

Mechanistic Study of Arylsilane Oxidation through ^{19}F NMR Spectroscopy

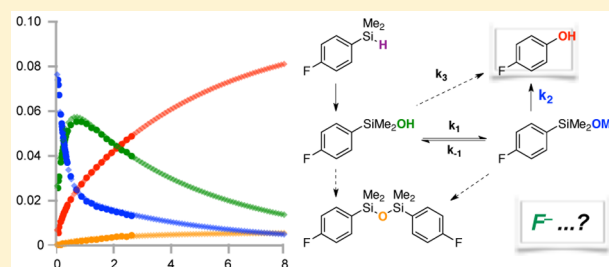
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Supporting Information

ABSTRACT: The mechanism of the oxidation of arylsilanes to phenols has been investigated using ^{19}F NMR spectroscopy. The formation of silanols in these reactions results from a rapid background equilibrium between silanol and alkoxyasilane; the relative rates of reaction of these species was evaluated by modeling of concentration profiles obtained through ^{19}F NMR spectroscopic reaction monitoring. Combining these results with a study of initial rates of phenol formation, and of substituent electronic effects, a mechanistic picture involving rapid and reversible formation of a pentavalent peroxide ate complex, prior to rate-limiting aryl migration, has evolved.



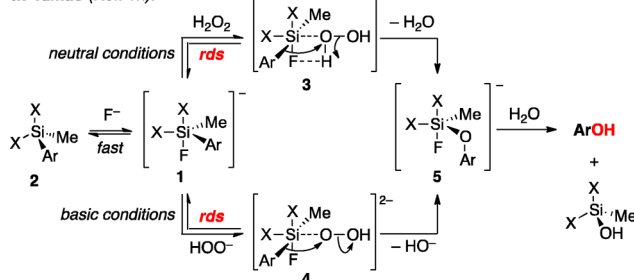
INTRODUCTION

Arylsilanes are highly versatile intermediates in organic synthesis, with a number of methods having recently been disclosed for both their preparation¹ and transformations.² Among these, the oxidation of arylsilanes to phenols is relatively underexploited compared to the equivalent conversion of alkyl and alkenylsilanes into aliphatic alcohols and ketones, respectively,^{3,4} and has only recently been developed as an efficient and general methodology.^{5,6} Despite the demonstrated synthetic utility of this oxidation,^{5g,7} mechanistic explorations of this phenol synthesis are limited to a study of arylfluorosilane oxidation by Tamao and co-workers,^{3h} and theoretical investigations on the oxidation of alkylfluorosilanes,⁸ and alkylalkoxyasilanes (and mixed alkoxyfluorosilane derivatives)⁹ by Mader and Norrby. Here we describe an experimental study of the mechanism of the H_2O_2 -mediated oxidation of arylalkoxyasilanes, a reaction that proceeds in the presence or absence^{3g,5a,10} of fluoride. In addition to shedding new light on the dynamic behavior of alkoxyasilanes, this work explores the effects of low concentrations of fluoride ion on the oxidation, which can be rationalized by consideration of the relative reactivity of different organosilane intermediates.

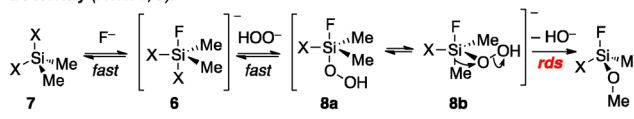
The Tamao group's seminal mechanistic studies on the hydrogen peroxide-mediated oxidation of fluorosilanes (and their corresponding fluoride ate complexes) led to their proposal (Scheme 1a) of a rate-limiting addition of hydrogen peroxide or hydroperoxide anion, under neutral or basic conditions respectively, to pentacoordinate ate complex **1** (formed by rapid and reversible addition of fluoride ion to **2**).^{3h} This peroxide association step was proposed to be rate-limiting, as the reaction was found to be first order with respect to H_2O_2 . Each pathway leads to a hexacoordinate species (**3** or **4**), and then to pentacoordinate aryloxyasilane **5** via aryl migration; a

Scheme 1. Mechanistic Paradigms in the Tamao Oxidation, and Previous Work from Our Group

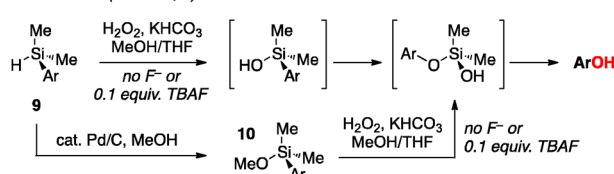
a: Tamao (Ref. 1h):



b: Norrby (Refs. 6, 7):



c: Our work (Refs. 3a, b):



concerted peroxide association/migration was not excluded. Tamao found that aryl groups migrate in preference to alkyl

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groups,¹¹ and proposed that the addition of fluoride ion is necessary for the oxidation to proceed.

Mader and Norrby subsequently calculated (Scheme 1b) that anionic substitution of anionic pentavalent silicates (e.g., **6**) is rapid,¹² and that hydroperoxide anion is more likely to attack pentacoordinate silicon (**6**) than the neutral species (**7**).^{8,9} They also proposed that addition of fluoride ions is not essential for the oxidation to proceed, but increases the rate of hydroperoxide attack at silicon via formation of a greater proportion of pentavalent trifluorosilicate species, which are more reactive toward substitution of F[−] by HOO[−] than neutral tetravalent difluorosilanes. Importantly, these authors concluded that alkyl migration from conformer **8b**, and not peroxide ion attack to generate hexacoordinate species such as **3** or **4**, is the rate-limiting step. Our own experimental work (Scheme 1c)^{5a} had shown that the oxidation of arylhydrosilanes **9**,^{5d} and arylalkoxysilanes **10**, proceeds under fluoride-promoted or fluoride-free conditions, thus supporting the notion that fluoride ion is a nonessential (but generally beneficial) component of the reaction.

