expanded the scope of the reaction enormously. The Hiyama reaction offers a number of advantages over more traditional organometallic coupling protocols; excellent substrate, mild reaction conditions, retention of regio- and stereochemistry during coupling, low toxicity and increased chemical stability.

The objective of this review is to provide a detailed overview of the various organosilicon species utilised in palladium catalysed cross-coupling reactions. The evolution of the major classes of organosilane coupling partner are discussed together with some selected examples illustrating their synthetic utility. Some excellent early seminal reviews, those detailing specific silanes, applications in natural product synthesis and personal research accounts have all been reported;[28–37] however, to date there has been no comprehensive review broadly encompassing all organosilanes. The scope, typical coupling conditions and key references for each organosilane is displayed clearly within an inclusive table allowing the reader to readily comprehend the different types of silane available.

David R. Spring

Dr David Spring is currently a Reader at the University of Cambridge within the Chemistry Department. He received his DPhil (1998) at Oxford University under Sir Jack Baldwin. He then worked as a Wellcome Trust Postdoctoral Fellow at Harvard University with Stuart Schreiber (1999–2001), after which he joined the faculty at the University of Cambridge. His research programme is focused on synthetic chemistry and chemical biology.

2. The advent of organosilicon cross-coupling

2.1 Trialkyl-, triallyl- and halosilanes

The addition of activators is necessary to facilitate the palladium catalysed cross-coupling of organosilicon reagents. Because of the low polarisation of the C–Si bond, a promoter is required to increase the nucleophilicity of the organosilicon species. Hiyama first achieved this in 1988 by the addition of fluoride ions, such as tetrabutylammonium fluoride (TBAF, $^{n}Bu_4N^+F^-$) and tris(diethylamino)sulfonium difluorotrimethylsilicate (TSAF ($(Et_2N)_3S^+(Me_3SiF_2)^-$) to vinyl, alkynyl or allyl substituted trimethylsilanes (see Table 1, silane 1).[27,37] Subsequently, trialkylsilanes have been utilised in the synthesis of polyenynes,[38] styrenes,[39] enynes[40] and aryl-substituted alkynylamides.[41]

The cross-coupling of 2-trimethylsilylpyridines **1** possessing electron withdrawing substituents was developed by Pierrat *et al.* allowing access to arylated pyridine derivatives **2** (Scheme 2).[42] The electron withdrawing substituent was necessary to increase the polarisation of the C–Si bond facilitating formation of the ate complex on addition of a fluoride source.[42] To expand the scope of the reaction further the coupling of unsubstituted 2-tri-methylsilylpyridine **3** with aryl iodides and bromides to furnish pyridines **4** has been achieved after additional reaction optimisation (Scheme 3).[43] The presence of Ag_2O in addition to TBAF was critical, as without the additive no cross-coupling product was observed.[43] On applying the optimised conditions good conversion to the biaryl products was observed with a variety of aryl iodides; however, only electron deficient aryl bromides resulted in moderate yields of the cross-coupled product.

The successful arylation of 2-trimethylsilylbenzofuran **5** to form derivatives of the general form **6** was accomplished by activation with AgF (Scheme 4). The promoter could be used directly or generated *in situ* with the combination of $AgNO_3$ and KF.[44] Homocoupling of the silane was observed (75% isolated yield) under similar conditions in the absence of the aryl iodide. Additional substitution of the benzofuran was not explored.

Base induced activation conditions were developed by Shindo *et al.* specifically for the coupling of (*Z*)-β-(trimethylsilyl)acrylic acids **7** with aryl iodides (Scheme 5).[45] The stable trimethylsilyl group was activated through intramolecular donation from the carbonyl oxygen of the carboxylic acid to the silicon, forming the necessary intramolecular pentacoordinate transition state. Electron rich, neutral and poor aryl iodides were coupled to produce a selection of tetra-substituted alkenes **8** in moderate to good yields.[45] To demonstrate the value of these substrates, compound **8d** was subsequently transformed into the anti-cancer drug, tamoxifen. A similar intramolecular activation approach has been described by Takeda and co-workers. Alkenyl- and aryl(trimethyl)silanes having a proximal hydroxyl group were found to undergo transmetallation from silicon to copper upon treatment with copper(I) *tert*-butoxide; the resulting copper species then underwent palladium-catalysed cross-coupling with aryl iodides.[46,47] A drawback of these examples is

Table 1 Organosilicon reagents; their scope, typical reaction conditions and references

Silane	R^2–X	Reaction conditions	Ref.
(1) Trialkylsilane  R = Me and R^1SiR_3 = R^1SiTBDMS R^1 = Alkenyl, Alkynyl, Allyl, Benzofuryl, 2-Pyridyl, (*Z*)-β-acrylic acid, naphthol derivatives (for R^1SiR_3 = R_1SiTBDMS)	R^2 = Aryl, Alkenyl, Allyl, Heteroaryl X = I, Br, OTf	Activator: TASF, KF/^{n}Bu$_4$NCl, TBAF·3H$_2$O, AgF, AgNO$_2$/KF Catalyst: [allylPdCl], Pd(PPh$_3$)$_4$, Pd(dba)$_2$, Pd(PPh$_3$)$_4$/AgI, PdCl$_2$(PPh$_3$)$_2$ Ligand: P(OEt)$_3$ Additive: Ag$_2$O Solvent: THF, HMPA, Toluene, DMF, DMSO Temp.: r.t. −100 °C OR Activator: Ag$_2$CO$_3$/^{n}Bu$_4$NCl, Cs$_2$CO$_3$ Catalyst: Pd(OAc)$_2$, PdCl$_2$(PPh$_3$)$_2$, Pd$_2$(dba)$_3$·CHCl$_3$, Pd(^{t}Bu$_3$)$_2$, [(allyl)PdCl] Ligand: PPh$_3$, 1,2-Bis(diphenylphosphino)ethane (dppe), AsPh$_3$ Solvent: THF, DME Temp.: 60 °C	27, 38–40, 42, 43 41, 45, 51
(2) Triallylsilane R^1-Si(allyl)$_3$ R^1 = Aryl	R^2 = Aryl, Heteroaryl X = Br, Cl	Activator: TBAF·3H$_2$O Catalyst: [allylPdCl], PdCl$_2$ Ligand: PCy$_3$, XPhos Solvent: DMSO/H$_2$O, THF/H$_2$O Temp.: 80 °C	61, 62
(3) Halosilane R^1-SiR$_n$X$_{3-n}$ R = Alkyl (Me, Et, Cyclohexyl) *n* = 0,1,2 X = Cl, F R^1 = Aryl, Alkenyl, Alkynyl	R^2 = Aryl, Heteroaryl, Alkenyl, Alkyl, solid supported Aryl X = Cl, Br, I, OTf	Activator: TBAF, TBAF (H$_2$O), TSAF, KF, CsF Catalyst: [allylPdCl], Pd(PPh$_3$)$_4$, Pd$_2$(dba)$_3$, (^{i}Pr$_3$P)$_2$PdCl$_2$, [(Et$_3$P)$_2$PdCl$_2$], [(dcpe)PdCl$_2$], Pd(OAc)$_2$, Pd(PPh$_3$)$_4$/CuI, NiCl$_2$·glyme Ligand/Additive: P(2-Furyl)$_3$, P(*o*-Tol)$_3$, norephedrine/LiHMDS, PPh$_3$, P(*o*-Tol)$_3$, dppf, dfpf Solvent: DMF, THF, DMI, DMA/H$_2$O, toluene, benzene, dioxane Temp.: r.t. −120 °C OR Activator: KOH Catalyst: Pd/C Solvent: H$_2$O Temp.: 100 °C	52–60, 140–142 59
(4) Oxysilane R^1-SiMe$_n$(OR)$_{3-n}$ R = Alkyl (Me, Et, CH_2CF_3, ^{i}Pr, TMS) *n* = 0,1,2	R^2 = Aryl, Alkenyl, Alkyl, Heteroaryl, Tropolone, Allyl X = Cl, Br, I, OTs, OMs, OCO$_2$Et	Activator: TBAF, polymer-supported ammonium fluoride, TBAT Catalyst: [allylPdCl], Pd(dba)$_2$, [Pd$_2$(dba)$_3$]·CHCl$_3$, Pd$_2$(dba)$_3$, PdCl$_2$, PdBr$_2$, Pd(OAc)$_2$, Pd(PPh$_3$)$_4$, Pd/P complex, ionic gel Pd catalyst, NiCl$_2$·glyme, K$_2$PdCl$_4$, Pd(acac)$_2$, PdCl(MeCN)$_2$ Ligand: P(OEt)$_3$, P(^{t}Bu)$_2$Me, PPh$_3$, P(*o*-tol)$_3$, XPhos, *N*-heterocyclic carbenes (NHC), thioureas, chiral diamines, phosphites, *H*-phosphonates,	64–70, 73, 75–78, 84, 88, 90–95, 97–100, 143–149

Table 1 (*continued*)

Silane	R^2–X	Reaction conditions	Ref.
R^1 = Aryl, Alkenyl, Heteroaryl		bisphosphines, hydrazones, β-diimines, DABCO, imidazolium chloride, N-Methyl-2-(2′- Dicyclohexylphosphinophenyl)indole (CM-phos), Iminoproazaphosphatrane-based ligands of the type R_2PN = $P(i\text{-}BuNCH_2CH_2)_3N$ (R = Ph, ^{i}Pr, ^{t}Bu) Additive: $InCl_3$, PEG-600, Acetic acid Solvent: THF, Toluene, Dioxane, *o*-Xylene, *p*-Xylene, ^{t}BuOH, DCM, DMF, MeCN Temp.: 0–90 °C OR Activator: NaOH Catalyst: $Pd(OAc)_2$, Pd nanoparticles, Pincer Pd complex, Palladacycle, $Pd(NH_3)_2Cl_2$, $[PdCl_2L_2]$ complexes, Pd-phosphinous acid, β-diketiminatophosphane palladium catalyst **20** Ligand: cationic bipyridyl ligands, crown-ether triarylphosphanes Additive: TBAB, PEG-2000, $InCl_3$ Solvent: H_2O, DMSO Temp.: 0–140 °C	71, 72, 78–83, 85, 87, 89, 96, 150
(5) Silanols  R = Alkyl (Me, Et, ^{i}Pr), Aryl R^1 = Aryl, Alkenyl, Alkynyl, Heteroaryl, Cyclopropyl	R^2 = Aryl, Alkenyl, Heteroaryl X = Br, I	Activator: Ag_2O, TBAF Catalyst: $Pd(PPh_3)_4$, $Pd(dba)_2$, $[allylPdCl]_2$ Additive: $BF_3(OEt)_2$ (for cyclopropyl silanols) Solvent: THF Temp.: rt −100 °C OR Activator: $KOSiMe_3$, Cs_2CO_3, NaO^{t}Bu, CsOH, NaH, NaHMDS Catalyst: $Pd(dba)_2$, [allylPdCl], $PdCl_2(PPh_3)_2$, $PdCl_2$, $[Pd_2(dba)_3]\cdot CHCl_3$ Ligand: Ph_3As, 1,4-bis(diphenylphosphino)butane (dppb) Additive: H_2O, CuI Solvent: DME, toluene, dioxane Temp.: rt −90 °C	102, 105–110, 151 29, 30, 32, 111–116
(6) Silonalates  M = Na, K, Cs R^1 = Alkenyl, Aryl, Allyl, Heteroaryl	R^2 = Aryl, Alkenyl X = Br, Cl	Activator (if formed *in situ*): NaH, NaHMDS, NaO^{t}Bu Catalyst: [allylPdCl], $Pd(dba)_2$, $Pd_2(dba)_3\cdot CHCl_3$ Ligands including: $Ph_3P(O)$, norbornadiene (nbd) Additive: CuI Solvent: THF, Dioxane, Toluene, DME Temp.: r.t. −90 °C	30, 119–123, 152
(7) Cyclic siloxanes	R^2 = Aryl X = I, Br	For R^1 = R^3 = Aryl Activator: TBAF Catalyst: $Pd(dba)_2$, $PdBr_2$ Ligand: $^t Bu_2$(biphenyl)P, Solvent: THF Temp.: r.t. −70 °C OR	128, 135, 153, 154

Table 1 (*continued*)

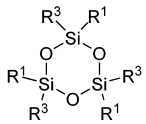
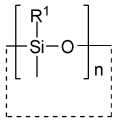
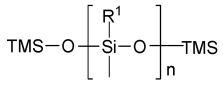
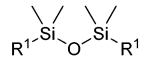
Silane	R^2–X	Reaction conditions	Ref.
For example:  $R^1 = R^3$ = Aryl R^1 = CH=CH_2 and R^3 = Me		Activator: $KOSiMe_3$ Catalyst: $Pd(dba)_2$ Ligand: $AsPh_3$ Solvent: DMF Temp.: r.t. For R^1 = CH = CH_2 and R^3 = Me Activator: KOH Catalyst: $Pd(OAc)_2$ Solvent: dioxane-H_2O (1 : 1), H_2O Temp: Reflux	136
(8) Silicone A:  B:  A: R^1 = Aryl, Alkenyl *n* = 3, 4 (for cyclic silicone species) B: R^1 = Ph *n* = 1, 2, 6, 20	R^2 = Aryl, X = I, Cl	Activator: TBAF, TBAF/H_2O Catalyst: $[Pd_2(dba)_3]\cdot CHCl_3$, $PdCl_2(PCy_3)_2$, $Pd(PPh_3)_4$ Additive: H_2O (for X = Cl) Solvent: THF Temp.: 60 °C OR Activator: Ag_2O, Cs_2CO_3, K_2CO_3, K_2CO_3-H_2O(for X = Cl), NaOH Catalyst: $Pd(dba)_2$, $Pd(PPh_3)_4$, $PdCl_2(PCy_3)_2$ Ligand: $AsPh_3$ Additive: H_2O (for X = Cl) Solvent: DMF, THF, 1,4-dioxane, toluene Temp.: r.t. −120 °C	155–157 156, 157
(9) Disiloxanes  R^1 = Aryl, Alkenyl	R^2 = Aryl X = Br, I	Activator: TBAF Catalyst: $Pd(dba)_2$, $Pd_2(dba)_3$ Solvent: THF, Dioxane Temp.: r.t. −80 °C OR Activator: KOH, $KOSiMe_3$. Catalyst: $Pd(dba)_2$ Ligand: P(*o*-tolyl)$_3$, X-Phos Solvent: MeOH, DMF Temp.: r.t. −70 °C	97, 98, 110, 128–130, 158, 159 113, 129

