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Tunable Cross Coupling of Silanols: Selective Synthesis of Heavily Substituted Allenes and Butadienes

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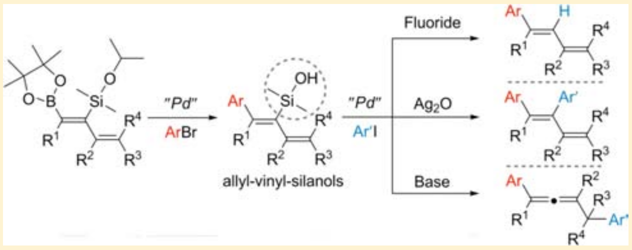
Supporting Information

ABSTRACT: 1,3-Dienyl-2-silanols with a wide range of substitution patterns are readily obtained by palladium-catalyzed silaboration of 1,3-enynes followed by Suzuki−Miyaura cross coupling with aryl bromides. Subsequent Hiyama−Denmark cross coupling with aryl iodides provides either 1,3- or 1,2-dienes in high yields. The site selectivity can be fully controlled by the choice of activator used in the coupling reaction. In the presence of strong bases such as NaO*t*-Bu, KO*t*-Bu, and NaH, clean formation of 1,2-dienes takes place via allylic rearrangement. In contrast, stereo- and site-selective formation of tetra- and trisubstituted 1,3-dienes results from use of Ag_2O and $Bu_4NF{\cdot}3H_2O$, respectively, as activators. Under microwave heating at 100 °C the base-mediated cross couplings are largely accelerated and are completed within one hour or less. The ratio of diastereomeric allenes varies depending on the substitution pattern of the silanol and ranges from >99:1 to 52:48.

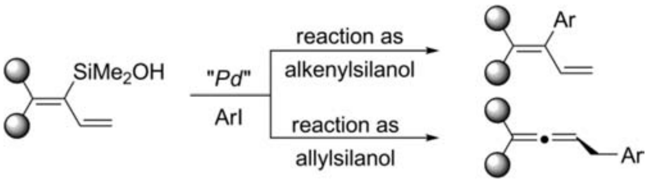


INTRODUCTION

Palladium-catalyzed cross-coupling reactions have emerged as efficient synthetic tools for the construction of carbon−carbon bonds. Among the various available methods, Hiyama−Denmark reactions are particularly attractive due to the low cost, low toxicity, and high chemical stability of the silicon compounds used as cross-coupling partners.[1] Cleavage of the strong carbon−silicon bond requires the presence of an activating agent for transmetalation to occur. With the introduction of organosilanols,[2] a viable alternative to the originally used fluoride activation became available, allowing the reactions to be performed under mild conditions in the presence of base.[3]

Organosilanols are available by several methods.[4] Although a variety of silanols, including aryl-, heteroaryl-, alkenyl-, alkynyl-, and allylsilanols, have been prepared, the substrate scope is still limited.[1,3,5] To allow for methodological extension, construction of new types of silanol substrates is important. During our current study, substrates containing 1,3-dienyl-2-silanol structural elements[6] were subjected to cross couplings with aryl iodides. Although coupling reactions of vinyl- and allylsilanols have been studied, no reports on reactions using these substrates, which contain both vinyl- and allylsilanol fragments, are available. Denmark and co-workers have demonstrated that vinylsilanols react with retention of olefin configuration[2b] and that allylic silanolate salts in the presence of dibenzylideneacetone (dba)-derived palladium catalysts react with aryl bromides to yield γ-coupled products with high site selectivity.[7] The present 1,3-dienyl-2-silanol substrates were thus expected to be able to react as alkenyl- as well as allylsilanols (Scheme 1). In consideration of the importance of both α-coupled (butadienes)[8] and γ-coupled products (allenes),[9] we decided to examine the influence of different activators on the coupling reaction.

Scheme 1. Palladium-Catalyzed Cross Coupling of 1,3-Dienyl-2-silanols



RESULTS AND DISCUSSION

Silaboration of Enynes. The required 1,3-dienyl-2-silanols were prepared starting from 1,3-enynes, which were readily obtained by Sonogashira couplings of vinyl bromides and alkynes. Silaborations of unsaturated organic compounds catalyzed by group 10 metal complexes[10] are known to provide access to adducts containing boron and silicon functions with orthogonal reactivity, thereby offering the opportunity for sequential introduction of functionality.[11] Although additions of silylboranes to alkynes have been extensively studied[12] and shown to generally proceed in a cis manner,[13] few examples of silaborations of 1,3-enynes are known.[14] Previous studies in our group demonstrated that the palladium-catalyzed addition of (dimethylphenylsilyl)pinacolborane to *E*- and *Z*-dodec-5-en-7-