Several points arise from this previous work. First, there is a general acceptance that stoichiometric amounts of fluoride are required for successful oxidation (albeit that fluoride ion may not be coordinated to silicon in the migration step itself), and that fluoride is sequestered in the course of the reaction by liberated silanes. Second, the peroxide-mediated oxidation of silanes featuring only one, or even no electronegative substituents, has not been studied from a mechanistic perspective. Third, no experimental correlation of Mader and Norrby's calculations on alkoxy silane oxidation has been achieved. Finally, the observation of silanols and disiloxanes, as intermediates or byproducts, has not been considered in detail. In this work, we disclose investigations of arylsilane oxidation which unite the various experimental and computational studies in the field, and provide a comprehensive picture of the equilibria that are at play during oxidation, as well as the influence of fluoride.

RESULTS AND DISCUSSION

In earlier work,^{5a,b} we had found that the addition of a fluoride source was not essential to achieve full conversion of arylsilanes to phenols, but that even substoichiometric amounts increase the overall efficiency of oxidation. This observation is mirrored in studies by Phillips and co-workers on the deprotection of silyl ethers using catalytic amounts of TBAF (0.1 equiv),¹³ which also demonstrate that fluoride ion can be recycled from fluorosilane byproducts (that fluorosilanes are formed irreversibly is an understandable assumption based on the strength of the Si–F bond, ~135 kcal mol^{−1}).¹⁴ Phillips found the deprotection of arylsilyl ethers to be especially rapid, underlining that these ethers are particularly susceptible to nucleophilic attack, and thus potentially more amenable to fluoride recycling as is also required in a fluoride-catalyzed oxidation manifold.¹⁵ Both our group and the Phillips group found the predominant fate of the organosilane to be the formation of a silanol (rather than fluorosilane, alkoxy silane, or disiloxane), again supporting the release of fluoride at some point after silyl ether cleavage.^{5a} With these observations in mind, we set out to study the processes at play during the oxidation of arylhydrosilanes and arylalkoxysilanes, under fluoride-free and fluoride-catalyzed reaction conditions.

Oxidation of Arylhdsilanes in THF/MeOH. We began this work by examining the oxidation of arylhydrosilanes

(ArMe₂SiH), substrates which do not contain an electronegative substituent as has previously been thought to be crucial for Tamao oxidation. The conversion of 4-(dimethylsilyl)benzonitrile **9a**, a substrate we had found to be among the more reactive toward oxidation, was monitored by ¹H NMR spectroscopy (Figure 1). To reproduce “standard”

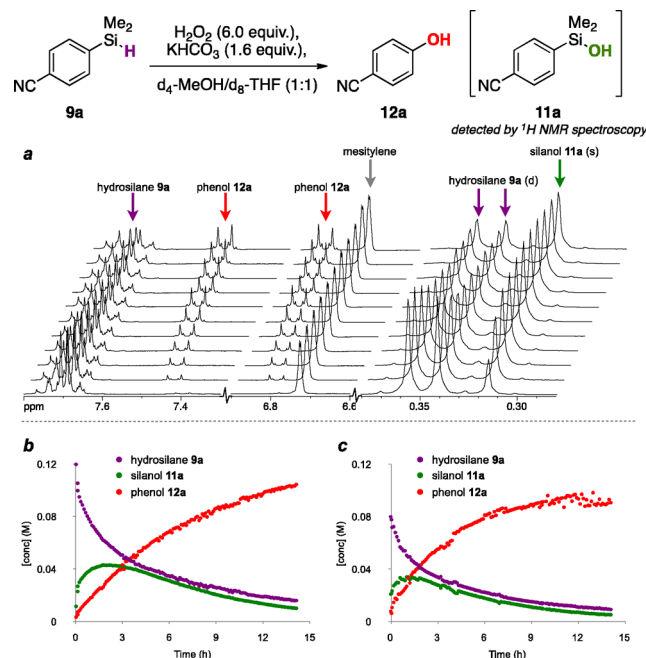


Figure 1. ¹H NMR spectroscopic reaction profiles of the oxidation of hydrosilane **9a** to phenol **12a**. (a) Reaction evolution as monitored by ¹H NMR spectroscopy. (b) Depiction of variation of concentration of **9a**, **12a**, and silanol **11a** with time. (c) Oxidation of a 4:1 mixture of hydrosilane **9a** and authentic silanol **11a**. Reactions run in 1:1 *d*₄-MeOH/*d*₈-THF (1:1, 0.3 M) at 298 K.

Tamao oxidation conditions, this experiment was performed in a mixed deuterated solvent system of *d*₄-MeOD/*d*₈-THF (1:1), with 6.0 equiv H₂O₂ (30% aq.) and 1.6 equiv KHCO₃. Although monitoring of the reaction was complicated by a broad water peak at 3.5–5.5 ppm, two regions of the spectrum proved informative (Figure 1a): the aromatic region (>6.5 ppm), where oxidation is characterized by an upfield shift of the aromatic protons; and the silane region (<0.5 ppm), where the silane substituents are characterized by their multiplicity (the methyl signals appear as a doublet in the hydrosilane, but as a singlet in compounds that do not contain Si–H). The profile of this reaction is shown in Figure 1b. This revealed a smooth consumption of hydrosilane **9a**, and the formation of a nonoxidized arylsilane species assigned as silanol **11a**,¹⁶ which was converted to phenol **12a** as the reaction proceeded. The identity of **11a** was confirmed through independent synthesis,^{17,18} and submission of a mixture of authentic **11a** and hydrosilane **9a** to the oxidation. Identical chemical shifts and a similar reaction profile were observed for this mixture as had been seen in the first oxidation, which confirmed the identity of **11a** in the mixed NMR solvent system.