Table 1 (*continued*)

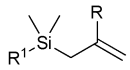
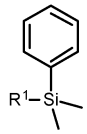
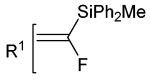
Silane	R^2–X	Reaction conditions	Ref.
(10) Silacyclobutanes  R = Me, Cl R^1 = Aryl, Alkenyl	R^2 = Aryl, Alkenyl X = Br, I	Activator: TBAF Catalyst: [allylPdCl], $Pd(dba)_2$ Ligand: $P(^tBu)_3$, $AsPh_3$ Solvent: THF Temp.: r.t. −60 °C	36, 101–104
(11) Allyldimethylsilane  R = H, Me R^1 = Alkenyl, 2-pyridyl	R^2 = Aryl X = I	For R^1 = alkenyl: Activator: TBAF Catalyst: $Pd_2(dba)_3$, $[allylPdCl]_2$ Solvent: THF/EtOH Temp.: r.t. For R^1 = 2-pyridyl: Activator: Ag_2O Catalyst: $Pd(PPh_3)_4$ Solvent: THF Temp.: 60 °C	160 161
(12) Phenyldimethylsilane  R^1 = Alkenyl	R^2 = Aryl X = I	Activator: ^tBuOK/TBAF Catalyst: $Pd_2(dba)_3$ Additive: 18-crown-6 Solvent: THF Temp.: r.t. OR Activator: None Catalyst: $Pd(OAc)_2$ Ligand: dppb Additive: NEt_3 Solvent: CH_3CN Temp.: 80 °C	127, 162 163
(13) Diphenylmethylsilane 	R^2 = Aryl X = I, Br, OTf	Activator: CsF. Catalyst: $Pd(PPh_3)_4$ Additive: CuI, $^nBu_4NI$ (for OTf only) Solvent: DMI/THF Temp.: r.t. −50 °C	140, 164

Table 1 (*continued*)

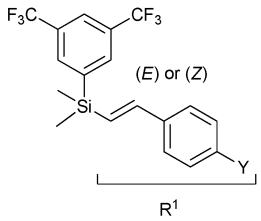
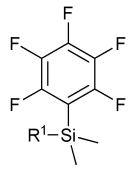
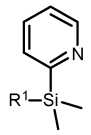
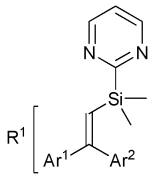
Silane	R^2–X	Reaction conditions	Ref.
(14) bis(3,5-trifluoromethylphenyl) dimethylsilane  Y = H, Br	R^2 = Aryl X = I	Activator: TBAF Catalyst: [Pd(η^3-allyl)(μ-Cl)] Solvent: THF Temp.: r.t.	165, 166
(15) Pentafluorophenyldimethylsilane  R^1 = Alkenyl	R^2 = Aryl X = I	Activator: TBAF Catalyst: $Pd(dba)_2$ Solvent: THF Temp.: r.t. OR Activator: KOH Catalyst: $Pd(dba)_2$ Solvent: MeOH Temp.: r.t.	127, 162, 165, 167
(16) Pyridyldimethylsilane  R^1 = Alkenyl	R^2 = Aryl, Alkenyl X = I, Br	Activator: TBAF Catalyst: $(PhCN)_2PdCl_2$ Solvent: THF Temp.: 0–60 °C	168–171
(17) Pyrimidinyldimethylsilane 	R^2 = Aryl X = I	Activator: *n*-Bu_4NI Catalyst: $PdCl_2(PhCN)_2$ Solvent: THF Temp.: 40–60 °C	171

Table 1 (*continued*)

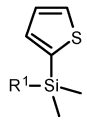
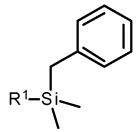
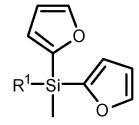
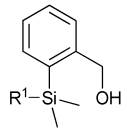
Silane	R^2–X	Reaction conditions	Ref.
(18) Thienyldimethylsilane  R^1 = Alkenyl	R^2 = Aryl X = I	Activator: TBAF Catalyst: $Pd(dba)_2$ Solvent: THF Temp.: r.t.	124, 172–175
(19) Benzyldimethylsilane  R^1 = Alkenyl	R^2 = Aryl X = I	Activator: TBAF Catalyst: $[Pd_2(dba)_3]\cdot CHCl_3$ Solvent: THF Temp.: r.t. −50 °C	124, 176–179
(20) Difurylmethylsilane  R^1 = Ph	R^2 = Aryl X = Br	Activator: TBAF Catalyst: $PdCl_2(dppf)$ Solvent: Dioxane/H_2O Temp.: 90 °C	180
(21) (2-hydroxymethyl)phenyl-dimethylsilane  R^1 = Alkenyl, aryl	R^2 = Aryl, Heteroaryl X = I, imidazol-1-ylsulfates	Activator: K_2CO_3 Catalyst: $PdCl_2$, $Pd(dppf)Cl_2$ Ligand: $(2\text{-furyl})_3P$ Additive: CuI Solvent: DMSO Temp.: 35–50 °C	48–50, 181, 182

Table 1 (*continued*)

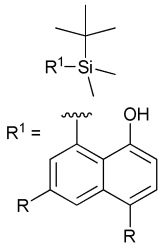
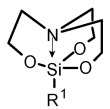
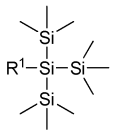
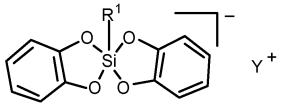
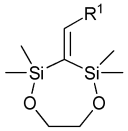
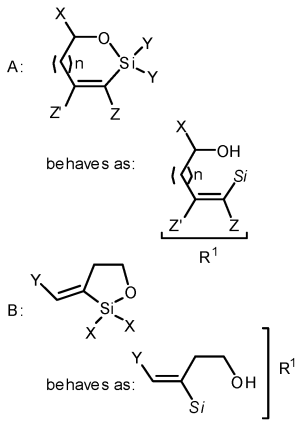
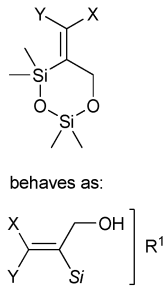
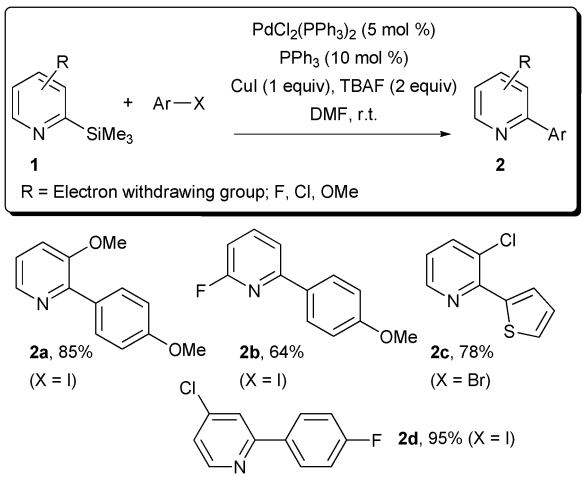
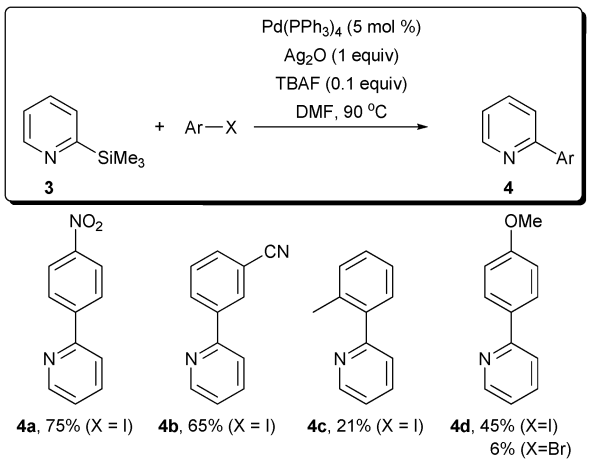
Silane	R^2–X	Reaction conditions	Ref.
(22) ^{t}Butyldimethylsilane  R = Alkyl	R^2 = Aryl X = I	Activator: Cs_2CO_3 Catalyst: $[(allyl)PdCl]_2$ Ligand: $AsPh_3$ Solvent: DME Temp.: 60 °C	183
(23) Silatranes  R^1 = aryl, 2-subsituted 1,3-butadiene	R^2 = Aryl X = I, Br, OTf	For R^1 = aryl (X = I, Br, OTf): Activator: TBAF Catalyst: $Pd(OAc)_2$, $Pd(dba)_2$ Ligand: PPh_3, $(Cy)_2P$(*o*-biphenyl) Solvent: THF Temp.: reflux For R^1 = 2-substituted 1,3-butadiene (X = I): Activator: TBAF Catalyst: $Pd(OAc)_2$ Ligand: PPh_3 Solvent: DMF/THF Temp: 90 °C	137–139
(24) Tris(trimethylsilyl)silanes  R^1 = Alkenyl	R^2 = Aryl, Heteroaryl, Alkenyl X = I, Br	Activator: H_2O_2/NaOH, TBAF Catalyst: $Pd(Ph_3)_4$ Solvent: THF Temp.: 55 °C	184, 185
(25) Bis(catecholato)silicates  R_1 = Alkenyl, Aryl; Y = $NHEt_3^+$, K^+ (for R^1 = 2-subsituted diene and X = I)	R^2 = Aryl (Ph only for Y = K^+) X = I, Br, OTf	For Y^+ = $NHEt_3^+$: Activator: Not required or TBAF Catalyst: $Pd(dba)_2$, $[allylPdCl]_2$ Ligand: Not required Solvent: THF Temp.: r.t. −153 °C For Y^+ = K^+: Activator: KF Catalyst: $[allylPdCl]_2$ Ligand: S-Phos Solvent: DMF Temp. Reflux	138, 186, 187 138

Table 1 (*continued*)

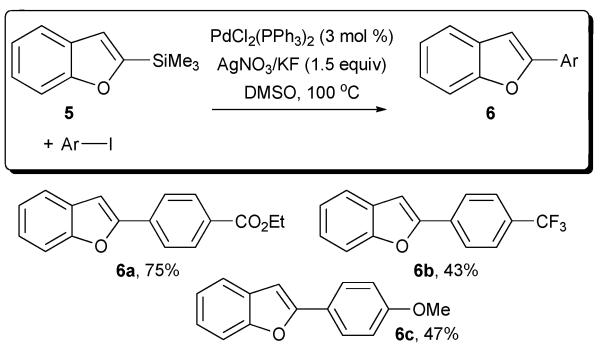
Silane	R^2–X	Reaction conditions	Ref.
(26) Cyclic 1,1-bis(silyl)alkenes  R^1 = H, Aryl	R^2 = Aryl, Vinyl X = I	Activator: TBAF Catalyst: $Pd_2(dba)_3$, $[allylPdCl_2]$ Solvent: THF Temp.: 65 °C	132, 188
(27) Cycloalkenylsiloxanes  A: X = Ph; Y = Me; Z = H, C_6H_{13}; Z' = H, Me B: X = ^{i}Pr, Me; Y = Me, *n*-Bu, CHO	R^2 = Aryl, vinyl X = I (aryl), Br (vinyl)	Activator: TBAF, KF/H_2O (for aldehyde coupling) Catalyst: $Pd(dba)_2$ (aryl coupling), $[allylPdCl]_2$ (vinyl coupling) Additive: None, CuI (for aldehyde coupling) Solvent: THF, DMF (for aldehyde coupling) Temp.: r.t. –45 °C	133, 189–192
(28) Cycloalkenyldisiloxanes  X = Me and Y = H or X = H and Y = Me	R^2 = Aryl X = I	Activator: TBAF Catalyst: $Pd(dba)_2$ Solvent: Dioxane Temp.: r.t. –40 °C	134



Scheme 2 Cross-coupling of substituted pyridyltrimethylsilanes.

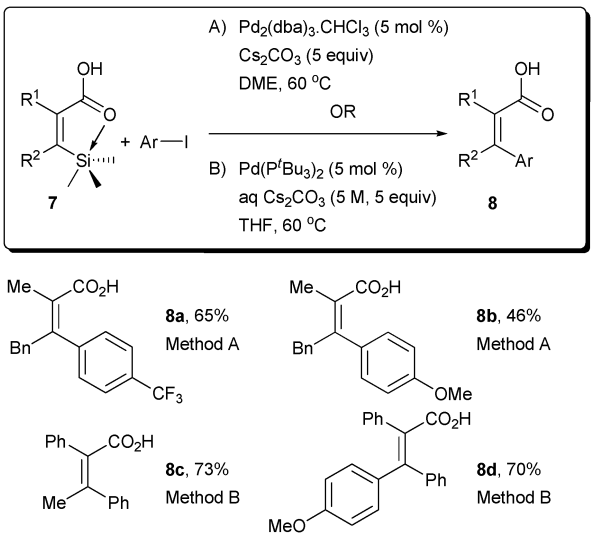


Scheme 3 Cross-coupling of unsubstituted pyridyltrimethylsilane.



