

ABSTRACT

Title of thesis: APPLICATION OF SILICON-BASED CROSS-
 COUPLING TECHNOLOGY TO ARYL TRIFLATES

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The goal of this research was to explore the use of aryl silatranes as a replacement for aryl siloxanes in the palladium-catalyzed cross-coupling reaction with aryl triflates. Phenylsilatrane underwent fluoride-induced cross-coupling with aryl triflates to provide unsymmetrical biaryl derivatives in good to excellent yields. Typically, better yields of adduct were obtained for aryl triflates bearing electron-donating substituents than electron withdrawing substituents. Optimization of cross-coupling reaction revealed that addition of small amounts of water, the Denmark modification, dramatically improved reaction yields. Phenylsilatrane was found also to cross-couple in good to excellent yields with aryl halides having either electron-donating or electron-withdrawing substituents, although the yields of biaryl are lower than with the corresponding siloxane derivatives. Aryl siloxanes that had previously failed to couple with aryl triflates can be employed for triflate couplings using the Denmark modification although the yields of biaryls are generally lower than the corresponding silatrane reactions.

APPLICATION OF SILICON-BASED CROSS-COUPLING TECHNOLOGY TO
ARYL TRIFLATES

by

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DEDICATION

To my husband Todd and family;

Huzzah

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My sincerest thanks to my advisor Philip DeShong for all your support and teaching me to teach. I would also like to thank the DeShong group, new and old, for their help and companionship. My many thanks to those who suffered with me from the beginning, especially Frank Kotch, LaTarsha Riddick, and Richard Keaton, your bulwark of support and commiseration were invaluable. Special thanks to my husband Todd for your faith in me and for giving me the courage to do what I love. And last but not least, a special thanks to my family for your unconditional love and support.

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LIST OF ABBREVIATIONS

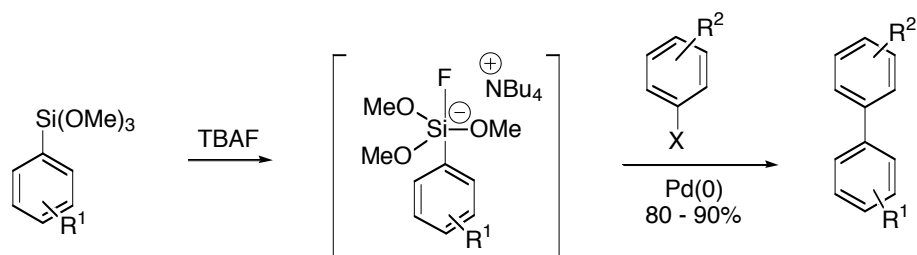
Ar	aryl
Ac	acetyl
Bu	butyl
Cy	cyclohexyl
dba	dibenzylideneacetone
DMF	<i>N,N</i> -dimethylformamide
Et	ethyl
equiv	equivalent(s)
GC	gas chromatograph
h	hour(s)
Hz	Hertz
IR	infrared
Me	methyl
mp	melting point
<i>n</i> -Bu	normal butyl
NMR	nuclear magnetic resonance
OAc	acetate
<i>o</i> -tol	<i>ortho</i> -tolyl
Ph	phenyl
rt	room temperature
TBAF	tetrabutylammonium fluoride
<i>t</i> -Bu	<i>tert</i> -butyl
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran

Introduction

“In the development of organic chemistry, the carbon-carbon bond formation has always been one of the most useful and fundamental reactions”.¹ The most common of these methods utilize organoboron²⁻⁴ or organotin⁵⁻⁸ reagents. Organosilicon reagents have played an increasingly important role in Pd(0)-catalyzed cross-coupling with organohalides to form unsymmetrical biaryls.^{2,9-28} Silicon derivatives are less toxic than the organotin reagents and more stable than organoborane reagents.

Our laboratory has developed the Pd(0)-catalyzed fluoride-promoted reaction of aryl halides coupling with aryl siloxanes. This methodology tolerates electron-deficient, electron-rich, and *ortho*-substituted systems, to provide the unsymmetrical biaryl adduct in good to excellent yields (Scheme 1).^{29,30}

Scheme 1



While siloxanes generally undergo cross-coupling with aryl halides in excellent yields, the coupling reaction failed with aryl triflates.³¹ When phenyltrimethoxysilane was cross-coupled with an aryl triflate, the major product was

hydrolyzed aryl triflate. When phenyltrimethoxysilane was cross-coupled with an aryl triflate, the major product was hydrolyzed aryl triflate.

The goal of this research was to explore the possibility of using phenylsilatrane (**1**) as a cross-coupling reagent with aryl triflates. Interest in phenylsilatrane (**1**) and its derivatives **2** is due to their intriguing molecular structure,³²⁻⁴⁰ patterns of chemical reactivity,^{13,41-43} and biological activity.⁴⁴⁻⁴⁷

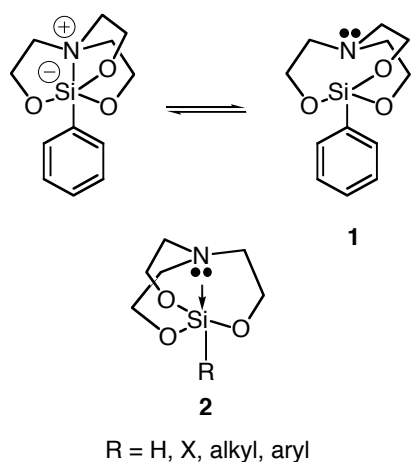


Figure 1. Silatrane structure and resonance between pentacoordinate and tetracoordinate silicon.

Silatrane structures were first synthesized in the 1960s by Frye.³⁹ They are a class of organosilicon compounds that feature a silicon atom that is formally neutral and pentacoordinate by virtue of the transannular interaction between the silicon and the electron pair from the nitrogen (Figure 1).⁴⁸ The existence of the Si-N transannular bond was demonstrated by Turley and Boer via a single-crystal X-ray study in 1968.³⁷ Silatrane structures consist of a distorted trigonal bipyramid at silicon, with nearly

equatorial oxygen atoms. The axial nitrogen is pyramidalized so that its lone pair points at silicon. Transannular distances in silatrane compounds **2** can range theoretically from the sum of the covalent radii of silicon and nitrogen to the sum of the van der Waals radii of these atoms (1.87 Å - 3.65 Å). A normal Si-N bond is 1.75 Å, shorter than the sum of the covalent radii of silicon and nitrogen. Most silatrane X-ray structures have transannular Si-N bond distances in the range 2.04 - 2.20 Å, considerably shorter than the sum of the van der Waals radii, but certainly longer than the typical single Si-N bond distance.⁴⁹

A series of optically active silatrane derivatives, [Si{N(CHRCH₂O)(CH₂CH₂O)₂}X] (R=Me, *i*-Pr; X=Ph, OMe) have been synthesized by Tasaka et al.⁵⁰ These derivatives were synthesized by the reaction of optically active triethanolamine derivatives with XSi(OMe)₃ (X = Ph or OMe) which were then characterized by ¹H NMR, ¹³C NMR, ²⁹Si NMR spectroscopy, and mass spectrometry. The structures were also determined by X-ray analysis. Taskaka et al. reached several conclusions: (1) the substituents (R) have a preference to take the equatorial orientation both in the solid phase and in solution, (2) the structures determined by X-ray analysis and by ¹H NMR spectroscopy are consistent with those from the MM2 calculations, (3) the bigger the steric hindrance of the substituent (R), the farther down field the corresponding ²⁹Si NMR signal shifts, and (4) even though the bond lengths of Si-N differ significantly in the five compounds, the individual Si-X, Si-C and Si-O bond lengths do not appreciably differ from one another.⁵⁰

During Frye's initial structural studies of silatrane, he proposed the steric influence of the silatrane cage enabled a resistance to hydrolysis and alcoholysis

under standard conditions. He came to this conclusion because prolonged time periods are required to hydrolyze silatrane derivatives, even in the presence of 0.1 N HClO₄ in glacial acetic acid at elevated temperatures.^{38,39} Subsequent X-ray diffraction analysis and theoretical calculations supported not only Frye's^{38,39} earlier conclusion, but suggested that the electronic influences of oxygens in the cage also contributed to the high hydrolytic resistance of silatrane.^{51,52}

Computational support of Fry's hypothesis was obtained by proton affinity studies of the oxygen atom in the silatrane cage.⁵³ *Ab initio* calculations with full geometry optimization have been used to investigate the oxygen and nitrogen atom proton affinities. Also the molecular structures of silatranes as well as the related compounds RSi(OCH₃)₃, RSi(OCH₂)₃CH, RSi(OCH₂CH₂)₃CH, where R = F, Cl, CH₃, SiH₃ have been investigated.

Table 1: Calculated Oxygen Proton Affinity for Silicon Compounds (kcal/mol)

	R = F	R = Cl	R = CH ₃	R = SiH ₃
RSi(OCH ₂ CH ₂) ₃ N	-205.5	-203.4	-210.0	-207.8
RSi(OCH ₃) ₃	-190.9	-191.0	-203.1	-201.0
RSi(OCH ₃) ₃ CH	-185.7	-187.9	-197.2	-197.9
RSi(OCH ₂ CH ₂) ₃ CH	-191.0	-192.0	-200.7	-200.0

These studies demonstrated that strong electron withdrawing and strong electron donating substituents have a significant effect upon the relative proton affinity. The standard difference between electron donating and withdrawing groups for the related silicon RSi(OR¹)₃ was ~10 kcal/mol (Table 1). There was found to be less variation between the proton affinities of the silatrane derivatives based on

electron withdrawing or donating (Table 1).⁵³ This is most likely because of the ability of the nitrogen to donate electrons to compensate for the protonation of the oxygen on the cage.