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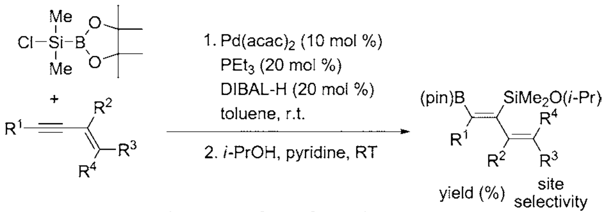
yne proceeds with high site selectivity and that high yields of the products obtained by exclusive addition to the alkyne function are obtained.[15] To allow for further elaboration of the primarily obtained products, a silyl function containing a heteroatom is required. We were therefore pleased to find that silaborations of enynes **1a**–**h** employing the more reactive (chlorodimethylsilyl)pinacolborane[16] proceeded in the presence of Pd(0), obtained by in situ reduction of Pd(acac)$_2$ with DIBAL-H, and PEt$_3$ in toluene at room temperature (Scheme 2). Addition of isopropanol and pyridine to the primarily formed products gave the stable isopropoxy derivatives **2a**–**h**, which could be isolated by chromatography in 50–73% yields. Products with a cis relationship between the silicon and boron functions, and with the configuration of the original olefinic bond unaffected by the addition, were obtained. The constitutional isomers having the silyl group at the internal position were obtained as main products, in all reactions except that involving 1-phenyl-substituted enyne **1d** in ratios of >96:4.

Scheme 2. Palladium-Catalyzed Silaboration of Enynes



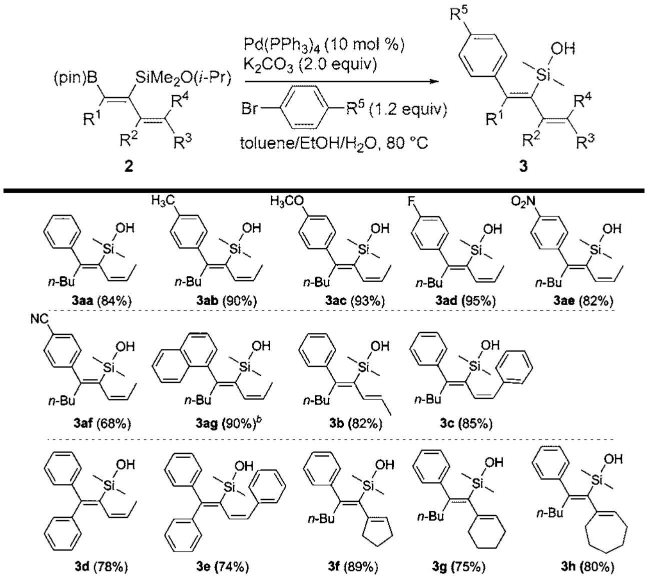
		yield (%)	site selectivity
1a	(R^1=n-C_4H_9, R^2=H, R^3=H, R^4=Me)	**2a** 62	97:3
1b	(R^1=n-C_4H_9, R^2=H, R^3=Me, R^4=H)	**2b** 73	98:2
1c	(R^1=n-C_4H_9, R^2=H, R^3=H, R^4=Ph)	**2c** 63	98:2
1d	(R^1=Ph, R^2=H, R^3=H, R^4=Me)	**2d** 62	90:10
1e	(R^1=Ph, R^2=H, R^3=H, R^4=Ph)	**2e** 55	>99:1
1f	(R^1=n-C_4H_9, R^2 R^3=-$(CH_2)_3$-, R^4=H	**2f** 68	>99:1
1g	(R^1=n-C_4H_9, R^2 R^3=-$(CH_2)_4$-, R^4=H	**2g** 50	98:2
1h	(R^1=n-C_4H_9, R^2 R^3=-$(CH_2)_5$-, R^4=H	**2h** 52	96:4

Suzuki–Miyaura Cross-Coupling Reactions. As expected, Suzuki–Miyaura cross couplings with a variety of aryl bromides, containing electron-donating as well as electron-attracting substituents, employing Pd(PPh$_3$)$_4$ as catalyst resulted in the arylated products **3**, with the isopropoxy group on silicon converted to a hydroxyl group and with unchanged configuration of the nonarylated olefinic bond. Single stereoisomers were obtained in high yields after chromatographic purification (Table 1). Even the sterically crowded compound **3ag** was obtained in 90% yield via coupling with 1-bromonaphthalene.

To understand the reason for the unexpected hydrolysis of the alkoxysilane,[17] the isopropoxy derivative of **3aa**, prepared in moderate yield by Suzuki–Miyaura cross coupling of **1a** with bromobenzene in the presence of Pd(OAc)$_2$, (*S*)-Phos, K$_3$PO$_4$, and H$_2$O (7 equiv) in toluene,[11] was treated with aqueous K$_2$CO$_3$ under the conditions used for the coupling reaction. Under these conditions no hydrolysis was, however, observed. Under the same conditions but with added tetrakis(triphenylphosphine)palladium, the silanol and the unreacted isopropoxysilane were isolated in a ratio of 0.4:1. It is possible that some intermediate formed in the reaction more efficiently catalyzes the hydrolysis.

Organosilanol-Based Cross-Coupling Reactions. For the subsequent coupling of the 1,3-dienyl-2-silanols **3** with aryl iodides, the influence of different activators was evaluated. To our surprise, we found that product formation was entirely dependent on the choice of activating agent.