Scheme 4 Cross-coupling of 2-trimethylsilylbenzofuran.

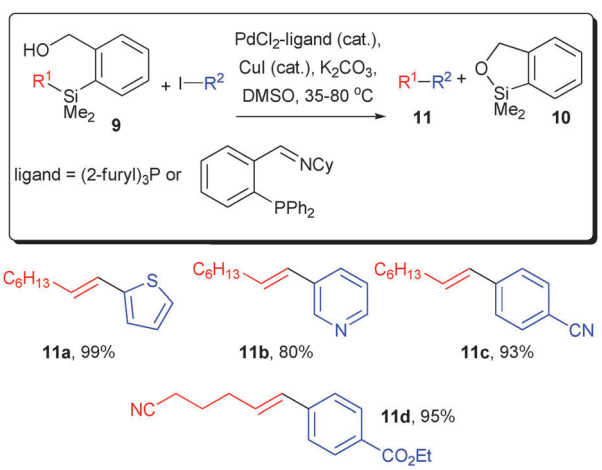
that one of the groups present in the products (*i.e.* a transferable group on the silicon) is always the oxygen-based activating functionality.[47] Hiyama *et al.* have introduced alkenyl- and aryl [2-(hydroxymethyl)phenyl]dimethylsilanes **9**; these stable tetraorganosilicon reagents possess an activating hydroxyl group which is independent of the transferable group on the silicon, allowing a diversity of groups on the silicon atom.[47] These silanes have been shown to couple with a broad range of aryl and alkenyl iodides in the presence of K_2CO_3 and Cu(I)I without any



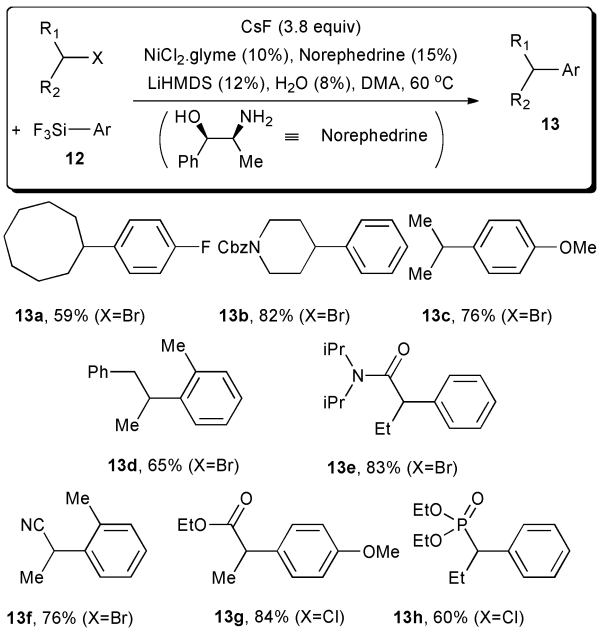
Scheme 5 Cross-coupling of (*Z*)-β-(trimethylsilyl)acrylic acids.

fluoride activators. The residual silicon species **10** is readily removed and resusable (Scheme 6).[47–50] Akai *et al.* have subsequently described fluoride free coupling reactions where a TBDMS group was substituted with an aryl group through intramolecular activation from a phenolic hydroxy group.[51]

The introduction of halogens on the silyl group of alkenylsilanes accelerated the fluoride-activated cross-coupling;[52] however, halosilanes have not seen widespread application despite their thermal stability possibly because of their hydrolytic sensitivity and difficulty in handling. Early research focused on expanding the scope of the fluoride-induced coupling of halosilanes to include; reactions with aryl halides and triflates,[52–54] development of solid supported synthesis[55,56] and employment of alkenyl, alkynyl and aryl halosilanes (see Table 1, silane 3).[52–54,57] Particular attention was also paid to understanding the mechanism in order to control the extent of isomerisation of the double bond observed when coupling alkenylhalosilanes.[37,58] The sensitivity to water was successfully exploited by Huang and Li for the development of base induced aryl-aryl coupling conditions in air and water.[59] A selection of aryl iodides and bromides were



Scheme 6 1 alkenyl- and aryl [2-(hydroxymethyl)phenyl]dimethylsilanes **9** have been employed in fluoride free cross-couplings.



Scheme 7 Cross-coupling of activated and unactivated secondary alkyl halides with arylhalosilanes.

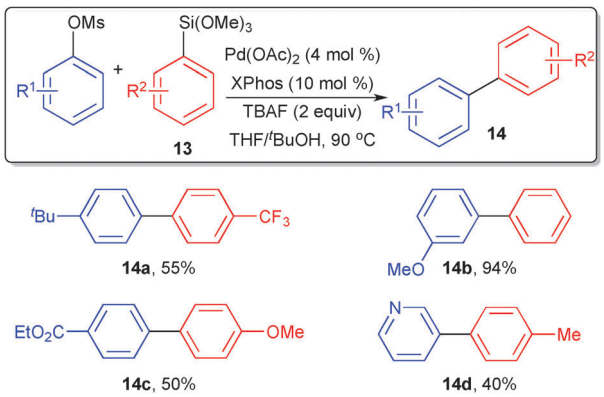
coupled with arylhalosilanes to produce the unsymmetrical biaryls in good to moderate yields.[59]

A recent report by Fu *et al.* described the coupling of activated and unactivated secondary alkyl halides with aryl fluorosilanes **12** by nickel/amino alcohol based catalysts (Scheme 7, unactivated and activated alkyl halides **13a–13d** and **13e–13h** respectively).[60] The addition of alkyl halides to the list of viable electrophilic partners for the coupling reaction offers a significant advance in the scope of the Hiyama reaction by expanding upon the nature of the substrates available.[60]

To increase the stability of the organosilyl species to moisture, acid and base, Hiyama *et al.* developed triallylsilanes as all-carbon-substituted silanes that readily cleave on the addition of a fluoride source (see Table 1, silane 2).[61,62] Aryltriallylsilanes were found to be an efficient coupling partner in the Hiyama reaction with a wide range of aryl/heteroaryl bromides[61,62] and chlorides.[61] Further research into differentially substituted triallylsilanes, expansion of the substrate scope and fluoride free coupling conditions would promote further use and applications of triallylsilanes.

2.2 Oxysilanes

Tamao was the first to develop the more robust and stable mono-, di-, or trialkoxysilanes as effective organonucleophiles in fluoride-promoted cross-coupling (see Table 1, silane 4).[63] Extensive research in the formative years enabled the development of milder and more efficient fluoride induced cross-coupling conditions; these were increasingly tolerant to a diverse range of alkoxysilanes including those containing sensitive functional groups.[64–70] The next notable advance was the development of alternative methods to active the oxysilane; to alleviate the requirement for the corrosive fluoride anions. 'Fluoride-free' approaches permit the use of silicon protecting groups common



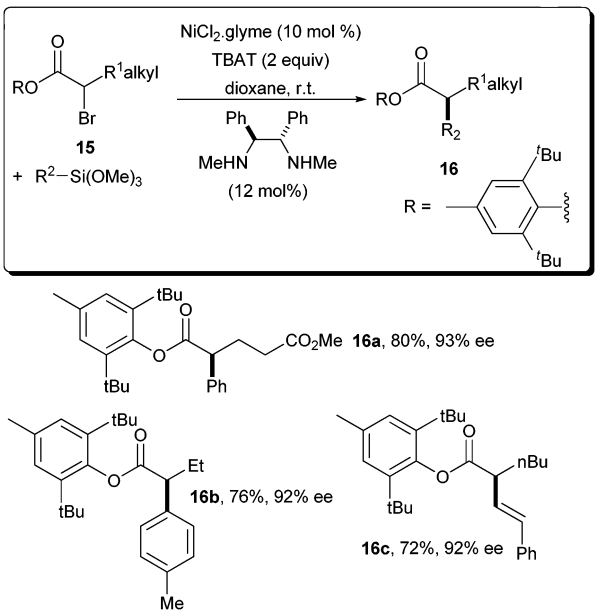
Scheme 8 Cross-coupling of aryl mesylates with aryl silanes.

in natural product synthesis and are more compatible with industrial processes.[71,72]

Research has focused over the past few years on expanding the scope of the coupling reaction with alkoxysilanes to include reactions with aryl chlorides, bromide, triflates and mesylates as the organoelectrophile.[73] The use of triflates and mesylates is an important advance as it allows access to a broader substrate scope by the derivatisation of substituted phenols. A report by Zhang *et al.* describes an efficient and general method to synthesise biaryls *via* a Hiyama coupling reaction between aryl tosylates and arylsilanes.[74] In a similar approach the first Hiyama cross-coupling with aryl mesylates was later reported by Zhang *et al.* (Scheme 8).[75] The trialkoxyaryl silanes **13** used were tolerant to a wide substrate scope including the presence of electron donating and electron withdrawing groups; additionally, those containing an *ortho*-substituent also produced the biaryls **14** in a good yield.[75] The electronic nature of the mesylate had a moderate effect on the biaryl formation, with electron donating groups leading to higher yields; however, the *ortho*-substituted 2-methylphenyl mesylate only yielded trace amounts of the coupled product.[75]

The first asymmetric Hiyama coupling of racemic α-bromo esters **15** to form derivatives of the general form **16** was reported recently by Fu and co-workers (Scheme 9).[67,76] The use of the sterically demanding ester (2,6-di-*tert*-butyl-4-methylphenol–BHT), TBAT ($[F_2SiPh_3]^-[NBu_4]^+$) as the fluoride source, the silane as well as the chiral ligand itself all significantly influenced the enantioselectivity and efficiency of the reaction. The yields obtained range between 64–84% with ee's of 75–99% for the 17 examples disclosed.[76]

A number of palladium catalysts have been developed and subsequently employed in the Hiyama reaction with the added advantage of lowering the catalyst loadings, recovery and recycling of the catalyst and creation of milder reaction conditions. These benefits have been achieved by a careful balance between maintaining the catalyst stability whilst increasing the reactivity. As a result excellent yields for the coupled products were generally obtained with a wide range of substrates.[71,77] For example the pincer-type palladium catalyst was employed in neat water under both fluoride and base induced conditions (Fig. 1, **17**),[78] the reactions with oxime-derived palladacycles were carried out in aqueous sodium hydroxide under ligand-free conditions (Fig. 1, **18** & **19**)[79–81] and palladium nanoparticles were reacted under



Scheme 9 Examples of the asymmetric synthesis of α-substituted esters.

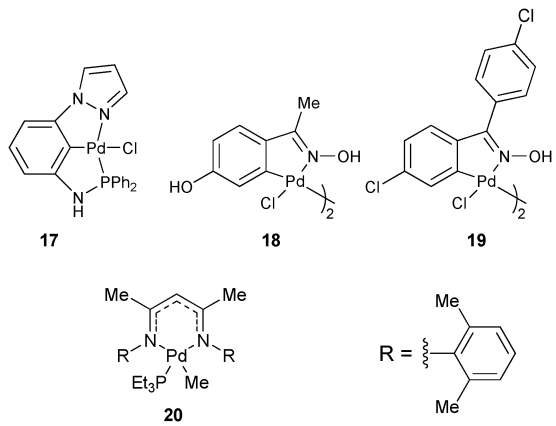
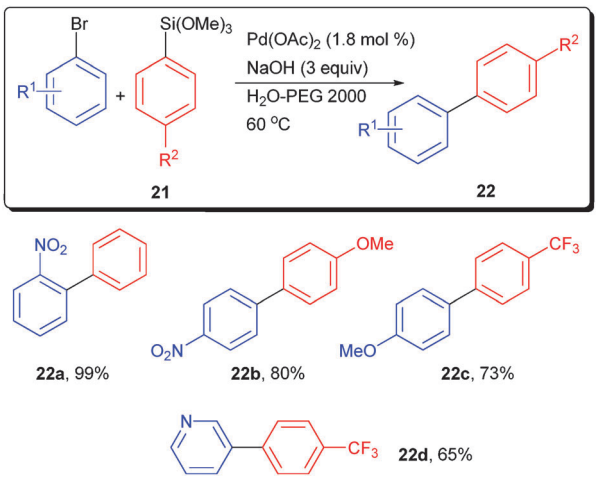


Fig. 1 Some palladium catalysts used for the coupling of siloxanes.

aqueous fluoride-free conditions or fluoride induced conditions with benzyl halides.[82–84] Palladium nanoparticles have been generated *in situ* from Na_2PdCl_4/sodium dodecyl sulfate[82] or formed using K_2PdCl_4 and a Fischer carbene complex as the reductant with PEG as the capping agent.[83] Similarly, complexes of the formula $[PdCl_2L_2]$, where L was a crown-ether containing triarylphosphane ligand were found to effectively cross-couple arylsiloxanes with a wide range of heterocyclic and aryl bromides in water under air.[85] Lee *et al.* have recently reported a novel β-diketiminatophosphane palladium catalyst **20** which was found to be highly effective in the mono and double Hiyama coupling reactions of unactivated aryl chlorides with aryltriethoxysilanes in water.[86]

Mild reaction conditions were developed by Shi and Zhang for the $Pd(OAc)_2$-catalysed coupling of *para*-substituted arylsiloxanes **21** with a range of aryl bromides promoted by base in a H_2O-PEG medium (Scheme 10).[87] The electronic nature and substitution of the aryl bromide did not affect the reaction outcome as yields of the biaryl products **22** obtained range from 60–99% for the 36 reactions highlighted.[87]



Scheme 10 Mild arylsiloxane-aryl bromide cross-coupling conditions.