O-Protonated silatranes have Si-N bond lengths shorter than average attributed to the increased electrophilicity of the Si atom (Table 2).⁵³

Table 2: Transannular Si-N Bond Distances in the Silatranes and their O-Protonated Compounds in Gas Phase

Silatrane	Neutral (Å)	Protonated (Å)
FSi(OCH ₂ CH ₂) ₃ N	2.531	2.108
ClSi(OCH ₂ CH ₂) ₃ N	2.555	2.153
MeSi(OCH ₂ CH ₂) ₃ N	2.733	2.295
H ₃ SiSi(OCH ₂ CH ₂) ₃ N	2.702	2.352

In 1991, Verkade and co-workers studied alkoxy-silatranes to explore the hypothesis that because of the transannular interaction between Si-N, electron density would find its way onto the equatorial oxygens and the axial R (or OR) group.³⁵ In the study, the silatranyl group was shown to be sufficiently electron releasing in methoxysilatrane (**3**) to allow isolation of the hydrogen-bonded adduct **4**, the cation **5**, and the oxonium ion **6** (Scheme 2).³⁵

Scheme 2

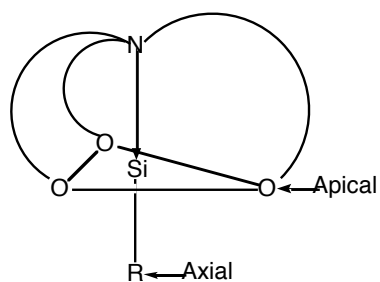
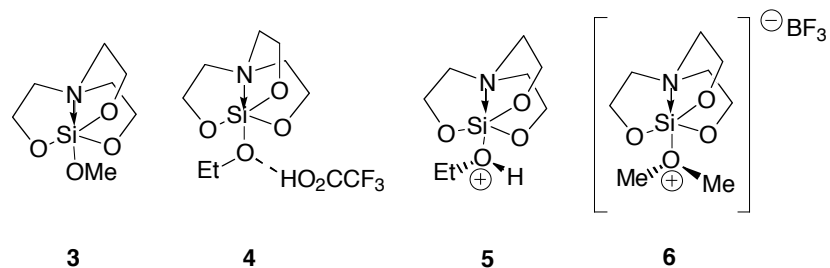


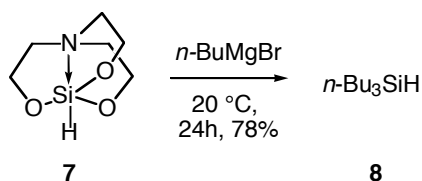
Figure 2. The relationship between axial and apical bond of the silatrane structure

After isolation and characterization of compounds **4-6**, the Si-N_{ax} bond length in compound **6** (1.965 Å) was found to be the shortest reported for a silatrane derivative and compound **4** had the shortest O(H)O distance recorded for an unsymmetrical hydrogen bond. The greatest downfield shifts of a ¹H or ¹³C resonance in alkoxy-silatrane in hydrogen bonding, protonating or alkylating environments was observed to occur at the O_{apical}-R group (Figure 2). A broadening of the resonances for OCH₂CH₂N protons of phenylsilatrane (**1**) in the presence of Me₃OBF₄ suggested that electrophilic attack can also occur at O_{eq} in solution.³⁵ The ¹H NMR studies of silatrane **3-6**, as a function of acid concentration, suggested equilibria involved protonation of both the equatorial and axial oxygen atoms. It was also found that the silatranyl group bound to an OR group was more basic than a

similarly bound (RO)₃Si moiety. The silatranyl group was less basic than a Me₃Si or ethyl group linked to an OR group.³⁵

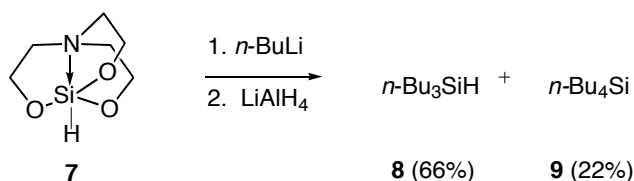
Many examples of the silatrane reactions that cleave at silicon replace the Si-O bond with Si-C or Si-H bonds. Silatrane **7** reacts with Grignard reagents to give the reduced silane **8** in good yield (Scheme 3), although normal butyllithium (*n*-BuLi) was found to reduce **7** with shorter reaction time (1h) and higher yield (90%).²¹

Scheme 3



n-BuLi, in excess, reacts readily with hydrosilatrane at room temperature to give a mixture of *n*-Bu₃SiH and *n*-Bu₄Si (Scheme 4).

Scheme 4

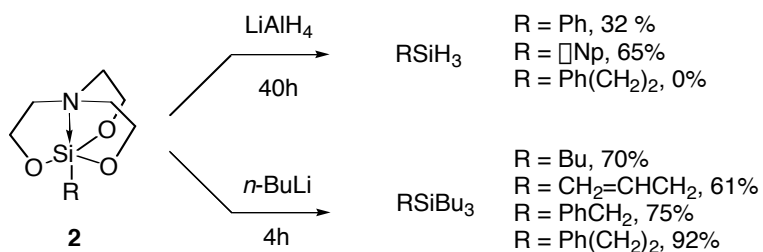


After addition of one or two molar equivalents of *n*-BuLi to hydrosilatrane, the reaction mixture was treated with lithium aluminum hydride (LiAlH₄) to remove any remaining Si-O bonds, a process which would result in formation of *n*-Bu₂SiH₂. The

reaction with *n*-BuLi on hydrosilatrane appears to proceed mainly by cleavage of the three Si-O bonds whatever the ratio hydrosilatrane/*n*-BuLi as only traces of *n*-Bu₂SiH₂ were detected.⁴⁸

Arylsilatrane are also reduced by LiAlH₄ to the corresponding arylsilane. *n*-BuLi converts both aryl and alkylsilatrane to the corresponding tetraorganosilane (Scheme 5).²¹

Scheme 5

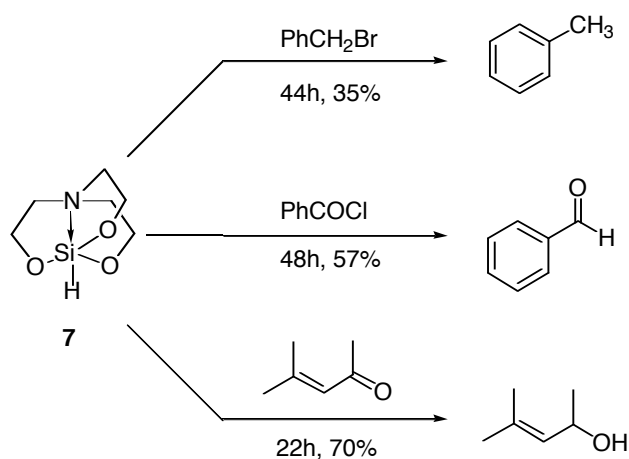


Reactions done with either LiAlH₄ or *n*-BuLi were performed at 20 °C. *n*-BuLi was found to be the better reducing agent giving higher yields and shorter reaction times.

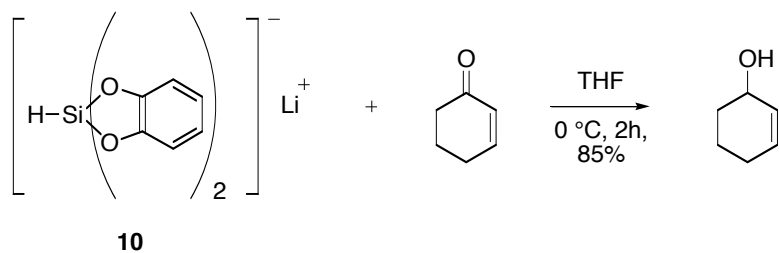
As seen with the nucleophilic reagents Grignard, LiAlH₄ or *n*-BuLi in Schemes 3 - 5, cleavage of the equatorial Si-O bonds occurs more readily than that of the apical Si-H bond.^{21,48} Results of substitution at the Si-R bond (**1**) have indicated that the reactivity of hypervalent species depends on the overall charge and structure.⁴⁸ Electron donating groups as the R group or on the silatrane cage, activate cleavage of the Si-O bond and lengthen the Si-N distance.⁴⁰

Silatranes, such as hydrosilatrane (**7**), react with carbonyl compounds, azoxybenzene, benzoyl chloride and benzyl bromide to give the reduced product. The reactivity of hydrosilatrane compared with that of other hydridosilicates, such as bis(1,2-benzenediolate)hydridosilicate **10**, was low, needing longer reaction times and higher temperatures (Scheme 6 and 7).^{48,54}