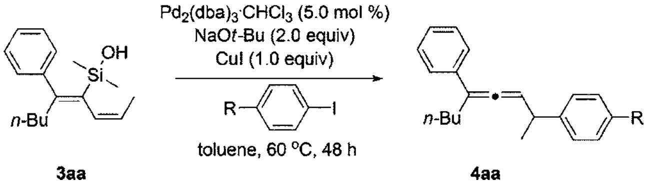
Table 1. Suzuki–Miyaura Cross-Coupling Reaction of 2 with Aryl Bromides[a,b]



[a] Unless stated otherwise, all reactions were carried out using Pd(PPh$_3$)$_4$ (11.6 mg, 10 mol %), K$_2$CO$_3$ (67.5 mg, 5.0 equiv), **2** (0.1 mmol), and aryl bromide (0.12 mmol, 1.2 equiv) in toluene/EtOH/H$_2$O (1.2/0.4/0.4 mL) at 80 °C under nitrogen for 24 h. Yields refer to isolated yields after chromatography. [b] 1-Bromonaphthalene as starting material.

Activation by Base. We first studied the effect of using strong base as activator. A variety of bases, such as NaH, NaO*t*-Bu, and KO*t*-Bu, promoted the reaction of **3** with aryl iodides, resulting in formation of 1,2-dienes **4** (see Table 2), thus demonstrating that under these conditions substrates **3** react as allylsilanes.[7] No 1,3-dienes were present in the reaction mixtures. The initial studies were performed on the cross coupling of **3aa** with 4-methoxyiodobenzene and 4-nitroiodobenzene in the presence of Pd$_2$(dba)$_3$·CHCl$_3$ using NaO*t*-Bu as activator (Table 2). A high yield, 84%, of allene **4aaa** was obtained after 48 h at 60 °C from the reaction with 4-methoxyiodobenzene (entry 1). In contrast, use of electron-poor 4-nitroiodobenzene resulted in merely 23% yield of the product (entry 2). CuI has proven to have a beneficial effect on palladium-catalyzed couplings of unreactive silanols.[18] We

Table 2. Influence of CuI on Cross Coupling of 3aa[a]



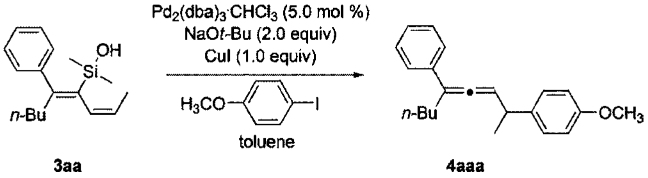
entry	R	additive	product	yield (%)[b]
1	OCH$_3$		**4aaa**	84
2	NO$_2$		**4aab**	23
3	OCH$_3$	CuI	**4aaa**	92
4	NO$_2$	CuI	**4aab**	52

[a] Reaction conditions: Pd$_2$(dba)$_3$·CHCl$_3$ (5 mol %), CuI (1.0 equiv), NaO*t*-Bu (2.0 equiv), **3aa** (0.036 mmol), and iodobenzene (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields after chromatography.

indeed found that addition of the copper salt increased the reactivity and provided the products in higher yields (92 and 52%, respectively, entries 3 and 4). We therefore decided to include the addition of CuI into our standard conditions.

To avoid the long reaction times needed for full conversion to product, we attempted to run the reactions at a higher temperature, 100 °C. This did, however, result in reduced yield due to Pd black formation (entry 2). Instead, we decided to use microwave conditions, which have been shown to result in largely reduced reaction times in a variety of palladium-catalyzed cross-coupling reactions,[19] including reactions with alkoxysilanes.[20] We were pleased to find that the time required for the reaction of **3aa** with 4-iodoanisole was dramatically shortened, and the reaction could be carried out in only 20 min at 100 °C (Table 3, entry 5), as compared to 48 h under conventional heating at 60 °C, with unaffected yields of product **4aa**.

Table 3. Optimization of Conditions for Cross Coupling of 3aa with 4-Iodoanisole[a]



entry	conditions	temperature (°C)	time	yield (%)[b]
1	Δ	60	48 h	92
2	Δ	100	40 h	85
3	MW	60	20 min	40
4	MW	80	20 min	66
5	MW	100	20 min	90

[a] Reaction conditions: $Pd_2(dba)_3 \cdot CHCl_3$ (5 mol %), CuI (1.0 equiv), NaO*t*-Bu (2.0 equiv), **3aa** (0.036 mmol), and 4-iodoanisole (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields of diastereomeric mixtures after chromatography.

The substrate range of the reaction was examined under these optimized conditions. Trisubstituted arylallenes were obtained as the sole products from tetrasubstituted silanols **3a–3e** (Table 4). High yields were observed, except in a reaction involving 4-nitroiodobenzene (entry 5) and in the reaction of sterically crowded **3ag** with 4-iodoanisole (entry 6). 1,1-Diphenyl-substituted silanols **3d** and **3e** required an extended reaction time of 60 min but gave high yields of products (entries 9 and 10). The diastereomeric ratios were, however, low, ranging from about 1:1 to 7:3.

The distribution of diastereomers proved to be essentially insensitive to the reaction conditions. Thus, reactions of **3aa** with 4-methoxyiodobenzene at room temperature, 60 °C, and 100 °C, resulted in similar diastereomeric ratios (dr, Table 5).

The presence of different ligands also proved to have a minor influence on the diastereomeric ratio of the product (see Table S1 of the Supporting Information); use of $Pd_2(dba)_3$ together with aryl- and alkylphosphines as well as an imidazoline carbene ligand resulted in essentially no change in product ratios, although the yields were somewhat affected (55–95% as compared to 87% in the absence of ligand).

