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Gas-Phase Acidity Studies of Dual Hydrogen-Bonding Organic Silanols and Organocatalysts

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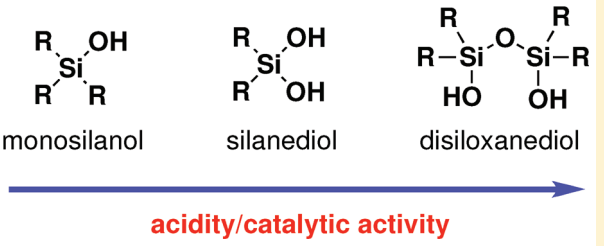
Supporting Information

ABSTRACT: The fundamental properties of a series of organic monosilanols, silanediols, disiloxanediols, and known hydrogen-bonding organocatalysts have been examined in the gas phase using computational and experimental mass spectrometry methods. The organosilicon diol molecules contain dual hydrogen-bonding groups that were designed as potential hosts and hydrogen-bonding catalysts. Newly measured acidities are reported, and implications regarding solvent effects, catalysis, and molecular recognition are discussed.



INTRODUCTION

Organic silanols and silanediols have great potential in molecular recognition and catalysis, due in large part to the ability to be both donor and acceptor.[1−7] A few studies of acidity exist in the gas phase and in solution for simple organic silanols, but no systematic study has been conducted, and no studies exist for more complex systems.[1,8] In this paper, we focus on a series of monosilanols, silanediols, and disiloxanediols, in comparison to several known hydrogen-bonding catalysts, in an effort to characterize their fundamental properties. Silanediols $R_2Si(OH)_2$ are of particular interest because they contain a geminal-diol bonding motif that is not commonly accessible for carbon analogues and has the potential to serve as a dual hydrogen-bonding group. Recent studies demonstrate that silanols can function as isosteres and transition state analogues in drug design, where the enhanced acidity of the silanol can improve binding to a receptor.[9−12] Antimicrobial activities of monosilanols have been reported where silanols exhibit greater biocidal properties relative to carbon analogues due to enhanced acidity and lipophilicity.[13] Studying silanol and silanediol groups may also be useful for understanding local surface sites and reactivity of silica materials for heterogeneous catalysis. The chosen substrates for this study (Figure 1) are targets for molecular recognition and catalysis.

RESULTS

We have conducted calculations and mass spectrometry experiments to obtain the gas-phase acidities of a fairly diverse range of silanols, including monosilanols, silanediols, and disiloxanediols, and compared these to several carbon analogues and organocatalysts (Figure 1). Studies on the fundamental properties of silanols have been primarily focused on monosilanols, which are the silicon analogues of alcohols.[1,14] By examining the intrinsic properties of molecules with dual hydrogen-bonding capabilities in the absence of solvent, we sought to explore the features that affect acidity, which in turn should affect hydrogen bonding, molecular recognition, and catalytic ability. The silanol substrates investigated here were largely chosen for their potential role in molecular recognition and as possible hydrogen-bonding catalysts, though the purpose of this specific study is to establish fundamental properties.[15a] The gas-phase acidities of a few common hydrogen-bonding catalysts were also explored, to provide fundamental data on these widely used organocatalysts and also for comparison to the silanols.[16]

Computational Results. The O−H acidity for the silanols and their carbon analogues were calculated at two levels: B3LYP/6-31+G(d) and B3LYP/6-311++G(2df,p) (Table 1).[17] The carbon analogues are of particular interest to examine by computation: carbon analogues of the monosilanols are known, stable compounds, whereas those of the diols can be computed but are generally unstable in aqueous solution, favoring structures that contain carbonyl groups. Although the carbon analogues are not experimentally accessible, calculating their properties is of interest in order to better understand the fundamental similarities and differences between analogous silicon and carbon species. We also calculated the acidities of some known hydrogen-bonding catalysts at the same computational levels (Table 2).[18]

Experimental Results. The acidity of the silanols was measured in the gas phase using both bracketing and Cooks kinetic methods.[19−25] In this paper, we report ΔH_{acid} values. Detailed bracketing