Scheme 6



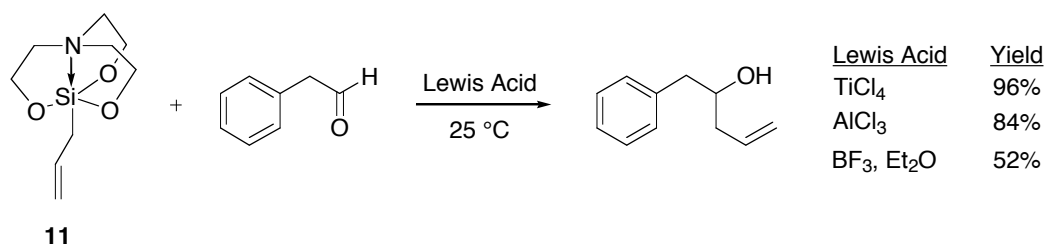
Scheme 7



Lewis acids activate silatranes for reactions with ketones and aldehydes via O-coordination.^{21,55} For example, allylsilatrane (**11**) reacted with phenylacetaldehyde in

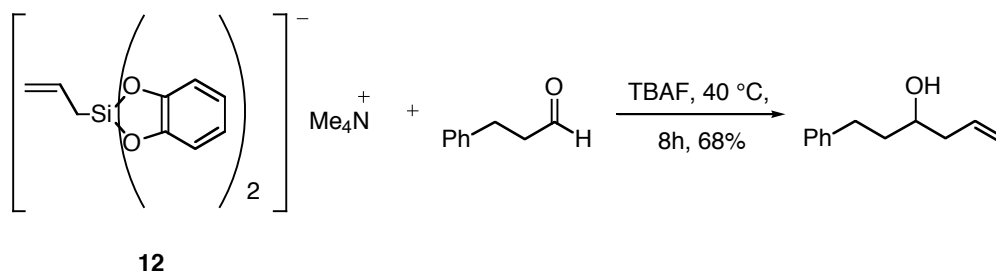
the presence of a catalytic amount of a Lewis acid to give the homoallylic alcohol (Scheme 8).^{42,56}

Scheme 8



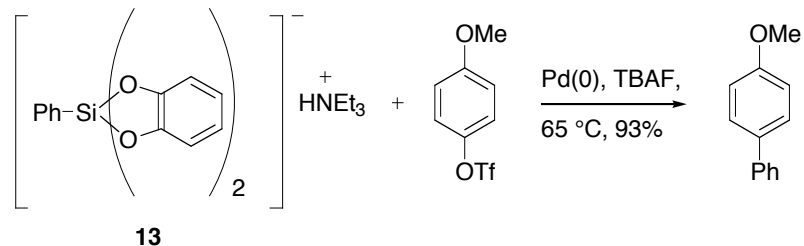
In contrast with the electrophilic conditions of silatrane, the catecholate bis(1,2-benzene-diolato)allylsilicate **12** transferred its allylic group by nucleophilic activation with tetrabutylammonium fluoride (TBAF) (Scheme 9).^{21,56,57}

Scheme 9



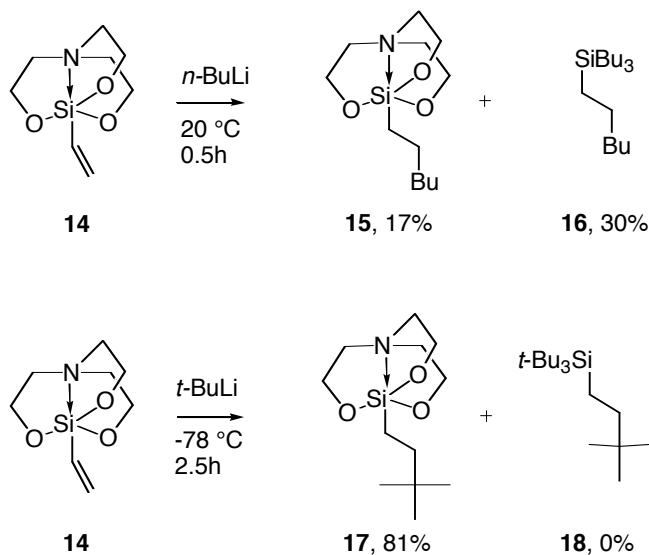
Recently our lab has developed cross-coupling technology utilizing (bis)catechol silicates with aryl triflates (Scheme 10).⁵⁸

Scheme 10



Unlike alkyl or arylsilatranes, *n*-BuLi simultaneously substituted the Si-O bonds and added to the C=C bond with vinylsilatranes. However, *t*-BuLi added only to the C=C bond without attacking the silatrane ring (Scheme 11).⁴⁸

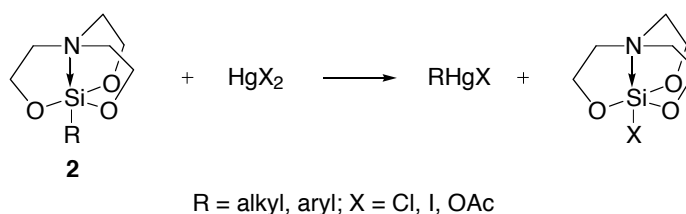
Scheme 11



The apical Si-C bond was found to be extraordinarily susceptible to direct electrophilic attack by mercury(II) to form the corresponding organomercurial compounds in protic or aprotic media (Scheme 12).⁵⁹ Under identical conditions,

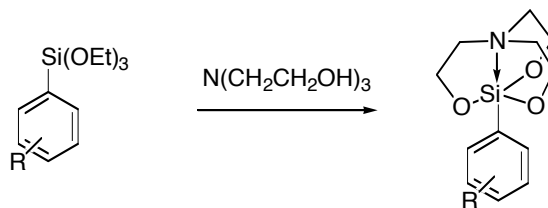
RSi(OEt)₃ compounds were inert. The reaction rate order for the R groups (**2**) was vinyl \approx phenyl \approx *p*-ClC₆H₄ > methyl > ethyl \approx propyl > *c*-hexyl \approx ClCH₂ \approx Cl₂CH \approx ethoxy. These results fall within the relative rates observed for Co-C bond cleavage by mercury(II), which were the result of both electronic and steric effects.^{59,60} As a consequence of the electron induction via the transannulation, there was an increase in the electrophilic character of the apical carbon of these silatranes.

Scheme 12



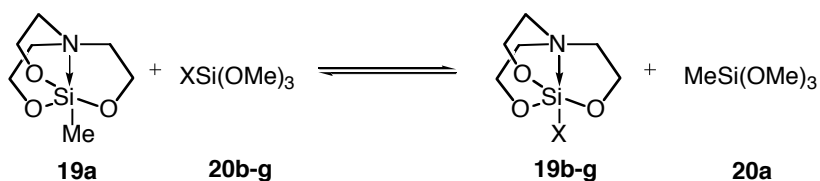
The transannular Si-N bond and the cage structure determine a number of features of chemical and physical properties of silatranes including methods for their preparation. The most common method for synthesis of silatrane is the alcoholysis of the corresponding trialkoxysilane by triethanolamine, leading to the exclusive formation of crystalline monomeric product in excellent yield (Scheme 13).^{38,39} In turn, the siloxane precursors for the synthesis of silatrane derivatives can be easily prepared using either a palladium(0) or rhodium(I) catalyst.⁶¹⁻⁶³

Scheme 13



Trans-silylation of silatranes by Si-substituted trimethoxysilane has been found to be a valid method for the synthesis of silatranes (Scheme 14).⁶⁴ Trans-silylation of silatranes by trialkoxysilanes was generally a reversible and highly chemoselective process. The equilibrium was shifted towards the formation of the silatrane bearing a stronger (shorter) transannular Si-N bond. Forward reactions between 1-methylsilatrane and Si-substituted trimethoxysilane lead to nearly the same resultant equilibrium mixtures as those produced in the reverse reactions between the silatranes bearing the corresponding substituent X and methyl trimethoxysilane (Table 3).⁶⁴

Scheme 14



X = CICH_2 (b), Cl_2CH (c), vinyl (d), Ph (e), MeO (f), Cl (g)

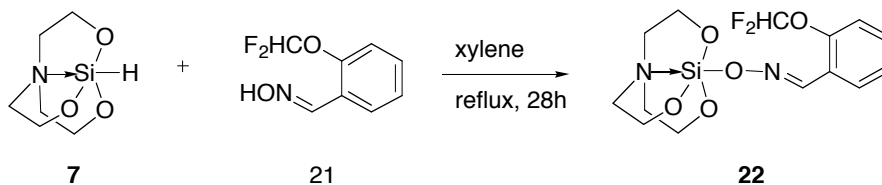
Table 3: Si-N Bond Lengths of the Silatranes *19b-g* in CDCl₃ and their Relative Content (*19b-g:19a*) in Equilibrium Mixtures as well as Isolated Yields in Reactions

Silatrane	d _{Si-N} Å	19b-g:19a	% Isolated Yield
19b	2.14	96:4	89
19c	2.10	100:0	81
19d	1.19	80:20	52
19e	2.18	91:9	78
19f	2.12	95:5	91
19g	2.05	100:0	58

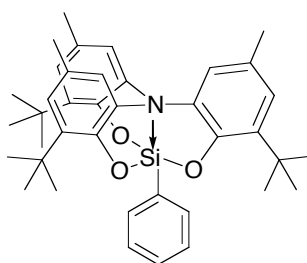
Similar results were obtained when these reactions were performed without solvent and when trimethoxysilane were replaced by the corresponding triethoxysilane.

