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Organocatalytic Oxidation of Organosilanes to Silanols

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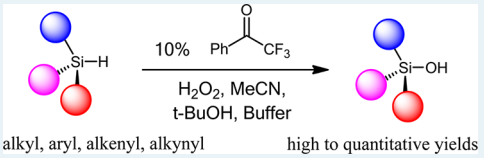
Supporting Information

ABSTRACT: The oxidation of organosilanes to silanols constitutes an attractive transformation for both industry and academia. Bypassing the need for stoichiometric oxidants or precious metal catalytic complexes, the first organocatalytic oxidation of silanes has been accomplished. Catalytic amounts of 2,2,2-trifluoroacetophenone, in combination with the green oxidant H_2O_2, lead to excellent to quantitative yields in a short reaction time. A variety of alkyl, aryl, alkenyl, and alkynyl substituents can be tolerated, providing an easy, cheap, efficient, and practical solution to a highly desirable transformation.



KEYWORDS: *green chemistry, hydrogen peroxide, organocatalysis, oxidation, perfluoroketones, silanols*

INTRODUCTION

Organosilicon compounds have attracted considerable interest because they find wide applications as versatile building blocks in both industry and academia.[1] In particular, silanols have been utilized in industry for the production of silicon-based polymeric materials,[2] for the derivatization of functional groups, and as nucleophilic partners in metal-catalyzed cross-coupling reactions in organic synthesis.[3] Organosilanols have also been identified as challenging bioactive agents in experimental pharmacology.[4] Very recently, organosilanols have been employed in catalysis,[5] because of their anion recognition ability.[6] Although the wide application of silanols requires efficient preparative protocols from readily available precursors, current synthetic approaches are limited to hydrolysis of chlorosilanes, alkali treatment of siloxanes, and oxidation of silanes (Figure 1).[7] The latter approach has stimulated the

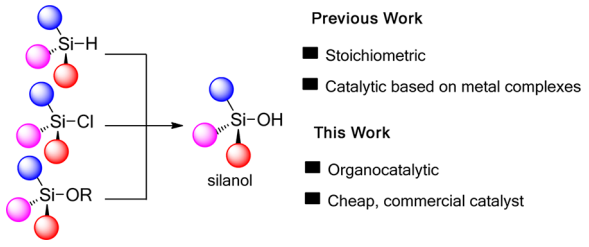


Figure 1. Approaches for the synthesis of silanols.

scientific community, and early attempts utilized stoichiometric oxidants like peracids,[8a] permanganates,[8b] dioxiranes,[8c,d] and oxaziridines.[8e] However, these methods suffer from low yields and selectivities, because undesirable byproducts, like disiloxanes, are formed. Transition metal catalysis has provided elegant solutions by employing a diverse set of catalytic conditions minimizing byproduct formation. Among the various metals utilized, Rh,[9a,b] Cu,[9c] Re,[9d,e] Pd,[9f] Ir,[9g] and W[9h] have been demonstrated to provide efficiently the oxidation of silanes. More recently, Ti-based,[10a] gold[10b,c] and silver[10d,e] nanoparticles have been synthesized and employed in the same transformation. Since 2000, organocatalysis, the use of small organic molecules as catalysts for organic transformations, has grown to such an extent that it today is considered the third major branch of asymmetric catalysis along with transition metal catalysis and biocatalysis.[11,12] Although much effort has been devoted to inventing novel reactivities, investigators researching organocatalysis have not been so actively involved in oxidation reactions. Only a number of examples exist in the literature, dealing mainly with the epoxidation reaction.[13−16] Because of their better environmental acceptance and their ability to act without requiring special reaction conditions, nonmetal organic oxidants have become available and have been employed in oxidation reactions. Furthermore, in the pharmaceutical industry, any contamination of the active pharmaceutical ingredients coming from metal catalysts is not usually acceptable [very low levels of metals (parts per million to parts per billion) are sometimes tolerated]. Along these lines, we became interested in developing the first organocatalytic protocol that could be efficiently applied in the catalytic oxidation of organosilanes.