Alternative ligands have also been explored which are air- and moisture stable and facilitate the generation of catalyst-recyclable systems. For example, the cyclic thiourea ligands are easily recovered by column chromatography[88] and cationic bipyridyl ligands assist by transporting the palladium(II) complex into the aqueous phase (Fig. 2, ligands **23** & **24** respectively).[89] Phosphite ligands were effectively used with TBAF as the additive to cross-couple electron deficient aryl bromides and chlorides as well as electron rich aryl bromides to form the biaryl products in good yields; however, *ortho*-substituents were not well tolerated (Fig. 2, **25**).[90] Similarly, the use of an *H*-phosphonate ligand facilitated the cross-coupling of aryl chlorides forming the 8 biaryls reported in yields ranging from 60–79% (Fig. 2, **26**).[91] A screen of phosphine ligands revealed that the bisphosphine ligand, ^{i}Pr-DPEphos (Fig. 2, **27**) gave the highest product yields when aryl bromides and chlorides were reacted under fluoride conditions.[92] The phosphine-free hydrazone ligand was also successfully employed in the fluoride induced coupling of aryl bromides with arylsiloxanes (Fig. 2, **28**).[93] Modification of the reaction conditions has led to improvements in the yield and efficiency of the Hiyama cross-coupling reaction.[94,95]

The success of coupling alkoxysilanes rapidly led onto the development of methodologies where the Hiyama reaction was

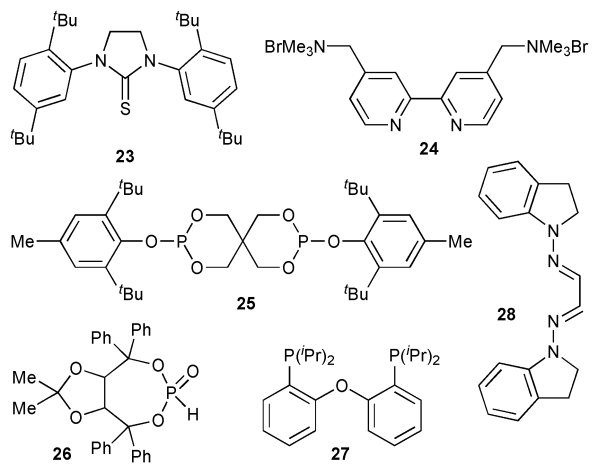
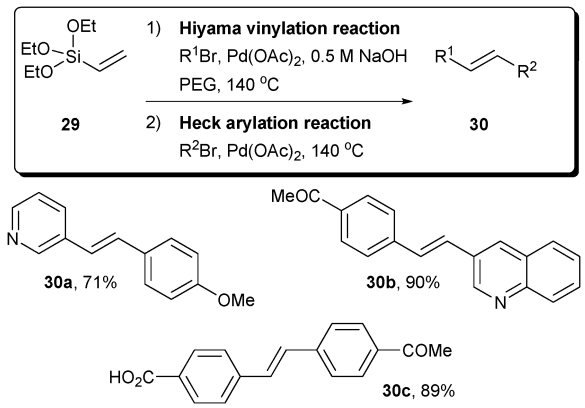


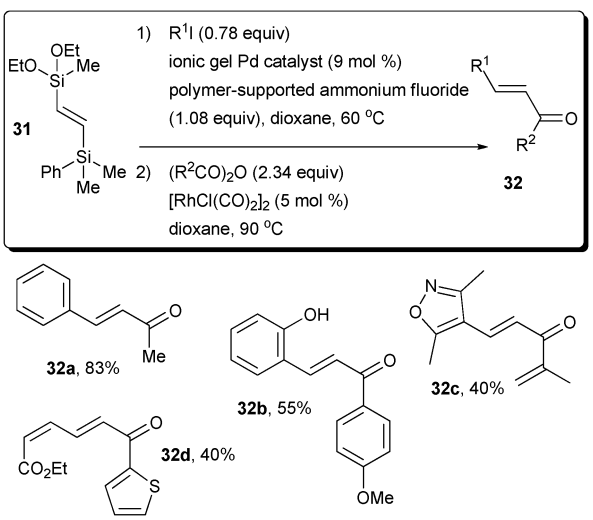
Fig. 2 Some ligands used in the coupling of siloxanes.



Scheme 11 Examples of products generated by a one-pot Hiyama-Heck reaction.

telescoped with other reactions to generate interesting and challenging scaffolds. Gordillo *et al*. recently reported the synthesis of unsymmetric (*E*)-1,2-diarylethenes by a consecutive one-pot Hiyama vinylation-Heck arylation reaction involving vinyl silanes **29** (Scheme 11).[96] Generally excellent selectivity and high yields were obtained for the unsymmetrical (*E*)-stilbenes **30**; only trace amounts of the symmetrical (*E*)-stilbene and/or 1,1-diarylethene were observed.[96] In an alternative approach Marciniec *et al*. synthesised derivatives of (*E*)-1,2-diarylethenes *via* a tandem cross-metathesis and Hiyama coupling.[97–99]

The versatile synthesis of α,β-unsaturated carbonyl motifs **32** was successfully accomplished by a sequential Hiyama/Narasaka acylation process starting with (*E*)-1,2-disilylethene **31** (Scheme 12).[100] The innate reactivity of the differentially substituted silyl groups was utilised to effectively react each group in a chemoselective manner. The use of a polymer-supported fluoride source for the Hiyama reaction followed by filtration was crucial in order to achieve good yields for the subsequent Narasaka acylation reaction. A diverse selection of α,β-unsaturated ketones were synthesised in yields ranging from 40–87% for the sequential two step procedure.[100]



Scheme 12 Synthesis of α,β-unsaturated ketones by a sequential Hiyama/Narasaka acylation process.

2.3 Silacyclobutanes

After the initial research into trialkylsilane, halosilane and oxysilanes, the heteroatom surrogate, silacyclobutanes (otherwise known as siletanes), were designed to have better chemical stability and enhanced reactivity (see Table 1, silane 11).[101] Vinylsiletanes cross-coupled with aryl halides with retention of stereochemistry and in good yields under standard fluoride conditions; ligandless palladium catalysts were superior and the selection of TBAF as the fluoride source was essential.[101] During the study of siletanes Denmark made the significant discovery that the four-membered siletane rapidly ring opened under the reaction conditions to reveal the corresponding silanol and disiloxane.[102] Subsequently, silanol and disiloxane analogues were synthesised and both were found to be effective partners in cross-coupling with TBAF·$3H_2O$, reacting *via* the pentacoordinate silicon intermediate.[102–104]

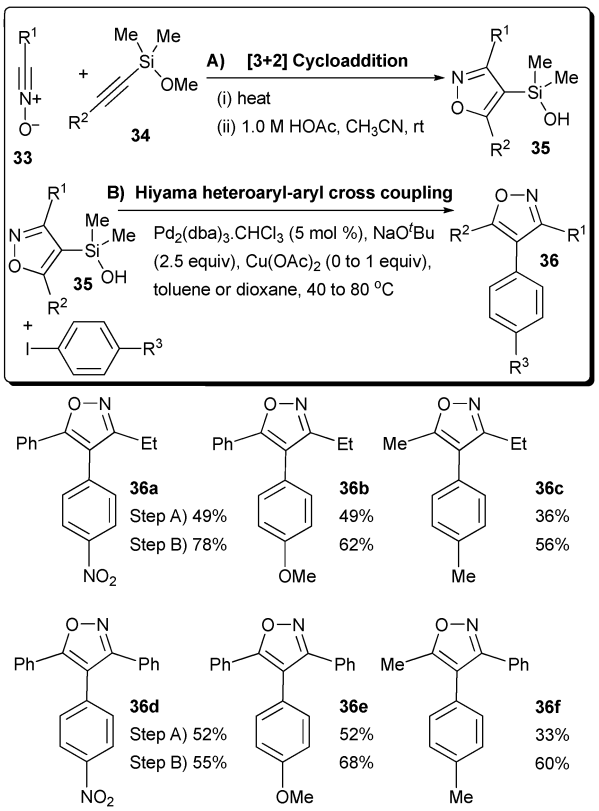
3. The development of organosilanols and its analogues as cross-coupling partners

3.1. Organosilanols

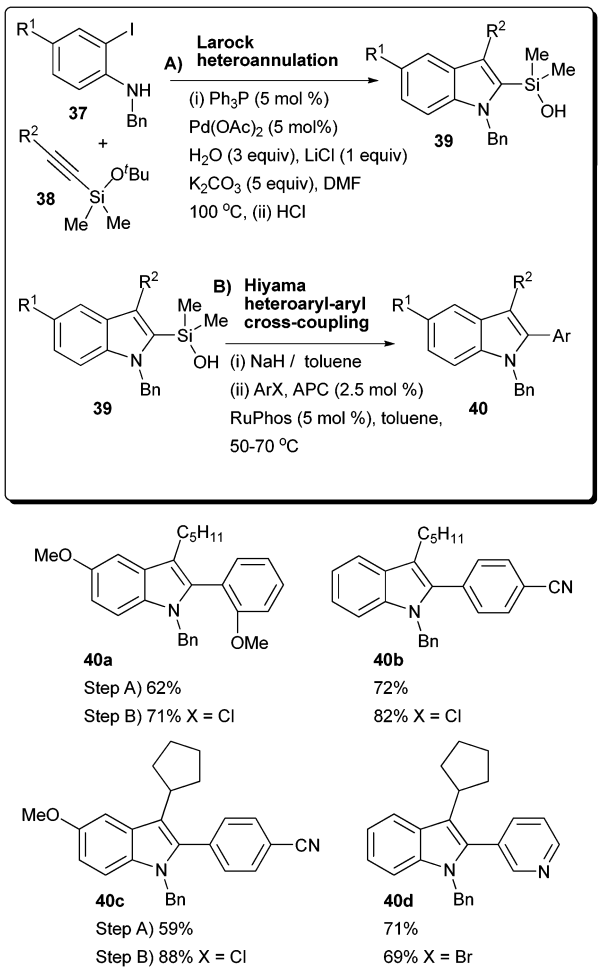
Building on the discoveries made during the research into silacyclobutanes, Denmark and Hiyama were fundamental in evolving silanols into effective organosilicon cross-coupling partners (see Table 1, silane 5). Initially alkenyl and aryl silanols were activated for cross-coupling with alkenyl or aryl halides under fluoride[102,105–107] or silver oxide[108,109] conditions.[110] To increase the scope and utility of the Hiyama cross-coupling further, investigations led onto the search for alternative methods of activation. The use of TBAF activation is incompatible for large scale synthesis and with silicon protecting groups commonly used in multi-step synthesis, it is also costly and can be problematic to handle.[111]

The significant breakthrough came with the discovery by Denmark *et al*. that vinylsilanols could be activated by base as a substitute for the conventional TBAF nucleophile, to promote the efficient 'fluoride free' palladium catalysed coupling of organosilanols.[111] The introduction of heteroatoms on the silicon species was critical to the success of the fluoride free cross-coupling reaction. The base induced cross-coupling of organosilanols has grown in scope to include the coupling of substituted and unsubstituted alkenyl,[111] aryl,[112,113] alkynyl[114] and heteroaryl[115,116] silanols with alkenyl, aryl and heteroaryl iodides and bromides. The metal silanolate is the active species in the cross-coupling and can be successfully generated using a number of bases, including; NaO^{t}Bu, NaH, Cs_2CO_3, KOTMS and K_3PO_4.[29,32] The cross-coupling of organosilanols typically occurs under mild conditions, for example, a base, $Pd(dba)_2$ or [allylPdCl_2] as the catalyst at room temperature, to obtain the products in good yields generally with retention of stereochemistry.[29,30]

The synthesis of heterocyclic silanols followed by their sequential cross-coupling has successfully led to the generation of numerous interesting substituted heterocycles. A series of 3,4,5-trisubstituted isoxazoles were synthesised *via* a sequential [3 + 2] cycloaddition and Hiyama cross-coupling.[117] The ethyl or phenyl nitrile oxides **33** required for the cycloaddition were generated *in situ* from 1-nitropropane and phenyl isocyanate



Scheme 13 Sequential [3 + 2] cycloaddition and Hiyama heteroaryl-aryl cross-coupling to synthesis 3,4,5-trisubstituted isoxazoles.



Scheme 14 Sequential Larock heteroannulation and Hiyama coupling.