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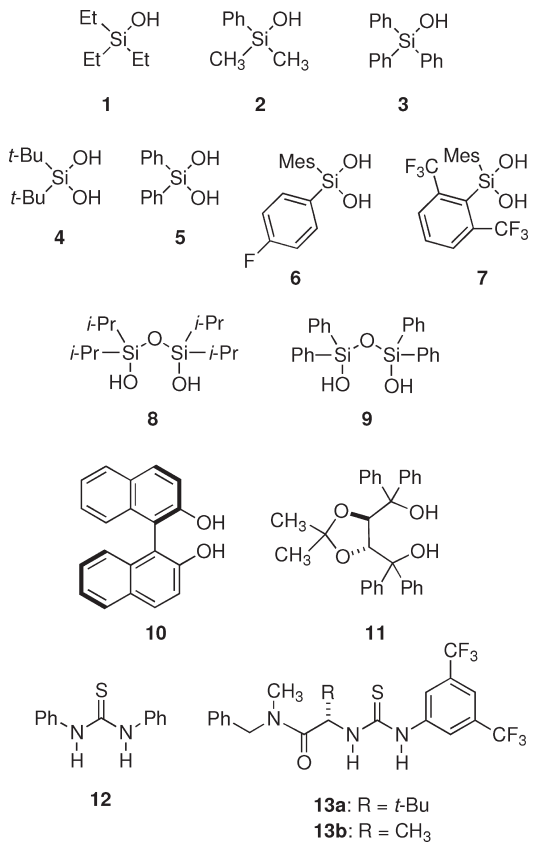


Figure 1. Silanols and other hydrogen-bonding molecules examined in this paper. Some carbon analogues were also examined and will be indicated by a prime; for example, **2′**, the carbon analogue of **2**, is $(Me)_2PhCOH$. Mes = mesityl.

tables (including ΔH_{acid} as well as ΔG_{acid} values) can be found in the Supporting Information.

*Monosilanols. a. Triethylsilanol (**1**).* The acidity of triethylsilanol was measured previously by Damrauer and co-workers to be between pyrrole (ΔH_{acid} = 359.5 ± 0.5 kcal mol^{-1}) and 2,2,2-trifluorethanol (ΔH_{acid} = 361.7 ± 2.5 kcal mol^{-1}), using a flowing afterglow-selected ion flow tube mass spectrometer.[14] A later equilibrium measurement by Bartmess and co-workers in an ion cyclotron resonance mass spectrometer yielded a comparable value.[26] In Damrauer's bracketing study, the reaction of the siloxide and the reference acid was monitored. We have repeated this measurement in our Fourier transform mass spectrometer; in our case, we were able to look at the reaction in both "directions": siloxide plus reference acid and the conjugate base of the reference acid plus the silanol. Our results are consistent with the previous results.

*b. Dimethylphenylsilanol (**2**).* We measured the acidity of dimethylphenylsilanol using two complementary methods: acidity bracketing and the Cooks kinetic method. In the bracketing experiment, dimethylphenylsiloxide deprotonates 3-methylpyrazole (ΔH_{acid} = 356.0 ± 2.1 kcal mol^{-1}), but not 3-(trifluoromethyl)aniline (ΔH_{acid} = 356.9 ± 2.1 kcal mol^{-1}). In the opposite direction, 3-(trifluoromethyl)anilide deprotonates dimethylphenylsilanol, but 3-methylpyrazolide does not. Therefore, we bracket the acidity of dimethylphenylsilanol to be ΔH_{acid} = 356 ± 3 kcal mol^{-1}.

Using the Cooks kinetic method with reference acids *p*-cresol (ΔH_{acid} = 350.3 ± 2.1 kcal mol^{-1}), 3-nitroaniline (ΔH_{acid} = 352.3 ± 2.1 kcal mol^{-1}), 4-(trifluoromethyl)aniline (ΔH_{acid} = 353.3 ± 2.1 kcal mol^{-1}), 3,5-dimethylpyrazole (ΔH_{acid} = 353.8 ± 2.1 kcal mol^{-1}), and benzamide (ΔH_{acid} = 354.0 ± 2.1 kcal mol^{-1}) yields a slightly lower acidity of 354 ± 3 kcal mol^{-1}.

Damrauer also measured the acidity of dimethylphenylsilanol.[14] The reaction was only followed in one direction (siloxide plus reference acid), and only two reference acids were used: they reported that dimethylphenylsiloxide deprotonates pyrrole but does not deprotonate trifluoroethanol, placing the acidity between 359.5 and 361.7 kcal mol^{-1}. As can be seen from Table 3, our results are different; we see no reaction between dimethylphenylsiloxide and pyrrole. Because we also examined the reaction in the reverse direction (deprotonated pyrrole plus dimethylphenylsilanol) and do see a reaction, we think it is likely that dimethylphenylsilanol is more acidic than pyrrole. Furthermore, the acidity measured by our secondary method (Cooks) is in agreement with our bracketed value.