Another method used to synthesize silatranes similar to trans-silylation was developed by Lukevics and co-workers.⁴³ *o*-Difluoromethoxybenzylideneiminoxy-silatrane was the first of its type to be synthesized from the oxime *o*-difluoromethoxybenzaloxime and hydrosilatrane (Scheme 15).⁴³ This reaction required no catalyst for formation of the silatrane derivative.

Scheme 15



Silatrane with six membered rings attached to the cage have also been synthesized from tri-(2-hydroxy-3-*tert*-butyl-5-methylbenzyl)amine (Figure 3).⁶⁵ The presence of the *tert*-butyl groups on the aryl ring system located adjacent to the axial R (R = Ph) group, introduced a steric effect that restricted the donor-acceptor interaction between the nitrogen and silicon leading to a narrower range for the Si-N bond distance when R was varied with electron withdrawing and donating groups.⁶⁵

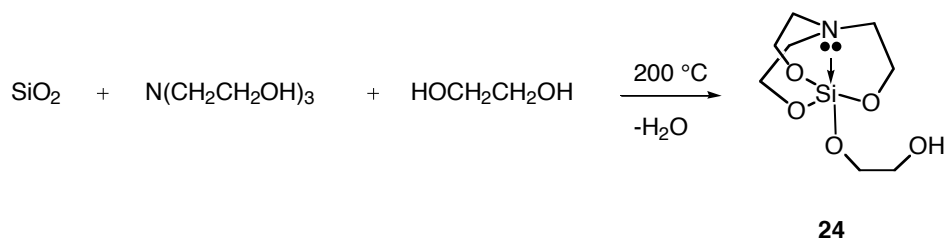


23

Figure 3: 1-Phenylsila-2,10,11-trioxa-6-aza-3,4;8,9;12,13-tris(4'-methyl, 6'-*tert*-butylbenzo)[4.4.4.0]tricyclotetradecane.

An inexpensive and efficient synthesis of silatrane used silica and neat triethanolamine to form hydroxysilatrane. With the addition of glycol and loss of water gave the silatrane **24** (Scheme 16).

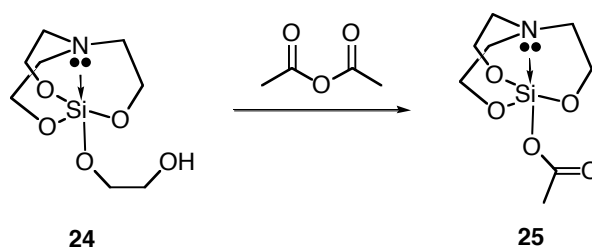
Scheme 16



24

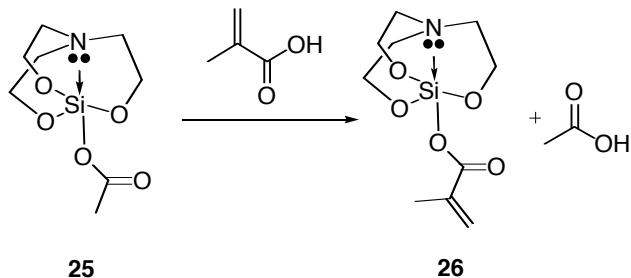
Cheng and Laine saw silatrane **24** as not only a precursor for trans-silylation but also as a precursor to a polymer with potential applications to flame resistant materials for aircraft interiors.⁶⁶ Unfortunately, the glycol derivative **24** was not able to undergo ligand exchange. Silatrane **24** was then reacted with acetyl anhydride which synthesized the acetate **25** (Scheme 17).

Scheme 17



Acetate **25** showed a very strong IR stretch at 1710 cm⁻¹ indicating no bidentate formation with silicon. Unlike silatrane **24**, acetate **25** underwent ligand exchange with methacrylic acid (Scheme 18) as well as allyl alcohol and 2-(propen-2-yloxy)ethanol.⁶⁶ This method gave an easy and cheap access to potentially useful monomeric silatranes to form polymer used as ceramic precursors or flame retardant chemicals.⁶⁶

Scheme 18



Silatrane dendrimers have been made with trimethoxy(glycidoxypropyl)silane and triisopropanolamine to form 1-glycidoxypropyl-3, 7, 10- trimethylsilatrane. Sequential addition of trimethoxy(glycidoxypropyl)silane and ethanol amine allow for desired dendritic silatrane wedges. Branching multiplicity was controlled with ammonia or diethanolamine instead of ethanolamine.^{67,68} Silatrane dendrimers represent potential ceramic precursors via hydrolytic sol-gel chemistry.^{67,69}

The most toxic silatranes are the 1-arylsilatranes, 4-XC₆H₄Si(OCH₂CH₂)₃N where X = CH₃, Cl or H. These compounds are twice as toxic as strychnine and hydrocyanic acid. Side effects of 1-arylsilatrane poisoning are evidenced as intensive stimulation of motor and respiratory centers when administered at lower than lethal doses (LD₅₀ = 0.15-0.4 mg/kg for white mice). Low doses also produce a local anaesthetic effect.⁴⁴ Vonokov and co-workers found the R group (**2**) must be in the para position to cause high toxicity levels, as both the meta and ortho compounds exhibit lower toxicity levels (0.40-73 mg/kg).⁴⁴ Phenylsilatrane (**1**) has effects like morphine, including shortness of breath at levels of 0.20-.25 mg/kg. The average dose of phenylsilatrane (**1**) needed to cause death in white mice was 0.43 mg/kg.

In 1971, M & T Chemicals used *p*-chlorophenylsilatrane as a rodenticide using the name RS-150. The advantage to using *p*-chlorophenylsilatrane was that the compound had to be ingested ($LD_{50} = 4000$ mg/kg needed to be considered non-toxic) and did not penetrate through the skin after the rat had died.^{44,52}

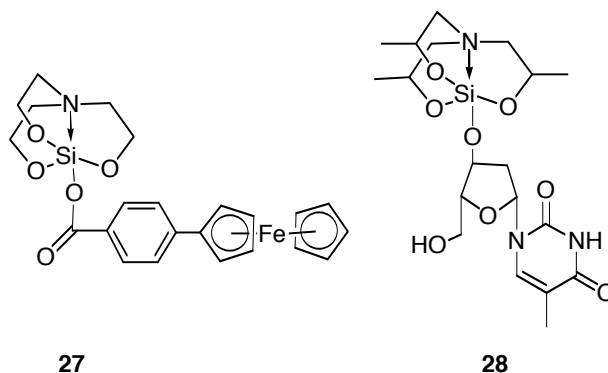


Figure 4: 1-ferrocenecarboxysilatrane **27** and 3'-*O*-(trimethylsilatranyl)thymidine **28**

In 1987, 1-alkylacyloxy silatrane s were reported as having low or medium toxicities and showed a decrease of Ehrlich cancer cell growth.⁷⁰ Recent work in 2003 has focused on ferrocene/silatrane compounds in an effort to decrease toxicity of 1-alkylacyloxy silatrane to acceptable levels for treatment.⁷⁰ The biological evaluation of the ferrocenylcarboxysilatrane compound **27** showed weak antibacterial activity giving relative inhibitory ratios (%) of 25, 25, 0, 0, and 23.5 for the following strains *in vitro*, *Gibberella saubinetii*, *Cladosporium fulvum*, *Bremia lactucae*, *Alternaria mali* and *Isariopsis clavispora*.⁷⁰

In 2002, 3'-*O*-(trimethylsilatranyl)thymidine (**28**) was sent to the National Cancer Institute (NCI) to be screened using a Developmental Therapeutics Program.⁷¹ The program assays the ability of a compound at a fixed concentration to inhibit the

growth of human breast, central nervous system and lung cancer cell lines over a 48h time period. The results of compound **28** were given in percentages compared with untreated cells (growth = 100%). The results for thymidine **28** were breast 54%, central nervous system 83% and lung 88%.⁷¹ NCI considers a compound for further testing that has growth percentage of less than or equal to 32% in any one of the three cell lines. While compound **28** did not meet these standards, the results were encouraging for these type of silatrane thymidine compounds.

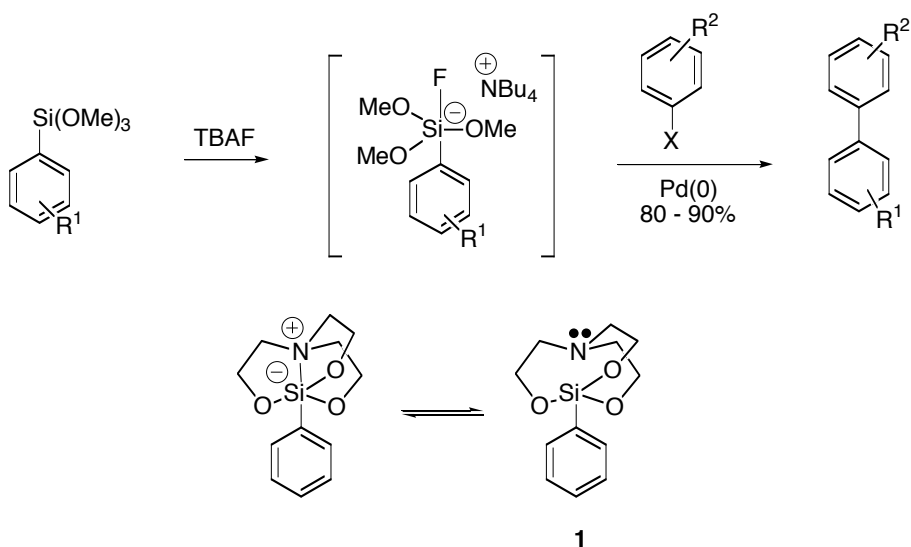
Other silatranes with beneficial biological activity include, 1-ethoxysilatrane and 1-isopropoxysilatrane, which have anticoagulants properties and 1-(chloromethyl)silatrane ointment, which reduced inflammation from small abrasions, burns and irritations of skin.⁴⁴

Silatranes and their derivatives have been most thoroughly studied in respect to structure, chemical patterns and biological activity. As will be discussed below, the goal of the following research was to expand the utility of phenylsilatrane as a potential cross-coupling partner to form unsymmetrical biaryls.