Finally, the influence of a sterically bulky silanol group on the product ratio was studied by employing the diphenylsilanol analogue of **3aa**, **3i**, as substrate. This compound was obtained analogously to **3aa** by the addition of (chlorodiphenylsilyl)-pinacolborane to (*Z*)-non-2-en-4-yne followed by the Suzuki–Miyaura coupling with bromobenzene. The two diastereomers of **4aaa** were however obtained in a ratio of 61:39, i.e., similar to that observed from **3aa**, although in lower yield (45%).

We next subjected pentasubstituted dienylsilanols **3f–h** to the same reaction conditions (Table 6). High yields of coupling products were observed, except in the reaction with electron-poor 4-nitroiodobenzene (entry 5). Excellent diastereoselectivities were observed in reactions with silanols **3g** and **3h** having the olefinic groups incorporated in six- and seven-membered rings, respectively. This procedure thus provides access to tetrasubstituted allenes as essentially pure diastereomers (entries 2–7). In contrast, from the reaction of cyclopentene derivative **3f** with 4-iodoanisole, a mixture of diastereomers was obtained.

Aryl bromides have previously been successfully used as electrophiles in coupling reactions with vinyl- as well as allylsilanols.[1] Reaction of silanol **3aa** with 4-methoxybromobenzene in the presence of $Pd_2(dba)_3$ resulted in the desired product, albeit in poor yield, at 60 °C as well as under microwave conditions at 100 °C (Table 7). Aryl bromides evidently exhibit insufficient reactivity toward the present silanols.

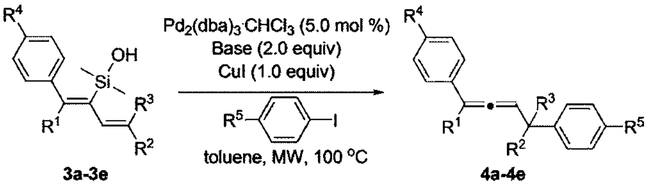
Activation by Fluoride. Attempted use of CsF as activator resulted in low conversion of starting material, and only a minor amount of coupling product was observed by ^1H NMR spectroscopy. No allene was detected in the mixture. Bearing in mind that the reaction has been shown to proceed via formation of a disiloxane,[21] the reluctance of **3** to form this type of sterically congested intermediate may provide an explanation for its failure to react. In the presence of $Bu_4NF \cdot THF$ (~5 wt % H_2O) or $Bu_4NF \cdot 3H_2O$ clean protiodesilylation[22] occurred to yield trisubstituted dienes **5aa** and **5b**, with retained configuration of the two olefinic bonds (97 and 98% yields, respectively, Scheme 4). No allenes were observed. As expected, products **5** were also obtained in the absence of iodoarene and palladium complex but under otherwise identical reaction conditions.

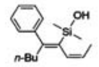
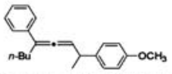
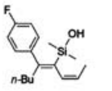
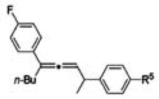
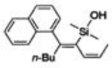
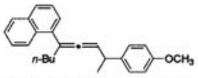
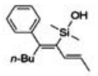
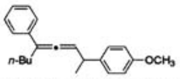
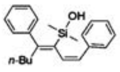
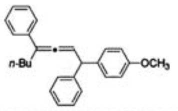
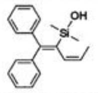
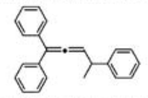
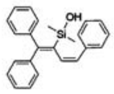
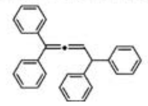
An alternative sequence for the preparation of compounds **5** starting from enynes **1** and consisting of hydroboration/Suzuki–Miyaura coupling would lead to mixtures of constitutional isomers since noncatalyzed hydroboration of the enyne suffers from low site selectivity.[23] The present procedure therefore constitutes a superior route to compounds **5**.

Activation by Silver Oxide. In contrast to the use of fluoride as activator, use of a stoichiometric amount of silver(I) oxide, introduced as coupling promotor by Hiyama and co-workers,[24] resulted in overall diarylation of the alkyne function (Table 8). The reactions proved to exhibit high stereoselectivity. Compounds **6**, with a cis relationship of the aryl groups, were obtained as major products, along with varying amounts of the trans isomers. The configuration of the nonarylated olefinic bond was preserved during the reaction. In contrast to reactions promoted by base, attempted reaction of sterically hindered naphthyl-substituted substrate **3ag** with 4-iodoanisole resulted in no product (entry 4). Tri- and tetraarylated 1,3-butadiene derivatives were also effectively obtained using **3c–3e** and differently substituted iodobenzenes (entries 5–9). This procedure thus constitutes a convenient method for the preparation of heavily substituted dienes with controlled site and stereochemistry.