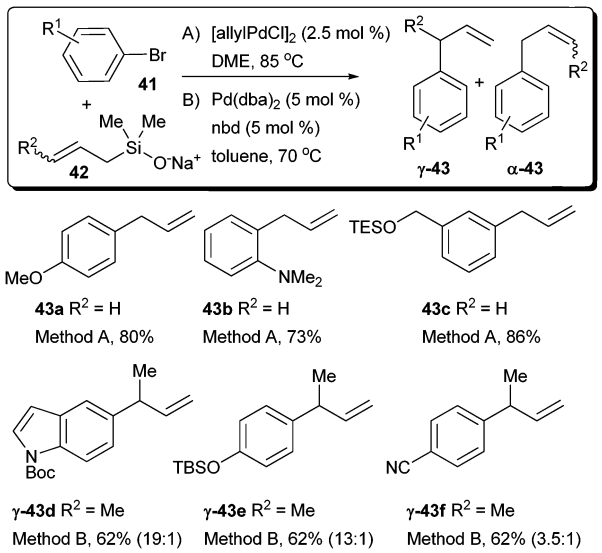
or chlorooxime and $KHCO_3$ respectively. The [3 + 2] cycloaddition between ethyl or phenyl nitrile oxides **33** and a silicon-substituted dipolarophile **34** occurred with reasonable regioselectivity to furnish derivatives **35**. The sequental Hiyama cross-coupling provided heterocyclic products **36** in yields ranging from 52–78%; however, sterically encumbered systems proved difficult to couple producing high proportions of protodesilylation by-products (Scheme 13).[117] Expanding upon this concept the successive Larock heteroannulation between anilines **37** and alkynyl silanes **38** and cross-coupling of the resulting indoles **39** produced 2,3-disubstituted indoles **40** in overall yields ranging from 44–63% (Scheme 14).[118]

Recent investigations by Denmark *et al*. have identified that the direct use of the silanolate can be advantageous in the palladium catalysed cross-coupling even though the formation of the silanolate constitutes an additional step (see Table 1, silane **6**).[30,119] Silanolates avoid the use of an activator, either base or fluoride, in the reaction mixture, therefore limiting the possibility of isomerisation of alkenyl silicon reagents, reducing the likehood of disiloxane formation and allowing the use of base sensitive substrates in the organic electrophile.[30,119] A wide range of nucleophilic substrates undergo efficient cross-coupling including alkenyl-,[120] allyllic-,[121] aryl-[30,119,122] and heteroaryl silanolates[30,119,123] with aryl chlorides, bromides and iodides.

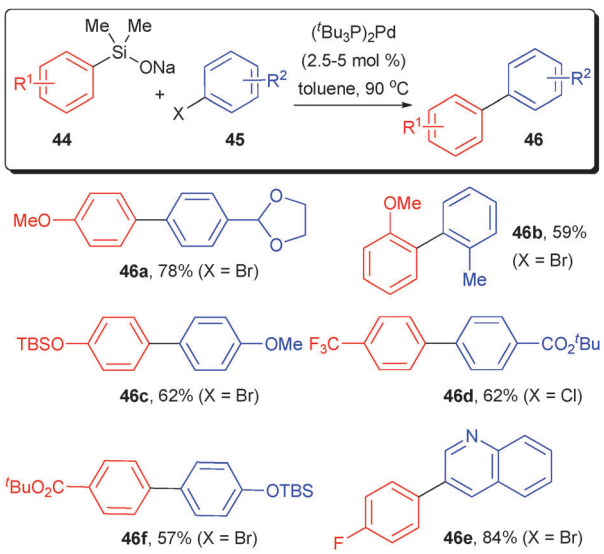
The allylation of electron rich and neutral substituted aryl bromides **41** with silanolates **42** to furnish compounds of the general form **43** proceeded smoothly in yields ranging from 71–95% (Scheme 15).[121] The desired product resulting from the allylation of electron deficient systems rapidly isomerised and underwent polymerisation, limiting the scope of the reaction to some extent.[121] After extensive optimisation the cross-coupling of electron rich and electron deficient aryl bromides with 2-butenyldimethylsilanolate (*E*/*Z* 80 : 20) proceeded in moderate yields and good selectivity for the γ-isomer.[121] Those bromides containing α-substituted coordinating groups resulted in lower yields and selectivity for the desired product.[121]

The cross-coupling of a wide range of aryl silanolates **44** (Scheme 16) and five-membered heterocyclic silanolates **47** (Scheme 17) with aromatic iodides, bromides and chlorides containing functional groups such as esters, ketones and silyl ethers **45** to furnish derivatives of the general form **46** and **48** respectively has recently been reported by Denmark *et al*.[119,123] In the cross-coupling reactions the isolated silanolate salt was used directly or was preformed *in situ*. The reactions typically proceed in high yields; however, lower yields were obtained with more sterically challenging substrates (yields range between 34–99%).[119,123]

Silanolates with nitrogen containing five-memberd ring heterocycles were significantly affected by the electronic nature of group attached to the nitrogen with electron withdrawing groups (such as Boc) reducing the reactivity.[123] A standard protocol was developed for the cross-coupling of aryl silanolates;



Scheme 15 Cross-coupling of allylic silanolate salts. nbd = norbornadiene.

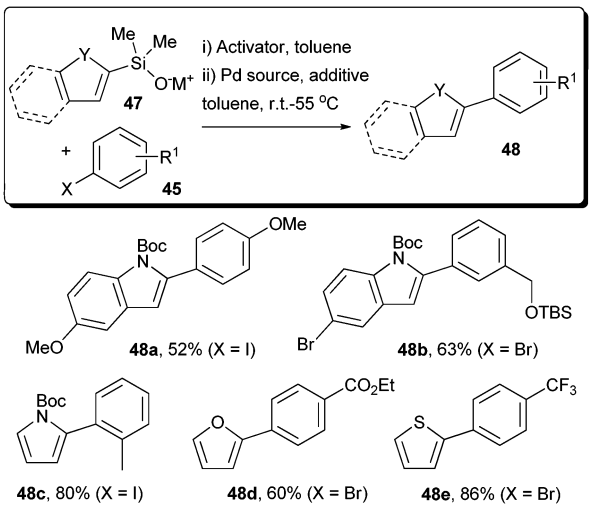


Scheme 16 Cross-coupling of aryl silanolates.

however, a separate protocol is needed for each heteroaromatic silanolate because of the variations in reactivity.[119,123]

3.2. 'Masked' silanols

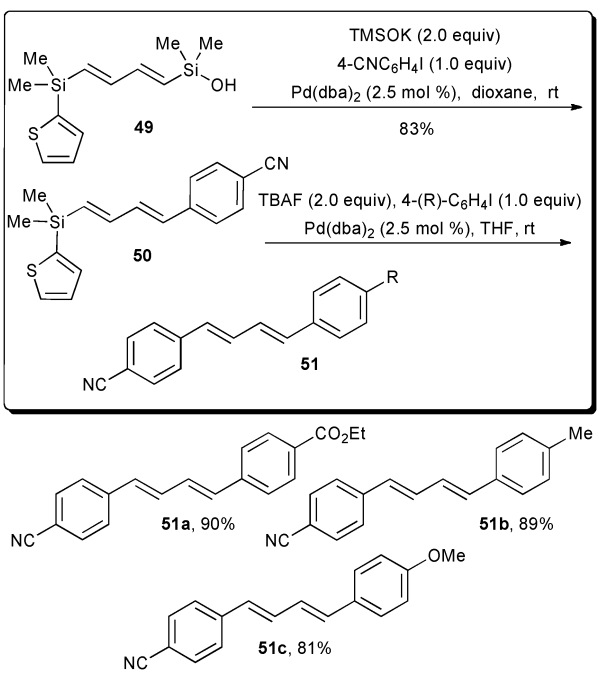
Siletanes, phenyl-, 2-pyridyl, 2-thienyl- and benzylsilanes were all established as viable organosilicon nucleophiles, which under appropriate hydrated fluoride reaction conditions unmasked to reveal the active silanol; consequently, these reagents were dubbed 'safety-catch' silanols or 'masked'silanols. Table 1 summarises these and various other 'masked' silanols, their scope and typical reaction conditions used in Hiyama coupling. 'Masked' silanols have the advantage of increased stability relative to silanols and therefore offer the possiblity of being carried through multiple synthetic steps, which could facilitate the application of silicon-based cross-coupling in complex molecule synthesis.



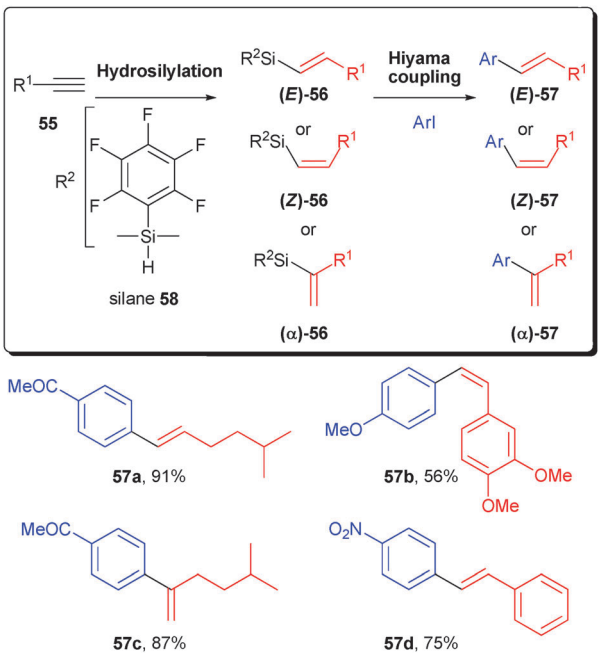
Scheme 17 Cross-coupling of five-membered ring heterocyclic silanolates.

There are numerous examples illustrating the synthetic utility of 'masked' silanols. For example, Denmark *et al.* have reported the synthesis of unsymmetrical 1,4-butadienes by the sequential cross-coupling of 1,4-bissilylbutadienes.[124] The best arrangement of silicon groups comprised of a silanol and a 2-thienylsilane. For example, silanol **49** was reacted under basic conditions to form **50** followed by the introduction of fluoride induced conditions required for the cross-coupling of the 2-thienylsilane with the aryl iodides to generate products of the general form **51** (Scheme 18).[124] The sequential cross-coupling methodology was successfully applied to the total synthesis of RK397.[125]

Spring and co-workers have developed a method for the diversity-oriented synthesis (DOS) of (*E*)- (*Z*)- and α-disubstituted



Scheme 18 An example of the sequential cross-coupling of 1,4-bissiylbutadienes.



Scheme 19 Diversity-oriented synthesis of alkenes using masked silanols. Yields refer to Hiyama cross-coupling step.

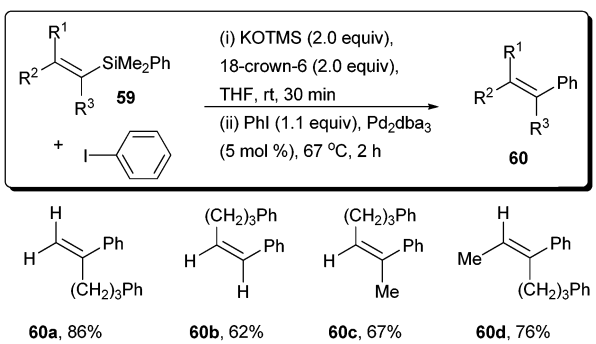
alkenes **57** from terminal alkynes **55** utilizing pentafluorophenyldimethylvinylsilanes **56** (generated *via* selective hydrosilylation with silane **58**) as 'masked' silanol intermediates (Scheme 19).[126]

The organosilicon intermediates were formed with excellent regio- and stereoselectivity and could be transformed into the corresponding alkenes without loss of selectivity.

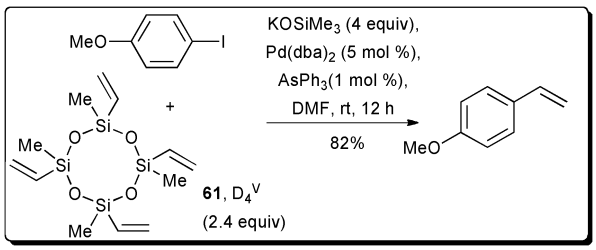
Fluoride free coupling using 'masked' silanols has also been reported. For example, Anderson *et al.* have described the base-mediated, palladium-catalysed vinylation of phenyl iodide to form products **60** using vinyldimethylphenylsilanes **59** as 'masked' silanols under fluoride free conditions (Scheme 20).[127]

Denmark *et al.* have also reported the vinylation of 4-iodoanisole using 1,3,5,7-tetravinyl-1,3,5,7-tetramethylcyclotetrasiloxane (**61**, D_4^V), a 'masked' silanol without the need for fluoride activation (Scheme 21, Cyclic silane derivatives are discussed in more detail in Section 3.3).[128]

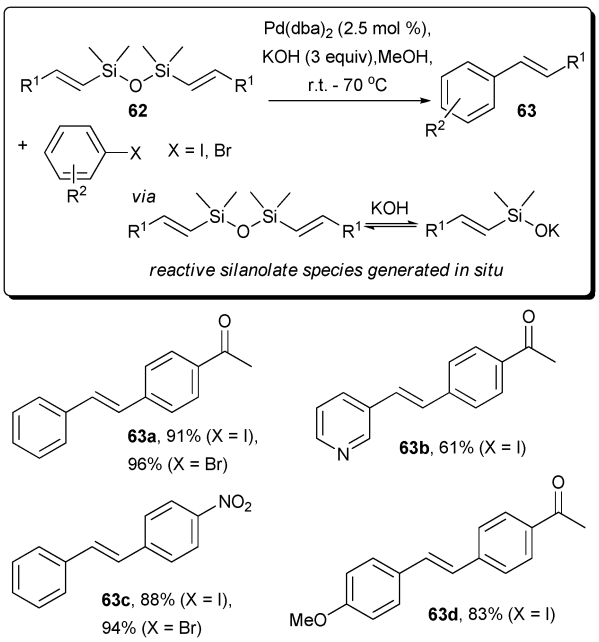
In recent years the use of disiloxanes as masked silanols in cross-coupling reactions has been reported. Disiloxanes have been shown to exist in equilibrium with the corresponding



Scheme 20 Fluoride free cross-coupling using vinyldimethylphenylsilanes **59** as 'masked' silanols.