We questioned whether the silanol observed in this oxidation was a necessary intermediate, or if direct hydrosilane oxidation could compete. Due to the limitations of observing the oxidation by ¹H NMR spectroscopy, we turned to *p*-fluorodimethylsilane (**9b**, Figure 2), which enabled reaction

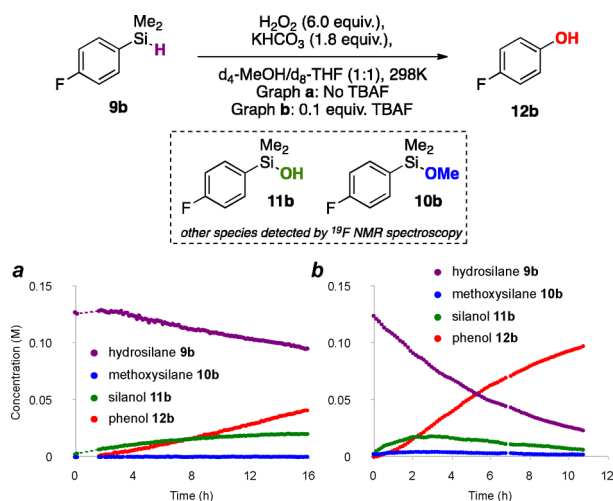


Figure 2. ^1H NMR spectroscopic reaction profiling of the oxidation of hydrosilane **9b** to phenol **12b**. (a) Reaction run in the absence of fluoride. (b) Reaction run in the presence of 0.1 equiv TBAF. Reactions run in 1:1 $d_4\text{-MeOH}/d_8\text{-THF}$ (1:1, 0.3 M) at 298 K.

monitoring by ^{19}F NMR spectroscopy. **9b** is significantly less reactive than benzonitrilesilane **9a**, but nonetheless revealed a similar trend of reactivity (Graph a), and allowed us to observe subtle details of the early phase of the oxidation, where a significant lag in the production of phenol was apparent until appreciable quantities of silanol had formed.¹⁸ This supports the intermediacy of the silanol in the oxidation, rather than a direct oxidation of the hydrosilane (i.e., migration of H is favored over Ar in the initial oxidation).

Interestingly, small amounts of methoxysilane **10b** were observed throughout the reaction. As expected, the equivalent oxidation of **9b** under fluoride-promoted conditions proceeded more rapidly (0.1 equiv TBAF, Graph b), although a delay in the production of phenol was again observed, with silanol **11b** being produced alongside small amounts of methoxysilane **10b** throughout the reaction.¹⁹ This suggests that an equivalent (but accelerated) reaction pathway operates in the presence of fluoride.

Oxidation of Silanols and Methoxysilanes in THF/MeOH. Although silanols were clearly intermediates in the oxidation of arylhydrosilanes under either fluoride-free or fluoride-promoted conditions, their reactivity relative to methoxysilanes, and the importance of exchange between these two species, was as yet unclear. To probe this, the fluoride-free oxidations of (4-fluorophenyl)dimethylsilanol **11b** and (4-fluorophenyl) methoxydimethylsilane **10b** were studied (Figure 3). We immediately noticed that oxidation of silanol **11b** (Figure 3a) proceeded at a much reduced rate compared to methoxysilane **10b** (Figure 3b), and that the latter oxidation featured significant quantities of silanol. Oxidation of **10b** under fluoride-promoted conditions (0.1 equiv TBAF, Figure 3c) proceeded at an overall rate broadly similar to that of the fluoride-free reaction. However, the composition of the various reaction intermediates was rather different, with silanol **11b** produced to a much greater extent, in addition to small amounts of a further silicon-containing species which was identified as disiloxane **13b**.¹⁸

While both the methoxysilane and silanol could potentially serve as substrates for oxidation, it was not clear whether both indeed did, given that these two components likely exist in equilibrium. To study this, methoxysilane **10b** was subjected to

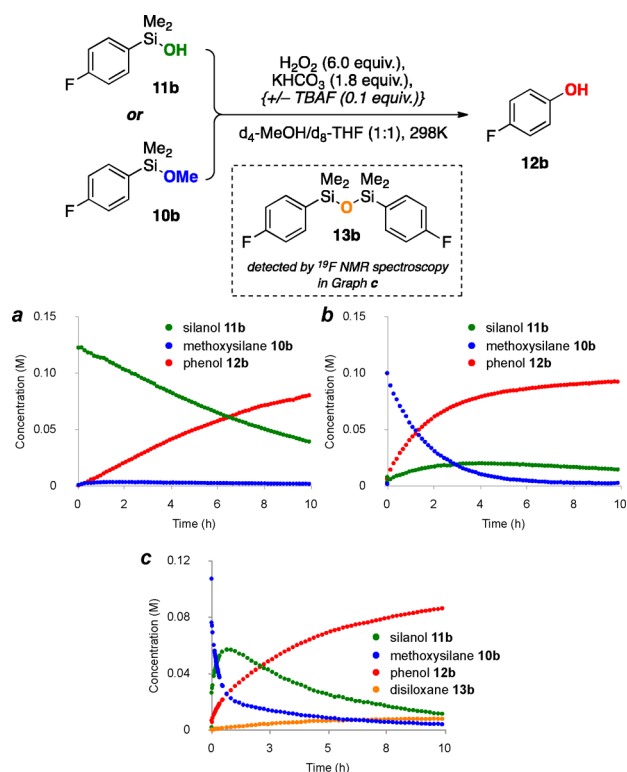


Figure 3. ^1H NMR spectroscopic reaction profiling in the oxidation of silanol **11b** and methoxysilane **10b** to phenol **12b**. Reactions run in $d_4\text{-MeOH}/d_8\text{-THF}$ (1:1, 0.1 M) at 298 K. (a) Fluoride-free oxidation of silanol **11b**. (b) Fluoride-free oxidation of methoxysilane **10b**. (c) Fluoride-promoted (0.1 equiv. TBAF) oxidation of methoxysilane **10b**.

basic conditions (KHCO_3) in deuterated THF/MeOH (1:1, plus a volume of water equivalent to that of the 30% aq. H_2O_2 used in the oxidations), in the presence and absence of TBAF. Under fluoride- and peroxide-free conditions (Figure 4, Graph