RESULTS AND DISCUSSION

Among the most promising organic oxidants are perhydrates and dioxiranes.[13a,b] These reagents are derived from ketones in conjunction with an oxygen source. Although, in principle, the oxidants mentioned above can be used catalytically, the vast majority of the literature utilizes, in the best case scenario, stoichiometric quantities. In most cases, a large excess (>5 equiv) is required for oxidations to reach completion. Attempts to reduce the amount of reaction promoter to substoichiometric quantities have met with limited success. Indeed, some excellent contributions from the groups of Denmark,[14] Yang,[15]

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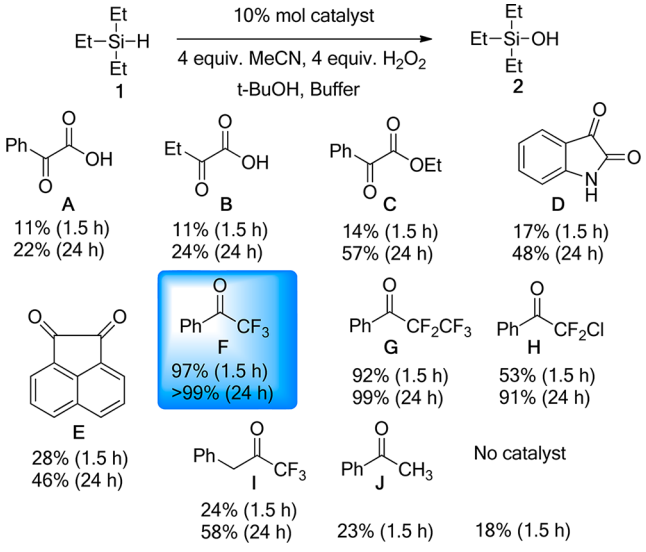
and Shi[16] have provided elegant solutions to both racemic and asymmetric epoxidation reactions. To fulfill our expectations for a process that would be acceptable for both academia and industry, we have focused on the development of a general strategy that allows the use of substoichiometric amounts (10 mol %) of a compound as a synthetically versatile and operationally trivial mode of activation of a green oxidant like H_2O_2. Today there is growing demand for the use oxidants such as H_2O_2, which are environmentally friendly and do not give rise to any waste products. We have been previously involved in the synthesis of activated ketones as potent and selective enzyme inhibitors.[17,18] Along with our own previous experience in organocatalysis,[19] we envisaged the use of activated ketones as catalysts. Hydrogen peroxide by itself is a poor oxidant for organic oxidations. Thus, it has to be coupled with a catalyst to create a reactive intermediate that will accelerate the oxidation. We anticipated that an activated ketone has the ability to perform in a manner similar to that of a metal and react with hydrogen peroxide. This intermediate will perform the oxidation of the substrate and will regenerate the catalyst.

A variety of activated ketones were tested as catalysts for the oxidation of triethyl silane to triethyl silanol using H_2O_2 as the oxidant (Scheme 1). Initially, ketoacids **A** and **B** and ketoester