Results and Discussion

Our laboratory has developed the Pd(0)-catalyzed fluoride-promoted reaction of aryl halides with aryl siloxanes. This methodology tolerates electron-deficient, electron-rich, and *ortho*-substituted systems, to provide the unsymmetrical biaryl adduct in good to excellent yields (Scheme 19).^{29,30}

Scheme 19

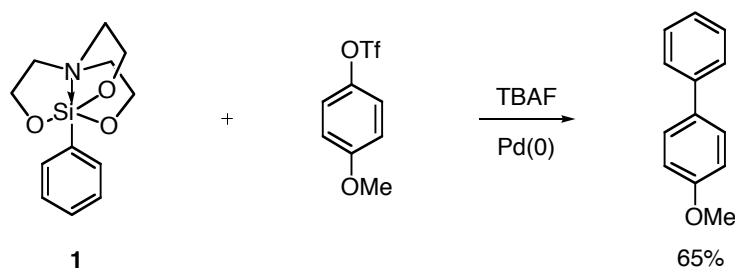


While siloxanes undergo cross-coupling with aryl halides in excellent yields, they failed to efficiently couple with aryl triflates.³¹ When phenyltrimethoxysilane was cross-coupled with an aryl triflate, the major product was the result of hydrolysis of the aryl triflate. The goal of this research was to explore the possibility of using phenylsilatrane as a cross-coupling reagent with aryl triflates, which are often more accessible than the halide derivatives.

One of the benefits of the silatrane derivatives is they have been found to be stable under standard hydrolysis and alcoholysis conditions.^{34,35,41,53} Also, they are crystalline solids, do not polymerize, are stable at room temperature and are easily prepared from their siloxane precursors. The synthesis of silatranes involves the alcoholysis of the corresponding trialkoxysilane by triethanolamine leading to the exclusive formation of crystalline monomeric product in excellent yield.^{38,39} In turn, the siloxane precursors for the synthesis of silatrane derivatives can be easily prepared using either a palladium(0) or rhodium(I) catalyst.⁶¹⁻⁶³ It was proposed that phenylsilatrane (**1**) would be adequately hypervalent to transfer its phenyl group without the need for activation by fluoride because silatrane and its derivatives constitute a class of formally pentacoordinate silicon compounds by virtue of the transannular Si-N bond.³⁷⁻³⁹

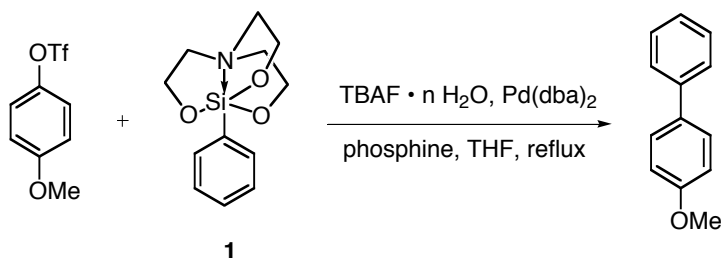
The initial studies involving phenylsilatrane as a phenyl transferring agent revealed that the dative bond in this pentacoordinate silicon system was not sufficient to promote transfer of phenyl. However, with TBAF activation, phenylsilatrane was found to couple with aryl triflates (Scheme 20).

Scheme 20



Recently, Denmark reported that the addition of water to his silanol coupling reactions would slow the rate of triflate hydrolysis, enabling a higher yield of coupled product.⁷² The original reaction conditions for couplings utilized TBAF as a 1M solution with a 3:1 mole ratio of H₂O to TBAF (Table 4, entry 1). In an attempt to increase the yield of coupled product, the amount of water in the TBAF solution was increased. Table 4 describes the results of varying first the amount of water added and then changing the phosphine ligand. Hydrated levels of TBAF were made by premixing appropriate amounts of water with TBAF • 3 H₂O. For entries 6 and 7, Table 4, 85% and 80% of aryl triflate was recovered.

Table 4. Optimization of the Coupling of 4-Methoxyphenyl Triflate with Phenylsilatrane



Entry	n	Phosphine	Time (h)	Yield (%)
1	3	29	12	65
2	10	29	12	83
3	20	29	12	90
4	30	29	24	93
5	20	30	24	35
6	20	PPh ₃	48	<5
7	20	P(<i>o</i> -tol) ₃	48	<5

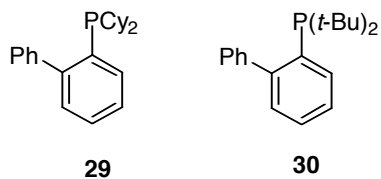


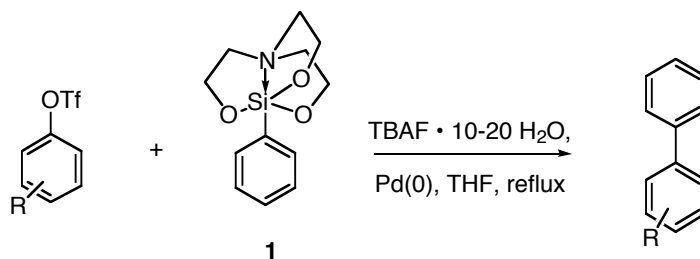
Figure 5: 2-(dicyclohexylphosphino)biphenyl and 2-(di-*tert*-butylphosphino)biphenyl

Upon addition of 20 to 1 H₂O/TBAF to the coupling medium, no hydrolyzed product was detected and an excellent yield of the coupled adduct was obtained (Table 4, entry 3). Table 4, entries 1 and 2 showed less than 10% hydrolyzed product and addition of water did not affect reaction time until after 30 equivalents of water had been added as seen in Table 4, entry 4. Assorted phosphines were surveyed as additives in the coupling reaction (Table 4, entries 5-7). Based on the results summarized in Table 4, the optimal reaction conditions for coupling of 4-methoxyphenyl triflate were 20 to 1 H₂O/TBAF and the use of the Buchwald ligand (**29**) (Figure 4) (Table 4, entry 3).⁷³⁻⁷⁵

After optimization of the coupling of phenylsilatrane with 4-methoxyphenyl triflate, other triflate substrates were investigated (Table 5). Interestingly, an electron-donating ortho substituent on the aryl triflate ring did not affect the coupling reaction, (Table 5, entries 2 and 3). Unfortunately, the sterically hindered 2,6-dimethoxyphenyl triflate does not couple with phenylsilatrane. Presumably, the aryl triflate is unable to undergo oxidative addition with the Pd(0) catalyst. Aryl substrates bearing strong electron-donating groups gave the best yields, although weaker donating groups also gave good yields of adduct (Table 5, entries 5 and 6). We also saw efficient coupling with 1-naphthalene triflate (68%). With electron-deficient aryl

triflates, (Table 5, entries 7-9), the yields were lower due to competing hydrolysis of aryl triflate. It is noteworthy that the rate of hydrolysis of the triflates in these instances is faster than the rate of the cross coupling reaction. Optimized conditions for electron rich aryl triflates differed from those of bearing electron donating groups. Table 5, entries 1-5 utilized 20 to 1 H₂O/TBAF and 2-(dicyclohexylphosphino)-biphenyl as the phosphine were as entries 7-9 utilized 10 to 1 H₂O/TBAF and PPh₃ as the phosphine. Table 5, entry 4, 56% of aryl triflate and 40% hydrolyzed aryl triflate was recovered. The major product for Table 5, entry 9 was hydrolyzed aryl triflate. Hydrolyzed aryl triflate was also observed as a major product in entries 7 and 8.

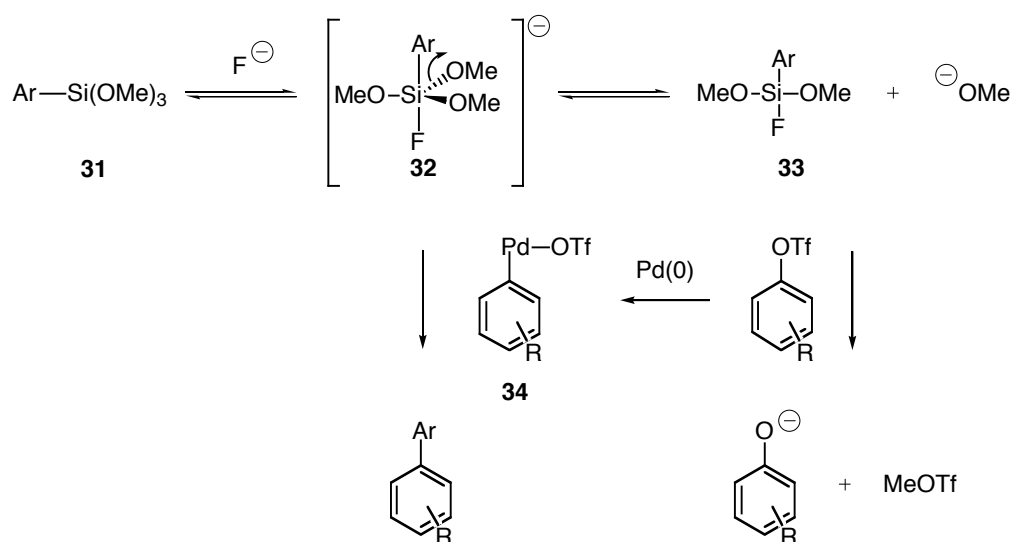
Table 5. Coupling of Phenylsilatrane with Aryl Triflates.