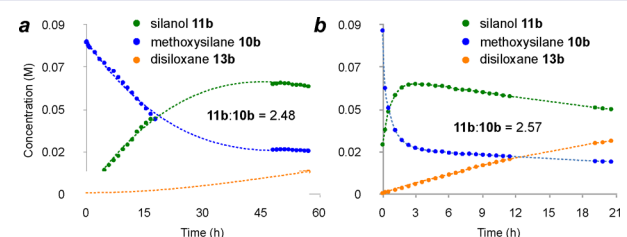


Figure 4. ^1H NMR spectroscopic profiling of the equilibria between methoxysilane **10b** and silanol **11b**. (a) Fluoride-free equilibrium. (b) Fluoride-promoted equilibrium (0.1 equiv TBAF). Reactions run in $d_4\text{-MeOH}/d_8\text{-THF}$ (1:1, 0.1 M substrate) at 298 K.

a), an equilibrium between **10b** and **11b** was established over ~48 h, which stabilized with an equilibrium constant of $K_{\text{eq}} = 2.48$ (in favor of silanol **11b**). The addition of TBAF greatly increased the rate at which equilibrium was reached, but not its position (Graph b, ~3 h, $K_{\text{eq}} = 2.57$; see the Supporting Information (SI) for further details on this equilibrium and the negligible effect of fluoride ion concentration). In both experiments, significant amounts of disiloxane **13b** were formed at the expense of the equilibrium mixture of silanol and methoxysilane; this side-reaction, which is to the detriment of oxidation,²⁰ was clearly promoted by fluoride. Under “true” oxidation conditions, the rate of equilibration could also be

affected by the nucleophilic hydroperoxide anion, particularly in the case of fluoride-free Graph 4a.

This suggested that under both sets of oxidation conditions, a dynamic equilibrium between the silanol and methoxysilane operates alongside the oxidation of either or both species, which is consistent with the exchange of ligands between different ate complexes. To elucidate the relative rates of these various processes, we modeled the timecourse kinetic data of the oxidation of methoxysilane **10b** in THF/MeOH using Berkeley Madonna software, based on the reaction scheme in Figure 5a. Graph b illustrates the experimental and modeled

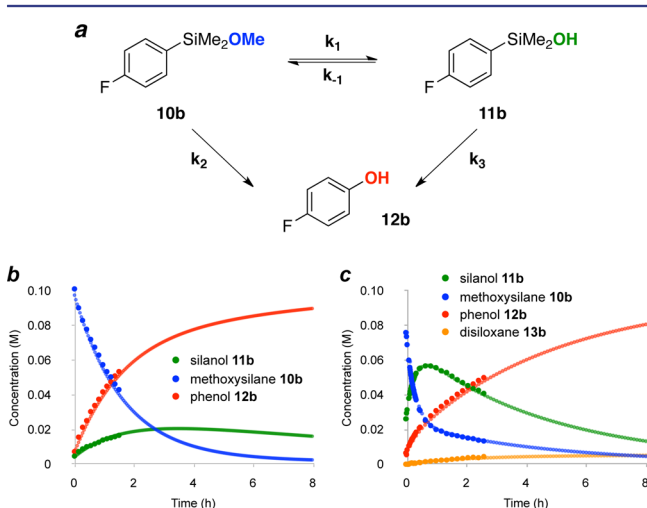


Figure 5. Modeling of kinetic data for oxidations of methoxysilane **10b**, as shown in Figure 3, using Berkeley Madonna. The model is based on experimental data up to 50% conversion (data points shown). (a) Modeled reaction pathways; (b) model for fluoride-free oxidation. (c) model for fluoride-promoted oxidation (0.1 equiv TBAF). Values are normalized relative to k_3 . Experimental data obtained at 0.1 M substrate, 0.6 M H_2O_2 , 1.8 equiv KHCO_3 in d_4 -MeOH/ d_8 -THF (1:1). Relative rate coefficients were obtained by best fit of parameters to the reaction profile a.

data for the fluoride-free oxidation of **10b**, and Graph c illustrates the data for fluoride-promoted oxidation.²¹ Best-fit correlations of the experimental data with the illustrated reaction scheme were obtained, which led to the relative rate coefficients depicted in the Table (Figure 5).²²

The modeling led to an excellent fit between experiment and theory, suggesting that the reaction scheme adopted is a valid depiction of the processes at play during the oxidation. Both models correlate with the equilibrium constants obtained experimentally ($K_{\text{eq}} \approx 2.5$, c.f. Figure 4), and give a qualitative indication that the rate of methoxysilane oxidation is around 10-fold that of silanol oxidation (i.e., $k_2 \gg k_3$). This may reflect the propensity of the silanol to form hydrogen bonds with methanol ($\text{Si}-\text{O}-\text{H} \cdots \text{O}(\text{H})\text{Me}$), which could increase electron density at the silicon atom and therefore deactivate it toward attack by hydroperoxide anion.²³ In the absence of TBAF, the rate of methoxysilane oxidation appears significantly faster than substitution at silicon by water/hydroxide ($k_2 \gg k_1 > k_{-1}$). Although hydroperoxide presumably serves as a highly competent nucleophile for ate complex formation (as evidenced by the more rapid interconversion of methoxysilane and silanol in its presence compared to the peroxide-free equilibrium experiment in Figure 4a), the peroxide ate complex formed from the methoxysilane seems more prone to undergo

(unimolecular) oxidation than (bimolecular) substitution. Equilibrium between methoxysilane and silanol is not reached until ~ 5 h reaction time (Figure 3b), such that a greater proportion of more reactive methoxysilane is present in the reaction before this time point. However, in the presence of TBAF (Figure 3c), the rate of substitution at silicon (i.e., the interconversion of methoxysilane and silanol) is increased to such an extent that it now outpaces the rate of oxidation ($k_1 > k_{-1} > k_2$). This seems reasonable, in that the interconversion of the methoxysilane and silanol would benefit significantly from fluoride (c.f. Figure 4b), and the rapid establishment of this equilibrium is to the detriment of methoxysilane oxidation.^{8,9} The culmination of these effects is that fluoride-free and fluoride-promoted methoxysilane oxidations proceed at similar overall rates, but by different compositions of intermediates.