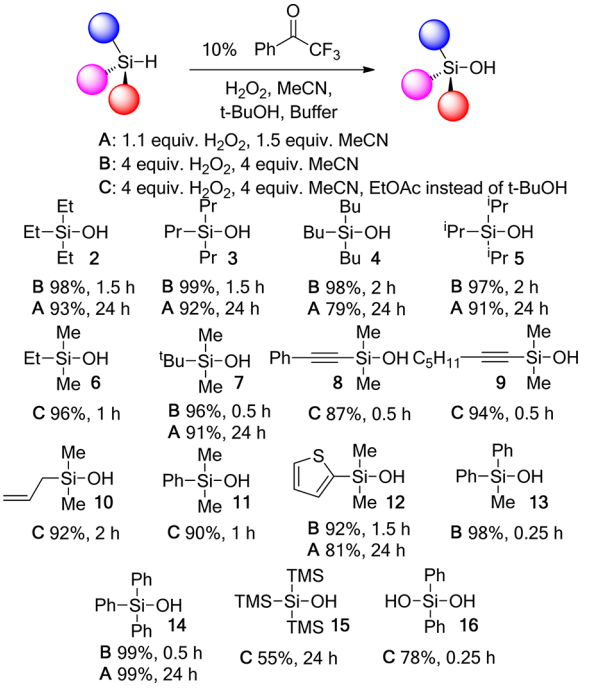
Scheme 1. Catalyst Screening for the Organocatalytic Oxidation of Triethyl Silane to Triethyl Silanol



C were employed as activated ketones. However, they led to low to moderate yields. Isatin **D** and strained 1,2-diketone **E** did not furnish the desired results. One of the most important classes of activated ketones consists of polyfluoroalkyl ketones. These ketones are known to be more activated than ketoacids and ketoesters, and these ketones exist in equilibrium with their hydrate form in aqueous environment. From this class of compounds, only some trifluoromethyl ketones have been employed in epoxidation reactions as catalysts. However, more than stoichiometric quantities are usually employed, or when substoichiometric amounts are used, lower yields, harsh reaction conditions, and longer reaction times are employed.[13] Once 2,2,2-trifluoroacetophenone **F** was employed, an excellent yield was obtained after a short reaction time (97% yield, 1.5 h). A prolonged reaction time led to a quantitative yield. Similar results were obtained when pentafluoroethylacetophenone (**G**) or heptafluoropropylacetophenone was employed.[20] Decreasing the potency of activation on the carbonyl, by either substituting one fluorine with one chlorine or utilizing a benzyl moiety instead of a phenyl, led to diminished reaction yields. Acetophenone (**J**) or the use of no catalyst led to very low levels of conversion underlying the role of the activated ketone for the catalytic activity.

After optimization,[20] we concluded that 10 mol % catalyst **F** in a *tert*-butanol aqueous buffer reaction medium can lead to excellent yields after 24 h utilizing 1.1 equiv of a MeCN/H_2O_2 mixture. The substrate scope of the protocol was then explored (Scheme 2). Initially, trialkyl and mixed alkyl silanes were

Scheme 2. Substrate Scope of the Organocatalytic Oxidation of Organosilanes



efficiently employed (silanols **2**–**7**). Unsaturated organosilanes bearing triple or double bonds can be utilized once the reaction medium is slightly altered to prevent product decomposition (EtOAc instead of *tert*-butanol). Both aromatic and aliphatic alkynyl substrates were employed, leading to high yields (silanols **8** and **9**). Substituting the alkynyl moiety with an alkene led to the isolation of silanol **10** in high yield. Aromatic moieties are also well-tolerated. The substitution of an aliphatic alkyl moiety with either a phenyl ring or a heteroaromatic thiophene moiety led to the isolation of silanols **11** and **12** in excellent yields. It has to be highlighted that a prolonged reaction time led to decreased yields via decomposition pathways. Further substitution of additional alkyl moieties with aromatic phenyl substituents led to faster reaction, leading to silanols **13** and **14** in almost quantitative yields. An organosilane bearing three TMS moieties was also employed successfully, leading to a good yield (**15**), although in this case a longer reaction time was necessary. Finally, the versatility of this method was also highlighted using diphenylsilane. This substrate usually suffers from the propensity upon oxidation to utilize metal oxidants to form not only the desired silanol **16** but also a mixture of disiloxanes, because a number of reaction pathways can be followed after the first oxidation. Our