Heating under microwave conditions has previously been shown to have no effect on Ag_2O mediated coupling of

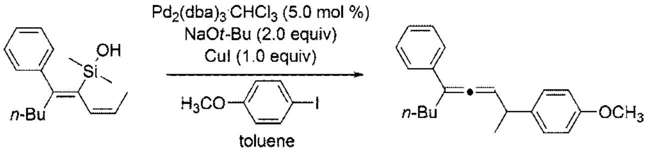
Table 4. Cross Couplings of 3a−3e with Aryl Iodides Using Base as Activator[a]



entry	silanol		R5	base	t (min)	product		yield (%)[b]	dr[c]
1		3aa	OCH_3	NaO*t*-Bu	20		4aaa	90	60:40
2		3ad	H	NaO*t*-Bu	20		4ada	86	58:42
3			OCH_3	NaO*t*-Bu	20		4adb	87	55:45
4			Br	NaO*t*-Bu	20		4adc	82	52:48
5			NO_2	KO*t*-Bu	60		4add	40	66:34
6		3ag	OCH_3	NaH	60		4ag	57	58:42
7		3b	OCH_3	NaO*t*-Bu	20		4b	91	47:53
8		3c	OCH_3	NaH	20		4c	90	68:32
9		3d	H	NaH	60		4d	88	-
10		3e	H	NaH	60		4e	83	-

[a] Unless stated otherwise, the reactions were carried out using $Pd_2(dba)_3\cdot CHCl_3$ (5 mol %), CuI (1.0 equiv), base (2.0 equiv), **3** (0.036 mmol), and aryl iodide (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields of diastereomeric mixtures after chromatography. [c] The diastereoselectivity was determined by high-performance liquid chromatography (OD-H column).

Table 5. Effect of Reaction Temperature on dr[a]

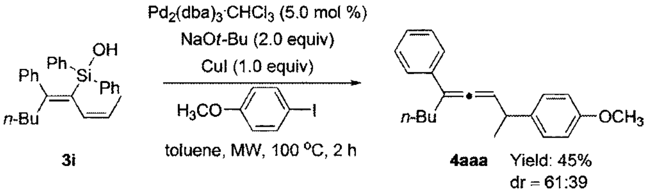


3aa **4aaa**

entry	normal heating	time (h)	yield (%)[b]	dr[c]
1	r.t.	48	33	58:42
2	60	48	92	60:40
3	100	40	85	55:45

[a] Reaction conditions: $Pd_2(dba)_3\cdot CHCl_3$ (5 mol %), CuI (1.0 equiv), NaO*t*-Bu (2.0 equiv), **3aa** (0.036 mmol), and 4-iodoanisole (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields of diastereomeric mixtures after chromatography. [c] The diastereoselectivity was determined by high-performance liquid chromatography (OD-H column).

Scheme 3. Cross-Coupling Reaction of Diphenylsilanol



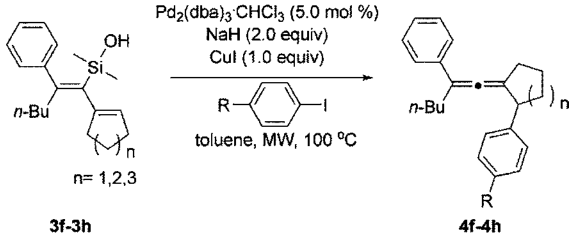
3i **4aaa**

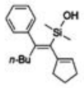
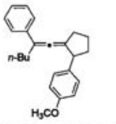
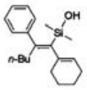
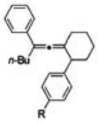
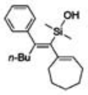
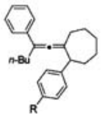
silanols.[25] Attempts to decrease the reaction time by performing the reaction of **3aa** with 4-iodoanisole under microwave conditions at 100 °C were unsuccessful, resulting in a poor yield of coupling product.

The isopropoxy analogue of silanol **3aa** proved not to be a competent coupling partner; treatment of this compound under the conditions used for Ag_2O-promoted coupling reactions resulted in only unreacted starting material.

We also attempted to use Ag_2O in combination with a catalytic amount of $Bu_4NF\cdot THF$ (0.1 equiv) to further improve the reaction efficiency. Under these conditions, higher reactivity than in reactions employing only Ag_2O has been observed.[25] In the present case these conditions resulted in the formation of products **5**, demonstrating that protiodesilylation is preferred

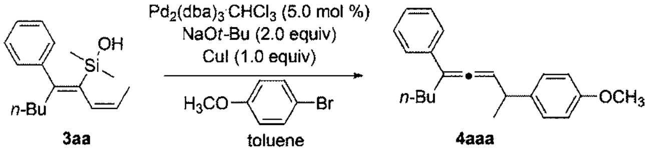
Table 6. Cross Couplings of 3f–3h with Aryl Iodides Using Base as Activator[a]



entry	silanol		R	t (min)	product		yield (%)[b]	dr[c]
1		3f	OCH_3	20		4f	90	58:42
2		3g	OCH_3	20		4ga	96	97:3
3			H	20		4gb	96	97:3
4			Br	20		4gc	94	98:2
5[d]			NO_2	60		4gd	45	>99:1
6		3h	H	20		4ha	93	92:8
7			OCH_3	20		4hb	93	93:7

[a] Unless stated otherwise, the reactions were carried out using $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %), CuI (1.0 equiv), NaH (2.0 equiv), **3** (0.036 mmol), and aryl iodide (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields of diastereomeric mixtures after chromatography. [c] The diastereoselectivity was determined by ^1H NMR analysis. [d] CuCl was used as additive instead of CuI.