Attempts to fit reaction parameters to the slower oxidation of the silanol (i.e., Figure 3a) proved more challenging: although these oxidations gave reproducible trends in 1:1 THF/MeOH, they did not afford reproducible relative rates of reaction, which prevented reliable parameter fitting. The reactions were found to be highly susceptible to agitation, with a momentary effervescence being observed which coincided with a marked “spike” (increase) in the rate of reaction. We surmised that this corresponded to release of carbon dioxide (from $\text{KHCO}_3/\text{H}_2\text{CO}_3$ decomposition), the evolution of which would have a dramatic effect on the acid–base equilibria of the reaction system and therefore presumably on the concentration of peroxide (or other) anions. This could be circumvented to an extent by purging the reaction mixture with argon, which displaced solubilized CO_2 . However, the most significant improvement was gained through the use of methanol alone as solvent, which now gave reproducible kinetic profiles.²⁴

The oxidations of the methoxysilane **10b** and silanol **11b** were monitored under these modified conditions (Figure 6), and the profiles modeled using Berkeley Madonna.²¹ Considering the fluoride-free oxidations of **10b** (Graph a) and **11b** (Graph b), it was immediately apparent that the rate of nucleophilic substitution at silicon was significantly enhanced in pure MeOH compared to MeOH/THF mixtures:²⁵ after initial rapid equilibration of silanol and methoxysilane (perhaps promoted by the higher solubility of KHCO_3 in MeOH), the two reaction profiles were very similar. Due to the high reproducibility of the reactions,²⁴ we were able to fit identical rate coefficients to the oxidation of both the silanol and methoxysilane, indicating that these oxidations operate under a Curtin–Hammett situation where rapid interconversion of **10b** and **11b** precedes rate-limiting oxidation—in other words, near identical reaction pathways operate from both arylsilanol and arylmethoxysilane substrates. The oxidation rate coefficients evaluated in the modeling suggest that although the silanol predominates at equilibrium, the vast majority of oxidation proceeds via the methoxysilane (i.e., $k_1 > k_{-1} \gg k_2 \gg k_3$).

The reaction profile of the fluoride-catalyzed oxidation of methoxysilane **10b** (0.1 equiv TBAF, Graph c) also revealed broadly similar kinetics, with a rapid equilibrium of methoxysilane and silanol compared to methoxysilane oxidation. TBAF might be expected to further enhance the rate of methoxysilane–silanol exchange, but no accompanying acceleration of oxidation was apparent. The reason for this was soon to become clear.

Influence of Reagent Concentration on Initial Rate of Reaction. The influence of the concentration of the various reagents was evaluated by measurement of initial rates of

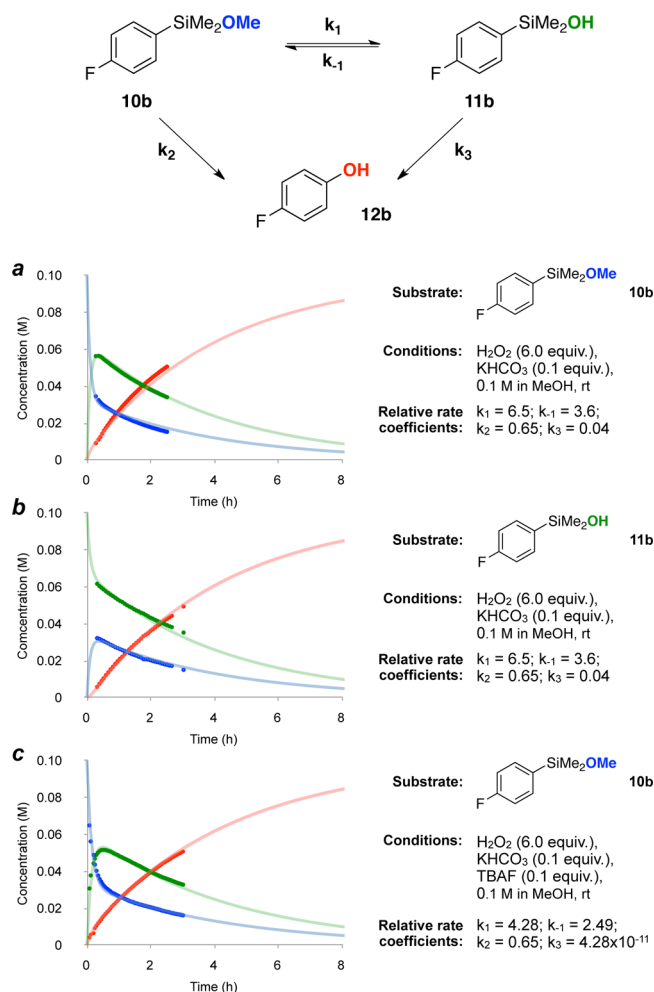


Figure 6. ^{19}F NMR spectroscopic observation, and modeled reaction parameters, for oxidations in MeOH. (a) Fluoride-free oxidation of methoxysilane **10b**; (b) fluoride-free oxidation of silanol **11b**; and (c) fluoride-promoted oxidation of **10b**. Experimental data obtained under the conditions indicated in d_4 -MeOH. Relative rate coefficients were obtained by best fit of parameters to the illustrated reaction profiles.

phenol formation in MeOH (Figure 7, experiments run in triplicate for each data point). Graph a shows the variation in initial rate of phenol formation with hydrogen peroxide concentration. As expected, the reaction shows a linear relationship to $[\text{H}_2\text{O}_2]$, but at higher concentrations a plateau effect is seen. We propose that this arises from the limiting concentration of KHCO_3 present in the reaction, which in turn limits the maximum concentration of active hydroperoxide anion. Similar results were obtained when the concentration of KHCO_3 was varied (Graph b): an increase in rate can again be seen with increasing concentration of base, with plateauing observed as the reaction mixture approaches a limit of base solubility at 0.3 equiv. KHCO_3 (i.e., 0.03 M).