*c. Triphenylsilanol (**3**).* The reaction of triphenylsilanol with 3-methoxyphenol (ΔH_{acid} = 348.0 ± 2.1 kcal mol^{-1}) proceeds in both directions, which indicates the acidities are comparable, ~348 kcal mol^{-1}. The Cooks kinetic experiments with reference acids 2-fluorophenol (ΔH_{acid} = 345.3 ± 2.2 kcal mol^{-1}), 2-*tert*-butylphenol (ΔH_{acid} = 345.8 ± 2.2 kcal mol^{-1}), 2-isopropylphenol (ΔH_{acid} = 347.5 ± 2.2 kcal mol^{-1}), 3-methoxyphenol (ΔH_{acid} = 348.0 ± 2.1 kcal mol^{-1}), and 4-*tert*-butylphenol (ΔH_{acid} = 348.5 ± 2.1 kcal mol^{-1}) give a comparable ΔH_{acid} of 347 ± 3 kcal mol^{-1}.

Silanediols. The acidities of silanediols have not previously been measured. The silanediols provide a unique opportunity to access a stable geminal-diol motif.

*a. Di-tert-butylsilanediol (**4**).* Deprotonated di-*tert*-butylsilanediol can deprotonate *p*-cresol but not 1-pentanethiol; 1-pentanethiolate deprotonates neutral di-*tert*-butylsilanediol, but *p*-cresolate does not. The bracketed acidity of di-*tert*-butylsilanediol is thus 352 ± 3 kcal mol^{-1}. The Cooks kinetic method with reference acids *m*-cresol (ΔH_{acid} = 349.6 ± 2.1 kcal mol^{-1}), *p*-cresol (ΔH_{acid} = 350.3 ± 2.1 kcal mol^{-1}), 4-hydroxyphenol (ΔH_{acid} = 350.4 ± 2.1 kcal mol^{-1}), 3-aminophenol (ΔH_{acid} = 350.6 ± 2.1 kcal mol^{-1}), and 4-aminophenol (ΔH_{acid} = 352.5 ± 2.1 kcal mol^{-1}) yields the same ΔH_{acid} of 352 ± 3 kcal mol^{-1}.

*b. Diphenylsilanediol (**5**).* While deprotonated diphenylsilanediol can deprotonate neutral acetic acid (ΔH_{acid} = 347.4 ± 0.5 kcal mol^{-1}) and more acidic compounds, it cannot deprotonate neutral *m*-cresol (ΔH_{acid} = 349.6 ± 2.1 kcal mol^{-1}) or less acidic compounds. In the opposite direction, *m*-cresolate deprotonates neutral diphenylsilanediol as do more basic bases. We therefore bracket the acidity of diphenylsilanediol as ΔH_{acid} = 349 ± 2 kcal mol^{-1}. By the Cooks kinetic method, we obtain an acidity of diphenylsilanediol of ΔH_{acid} = 347 ± 3 kcal mol^{-1}, using reference acids pivalic acid (ΔH_{acid} = 344.6 ± 2.1 kcal mol^{-1}), isovaleric acid (ΔH_{acid} = 345.5 ± 2.1 kcal mol^{-1}), valeric acid (ΔH_{acid} = 346.2 ± 2.1 kcal mol^{-1}), butyric acid (ΔH_{acid} = 346.8 ± 2.0 kcal mol^{-1}), and *m*-cresol (ΔH_{acid} = 349.6 ± 2.1 kcal mol^{-1}).

*c. (4-Fluorophenyl)(mesityl)silanediol (**6**).* Proton transfer occurs in both "directions" with acetic acid, which implies that the acidity of (4-fluorophenyl)(mesityl)silanediol is close to the acidity of acetic acid (ΔH_{acid} = 347.4 ± 0.5 kcal mol^{-1}). Cooks kinetic studies were difficult due to the inability to generate enough protonated dimer signal with reference acids.

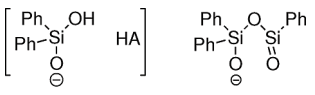
Table 1. Computational Results for Acidity of Silanols and Their Carbon Analogues

	B3LYP/6-31+G(d) (ΔH, kcal mol^{-1})		B3LYP/6-311++G(2df, p) (ΔH, kcal mol^{-1})	
silanols	silanols	carbon analogues	silanols	carbon analogues
triethylsilanol (**1**)	355.3	367.4	358.5	370.3
dimethylphenylsilanol (**2**)	351.9	361.8	355.3	365.1
triphenylsilanol (**3**)	344.5	351.3	347.6	354.0
di-*tert*-butylsilanediol (**4**)	348.4	348.6	352.2	351.9
diphenylsilanediol (**5**)	344.2	347.5	348.4	350.8
(4-fluorophenyl)-(mesityl)silanediol (**6**)	340.3	339.1	345.0	343.1
(2,6-bis(trifluoromethyl)phenyl)(mesityl)silanediol (**7**)	339.0	335.1	342.8	338.5
1,1,3,3-tetraisopropyldisiloxane-1,3-diol (**8**)	336.7	339.6	338.8	342.3
1,1,3,3-tetraphenyldisiloxane-1,3-diol (**9**)	329.4	331.7	333.1	334.6