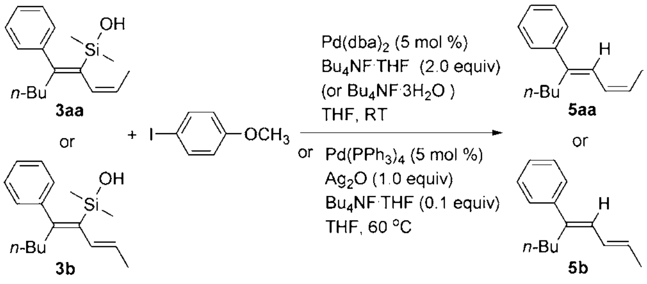
Table 7. Cross-Coupling Reaction of 3aa with 4-Bromoanisole[a]



entry	heating source	temperature (°C)	time (h)	isolated yield (%)[b]
1	oil bath	60	48	9
2	MW	100	3	26

[a] Unless stated otherwise, the reactions were carried out using $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %), CuI (1.0 equiv), NaO*t*-Bu (2.0 equiv), **3aa** (0.036 mmol), and 4-bromoanisole (0.043 mmol) in toluene (0.5 mL) under nitrogen. [b] Yields refer to isolated yields after chromatography.

Scheme 4. Palladium-Catalyzed Cross Couplings Using Fluoride as Activator



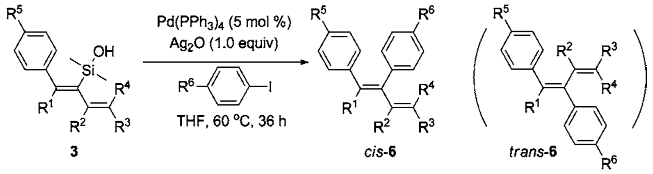
even in the presence of only minor amounts of water (Scheme 4).

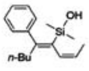
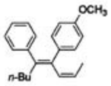
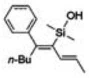
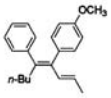
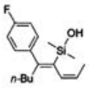
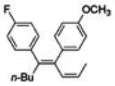
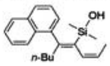
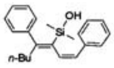
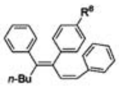
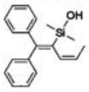
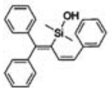
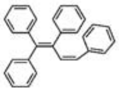
Origin of Site Selectivity. Denmark has demonstrated that in the coupling of allylsilanols, the nature of the catalyst has a dramatic influence on the α/γ ratio of the product.[7] To elucidate whether the type of product formed (1,2- or 1,3-diene) was affected not only by the activator but also by the choice of catalyst, Ag_2O-promoted coupling of **3aa** with 4-methoxyiodobenzene was performed in the presence of $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol %) in place of $Pd(PPh_3)_4$. Also under these conditions only 1,3-diene was obtained, albeit in lower yield (40% after 36 h at 60 °C as compared to 63% in the presence of $Pd(PPh_3)_4$. We also employed $Pd(PPh_3)_4$ (5 mol %) in combination with NaO*t*-Bu for the coupling of **3aa** with 4-methoxyiodobenzene. This led to exclusive formation of allene **4aa**, although in merely 52% yield (as compared to 90% using $Pd_2(dba)_3{\cdot}CHCl_3$). As described above, $Pd_2(dba)_3{\cdot}CHCl_3$ in combination with base and different ligands also led exclusively to 1,2-dienes. These experiments clearly demonstrate that the site selectivity is a function of the activator.

Mechanism and Stereochemistry. The contrasting reactivity of 1,3-dienyl-2-silanols **3** in the presence of different activating agents may be explained by different intermediates/transition states for the reactions. Denmark has demonstrated that, in the presence of base, silanol-based cross couplings proceed via formation of a silanolate, which reacts with Pd(II) to yield a complex with a Si–O–Pd linkage prior to transmetalation.[26]

In the initially planar palladium diene complex (part A of Scheme 5), the metal can coordinate to any of the enantiotopic faces of the olefin. Formation of the allene requires rotation around the C_2–C_3 single bond. The mode of coordination determines the sense of rotation and, as a consequence, the configuration of both newly formed stereogenic elements (axis

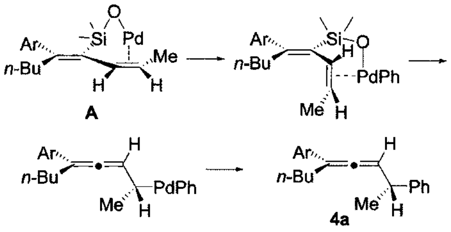
Table 8. Cross Couplings of 3 with Aryl Iodides Using Ag_2O as Activator[a]



entry	silanol		R^6	product		yield (%)[b]	cis:trans[c]
1		**3aa**	OCH_3		**6aa**	63	97:3
2		**3b**	OCH_3		**6b**	79	97:3
3		**3ad**	OCH_3		**6ad**	70	>99:1
4[d]		**3ag**	OCH_3	NR[e]	-	-	-
5		**3c**	OCH_3		**6ca**	76	94:6
6			Br		**6cb**	62	>99:1
7[d]			NO_2		**6cc**	58	93:7
8		**3d**	H		**6d**	63	-
9		**3e**	H		**6e**	55	-

[a] Unless stated otherwise, the reactions were carried out using $Pd(PPh_3)_4$ (5 mol %), Ag_2O (1.0 equiv), 3 (0.036 mmol), and aryl iodide (0.043 mmol, 1.2 equiv) in THF (0.5 mL) at 60 °C under nitrogen. [b] Yields refer to isolated yields after chromatography. [c] Cis/trans isomer ratios were determined by ^1H NMR spectroscopy. [d] Reaction was carried out at 70 °C for 48 h. [e] No reaction.