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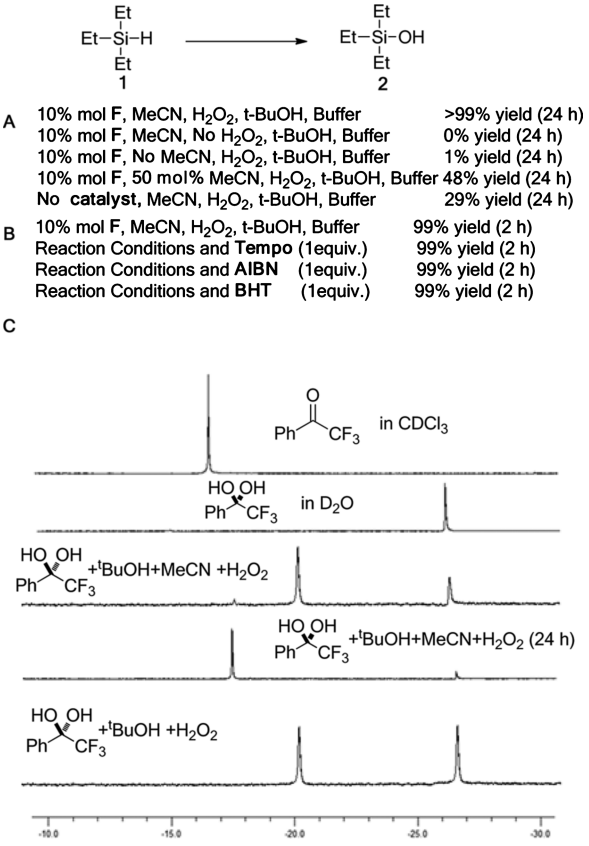
organocatalytic protocol led to a high yield of silanol **16**, and no other byproduct could be identified by nuclear magnetic resonance (NMR) and gas chromatography−mass spectrometry (GC−MS) analysis of the reaction mixture, although the reaction time and medium were quite crucial for the reaction outcome. A longer reaction time led to decreased yields because of decomposition of the product to phenol.

We then turned our attention to elucidating the reaction mechanism. A number of experiments were performed to shed more light on the reactive intermediates and key active species.

In the absence of H_2O_2, no reaction occurred. H_2O_2 was not capable by itself or in combination with the catalyst of performing the oxidation, because in the absence of MeCN, oxidation did not take place (Scheme 3A). Furthermore, when

Scheme 3. (A) Control Experiments for Probing the Reaction Mechanism, (B) Experiments for Ruling Out the Possibility of Radical Intermediates, and (C) ^{19}F NMR Experiments for Probing the Active Oxidant Species



only 0.5 equiv of MeCN was employed, only 48% of the oxidation occurred.[20] We assume that there is an intermediate oxidant, which is a peroxycarboximidic acid, similar to the intermediate that Payne and co-workers have proposed in their epoxidation reaction.[21] Furthermore, this intermediate oxidant is also not capable of promoting the reaction by itself, because in the absence of the catalyst an only 29% yield is obtained (Scheme 3A). It is our belief that H_2O_2, which is not capable of performing the oxidation by itself, has to react with acetonitrile to afford the more reactive oxidant intermediate, which in turn is not capable of performing the full oxidation but in the presence of the hydrate form of the catalyst can react and form the final oxidant that performs the reaction. Evidence that supports the peroxycarboximic acid intermediate is the observation of acetamide formation at the end of the reaction by both GC−MS analysis and ^{1}H NMR. At this stage, the crucial role of the pH of the solution has to be highlighted for the peroxycarboximic acid intermediate to be generated (see the Supporting Information). The reaction outcome was independent of the addition of the radical traps, like Tempo, AIBN, and BHT, indicating that this protocol does not contain any radical intermediates (Scheme 3B). Stemming from previous knowledge acquired in our laboratory for fluoroketones,[17] ^{19}F NMR experiments showed that although in organic solvents the equilibrium was toward the ketone form, in the aqueous medium of the reaction, the hydrate was the main form (Scheme 3C; see also the Supporting Information). Following the reaction mixture by ^{19}F NMR, infrared, and MS spectroscopy, new species containing fluorine were identified (Scheme 3C). Although 2,2,2-trifluoroacetophenone exists in the keto form in organic solvents, in the D_2O/buffer solution, the hydrate form is the predominant species (Scheme 3C). Upon addition of *t*-BuOH and MeCN, no change was observed. Once H_2O_2 was added, immediately a new peak was observed in ^{19}F NMR. This is presumably compound **IV**, a perhydrate, because the same compound was obtained when no MeCN was added to the reaction mixture (Scheme 3C, bottom). It seems that MeCN has a dual role in the oxidation via the formation of the peroxycarboximidic acid. First, it helps in the formation of higher concentrations of the perhydrate via oxidation, and second, the perhydrate with the peroxycarboximidic acid forms the active oxidant species. If no silane was added, the perhydrate was slowly transformed to a new compound, which was thought to be the corresponding dihydroperoxide. This compound is capable of promoting the oxidation, but its oxidation reaction rate is slower (24% yield, 1 h; 94% yield, 24 h). Monitoring the reaction mixture leads to the conclusion that the perhydrate is decaying while the concentration of the dihydroperoxide increases.