*d. (2,6-Bis(trifluoromethyl)phenyl)(mesityl)silanediol (**7**).* We were unable to vaporize **7** for FTMS bracketing experiments. The Cooks kinetic method is prohibited by the high molecular mass of the protonated dimers; dissociation of those protonated dimers yields peaks at too low m/z values to observe (due to instrumental software limitations).

*Disiloxanediols. a. 1,1,3,3-Tetraisopropyldisiloxane-1,3-diol (**8**).* Deprotonated 1,1,3,3-tetraisopropyldisiloxane-1,3-diol can deprotonate neutral methyl cyanoacetate (ΔH_{acid} = 340.8 ± 0.6 kcal mol^{-1}) but not neutral ethoxyacetic acid (ΔH_{acid} = 342.0 ± 2.2 kcal mol^{-1}). In the opposite direction, 1,1,3,3-tetraisopropyldisiloxane-1,3-diol reacts with ethoxyacetate, but there is no proton transfer observed in the reaction of 1,1,3,3-tetraisopropyldisiloxane-1,3-diol and deprotonated methyl cyanoacetate. Thus, we bracket the acidity to be 342 ± 2 kcal mol^{-1}. Measurement by the Cooks kinetic method gives the same acidity, using L-phenylalanine (ΔH_{acid} = 336.5 ± 3.1 kcal mol^{-1}), 3-hydroxybenzoic acid (ΔH_{acid} = 338.6 ± 2.1 kcal mol^{-1}), trifluoro-*m*-cresol (ΔH_{acid} = 339.3 ± 2.1 kcal mol^{-1}), and 2-chlorophenol (ΔH_{acid} = 343.4 ± 2.3 kcal mol^{-1}).

*b. 1,1,3,3-Tetraphenyldisiloxane-1,3-diol (**9**).* Attempts to bracket the acidity of **9** were hindered by its proclivity to fragment under mass spectrometry conditions. For example, with α,α,α-trifluoro-*m*-cresol, ions at m/z 377 and 335 are observed; possible structures **9a** and **9b** are shown below (where HA is the cresol).



m/z = 377 **9a** m/z = 335 **9b**

We therefore measured the acidity using the Cooks kinetic method. Using reference acids perfluoro-*tert*-butanol (ΔH_{acid} = 331.6 ± 2.2 kcal mol^{-1}), 3-(trifluoromethyl)benzoic acid (ΔH_{acid} = 332.2 ± 2.1 kcal mol^{-1}), 4-acetylbenzoic acid (ΔH_{acid} = 334.3 ± 2.1 kcal mol^{-1}), 3,5-dichlorophenyl (ΔH_{acid} = 334.4 ± 2.1 kcal mol^{-1}), and L-phenylalanine (ΔH_{acid} = 336.5 ± 3.1 kcal mol^{-1}), the acidity of 1,1,3,3-tetraphenyldisiloxane-1,3-diol is measured to be ΔH_{acid} = 334 ± 3 kcal mol^{-1}.

Carbon Analogues. Two carbon analogues (**2′** and **3′**) of monosilanols **2** and **3** are known, and the acidity can be measured for comparison.

Table 2. Computational Results for Acidity of Known Hydrogen-Bonding Catalysts

commercial catalyst	B3LYP/ 6-31+G(d) (ΔH, kcal mol^{-1})	B3LYP/ 6-311++G(2df, p) (ΔH, kcal mol^{-1})
BINOL (**10**)	321.4	323.1
TADDOL (**11**)	328.5	330.4
N,*N*-diphenylthiourea (**12**)	328.2	330.5
2-[[3,5-bis(trifluoromethyl)-phenyl]thioureido]-*N*-benzyl-*N*-methylbutanamide (**13b**)	322.2	325.2

*a. 2-Methyl-2-phenylethanol (**2′**).* 2-Methyl-2-phenylethanol is the carbon analogue of dimethylphenylsilanol. 2-Methyl-2-phenylethoxide deprotonates aniline (ΔH_{acid} = 366.4 ± 2.1 kcal mol^{-1}) but not acetone (ΔH_{acid} = 368.8 ± 2.0 kcal mol^{-1}); also, deprotonated acetone deprotonates neutral 2-methyl-2-phenylethanol, but the anilide does not. We therefore bracket the acidity of 2-methyl-2-phenylethanol to be 368 ± 3 kcal mol^{-1}.