Scheme 21 Fluoride free cross-coupling using D_4^V.



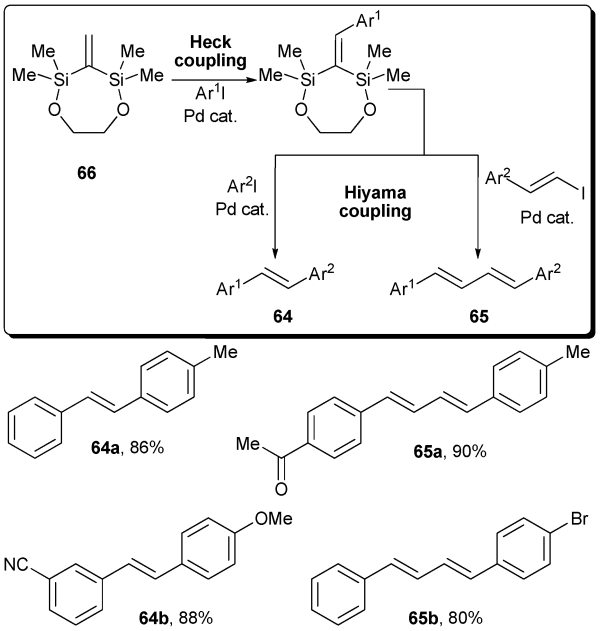
Scheme 22 Disiloxanes used as 'masked' silanols in fluoride free cross-couplings.

silanolate species under basic conditions (Scheme 22).[113,128,129] This phenomenon has been exploited by the research group of Denmark for the development of methods which allowed the cross-coupling reaction of vinyldisiloxanes with aryl iodides using fluoride activation[130] and also the coupling of divinyltetramethyldisiloxane with aromatic halides under fluoride free conditions to furnish styrene derivatives.[128] Spring *et al.* have reported the development of operationally simple protocols for the base-induced cross-coupling of a range of aryl substituted vinyldisiloxanes **62** with aryl and heteroaryl bromides under fluoride free conditions, providing access to (*E*)-stilbene derivatives **63** in good-to-excellent yields with excellent levels of geometric purity (Scheme 22).[129,131]

3.3. Cyclic variants

In addition to silacyclobutanes (Section 2.3) various other organosilicon species containing a silicon moiety embedded in a ring system, including cyclic silyl ethers (Table 1, silanes 27 and 28), cyclic siloxanes (Table 1 silanes 7 and 8) and silatranes (Table 1 silane 24) have been employed as substrates in palladium catalysed cross-coupling reactions.

Pawluc *et al.* have reported a strategy for the stereoselective synthesis of unsymmetrical (*E*)-stilbenes **64** and (*E*,*E*)-1,4-diarylbuta-1,3-dienes **65** based upon the use of cyclic 1,1-bis(silyl)ethene

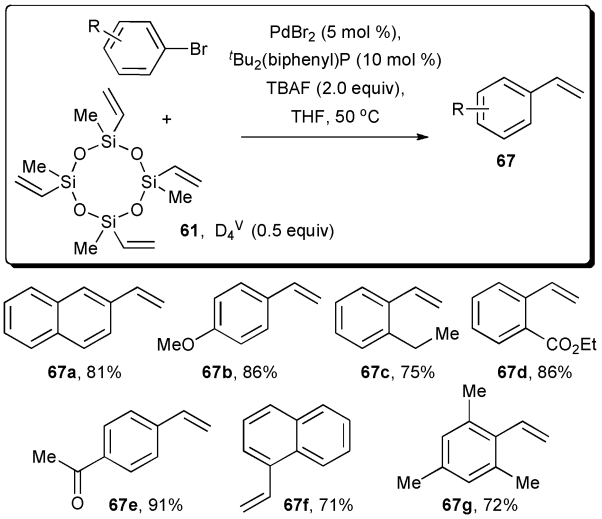


Scheme 23 Cyclic 1,1-bis(silyl)alkenes **66** as building blocks in alkene synthesis. Yields refer to the Hiyama coupling step.

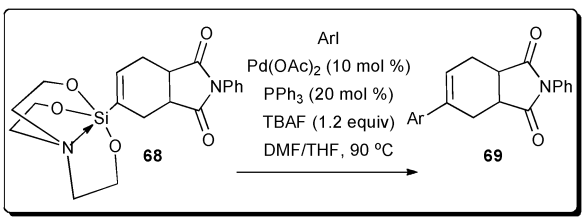
66 as a 'platform' onto which aryl groups could be sequentially installed onto the alkene core using both Heck and fluoride-activated Hiyama couplings (Scheme 23).[98] A related protocol for the one-pot, stereoselective synthesis of (*E*)-poly(arylene-vinlene)s has also been described.[132]

Unsaturated cycloalkenylsiloxanes have proven to be viable coupling partners in Hiyama-type cross-coupling reactions (Table 1 silane 28). The ease with which the oxasilyl group can be introduced into organic structures with concomitant formation of geometrically defined alkene geometries has been highlighted as a significant feature of cross-coupling strategies employing organosilicon nucleophiles of this sort.[133,134] Denmark *et al*. have reported three such methods: (1) intramolecular hydrosilylation of homopropargyl alcohols, (2) intramolecular silylformylation of homopropargyl alcohols and (3) ring-closing methathesis.[134] The siloxane derivatives resulting from these transformations have been successfully employed in fluoride-activated cross-coupling reactions which typically proceeded with high levels of stereoselectivity.[134] In addition cycloalkenyldisiloxanes have been shown to undergo cross-coupling reactions with a range of aryl iodides to afford trisubsituted allylic alchohols with high levels of stereoselectivity (Table 1 silane 29).[134]

Palladium-catalysed vinylation of aryl halides using cyclic siloxanes has been reported (Table 1 entry 7). For example, D_4^V (**61**) has been shown to be a competent vinyl donor in fluoride-activated cross-coupling reactions with aryl bromides to furnish derivatives **67**,[135] as well as fluoride free reactions with aryl iodides (Scheme 24).[128] Organosilicon reagents of this sort are typically inexpensive, air stable and widely available.[128] Hexaaryltrisiloxane derivatives have also been utilised as aryl donors in fluoride-free palladium-catalyzed cross-couplings with aryl iodides and bromides (Table 1 entry 7). In most cases, both of the aryl groups attached to the silicon atom can be utilised for the desired carbon–carbon bond forming process; consequently



Scheme 24 Cross-coupling of aryl bromides using D_4^V as a vinyl donor.



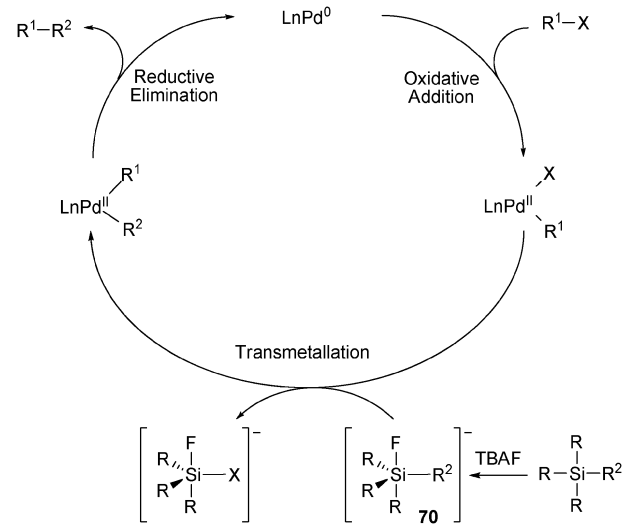
Scheme 25 Hiyama coupling using silyl substituted cycloadduct **68**.

the rest of the reagent becomes inorganic during the course of the reaction, facilitating product isolation and purification.[136]

Aryl- and alkynylsilatranes have also been employed as viable organosilicon nucleophiles in cross-coupling reactions. Riggleman *et al*. have described the use of phenylsilatrane in fluoride-induced cross-couplings with aryl triflates and halides to furnish unsymmetrical biaryl derivatives (Table 1 entry 23).[137] Pidaparthi *et al*. have also reported the preparation of a silatrane-substituted 1,3-diene derivative which readily participated in a Diels–Alder reaction with *N*-phenylmaleimide; the resulting silicon-substituted cycladducts **68** in turn served as a viable substrate in TBAF-assisted palladium-catalyzed Hiyama cross-coupling reactions with aryl iodides to form arylated derivatives **69** (Scheme 25). A similar reaction sequence employing a catechol-subsituted silane analogue (Table 1, silane 26) has also been reported.[138,139]

Mechanistic considerations

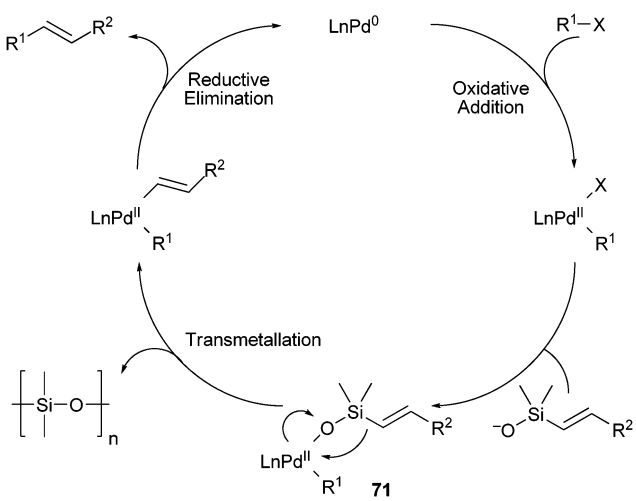
The high affinity of silicon and fluoride ions for one another assists in lowering the activation barrier for transmetallation by promoting the formation of a stable pentacoordinate siliconate intermediate (Scheme 26, **70**), which then readily participates in palladium catalysed cross-coupling; it was long assumed that formation of this pentacoordinate intermediate is essential for cross-coupling to occur, though recent studies suggest that this is not the case (*vide infra*).[193] The catalytic cycle follows a similar path to other transition metal catalysed reactions: oxidative addition, facile transmetallation of the activated pentacoordinate siliconate and finally reductive



Scheme 26 Proposed mechanism for the fluoride promoted cross-coupling of organo halides with organonsilanes and TBAF as the fluoride source.

elimination (Scheme 26). Detailed studies to build upon the understanding of the mechanism of allylic coupling were conducted by DeShong and co-workers.[143] They discovered that formation of both the π-allyl palladium complex and the hypercoordinate silicate species were rapid and reversible; therefore, the rate-determining step was either the transmetallation or reductive elimination.[143] Although it was not possible to unambiguously determine which of these two was the rate determining step, on examining additional evidence it was postulated that transmetallation is the likely slower process.[143]

In depth studies on the Hiyama coupling of alkenylsilanolates have revealed that reactions activated using a nucleophilic base proceed *via* a different mechanism (Scheme 27) to those which are activated by fluoride.[194] Following a general catalytic cycle the first step is the oxidative addition of the palladium to the organo halide. The transmetallation step is initiated by the silanolate species obtained through deprotonation of the silanol or the direct use of a silanolate salt. This activated silanolate species rapidly adds to the palladium to form a tetracoordinate palladium-silanolate complex **71** containing a covalent Pd–O–Si bond, without further activation needed. This is followed by reductive elimination to form the cross-coupled product. Through extensive kinetic studies, a clearer picture of the transmetallation process has evolved, highlighting that breakdown of the tetracoordinate complex **71** is the rate limiting step within the catalytic cycle (Scheme 27).[32,194] An X-ray crystal structure of **71** has been provided by Denmark as further evidence for this modified mechanism.[29]



Scheme 27 Proposed mechanism for the fluoride-free cross-coupling of alkenylsilanolates using a base as the activator.[32]

Applications

The transition metal catalysed cross-coupling of organosilicon reagents has emerged only more recently as a viable alternative to the more established C–C bond forming techniques; consequently, there are limited applications of this methodology to natural product and pharmaceutical synthesis. However, there are some examples which illustrate the synthetic utility of Hiyama coupling in these contexts. (Fig. 3).

Denmark effectively used the fluoride-promoted coupling of a vinyl silanol with a (*Z*)-alkenyl iodide and found the equivalents of water were critical to the success of the reaction; using TBAF·8H_2O ($^nBu_4N^+F^-$) resulted in a 92% yield of the fully protected natural product Isodomoic acid H (**72**).[195] In the synthesis of (+)-Papulacandin D (**73**), Denmark *et al*. described the base-activated coupling of an elaborate silicon-protected silanol; thus, clearly demonstrating the beneficial advantages of developing fluoride-free silicon cross-coupling methodology.[196] The synthesis of Picropodophyllin analogues (**74**) was achieved by a sequential intramolecular allylic alkylation and subsequent fluoride-activated Hiyama cross-coupling of the (2-thienyl)-vinylsilane lactone intermediate.[172] The coupling of a sterically hindered di-*ortho*-substituted siloxane was successfully achieved during the synthesis of *N*-acetyl colchinol-*O*-methyl ester (**73**), using $Pd(OAc)_2$, PPh_3 with TBAF as the activator.[146,197]

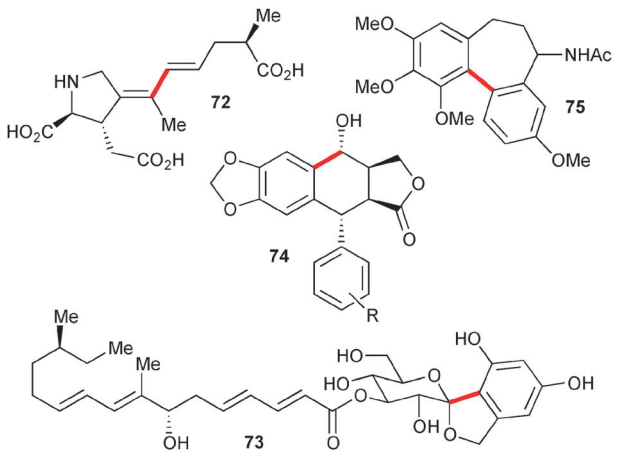


Fig. 3 Hiyama reactions in the synthesis of Isodomoic acid H (**72**), (+)-Papulacandin D (**73**), Picropodophyllin analogues (**74**) *N*-acetyl colchinol-*O*-methyl ester (**75**). Bonds formed *via* Hiyama reaction are highlighted in red.