Entry	R	Time (h)	Yield (%)
1	4-OMe	12	90
2	2-OMe	12	90
3	2,3-dimethoxy	12	73
4	2,6-dimethoxy	48	0
5	4-H	12	75
6	4-Me	12	87
7	4-NO ₂	1	50
8	4-Ac	1	56
9	4-CO ₂ Me	1	21

There are two main strategies in dealing with the hydrolysis of the aryl triflate: (1) the use of silatrane derivatives to decrease hydrolyzed triflate; and (2) the use of water to control the rate of hydrolysis. We propose that hydrolysis of the aryl triflate occurs via the mechanism described in Scheme 21 and is in fact, not hydrolysis, but alcoholysis.

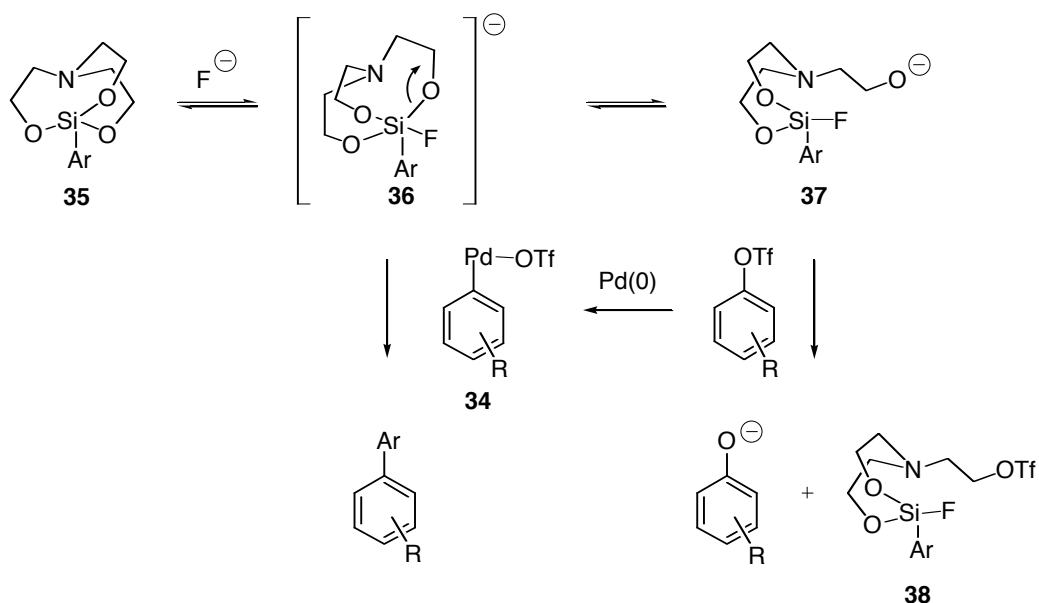
Scheme 21



First, siloxane **31** undergoes hypervalent silicate formation with fluoride to give silicate **32**. Cerveau et al.⁵⁶ showed that for allyltrimethoxysilane, KF promotes cleavage of the Si-O bond rather than the Si-C bond in the tetracoordinate silicon compound. In these reaction the allyl transfer is not observed; instead a crotonization or Cannizzaro reaction takes place as a result of the generation of methoxide.⁵⁶ In accordance with the earlier study, silicate **32** is in equilibrium with silyl fluoride **33** and methoxide. The methoxide would then be responsible for hydrolysis of the aryl

triflate. If the rate of methanolysis of the triflate is faster than either aryl transfer of silicate **32** to aryl palladium intermediate **34** or the rate of oxidative addition of Pd(0) into the triflate, then hydrolysis of the triflate will occur faster than oxidative addition and cross coupling. The goal was to inhibit alcoholysis either by decreasing the effective concentration of methoxide or by decreasing the rate of triflate alcoholysis.

Scheme 22

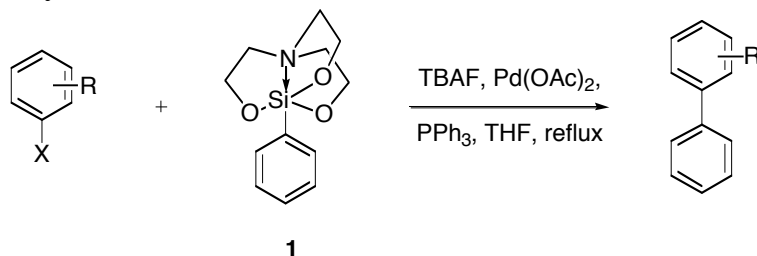


One effective tactic to accomplish this goal was to employ silatrane **35** rather than siloxane reagents. The rate of alcoholysis of the triflate substrate was dramatically reduced when using phenylsilatrane. Fluoride addition to silatrane **35** gave silicate **36** which can undergo alkoxide loss (**37** in Scheme 22). Unlike the situation with siloxane reagents (Scheme 21), however, the effective concentration of compound **37** is low because of the intramolecular (unimolecular) return to silicate.

The bimolecular alcoholysis reaction becomes less competitive. The end result is that the rate of coupling exceeds the rate of alcoholysis.

Having demonstrated that aryl triflates underwent coupling with phenylsilatrane, aryl halides were also attempted (Table 6). As with phenyltrimethoxysilane, phenylsilatrane gives higher yields with aryl iodides (Table 6, entries 1 and 2) than with aryl bromides (Table 6, entries 3-5). Electron-withdrawing and -donating groups did not greatly effect the reactivity of iodides or bromides. Entry 5 is particularly noteworthy, demonstrating that phenylsilatrane will couple with sterically hindered systems. Phenylsilatrane does not couple well with aryl chlorides (0-30%). For comparison, Table 6 also includes results for siloxane couplings reported by Mowery.⁷⁶

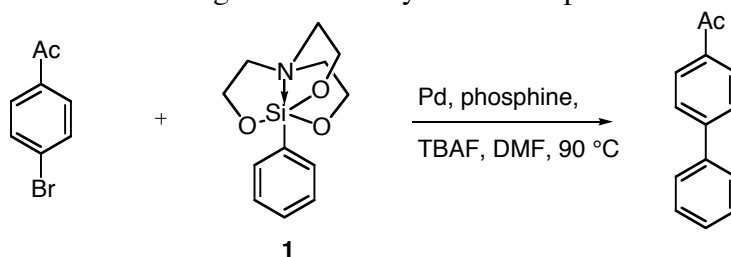
Table 6. Phenylsilatrane Coupling with Aryl Halides Compared with Phenyltrimethoxysilane



Entry	X	R	Yield (silatrane)	Yield (siloxane) ⁷⁶
1	I	4-Ac	80	77
2	I	4-OMe	78	91
3	Br	4-Ac	71	86
4	Br	4-OMe	73	74
5	Br	2,6-dimethyl	65	85

Coupling of aryl halides with silatrane tolerates changes in phosphine and palladium catalyst (Table 7). The Pd(OAc)₂ was better suited as a catalyst for the purpose of comparing silatrane reactions with those of the optimized siloxane reactions. For coupling of aryl halides with phenylsilatrane, high levels of water were not necessary and only 1.5 equiv. of TBAF were required for good yields (entry 4).

Table 7: Dependency of TBAF for Coupling of Phenylsilatrane with 4-Bromoacetophenone and Changes in Pd-catalyst and Phosphine.

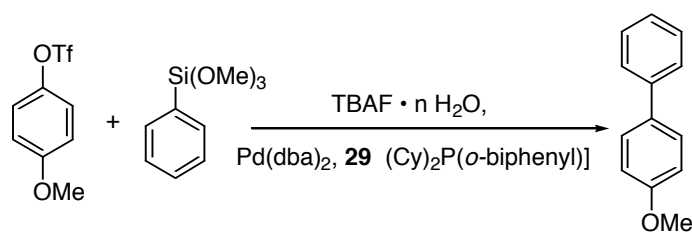


Entry	TBAF equiv.	Catalyst	Phosphine	Yield (%)
1	0.0	Pd(OAc) ₂	PPh ₃	0
2	0.5	Pd(OAc) ₂	PPh ₃	25
3	1.0	Pd(OAc) ₂	PPh ₃	32
4	1.5	Pd(OAc) ₂	PPh ₃	70
5	2.0	Pd(OAc) ₂	PPh ₃	71
6	2.0	Pd(OAc) ₂	P(<i>o</i> -tol) ₃	61
7	2.0	Pd(OAc) ₂	(Cy) ₂ P(<i>o</i> -biphenyl)	40
8	2.0	Pd(dba) ₂	PPh ₃	67

Unlike trimethoxysilane, phenylsilatrane forms no biphenyl byproduct from its coupling reactions with either aryl halide or triflate. Small amounts of the homocoupling byproduct were seen for aryl halides and reduction of starting aryl halide was only seen when electron withdrawing groups were present on the aryl halide ring.