Taking into consideration these data, we proposed the following catalytic cycle (Figure 2). Initially, the perfluoroalkyl

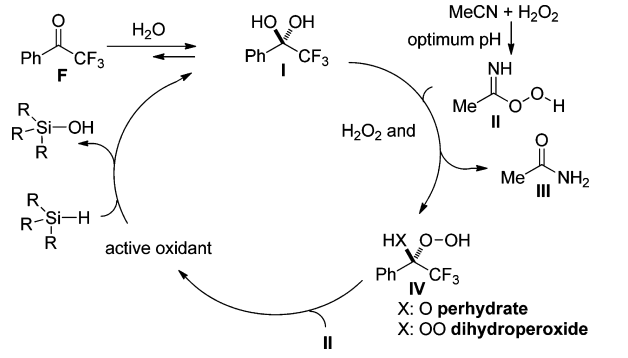


Figure 2. Proposed catalytic cycle of the oxidation.

ketone is hydrated in the presence of water, leading to its hydrate form **I**. Once the optimal pH is utilized, acetonitrile and H_2O_2 react to form peroxycarboximidic acid **II**. The hydrate form of the perfluoroalkyl ketone is oxidized by H_2O_2 and **II**, forming perhydrate **IV** and leaving acetamide **III** as a byproduct of the peroxycarboximidic acid. The presence of a new intermediate after addition of acetonitrile and H_2O_2 to the solution of the catalyst in the reaction medium was identified by ^{19}F NMR (see the Supporting Information). Perhydrate **IV**

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then reacts with **II**, forming the active oxidant species of the oxidation.[22] Upon addition of the silane, the oxidation to the corresponding silanol occurs. Finally, the silanol derivative is obtained, and at the same time, recycling of the catalyst occurs through generation of hydrate **I**. If no silane is added to the reaction medium, perhydrate is transformed to another species, the dihydroperoxide, which is capable of promoting the oxidation but at a slower rate [based on the observation of ^{19}F NMR (see the Supporting Information)].

CONCLUSIONS

In conclusion, the first highly selective organocatalytic oxidation protocol of organosilanes to silanols is described. Perfluoroalkyl aryl ketones can be employed as catalysts (10 mol %) in a such a reaction leading to excellent to quantitative yields in short reaction times. To the best of our knowledge, this is the first example of such a catalytic oxidation utilizing a cheap and commercially available metal-free organic molecule. The substrate scope of the reaction is very general, and a variety of alkyl, alkenyl, alkynyl, aryl, and heteroaryl substituents can be tolerated. The mechanism of the reaction was studied, and active intermediates are proposed.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, optimization of catalysts and conditions, including NMR and GC data, and mechanistic investigations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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