The effect of TBAF concentration was next examined. Here we were surprised to observe an overall *inhibitory* effect of fluoride in the initial rate profiles (Graph c). Fluoride ions increase the rate of nucleophilic substitution around tetravalent silicon by increasing the electrophilicity of the silicon center in a pentavalent silicon-fluoride ate complex, where negative charge is dispersed onto the electronegative apical ligands; nucleophilic attack at pentavalent silicon can be up to 150 times faster than at tetravalent silicon.^{12b,26} However, in the oxidation

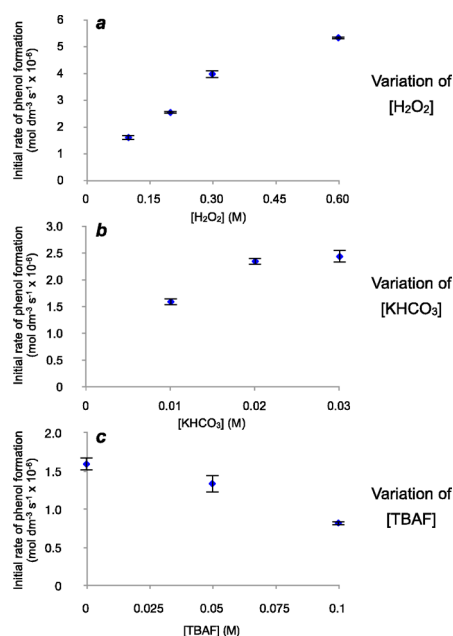


Figure 7. Order of reaction for the oxidation of methoxysilane **10b** with respect to reagents. Reactions run 0.1 M in substrate, in MeOH. Variation of concentration of (a) H_2O_2 (0.1 equiv. TBAF, 0.1 equiv. KHCO_3); (b) KHCO_3 (0.1 equiv. TBAF, 6.0 equiv. H_2O_2); (c) TBAF (0.1 equiv. KHCO_3 , 6.0 equiv. H_2O_2). Data points represent the mean rate coefficient of three reactions. Error bars indicate one standard deviation from the mean. See the SI for raw data sets.

reaction, we suggest that this effect is offset by an increased rate of interconversion of the various tetracoordinate and pentacoordinate silicon species, including the possibility that fluoride could retard the overall rate of oxidation by competitive displacement of hydroperoxide from preoxidation ate complexes, thereby decreasing the overall rate of reaction. Finally, the effect of water present in the reaction was examined, as this would likely also affect the concentration of the two silane species, and hence the rate of oxidation. Figure 8 illustrates the influence of water on the methoxysilane–silanol equilibrium constant. Not only is there a clear correlation between K_{obs} and the concentration of water, but also with the nature of the cosolvent, with a higher proportion of silanol being observed in THF/MeOH mixtures (Series A) compared

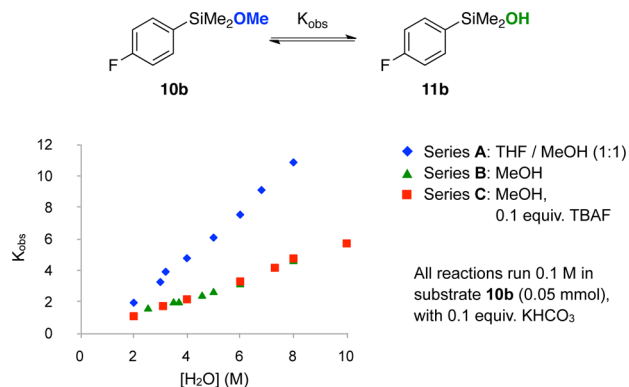


Figure 8. Effect of water on the methoxysilane/silanol equilibrium. All experiments employed 0.05 mmol **10b** and 0.1 equiv. KHCO_3 . Series A: THF/MeOH (1:1). Series B: MeOH. Series C: MeOH, 1 equiv. TBAF.

to MeOH alone (Series B, C). It is again notable in the latter solvent that fluoride does not affect the position of equilibrium. These results suggest that increasing amounts of water are likely to inhibit oxidation, albeit the inorganic base will be better solubilized.

Aryldimethylfluorosilane Intermediacy. The importance of fluoride ions in silicon chemistry merited a search for fluorosilane intermediates, which we expected would likely be present during the oxidation. To study this, we prepared the *p*-fluorophenyl dimethylfluorosilane (4-FC₆H₄SiMe₂F), and recorded its ¹⁹F NMR spectrum, which showed two signals at −113.5 (C–F) and −165.1 (Si–F)²⁷ ppm (in MeOH, Figure 9a).²⁸ Close inspection of the reaction profiles of the oxidation

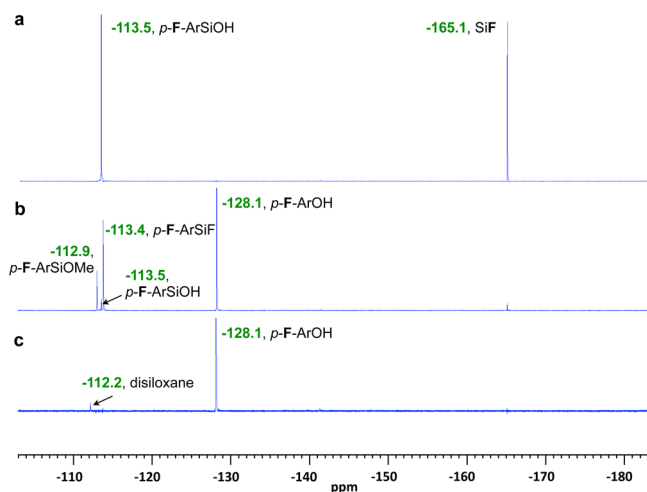


Figure 9. ¹⁹F NMR spectra of 4-FC₆H₄SiMe₂F, and oxidation of **10b**, in MeOH. (a) Authentic sample of fluorosilane. (b) Oxidation of **10b** after 4 h reaction time. (c) Spectrum of reaction mixture of oxidation of **10b** at completion (36 h), showing consumption of the fluorosilane.

of methoxysilane **10b** in MeOH, using 0.1 equiv TBAF and 3 or 6 equiv of H₂O₂, revealed a small amount of this fluorosilane to be rapidly formed in these reactions (Figure 9b, 6 equiv H₂O₂). The proportion of fluorosilane observed was inversely proportional to the concentration of H₂O₂, and the fluorosilane peak completely disappeared in the reaction using 6 equiv of H₂O₂ once this reaction reached completion (Figure 9c).²⁹ These observations substantiate the notion that fluorosilane formation is indeed influential on reaction progress, and that fluoride ion can be recycled from silane intermediates.