Conclusion

The Hiyama coupling has evolved over the past three decades into an attractive alternative to existing cross-coupling methods.[198] The Hiyama reaction has a number of advantages, including mild reaction conditions, functional group tolerance, stability to be carried through a number of transformations, retention of stereochemistry and non-toxic by-products.[29,30,198] This is an active area of research with numerous silanes and alternative reaction conditions continuing to be developed. For example, the use of π-acidic alkene ligands in Hiyama-type reactions involving palladium nanoparticles has recently been reported.[199] Advancements of this sort should help to expand the scope and applicability of silicon-based cross-coupling reactions even further.

Notes and references

1 F. Diederich and P. J. Stang, *Metal-catalyzed Cross-coupling Reactions*, Wiley-VCH, Weinheim, 1998.
2 K. C. Nicolaou, P. G. Bulger and D. Sarlah, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442.
3 K. Tamao, K. Sumitani and M. Kumada, *J. Am. Chem. Soc.*, 1972, **94**, 4374.
4 R. J. P. Corriu and J. P. Masse, *J. Chem. Soc., Chem. Commun.*, 1972, 144a.
5 K. Tamao, K. Sumitani, Y. Kiso, M. Zembayashi, A. Fujioka, S.-i. Kodama, I. Nakajima, A. Minato and M. Kumada, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 1958.
6 E.-i. Negishi and S. Baba, *J. Chem. Soc., Chem. Commun.*, 1976, 596.
7 S. Baba and E.-i. Negishi, *J. Am. Chem. Soc.*, 1976, **98**, 6729.
8 E.-i. Negishi and D. E. Van Horn, *J. Am. Chem. Soc.*, 1977, **99**, 3168.
9 A. O. King, N. Okukado and E.-i. Negishi, *J. Chem. Soc., Chem. Commun.*, 1977, 683.
10 E.-i. Negishi, A. O. King and N. Okukado, *J. Org. Chem.*, 1977, **42**, 1821.
11 A. O. King and E.-i. Negishi, *J. Org. Chem.*, 1978, **43**, 358.
12 D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1979, **101**, 4992.
13 D. Milstein and J. K. Stille, *J. Am. Chem. Soc.*, 1978, **100**, 3636.
14 M. Kosugi, Y. Shimizu and T. Migita, *J. Organomet. Chem.*, 1977, **129**, C36.
15 D. Azarian, S. S. Dua, C. Eaborn and D. R. M. Walton, *J. Organomet. Chem.*, 1976, **117**, C55.
16 D. Milstein and J. K. Stille, *J. Org. Chem.*, 1979, **44**, 1613.
17 M. Kosugi and K. Fugami, *J. Organomet. Chem.*, 2002, **653**, 50.
18 T. N. Mitchell, *Synthesis*, 1992, 803.
19 J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508.
20 N. Miyaura and A. Suzuki, *J. Chem. Soc., Chem. Commun.*, 1979, 866.
21 N. Miyaura, K. Yamada and A. Suzuki, *Tetrahedron Lett.*, 1979, **20**, 3437.
22 N. Miyaura, *Bull. Chem. Soc. Jpn.*, 2008, **81**, 1535.
23 S. Kotha, K. Lahiri and D. Kashinath, *Tetrahedron*, 2002, **58**, 9633.
24 S. R. Chemler, D. Trauner and S. J. Danishefsky, *Angew. Chem., Int. Ed.*, 2001, **40**, 4544.
25 A. Suzuki, *J. Organomet. Chem.*, 1999, **576**, 147.
26 N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.
27 Y. Hatanaka and T. Hiyama, *J. Org. Chem.*, 1988, **53**, 918.
28 S. E. Denmark and J. H. C. Liu, *Angew. Chem., Int. Ed.*, 2010, **49**, 2978.
29 S. E. Denmark, *J. Org. Chem.*, 2009, **74**, 2915.
30 S. E. Denmark and C. S. Regens, *Acc. Chem. Res.*, 2008, **41**, 1486.
31 S. E. Denmark, L. Neuville, M. E. L. Christy and S. A. Tymonko, *J. Org. Chem.*, 2006, **71**, 8500.
32 S. E. Denmark and J. D. Baird, *Chem.–Eur. J.*, 2006, **12**, 4954.
33 C. J. Handy, A. S. Manoso, W. T. McElroy, W. M. Seganish and P. DeShong, *Tetrahedron*, 2005, **61**, 12201.
34 A. C. Spivey, C. J. G. Gripton and J. P. Hannah, *Curr. Org. Synth.*, 2004, **1**, 211.
35 S. E. Denmark and R. F. Sweis, *Chem. Pharm. Bull.*, 2002, **50**, 1531.
36 S. E. Denmark and R. Sweis, *Acc. Chem. Res.*, 2002, **35**, 835.
37 Y. Hatanaka and T. Hiyama, *Synlett*, 1991, 845.
38 Y. Hatanaka, K. Matsui and T. Hiyama, *Tetrahedron Lett.*, 1989, **30**, 2403.
39 T. Jeffery, *Tetrahedron Lett.*, 1999, **40**, 1673.
40 P. Bertus, U. Halbes and P. Pale, *Eur. J. Org. Chem.*, 2001, 4391.
41 Y. Koseki, K. Omino, S. Anzai and T. Nagasaka, *Tetrahedron Lett.*, 2000, **41**, 2377.
42 P. Pierrat, P. Gros and Y. Fort, *Org. Lett.*, 2005, **7**, 697.
43 S. Napier, S. M. Marcuccio, H. Tye and M. Whittaker, *Tetrahedron Lett.*, 2008, **49**, 6314.
44 S. Matsuda, M. Takahashi, D. Monguchi and A. Mori, *Synlett*, 2009, 1941.
45 M. Shindo, K. Matsumoto and K. Shishido, *Synlett*, 2005, 176.
46 H. Taguchi, K. Ghoroku, M. Tadaki, A. Tsubouchi and T. Takeda, *J. Org. Chem.*, 2002, **67**, 8450.
47 Y. Nakao, A. K. Sahoo, H. Imanaka, A. Yada and T. Hiyama, *Pure Appl. Chem.*, 2006, **78**, 435.
48 Y. Nakao, H. Imanaka, A. K. Sahoo, A. Yada and T. Hiyama, *J. Am. Chem. Soc.*, 2005, **127**, 6952.
49 Y. Nakao, J. Chen, M. Tanaka and T. Hiyama, *J. Am. Chem. Soc.*, 2007, **129**, 11694.
50 Y. Nakao, A. K. Sahoo, A. Yada, T. Hiyama and J. Chen, *Sci. Technol. Adv. Mater.*, 2006, **7**, 536.
51 S. Akai, T. Ikawa, S. I. Takayanagi, Y. Morikawa, S. Mohri, M. Tsubakiyama, M. Egi, Y. Wada and Y. Kita, *Angew. Chem., Int. Ed.*, 2008, **47**, 7673.
52 T. Hiyama and Y. Hatanaka, *J. Org. Chem.*, 1989, **54**, 268.
53 Y. Hatanaka and T. Hiyama, *Tetrahedron Lett.*, 1990, **31**, 2719.
54 K. i. Gouda, E. Hagiwara, Y. Hatanaka and T. Hiyama, *J. Org. Chem.*, 1996, **61**, 7232.
55 F. Homsi, K. Hosoi, K. Nozaki and T. Hiyama, *J. Organomet. Chem.*, 2001, **624**, 208.
56 F. Homsi, K. Nozaki and T. Hiyama, *Tetrahedron Lett.*, 2000, **41**, 5869.
57 Y. Hatanaka, K.-i. Goda, Y. Okahara and T. Hiyama, *Tetrahedron*, 1994, **50**, 8301.
58 Y. Hatanaka, K.-i. Goda and T. Hiyama, *J. Organomet. Chem.*, 1994, **465**, 97.
59 T. Huang and C.-J. Li, *Tetrahedron Lett.*, 2002, **43**, 403.
60 N. A. Strotman, S. Sommer and G. C. Fu, *Angew. Chem., Int. Ed.*, 2007, **46**, 3556.
61 T. Hiyama, A. K. Sahoo, T. Oda and Y. Nakao, *Adv. Synth. Catal.*, 2004, **346**, 1715.
62 Y. Nakao, T. Oda, A. K. Sahoo and T. Hiyama, *J. Organomet. Chem.*, 2003, **687**, 570.
63 K. Tamao, K. Kobayashi and Y. Ito, *Tetrahedron Lett.*, 1989, **30**, 6051.
64 L. Li and N. Navasero, *Org. Lett.*, 2004, **6**, 3091.
65 A. Mori, E. Takahisa, Y. Yamamura, T. Kato, A. P. Mudalige, H. Kajiro, K. Hirabayashi, Y. Nishihara and T. Hiyama, *Organometallics*, 2004, **23**, 1755.
66 W. M. Seganish and P. DeShong, *J. Org. Chem.*, 2004, **69**, 6790.
67 G. C. Fu and J.-Y. Lee, *J. Am. Chem. Soc.*, 2003, **125**, 5616.
68 M. E. Mowery and P. DeShong, *J. Org. Chem.*, 1999, **64**, 1684.
69 K. Shibata, K. Miyazawa and Y. Goto, *Chem. Commun.*, 1997, 1309.
70 H. M. Lee and S. P. Nolan, *Org. Lett.*, 2000, **2**, 2053.
71 C. Wolf and R. Lerebours, *Org. Lett.*, 2004, **6**, 1147.
72 M. Murata, R. Shimazaki, S. Watanabe and Y. Masuda, *Synthesis*, 2001, 2231.
73 M. E. Mowery and P. DeShong, *Org. Lett.*, 1999, **1**, 2137.
74 L. Zhang and J. Wu, *J. Am. Chem. Soc.*, 2008, **130**, 12250.
75 L. Zhang, J. Qing, P. Yang and J. Wu, *Org. Lett.*, 2008, **10**, 4971.
76 X. Dai, N. A. Strotman and G. C. Fu, *J. Am. Chem. Soc.*, 2008, **130**, 3302.
77 C. Wolf, R. Lerebours and E. H. Tanzini, *Synthesis*, 2003, 2069.
78 B. Ines, R. SanMartin, F. Churruca, E. Dominguez, M. K. Urtiaga and M. I. Arriortua, *Organometallics*, 2008, **27**, 2833.
79 E. Alacid and C. Nájera, *J. Org. Chem.*, 2008, **73**, 2315.
80 E. Alacid and C. Nájera, *Adv. Synth. Catal.*, 2006, **348**, 945.
81 E. Alacid and C. Nájera, *Adv. Synth. Catal.*, 2006, **348**, 2085.