Previously, we had reported that aryl triflates were not viable substrates for coupling with siloxanes due to rapid alcoholysis of the aryl triflate under standard coupling conditions.³¹ However, by adding excess water to the reaction mixture as noted by Denmark,⁷² alcoholysis of the triflate was dramatically suppressed and the coupling of the siloxane derivatives proceeded in good yields (Table 8). Table 8, entry 1 used “anhydrous” TBAF solutions purchased from Acros (contains <5% water) and the results reported are from Mowery.³¹ For Table 8, entries 1-3, the remaining material isolated was alcoholized aryl triflate. In entry 4, Table 8, no alcoholysis of starting aryl triflate was observed, while there was significant alcoholysis of the aryl triflate with lesser than 20 equiv. of water in the reaction media. Reported yields for entries 4 and 5 from Table 8 are the average yields of three experiments.

Table 8. Coupling 4-Methoxyphenyl Triflate with Phenyltrimethoxysilane



Entry	n	Time (h)	Yield (%)
1	0	12	<10
2	3	12	36
3	10	12	53
4	20	12	79
5	30	24	72

In conclusion, phenylsilatrane has been shown to undergo palladium-catalyzed cross-coupling with aryl triflates and halides to give unsymmetrical biaryls in good yields. Phenylsilatrane has been found to be stable to standard hydrolysis and alcoholysis conditions.^{34,35,41,53} Also, it is a crystalline solid, does not polymerize, is stable at room temperature and easily prepared from the commercially available siloxane precursor. Addition of water to the reaction medium was observed to increase the yields of the coupled adduct using either the silatrane or siloxane derivative in coupling with aryl triflates.

Experimental Section

General. All ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX400 spectrometer in CDCl_3 unless otherwise noted. Chemical shifts were reported in parts per million (δ) downfield from tetramethylsilane (TMS). Coupling constants (J values) are given in Hertz (Hz) and spin multiplicities are indicated by standard notation.

Infrared spectra were recorded on a Nicolet 5DXC FT-IR spectrophotometer with samples dissolved in carbon tetrachloride (CCl_4) unless otherwise noted. Band positions are given in reciprocal centimeters (cm^{-1}) and relative intensities are listed as: br (broad), vs (very strong), s (strong), m (medium), or w (weak).

Melting points were taken in Kimax soft glass capillary tubes using a Thomas-Hoover Uni-Melt capillary melting point (Model 6406 K) equipped with a calibrated thermometer.

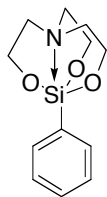
Flash chromatography was performed using thick-walled glass columns and "medium-pressure" silica gel (Sorbent Technologies, 40-75 μm). Flash chromatography data were reported as (column diameter in mm, column height in cm, solvent).

N,N-Dimethylformamide (DMF) was distilled from molecular sieves. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl. Glassware used in the reactions described herein was dried in an oven at 120 $^\circ\text{C}$ for a minimum of 12 h. All reactions were performed under argon unless otherwise indicated.

Tetrabutylammonium fluoride (TBAF) was purchased from Fluka in the form of crystalline tetrabutylammonium fluoride trihydrate and used as a 1.0 M solution in

distilled THF. 4-Nitrophenyl trifluoromethanesulfonate, 4-cabomethoxyphenyl trifluoromethanesulfonate, 1-naphthalene trifluoromethanesulfonate, 4-methoxyphenyl trifluoromethanesulfonate, phenyltrifluoromethanesulfonate and 4-methylphenyl trifluoromethanesulfonate were prepared using a modified procedure of Ritter.⁷⁷ All other materials were purchased from Aldrich and used as received, with the following exceptions: bis(dibenzylideneacetone)palladium (Pd(dba)₂) and palladium diacetate (Pd(OAc)₂) were purchased from Acros and triphenylphosphine (PPh₃) was recrystallized from hexanes prior to use. All compounds were determined to be >95% pure by GC and ¹H NMR spectroscopy unless otherwise indicated.

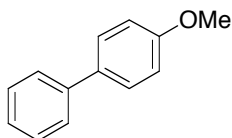
CAUTION: *Silatrane derivatives are toxic when ingested and should be handled with caution.*⁴⁴



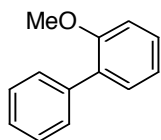
Preparation of Phenylsilatrane (1). The following procedure was modified from Frye et. al.³⁹ To a solution of triethanolamine (17.0 g, 114 mmol) in 50 mL of toluene was added phenyltriethoxysilane (18.8 mL, 101 mmol). The clear and colorless solution was heated in a 85 °C oil bath until all ethanol had distilled away (5h) [bp. (EtOH/toluene azeotrope = 76.7 °C)].⁷⁸ When the reaction mixture had cooled to room temperature, a white precipitate formed. Recrystallization from toluene gave 25.4 g (92%) of phenylsilatrane as a white crystalline solid: mp 203-204 °C (lit. 208-209 °C)³⁹; IR 3069 (w), 2967(w), 2912 (w), 2871 (m), 2364 (w), 1135

(vs), 1121 (vs) 1112 (vs); $^1\text{H NMR}$ δ 2.88 (t, $J = 6.0$, 6H), 3.88 (t, $J = 6.0$, 6H), 7.20-7.30 (m, 3H), 7.70-7.75 (m, 2H); $^{13}\text{C NMR}$ δ 51.2, 57.9, 127.4, 127.8, 134.2, 145.0. The spectroscopic properties were identical to previously reported values.³⁹

Cross-Coupling Reactions Utilizing Aryl Triflates and Phenylsilatrane

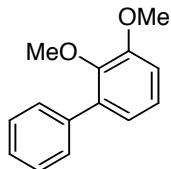


4-Methoxybiphenyl (Table 1, entry 1). A 1M solution of TBAF • 3 H₂O in THF (1.60 mL, 1.60 mmol) was added to a solution of phenylsilatrane (392 mg, 1.56 mmol), 2-(dicyclohexylphosphino)biphenyl (55 mg, 0.156 mmol) and Pd(dba)₂ (45 mg, 0.078 mmol) in 10 mL THF. The substrate 4-methoxyphenyl triflate (200 mg, 0.781 mmol) was then added. The reaction mixture was degassed to remove oxygen via one freeze pump thaw cycle and placed in a 75 °C oil bath. After heating for 12h at 75 °C, the reaction mixture was quenched with 50 mL of H₂O and the aqueous layer was extracted with 4 x 50 mL of Et₂O. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. Purification of residue by flash chromatography (30, 24, 2:3 CH₂Cl₂:hexanes) gave 93 mg (65%) of 4-methoxybiphenyl: mp 84-85 °C (lit. 90 °C (EtOH));⁷⁹ the spectroscopic properties were identical to previously reported values.^{29,30}



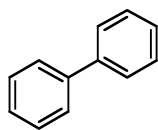
2-Methoxybiphenyl (Table 2, entry 2). Following the method

described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 20 H₂O in THF (1.60 mL, 1.60 mmol) was added to a solution of phenylsilatrane (392 mg, 1.56 mmol), 2-(dicyclohexylphosphino)biphenyl (54.7 mg, 0.156 mmol) and Pd(dba)₂ (44.9 mg, 0.0781 mmol) in 10 mL THF. The 2-methoxyphenyl triflate (200 mg, 0.781 mmol) was then added. Heating the reaction for 12 h gave 190 mg (90%) of 2-methoxybiphenyl by flash chromatography (30, 24, 2:3 CH₂Cl₂:hexanes) as a colorless oil; the spectral properties were identical to previously reported values.⁸⁰

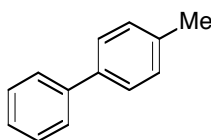


2,6-Dimethoxybiphenyl (Table 2, entry 3). Following the method

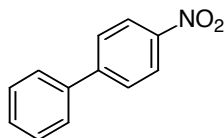
described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 20 H₂O in THF (1.60 mL, 1.60 mmol) was added to a solution of phenylsilatrane (526.9 mg, 2.10 mmol), 2-(dicyclohexylphosphino)biphenyl (73.5 mg, 0.210 mmol) and Pd(dba)₂ (60.3 mg, 0.0105 mmol) in 10 mL THF. The 2,6-dimethoxyphenyl triflate (300 mg, 1.05 mmol) was then added. Heating the reaction for 12 h gave 163.2 mg (73%) of 2,6-dimethoxybiphenyl by flash chromatography (30, 24, 2:3 CH₂Cl₂:hexanes) as a white solid: mp 47-48 °C (lit. 45-46 °C)⁸¹; the spectral properties were identical to previously reported values.⁸²



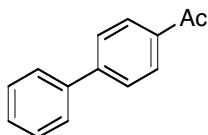
Biphenyl (Table 2, entry 5). Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 20 H₂O in THF (1.80 mL 1.80 mmol) was added to a solution of phenylsilatrane (444 mg, 1.77 mmol), 2-(dicyclohexylphosphino)biphenyl (62.0 mg, 0.177 mmol) and Pd(dba)₂ (50.8 mg, 0.0884 mmol) in 10 mL THF. The phenyl triflate (200 mg, 0.884 mmol) was then added. Heating the reaction for 12 h gave 101 mg (75%) of biphenyl by flash chromatography (30, 24, hexanes): mp: 63-64 °C (lit 71 °C)⁸³; the spectroscopic properties were identical to previously reported values.⁸⁴