Charge Development in the Rate-Limiting Step. The experimental data obtained supports a rapid exchange of electronegative ligands around silicon (methoxide, hydroxide, hydroperoxide, and fluoride) as a prelude to a slower, rate-determining migration. In methanol, the rate of ligand exchange approaches a Curtin–Hammett situation, with the majority of the oxidation proceeding via the less abundant, but far more reactive methoxysilane. Given its greater intrinsic nucleophilicity, the reaction of tetravalent silicon with hydroperoxide anion itself is likely to be significantly faster than methoxide or hydroxide.

To further investigate this, we compared the relative rates of oxidation of a variety of para-substituted arylmethoxysilanes, which would enable the construction of linear free-energy relationship (LFER) plots and evaluation of associated reaction parameters. The relative rates of oxidation of these arylmethoxysilanes were measured by reaction of an equimolar

mixture of two silanes in the presence of 6 equiv H₂O₂. Five arylsilanes were investigated (*p*-OMe, Me, F, Br, CN), each run in competition with the *p*-F arylsilane. In each case, the proportion of products was measured by ¹H NMR spectroscopic monitoring of the reaction (experiments run in triplicate, ratios, which were consistent, were taken up to ~50% conversion). To compare solvent effects, each set of experiments was performed in THF/MeOH (1:1), and MeOH.

The resultant LFER plots are depicted in Figure 10. Graph a shows the Hammett plot in 1:1 THF/MeOH, and Graph b the

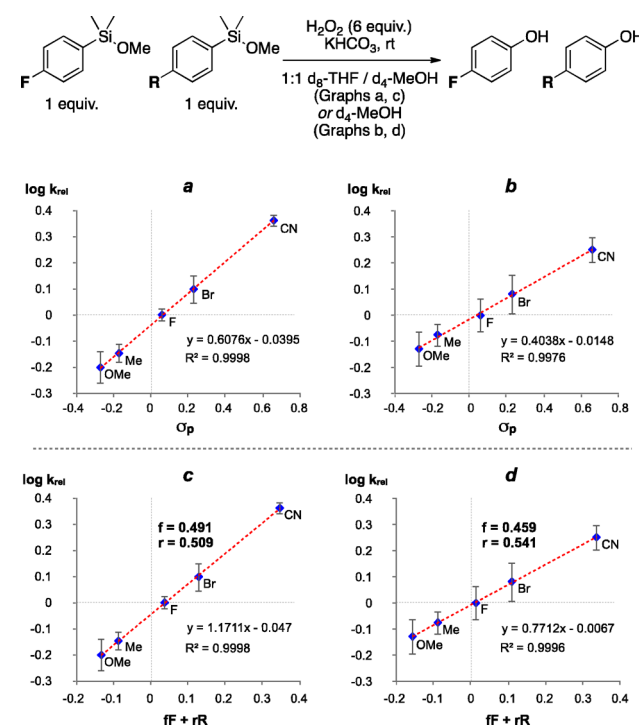


Figure 10. LFER plots for the oxidations of *p*-substituted ArSiMe₂OMe. (a) Hammett plot in 1:1 *d*₈-THF/*d*₄-MeOH; (b) Hammett plot in *d*₄-MeOH; (c) Swain–Lupton plot in 1:1 *d*₈-THF/*d*₄-MeOH; (d) Swain–Lupton plot in *d*₄-MeOH. All reactions run with 1.0 equiv each of two arylsilanes, 6 equiv H₂O₂, 16 h, rt, with (a) 0.5 equiv. KHCO₃, 0.1 M in THF/MeOH (1:1); (b) 0.5 equiv. KHCO₃, 0.1 M MeOH, reaction progress monitored by ¹H NMR spectroscopy. All reactions run in competition with 4-FC₆H₄SiMe₂OMe. $k_{rel} = [p\text{-XC}_6\text{H}_4\text{OH}]/[p\text{-FC}_6\text{H}_4\text{OH}]$, as determined by ¹H NMR spectroscopic analysis of each reaction. Error bars show one standard deviation from the mean.

Hammett plot in MeOH, which pleasingly show an excellent straight line fit, with reaction constants of $\rho = +0.60$ and $\rho = +0.45$ for Graphs a and b, respectively. Mindful that mesomeric effects might play a limited role during a rate-limiting migration step, we also explored Swain–Lupton plots of these data;³⁰ Graph c shows the Swain–Lupton plot in 1:1 THF/MeOH ($\rho_{SL} = 1.17$), and Graph d in MeOH ($\rho_{SL} = 0.77$). Of great intrigue is the balance of Swain–Lupton sensitivity factors *f* (field/inductive) and *r* (resonance), which were obtained using Dual Obligation Vector Evaluation (DOVE) as reported by Swain et al.³⁰ In MeOH/THF, $f = 0.491$, $r = 0.509$; while in MeOH, $f = 0.459$, $r = 0.541$. These values show that mesomeric and inductive effects play an equal role in the rate-determining step of the oxidation.