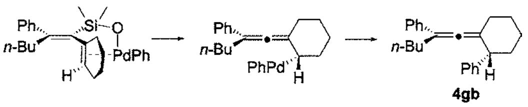
Scheme 5. Expected Stereochemistry of Base-Promoted Coupling



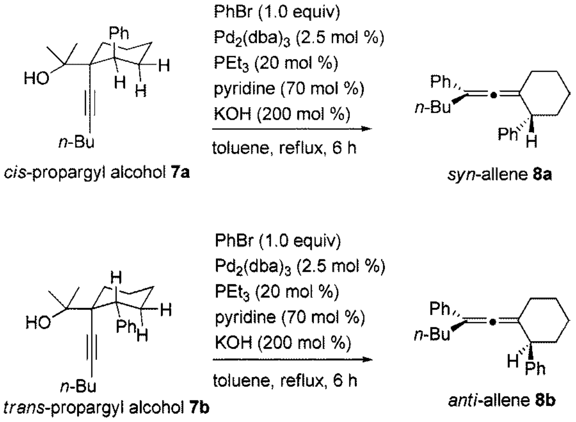
and center). Thus, whereas **3aa** is expected to lead to the *R**,*R** diastereomer (Scheme 5), the E isomer **3b** should lead to the *R**,*S** product.

According to these assumptions, the product obtained from silanol **3g** should have syn stereochemistry (Scheme 6). To verify this assumption, the two diastereomers were prepared independently employing a published procedure involving stereospecific palladium-catalyzed retro-propargylation of *syn*- and *anti*-propargyl alcohols **7a** and **7b**, respectively (Scheme 7).[27] The two alcohols were prepared in a mixture and separated by column chromatography. ^1H NMR spectroscopy ($^1H-^1H$ coupling constants and nuclear Overhauser enhancement spectroscopy (NOESY)) allowed unambiguous assignment of their stereochemistry, which in turn permitted the

Scheme 6. Stereochemistry for Fomation of 4gb from 3g



Scheme 7. Palladium-Catalyzed Retro-Propargylation[27]

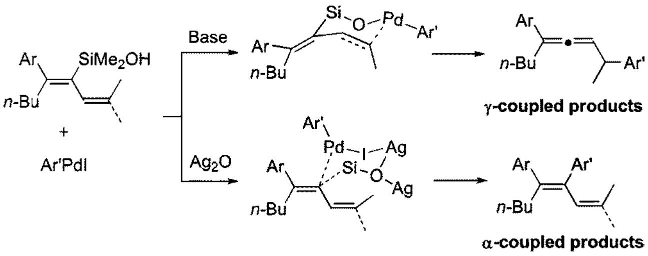


stereochemistry of the products **8a** and **8b** to be determined. In line with our hypothesis, the *syn*-allene **8a** was identical to the product obtained by the silanol coupling (**4gb**).

The observation of mixtures of diastereomers may be the result of isomerization around one of the olefinic bonds or, alternatively, of facial exchange of palladium.

The mechanism of reactions promoted by Ag_2O are less well-known. Hiyama suggested a transition state with a Si−O−Ag bond (Scheme 8).[24] Alternatively, the role of silver may be to help to ionize the Pd−I bond, thereby increasing the reactivity of the palladium complex.[28] The suggestion that different palladium complexes are involved in the two types of reactions is supported by the observation that a silyloxyplatinum complex is not an intermediate in the analogous platinum-catalyzed cross coupling of a silanol with an aryl iodide promoted by Ag_2O.[29]

Scheme 8. Possible Routes for Formation of α- and γ-Coupled Products



CONCLUSION

In summary, we have demonstrated that silaborations of 1,3-enynes provide adducts that can serve as 1,2- as well as 1,4-dianion equivalents. The type of product obtained from sequential Suzuki−Miyaura and Hiyama−Denmark cross-coupling reactions can be controlled by the choice of activator used in the last step. As a result, highly selective overall monofunctionalization, 1,2-, or 1,4-difunctionalization of the 1,3-enyne to give tri- or tetrasubstituted 1,3-dienes or 1,2-dienes, is observed. The reactions are examples of chemical control of the chemo-, regio-, or diastereoselectivity from identical starting materials, which is an attractive but challenging concept to implement.