82 B. C. Ranu, R. Dey and K. Chattopadhyay, *Tetrahedron Lett*., 2008, **49**, 3430.
83 D. Srimani, S. Sawoo and A. Sarkar, *Org. Lett*., 2007, **9**, 3639.
84 D. Srimani, A. Bej and A. Sarkar, *J. Org. Chem*., 2010, **75**, 4296.
85 Ã. Gordillo, E. de Jesus and C. Lopez-Mardomingo, *Org. Lett*., 2006, **8**, 3517.
86 M. J. Jin, D. H. Lee and J. Y. Jung, *Chem. Commun*., 2010, **46**, 9046.
87 S. Shi and Y. Zhang, *J. Org. Chem*., 2007, **72**, 5927.
88 Z.-s. Wu, M. Yang, H.-l. Li and Y.-x. Qi, *Synthesis*, 2008, 1415.
89 S.-N. Chen, W.-Y. Wu and F.-Y. Tsai, *Tetrahedron*, 2008, **64**, 8164.
90 J. Ju, H. Nam, H. M. Jung and S. Lee, *Tetrahedron Lett*., 2006, **47**, 8673.
91 L. Ackermann, C. J. Gschrei, A. Althammer and M. Riederer, *Chem. Commun*., 2006, 1419.
92 M. Murata, S. Yoshida, S.-i. Nirei, S. Watanabe and Y. Masuda, *Synlett*, 2006, 0118.
93 T. Mino, Y. Shirae, T. Saito, M. Sakamoto and T. Fujita, *J. Org. Chem*., 2006, **71**, 9499.
94 J.-H. Li, C.-L. Deng and Y.-X. Xie, *Synthesis*, 2006, 969.
95 J.-H. Li, C.-L. Deng, W.-J. Liu and Y.-X. Xie, *Synthesis*, 2005, 3039.
96 A. Gordillo, E. d. Jesus and C. Lopez-Mardomingo, *Chem. Commun*., 2007, **39**, 4056.
97 W. Prukala, M. Majchrzak, K. Posala and B. Marciniec, *Synthesis*, 2008, 3047.
98 W. Prukala, B. Marciniec, M. Majchrzak and M. Kubicki, *Tetrahedron*, 2007, **63**, 1107.
99 W. Prukala, M. Majchrzak, C. Pietraszuk and B. Marciniec, *J. Mol. Catal. A: Chem*., 2006, **254**, 58.
100 C. Thiot, C. Mioskowski and A. Wagner, *Eur. J. Org. Chem*., 2009, 3219.
101 S. E. Denmark and J. Y. Choi, *J. Am. Chem. Soc*., 1999, **121**, 5821.
102 S. E. Denmark, D. Wehrli and J. Y. Choi, *Org. Lett*., 2000, **2**, 2491.
103 S. E. Denmark and Z. Wu, *Org. Lett*., 1999, **1**, 1495.
104 S. E. Denmark and Z. Wang, *Synthesis*, 2000, 999.
105 S. E. Denmark and L. Neuville, *Org. Lett*., 2000, **2**, 3221.
106 S. E. Denmark and D. Wehrli, *Org. Lett*., 2000, **2**, 565.
107 S. E. Denmark and W. Pan, *J. Organomet. Chem*., 2002, **653**, 98.
108 T. Hiyama, K. Hirabayashi, J. Kawashima, Y. Nishihara and A. Mori, *Org. Lett*., 1999, **1**, 299.
109 K. Hirabayashi, A. Mori, J. Kawashima, M. Suguro, Y. Nishihara and T. Hiyama, *J. Org. Chem*., 2000, **65**, 5342.
110 S. Napier, S. M. Marcuccio, H. Tye and M. Whittaker, *Tetrahedron Lett*., 2008, **49**, 3939.
111 S. E. Denmark and R. F. Sweis, *J. Am. Chem. Soc*., 2001, **123**, 6439.
112 S. E. Denmark and M. H. Ober, *Org. Lett*., 2003, **5**, 1357.
113 S. E. Denmark and M. H. Ober, *Adv. Synth. Catal*., 2004, **346**, 1703.
114 S. E. Denmark and S. A. Tymonko, *J. Org. Chem*., 2003, **68**, 9151.
115 S. E. Denmark and J. D. Baird, *Org. Lett*., 2004, **6**, 3649.
116 H. Fuwa and M. Sasaki, *Org. Biomol. Chem*., 2007, **5**, 2214.
117 S. E. Denmark and J. M. Kallemeyn, *J. Org. Chem*., 2005, **70**, 2839.
118 S. E. Denmark and J. D. Baird, *Tetrahedron*, 2009, **65**, 3120.
119 S. E. Denmark, R. C. Smith, W.-T. T. Chang and J. M. Muhuhi, *J. Am. Chem. Soc*., 2009, **131**, 3104.
120 S. E. Denmark and J. M. Kallemeyn, *J. Am. Chem. Soc*., 2006, **128**, 15958.
121 S. E. Denmark and N. S. Werner, *J. Am. Chem. Soc*., 2008, **130**, 16382.
122 S. E. Denmark, R. C. Smith and S. A. Tymonko, *Tetrahedron*, 2007, **63**, 5730.
123 S. E. Denmark, J. D. Baird and C. S. Regens, *J. Org. Chem*., 2008, **73**, 1440.
124 S. E. Denmark and S. A. Tymonko, *J. Am. Chem. Soc*., 2005, **127**, 8004.
125 S. E. Denmark and S. Fujimori, *J. Am. Chem. Soc*., 2005, **127**, 8971.
126 H. F. Sore, D. T. Blackwell, S. J. F. MacDonald and D. R. Spring, *Org. Lett*., 2010, **12**, 2806.
127 J. C. Anderson and R. H. Munday, *J. Org. Chem*., 2004, **69**, 8971.
128 S. E. Denmark and C. R. Butler, *J. Am. Chem. Soc*., 2008, **130**, 3690.
129 H. F. Sore, C. M. Boehner, S. J. F. MacDonald, D. Norton, D. J. Fox and D. R. Spring, *Org. Biomol. Chem*., 2009, **7**, 1068.
130 S. E. Denmark and Z. Wang, *Org. Lett*., 2001, **3**, 1073.
131 D. R. Spring, H. F. Sore, C. M. Boehner, L. Laraia, P. Logoteta, C. Prestinari, M. Scott, K. Williams and W. R. J. D. Galloway, *Org. Biomol. Chem*., 2011, **9**, 504.
132 W. Prukala, P. Pawluc, K. Posala and B. Marciniec, *Synlett*, 2008, 41.
133 S. E. Denmark and S.-M. Yang, *Tetrahedron*, 2004, **60**, 9695.
134 S. E. Denmark and W. Pan, *Org. Lett*., 2003, **5**, 1119.
135 S. E. Denmark and C. R. Butler, *Org. Lett*., 2006, **8**, 63.
136 M. Endo, T. Sakurai, S. Ojima, T. Katayama, M. Unno, H. Matsumoto, S. Kowase, H. Sano, M. Kosugi and K. Fugami, *Synlett*, 2007, 749.
137 S. Riggleman and P. DeShong, *J. Org. Chem*., 2003, **68**, 8106.
138 R. R. Pidaparthi, C. S. Junker, M. E. Welker, C. S. Day and M. W. Wright, *J. Org. Chem*., 2009, **74**, 8290.
139 R. R. Pidaparthi, M. E. Welker, C. S. Day and M. W. Wright, *Org. Lett*., 2007, **9**, 1623.
140 T. Hanamoto, T. Kobayashi and M. Kondo, *Synlett*, 2001, 281.
141 S. F. Wnuk, J. P. Pitteloud, Z. T. Zhang, Y. Liang and L. Cabrera, *J. Org. Chem*., 2010, **75**, 8199.
142 T. Bach and S. A. Schweizer, *Synlett*, 2010, 81.
143 K. H. Shukla and P. DeShong, *J. Org. Chem*., 2008, **73**, 6283.
144 C. Pan, M. Liu, L. Zhao, H. Wu, J. Ding and J. Cheng, *Catal. Commun*., 2008, **9**, 1685.
145 C. Thiot, M. Schmutz, A. Wagner and C. Mioskowski, *Chem.–Eur. J*., 2007, **13**, 8971.
146 W. M. Seganish and P. DeShong, *Org. Lett*., 2006, **8**, 3951.
147 D. Domin, D. Benito-Garagorri, K. Mereiter, J. Frohlich and K. Kirchner, *Organometallics*, 2005, **24**, 3957.
148 C. M. So, H. W. Lee, C. P. Lau and F. Y. Kwong, *Org. Lett*., 2009, **11**, 317.
149 S. M. Raders, J. V. Kingston and J. G. Verkade, *J. Org. Chem*., 2010, **75**, 1744.
150 A. Gordillo, E. de Jesus and C. Lopez-Mardomingo, *J. Am. Chem. Soc*., 2009, **131**, 4584.
151 A. B. Charette, L. P. B. Beaulieu and L. B. Delvos, *Org. Lett*., 2010, **12**, 1348.
152 S. E. Denmark and J. D. Baird, *Org. Lett*., 2006, **8**, 793.
153 S. E. Denmark and Z. Wang, *J. Organomet. Chem*., 2001, **624**, 372.
154 B. Marciniec, J. Waehner, P. Pawluc and M. Kubicki, *J. Mol. Catal. A: Chem*., 2007, **265**, 25.
155 M. Suguro, Y. Yamamura, T. Koike and A. Mori, *React. Funct. Polym*., 2007, **67**, 1264.
156 T. Koike and A. Mori, *Synlett*, 2003, 1850.
157 A. Mori and M. Suguro, *Synlett*, 2001, 845.
158 W. Prukala, *Synlett*, 2008, 3026.
159 K. G. Sunil, S. Rekha and C. S. Gobind, *Eur. J. Org. Chem*., 2004, 4141.
160 L. Li and N. Navasero, *Org. Lett*., 2006, **8**, 3733.
161 T. Nokami, Y. Tomida, T. Kamei, K. Itami and J.-i. Yoshida, *Org. Lett*., 2006, **8**, 729.
162 J. C. Anderson, S. Anguille and R. Bailey, *Chem. Commun*., 2002, **18**, 2018.
163 D. Alvisi, E. Blart, B. F. Bonini, G. Mazzanti, A. Ricci and P. Zani, *J. Org. Chem*., 1996, **61**, 7139.
164 T. Hanamoto and T. Kobayashi, *J. Org. Chem*., 2003, **68**, 6354.
165 H. Katayama, M. Nagao, F. Ozawa, M. Ikegami and T. Arai, *J. Org. Chem*., 2006, **71**, 2699.
166 F. Ozawa, H. Katayama, K. Taniguchi, M. Kobayashi, T. Sagawa and T. Minami, *J. Organomet. Chem*., 2002, **645**, 192.
167 I. Fleming, R. Henning, D. C. Parker, H. E. Plaut and P. E. J. Sanderson, *J. Chem. Soc., Perkin Trans. 1*, 1995, 317.
168 K. Itami, T. Nokami and J.-I. Yoshida, *J. Am. Chem. Soc*., 2001, **123**, 5600.
169 K. Itami, T. Nokami, Y. Ishimura, K. Mitsudo, T. Kamei and J.-I. Yoshida, *J. Am. Chem. Soc*., 2001, **123**, 11577.
170 K. Itami, K. Mitsudo, T. Nokami, T. Kamei, T. Koike and J.-i. Yoshida, *J. Organomet. Chem*., 2002, **653**, 105.
171 K. Itami, Y. Ohashi and J.-i. Yoshida, *J. Org. Chem*., 2005, **70**, 2778.

172 M. Vitale, G. Prestat, D. Lopes, D. Madec, C. Kammerer, G. Poli and L. Girnita, *J. Org. Chem.*, 2008, **73**, 5795.
173 K. Hosoi, K. Nozaki and T. Hiyama, *Chem. Lett.*, 2002, **31**, 138.
174 M. Vitale, G. Prestat, D. Lopes, D. Madec and G. Poli, *Synlett*, 2006, 2231.
175 K. Hosoi, K. Nozaki and T. Hiyama, *Proc. Jpn. Acad., Ser. B, Phys. Biol. Sci.*, 2002, **78**, 154.
176 B. M. Trost, M. R. Machacek and Z. T. Ball, *Org. Lett.*, 2003, **5**, 1895.
177 S. E. Denmark and J. H.-C. Liu, *J. Am. Chem. Soc.*, 2007, **129**, 3737.
178 Y. Nishihara, D. Saito, K. Tanemura, S. Noyori and K. Takagi, *Org. Lett.*, 2009, **11**, 3546.
179 C. Morrill and N. S. Mani, *Org. Lett.*, 2007, **9**, 1505.
180 M. Murata, H. Ohara, R. Oiwa, S. Watanabe and Y. Masuda, *Synthesis*, 2006, 1771.
181 Y. Nakao, A. K. Sahoo, A. Yada, T. Hiyama and J. Chen, *J. Organomet. Chem.*, 2007, **692**, 585.
182 S. J. Shirbin, B. A. Boughton, S. C. Zammit, S. D. Zanatta, S. M. Marcuccio, C. A. Hutton and S. J. Williams, *Tetrahedron Lett.*, 2010, **51**, 2971.
183 A. Shuji, I. Takashi, T. Sho-ichi, M. Yuki, M. Shinya, T. Masaya, E. Masahiro, W. Yasufumi and K. Yasuyuki, *Angew. Chem., Int. Ed.*, 2008, **47**, 7673.
184 Z. Wang, J.-P. Pitteloud, L. Montes, M. Rapp, D. Derane and S. F. Wnuk, *Tetrahedron*, 2008, **64**, 5322.
185 S. F. Wnuk, P. I. Garcia and Z. Wang, *Org. Lett.*, 2004, **6**, 2047.
186 W. M. Seganish and P. DeShong, *J. Org. Chem.*, 2004, **69**, 1137.
187 W. M. Seganish and P. DeShong, *Org. Lett.*, 2004, **6**, 4379.
188 P. Pawluc, G. Hreczycho, A. Suchecki, M. Kubicki and B. Marciniec, *Tetrahedron*, 2009, **65**, 5497.
189 S. E. Denmark and T. Kobayashi, *J. Org. Chem.*, 2003, **68**, 5153.
190 S. E. Denmark and W. Pan, *Org. Lett.*, 2002, **4**, 4163.
191 S. E. Denmark and S.-M. Yang, *Org. Lett.*, 2001, **3**, 1749.
192 S. E. Denmark and W. Pan, *Org. Lett.*, 2000, **3**, 61.
193 S. E. Denmark, R. F. Sweis and D. Wehrli, *J. Am. Chem. Soc.*, 2004, **126**, 4865.
194 S. E. Denmark and R. F. Sweis, *J. Am. Chem. Soc.*, 2004, **126**, 4876.
195 S. E. Denmark, J. H.-C. Liu and J. M. Muhuhi, *J. Am. Chem. Soc.*, 2009, **131**, 14188.
196 S. E. Denmark, C. S. Regens and T. Kobayashi, *J. Am. Chem. Soc.*, 2007, **129**, 2774.
197 W. M. Seganish, C. J. Handy and P. DeShong, *J. Org. Chem.*, 2005, **70**, 8948.
198 Y. Nakao and T. Hiyama, *Chem. Soc. Rev.*, 2011, **40**, 4893.
199 P. S. Bäuerlein, I. J. S. Fairlamb, A. G. Jarvis, A. F. Lee, C. Müller, J. M. Slattery, R. J. Thatcher, D. Vogt and A. C. Whitwood, *Chem. Commun.*, 2009, 5734.