Despite a significant change in the rates of nucleophilic substitution at silicon when the solvent system is changed from

THF/MeOH to pure MeOH (Compare Figures 4 and 6, respectively), the somewhat similar ρ values observed for these two reactions under both Hammett and Swain–Lupton analyses further argues against nucleophilic attack of hydrogen peroxide at silicon being rate-determining, albeit H_2O_2 concentration clearly has a rate-influencing effect. These values are, nonetheless, indicative of modest negative charge development in the transition state of the rate-limiting step, which may reflect a positioning of the migrating group in the (charge dense) apical position around pentacoordinate silicon prior to/ during the migration step itself. The balance of inductive and mesomeric effects is harder to interpret, as these could affect both migration, or HOO^- coordination to the silane, but provide an additional interesting insight into the electronic characteristics of the RDS. The effect of the solvent on the extent of negative charge development adjacent to the arene in the RDS may reflect a change in the position of the transition state. For instance, it seems reasonable to suppose that O–O bond breaking may be more advanced in MeOH due to better solvation of the hydroxide leaving group.

Finally, we note that these reaction constants are similar in magnitude to the results of an intramolecular competition study of aryl migration conducted by the Tamao group (Scheme 2, eq

these studies offer new insight into organosilane reactivity for the design of silicon-based organic reactions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b00357.

Experimental procedures and data sets for NMR timecourse experiments. Characterization data and copies of NMR spectra for reaction intermediates (PDF)

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Notes

The authors declare no competing financial interest.

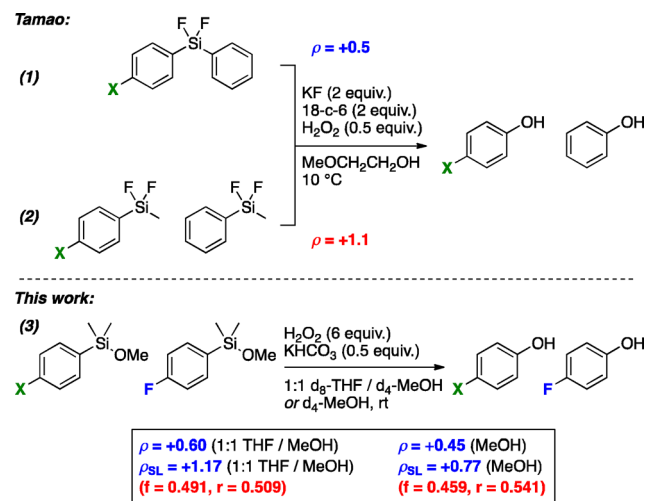
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Scheme 2. Summary of Results of Linear Free Energy Relationship Experiments



1), which was attributed to electronic effects on aryl migration alone,^{3h} but lower than a related intermolecular competition (eq 2) which Tamao concluded implied a rate-limiting attack of peroxide at silicon.³¹

■ CONCLUSIONS

By observing the oxidation of arylsilanes using ^{19}F NMR spectroscopy, the major reaction components of the oxidation have been identified and the reaction profiles characterized. A significant formation of silanol during the oxidations was revealed, as well as a sensitivity of the oxidation to solvent effects. The rapid rate of nucleophilic substitution at silicon in MeOH compared to THF/MeOH, but the similarity between the LFER reaction parameters for the oxidation in MeOH and THF/MeOH mixtures, indicates that hydrogen peroxide coordination is *not* a rate-limiting process. Instead, aryl migration is proposed to be the rate limiting step, supporting the conclusions of previous theoretical work. The results of

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- (18) See the SI for details of the identification of various key reaction intermediates through comparison with authentic materials.
- (19) We suggest that the lack of an observable lag in product formation from the *p*-CN hydrosilane (Figure 1) is due to a much higher rate of silanol-methoxysilane equilibration, and methoxysilane oxidation, which masks the expected lag.
- (20) Aryldisiloxanes are poor substrates for oxidation, see ref 5a.
- (21) Modelling is based on the first 50% conversion, with the concentration of H₂O₂ assumed constant. See the SI for details.
- (22) Relative rate coefficients have been normalized with respect to silanol oxidation ($k_{\text{rel}} = 1 \text{ s}^{-1}$). Relative second order rate coefficients for the formation of the disiloxane 13b were also modeled. The relative rate coefficient for formation of 13b from 10b and 11b was $k_3 = 20.2 \text{ s}^{-1} \text{ mol}^{-1} \text{ dm}^3$. The relative rate coefficient for the formation of 13b from two molecules of 11b was $4.1 \times 10^{-7} \text{ s}^{-1} \text{ mol}^{-1} \text{ dm}^3$. The concentration of H₂O₂ is assumed constant in these calculations.
- (23) The extreme of this interaction in a basic medium would be deprotonation of the silanol; however, the presence of silanolate ions was not detected spectroscopically.
- (24) These experiments were run in triplicate. See the SI for reaction profiles, which gave identical rate data. For example, the oxidation of the methoxysilane under fluoride-free conditions in d₄-MeOD using a standardized degassing procedure gave three initial rate coefficients of 5.316×10^{-6} , 5.322×10^{-6} and $5.312 \times 10^{-6} \text{ mol dm}^{-3} \text{ s}^{-1}$, with r^2 values of 0.92, 0.99, and 0.99 respectively; %RSD (relative standard deviation) = 0.082.
- (25) For this reason, reactions in MeOH were run at increased dilution (0.1M). See the SI for details of the optimization of conditions, and consistency of kinetic data.
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- (28) The Si–F ¹⁹F NMR peak at –165.1 ppm is masked when using hexafluorobenzene as internal standard. These NMR spectra are run in the absence of this internal standard.
- (29) Reaction using 3 equiv of H₂O₂ did not reach completion after 24 h, and fluorosilane remained after this time. We note that the fluorosilane could arise from a number of reaction pathways, including breakdown of fluoride-peroxide ate complexes.
- (30) We thank a reviewer for the helpful suggestion to analyze the LFER data using the Swain–Lupton method. See: Swain, C. G.; Unger, S. H.; Rosenquist, N. R.; Swain, M. S. *J. Am. Chem. Soc.* **1983**, 105, 492–502.
- (31) We suggest that the reduced susceptibility of the diarylsilane to electronic effects could reflect the difference in reactivity effects for this substrate class, as opposed to an arylmethylsilane.