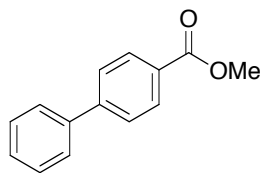
4-Methylbiphenyl (Table 2, entry 6). Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 20 H₂O in THF (1.70 mL, 1.70 mmol) was added to a solution of phenylsilatrane (418 mg, 1.67 mmol), 2-(dicyclohexylphosphino)biphenyl (58.4 mg, 0.167 mmol) and Pd(dba)₂ (47.9 mg, 0.0833 mmol), 10 mL THF. The 4-methylphenyl triflate (200 mg, 0.833 mmol) was then added. Heating the reaction for 12 h gave 121 mg (87%) of 4-methylbiphenyl by flash chromatography (30, 24, hexanes): mp: 47-48 °C (lit 47-48 °C)⁸⁵; the spectroscopic properties were identical to previously reported values.^{29,30}



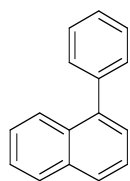
4-Nitrobiphenyl (Table 2, entry 7). Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 10 H₂O in THF (1.50 mL, 1.50 mmol) was added to a solution of phenylsilatrane (370 mg, 1.48 mmol), PPh₃ (38.7 mg, 0.148 mmol) and Pd(dba)₂ (55.1 mg, 0.0959 mmol) 10 mL THF. The 4-nitrophenyl triflate (200 mg, 0.738 mmol) was then added. Heating the reaction for 2 h gave 73 mg (50%) of 4-nitrobiphenyl by flash chromatography (20, 14, 2:3 CH₂Cl₂:hexanes) as a light yellow solid: mp: 112-113 °C (lit 115-116 °C)⁸⁴; the spectroscopic properties were identical to previously reported values.⁸⁰



4-Acetylbiphenyl (Table 2, entry 8). Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 10 H₂O in THF (1.50 mL, 1.50 mmol) was added to a solution of phenylsilatrane (375 mg, 1.49 mmol), PPh₃ (39.1 mg, 0.149 mmol) and Pd(dba)₂ (55.7 mg, 0.0969 mmol) 10 mL THF. The 4-acetylphenyl triflate (200 mg, 0.746 mmol) was added. Heating the reaction for 2 h gave 82 mg (56%) of 4-acetylbiphenyl by flash chromatography (30, 24, 2:3 CH₂Cl₂:Hexanes) as a white solid: mp 119-120 °C (lit. 119-120°C (EtOH))¹⁴; the spectroscopic properties were identical to previously reported values.^{29,30}



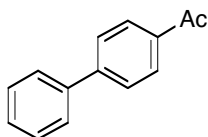
4-Carbomethoxybiphenyl (Table 2, entry 9). Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 10 H₂O in THF (1.40 mL, 1.40 mmol) was added to a solution of phenylsilatrane (354 mg, 1.41 mmol), PPh₃ (36.9 mg, 0.141 mmol) and Pd(dba)₂ (52.6 mg, 0.0915 mmol) in 10 mL THF. The 4-carbomethoxyphenyl triflate (200 mg, 0.746 mmol) was added. Heating reaction for 2 h gave 32 mg (22%) of 4-carbomethoxybiphenyl by flash chromatography (30, 24, 2:3 CH₂Cl₂:hexanes): mp: 114-115 °C (lit 119-120 °C)⁸⁶; ¹H NMR δ 3.95 (s, 3H), 7.40-7.45 (m, 1H), 7.45-7.50 (m, 2H), 7.60-7.70 (m, 4H), 8.10-8.15 (m, 2H); ¹³C NMR δ 52.6, 127.5, 127.7, 128.6, 129.3, 129.4, 130.5, 140.4, 146.0, 167.4. The spectroscopic properties were identical to previously reported values.^{87,88}



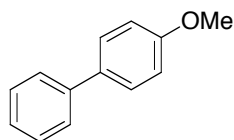
1-Phenylnaphthalene. Following the method described for the preparation of 4-methoxybiphenyl (Table 1, entry 1), a 1M solution of TBAF • 20 H₂O in THF (1.50 mL, 1.50 mmol) was added to a solution of phenylsilatrane (364 mg, 1.45 mmol), 2-(dicyclohexylphosphino)biphenyl (50.8 mg, 0.145 mmol) and Pd(dba)₂ (41.6 mg, 0.0724 mmol) in 10 mL THF. The 1-naphthalene triflate (200 mg, 0.724 mmol) was added. Heating the reaction for 12 h gave 101 mg (69%) of 4-

methylbiphenyl by flash chromatography (30, 24, hexanes) as a colorless oil: ^1H NMR δ 7.40-7.55 (m, 9H), 7.85-7.90 (m, 3H); ^{13}C NMR δ 125.3, 125.7, 126.0, 126.9, 127.2, 127.6, 128.2, 130.1, 131.6, 133.8, 140.2, 140.7. The spectroscopic properties were identical to previously reported values.⁸⁴

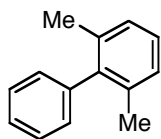
Cross-Coupling Reactions Utilizing Aryl Iodides and Bromides



4-Acetylbiphenyl (Table 3, entry 1). A 1M solution of TBAF • 3 H₂O in THF (1.63 mL, 1.63 mmol) was added to a solution of 4-iodoacetophenone (200 mg, 0.813 mmol), phenylsilatrane (408 mg, 1.63 mmol), PPh₃ (43 mg, 0.163 mmol) and Pd(OAc)₂ (19 mg, 0.0813 mmol) in 10 mL DMF. The reaction mixture was degassed to remove oxygen via one freeze pump thaw cycle and then placed in a 90 °C oil bath. After heating for 2h at 90 °C, the reaction mixture was quenched with 50 mL of H₂O and the aqueous layer was extracted with 4 x 50 mL of Et₂O. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. Purification of residue by flash chromatography (30, 24, 2:3 CH₂Cl₂/hexanes) gave 127 mg (80%) of 4-acetylbiphenyl. The spectroscopic properties were identical to previously reported values.^{29,30}



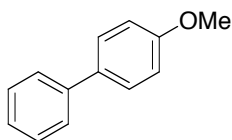
4-Methoxybiphenyl (Table 3, entry 2). Following the method described for the preparation of 4-acetylbiphenyl (Table 3, entry 1), a 1M solution of TBAF • 3 H₂O in THF (1.70 mL, 1.70 mmol) was added to a solution of 4-iodoanisole (200 mg, 0.855 mmol), phenylsilatrane (430 mg, 1.71 mmol), PPh₃ (45 mg, 0.171 mmol) and Pd(OAc)₂ (20 mg, 0.086 mmol) in 10 mL DMF. Heating the reaction gave 154 mg (78%) of 4-methoxybiphenyl by flash chromatography (30, 24, 2:3 CH₂Cl₂/hexanes): mp 84-85 °C (lit. 90 °C (EtOH)⁷⁹; the spectroscopic properties were identical to previously reported values.^{29,30}



2,6-Dimethylbiphenyl (Table 3, entry 5). Following the method described for the preparation of 4-acetylbiphenyl (Table 3, entry 1), a 1M solution of TBAF • 3 H₂O in THF (2.20 mL, 2.20 mmol) was added to a solution of 2-bromo-*m*-xylene (200 mg, 1.08mmol), phenylsilatrane (543 mg, 2.16 mmol), PPh₃ (57 mg, 0.216 mmol) and Pd(OAc)₂ (25 mg, 0.182 mmol) in 10 mL DMF. Heating the reaction gave 128 mg (65%) of 2,6-dimethylbiphenyl and 3 mg (1.5%) of biphenyl. 2,6-dimethylbiphenyl was 96% pure by GC analysis and biphenyl was unable to be removed from major product by column chromatography or distillation. The impurities were identified by comparison of GC retention times of authentic samples and with ¹H NMR of authentic samples; IR 3061 (s), 3022 (s), 2957 (vs), 2857 (s),

1945 (w), 1602 (m), 1582 (m); ^1H NMR δ 2.00 (s, 6H), 7.05-7.15 (m, 5H), 7.25-7.35 (m, 1H), 7.40-7.45 (m, 2H); ^{13}C NMR δ 26.9, 127.5, 127.6, 128.5, 129.2, 129.3, 136.1, 140.1, 146.0. The spectroscopic properties were identical to previously reported values.^{80,89}

Cross-Coupling Reactions Utilizing Aryl Triflates and Phenyltrimethoxysilane



4-Methoxybiphenyl (Table 4, entry 1). Following the method described for the preparation of 4-methoxybiphenyl (Table 2, entry 1), a 1M solution of TBAF \cdot 3 H₂O in THF (1.70 mL, 1.70 mmol) was added to a solution of phenyltrimethoxysilane (310 mg, 1.56 mmol), 2-(dicyclohexylphosphino)biphenyl (54.7 mg, 0.156 mmol) and Pd(dba)₂ (44.9 mg, 0.0781 mmol) 10 mL THF. The 4-methoxyphenyl triflate (200 mg, 0.781 mmol) was added. Heating the reaction for 12 h gave 52.5 mg (36%) of 4-methoxybiphenyl. The spectroscopic properties were identical to previously reported values.^{29,30}

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