EXPERIMENTAL SECTION

Typical Procedures for Base-, Fluoride-, and Ag_2O-Activated Cross Coupling of 1,3-Dienyl-2-silanols. *Base-Activated Cross Coupling.* To a solution of silanol **3g** (11.3 mg, 0.036 mmol) in 0.5 mL of toluene was added NaH (1.7 mg, 0.072 mmol, 2 equiv). After stirring for 10 min at room temperature, iodobenzene (4.8 μL, 0.043 mmol, 1.2 equiv), CuI (6.8 mg, 1.0 equiv), and $Pd_2(dba)_3 \cdot CHCl_3$ (1.9 mg, 5 mol %) were sequentially added. The resulting brown solution was stirred under microwave heating at 100 °C for 20 min. After removal of the solvents, the residue was purified by column chromatography (hexane) to give **4gb** as a colorless liquid (96%). ^{1}H NMR (400 Hz, $CDCl_3$): δ 7.28−7.35 (m, 4H, Ph-*H*), 7.09−7.20 (m, 6H, Ph-*H*), 3.33 (dd, *J* = 3.2, 9.0 Hz, 1H, Cy-*H*), 2.50 (dt, *J* = 3.2, 10.0 Hz, 1H, Cy-*H*), 2.26 (td, *J* = 3.2, 10.0 Hz, 1H, Cy-*H*), 2.06−2.14 (m, 3H), 1.92−1.99 (m, 3H, Cy-*H*), 1.59−1.69 (m, 2H, Cy-*H*), 1.08−1.20 (m, 4H, $-CH_2CH_2CH_3$), 0.83 (t, *J* = 5.6 Hz, 3H, $-CH_2CH_3$). ^{13}C NMR (125 Hz, $CDCl_3$): δ 199.82, 144.16, 138.50, 128.43, 128.38, 128.05, 126.35, 126.19, 126.05, 110.57, 106.15, 48.49, 34.74, 32.66, 30.45, 30.12, 28.33, 26.64, 22.68, 14.39. IR (film): ν 3088, 3063, 3024, 2938, 2854, 1953, 1604, 1496, 1453, 1246, 1034, 756 cm^{-1}.

Fluoride-Activated Cross Coupling. To a solution of silanol **3aa** (9.8 mg, 0.036 mmol) in 0.5 mL of THF was added $Pd(dba)_2$ (1.0 mg, 5 mol %), 4-iodoanisole (10.0 mg, 0.043 mmol, 1.2 equiv), and $Bu_4NF \cdot THF$ (0.072 mmol, 2.0 equiv). The resulting solution was stirred at 25 °C for 20 h. After the completed reaction, the solvent was removed, and the residue was purified by column chromatography (hexane/EtOAc = 80:1) to yield **5aa** as a colorless liquid (97%). ^{1}H NMR (400 Hz, $CDCl_3$): δ 7.42 (d, *J* = 6.4 Hz, 2H, Ph-*H*), 7.33 (t, *J* = 6.4 Hz, 2H, Ph-*H*), 7.24 (t, *J* = 6.4 Hz, 1H, Ph-*H*), 6.59 (d, *J* = 9.2 Hz, 1H, Ph−C*H*-), 6.39 (dt, *J* = 0.4, 9.2 Hz, 1H, $-CH{=}CHCH_3$), 5.63 (dq, *J* = 5.6, 9.2 Hz, 1H, $-CH{=}CHCH_3$), 2.63 (t, *J* = 6.4 Hz, 2H, $-CH_2CH_2CH_2CH_3$), 1.83 (d, *J* = 5.6 Hz, 3H, $-CH{=}CHCH_3$), 1.30−1.42 (m, 4H, $-CH_2CH_2CH_3$), 0.88 (t, *J* = 5.6 Hz, 3H, $-CH_2CH_3$). ^{13}C NMR (125 Hz, $CDCl_3$): δ 143.52, 141.80, 128.62, 127.33, 127.21, 126.66, 126.13, 122.64, 31.67, 29.95, 23.09, 14.28, 13.76.

Ag_2O-Activated Cross Coupling. Silanol **3ad** (10.5 mg, 0.036 mmol) and tetrakis(triphenylphosphine)palladium(0) (2.0 mg, 5 mol %) were added to 4-methoxyiodobenzene (10 mg, 0.043 mmol, 1.2 equiv) and silver(I) oxide (8.2 mg, 1.0 equiv) in 0.5 mL of THF. The resulting suspension was stirred at 60 °C for 36 h and then filtered and washed with CH_2Cl_2. After removal of the solvents, the residue was purified by column chromatography (hexane/CH_2Cl_2 = 5:1) to yield **6ad** as a colorless liquid (75%). ^{1}H NMR (400 Hz, $CDCl_3$): δ 6.95−6.98 (m, 2H, Ph-*H*), 6.79−6.86 (m, 4H, Ph-*H*), 6.60 (d, *J* = 8.6 Hz, 2H, Ph-*H*), 6.32 (d, *J* = 11.2 Hz, 1H, $-CH{=}CHCH_3$), 5.66 (dq, *J* = 7.0, 8.6 Hz, 1H, $-CH{=}CHCH_3$), 3.72 (s, 3H, $-OCH_3$), 2.53 (t, *J* = 7.0 Hz, 2H, $-CH_2CH_2CH_2CH_3$), 1.39 (d, *J* = 7.0 Hz, 3H, $-CH{=}CHCH_3$), 1.28−1.30 (m, 4H, $-CH_2CH_2CH_3$), 0.86 (t, *J* = 7.0 Hz, 3H, $-CH_2CH_3$). ^{13}C NMR (125 Hz, $CDCl_3$): δ 156.01, 137.66, 132.94, 132.66, 129.78, 129.60, 129.02, 126.12, 113.17, 112.96, 111.48, 53.55, 33.77, 30.10, 28.38, 21.34, 13.40, 12.49. IR (film): ν 3017, 2966, 2940, 2864, 2938, 1601, 1519, 1460, 1298, 1256, 1181, 1045, 830 cm^{-1}.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures, analytical data, and ^{1}H NMR, ^{13}C NMR, and IR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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