*b. Triphenylmethanol (**3′**).* Triphenylmethanol is the carbon analogue of triphenylsilanol. Triphenylmethoxide deprotonates 3-methylpyrazole (ΔH_{acid} = 356.0 ± 2.1 kcal mol^{-1}) but not 3-(trifluoromethyl)aniline (ΔH_{acid} = 356.9 ± 2.1 kcal mol^{-1}). In the opposite direction, 3-(trifluoromethyl)anilide deprotonates triphenylmethanol, but 3-methylpyrazolide does not. Therefore, we bracket the acidity of triphenylmethanol to be 356 ± 3 kcal mol^{-1}.

*Commercial Hydrogen-Bonding Organocatalysts. a. BINOL (**10**).* Reaction occurs in both directions for 1,1,1,-trifluoro-2,4-pentanedione (ΔH_{acid} = 328.3 ± 2.9 kcal mol^{-1}) and difluoroacetic acid (ΔH_{acid} = 331.0 ± 2.2 kcal mol^{-1}, Table 4). Deprotonated BINOL does not deprotonate 3,5-bis(trifluoro-2,4-pentanedione) (ΔH_{acid} = 329.8 ± 2.1 kcal mol^{-1}), but the reaction in the opposite direction does proceed. We therefore can bracket only an acidity range, between the pentadione and difluoroacetic acid (328−331 kcal mol^{-1}). The Cooks kinetic method yields a ΔH_{acid} of 330 ± 3 kcal mol^{-1} (using reference acids 2-hydroxybenzoic acid (ΔH_{acid} = 325.5 ± 2.2 kcal mol^{-1}), pentafluorophenol (ΔH_{acid} = 328.0 ± 2.2 kcal mol^{-1}), dichloroacetic acid (ΔH_{acid} = 328.4 ± 2.1 kcal mol^{-1}), 3,5-bistrifluoromethylphenol (ΔH_{acid} = 329.8 ± 2.1 kcal mol^{-1}), and L-asparagine (ΔH_{acid} = 331.7 ± 3.1 kcal mol^{-1})).

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Table 3. Summary of Results for Acidity Bracketing of Dimethylphenylsilanol (2)

reference compound	ΔH_{acid}[a] (kcal mol^{-1})	proton transfer[b] reference acid	proton transfer[b] conjugate base
acetic acid	347.4 ± 0.5	+	−
p-cresol	350.3 ± 2.1	+	−
1-pentanethiol	352.5 ± 2.3	+	−
1-propanethiol	354.2 ± 2.2	+	−
3-methylpyrazole	356.0 ± 2.1	+	−
3-(trifluoromethyl)aniline	356.9 ± 2.1	−	+
fluoroacetone	357.7 ± 3.6	−	+
pyrrole	359.5 ± 0.5	−	+
2,2,2-trifluoroethanol	361.7 ± 2.5	−	+
2-fluoroaniline	362.6 ± 2.2	−	+
N-ethylaniline	364.1 ± 2.1	−	+
aniline	366.4 ± 2.1	−	+

[a] Acidities are in kcal mol^{-1}.[27] [b] A "+" indicates the occurrence and a "−" indicates the absence of proton transfer.

Table 4. Summary of Results for Acidity Bracketing of BINOL (10)

reference compound	ΔH_{acid}[a] (kcal mol^{-1})	proton transfer[b] reference acid	proton transfer[b] conjugate base
1,1,1,-trifluoro-2,4-pentanedione	328.3 ± 2.9	+	+
3,5-bis(trifluoromethyl)-phenol	329.8 ± 2.1	−	+
difluoroacetic acid	331.0 ± 2.2	+	+
perfluoro-*tert*-butanol	331.6 ± 2.2	−	+
pyruvic acid	333.5 ± 2.9	−	+
2-chloropropanoic acid	337.0 ± 2.1	−	+
trifluoro-*m*-cresol	339.3 ± 2.1	−	+

[a] Acidities are in kcal mol^{-1}.[27] [b] A "+" indicates the occurrence and a "−" indicates the absence of proton transfer.

*b. TADDOL (**11**).* The conjugate base of TADDOL deprotonates perfluoro-*tert*-butanol (ΔH_{acid} = 331.6 ± 2.2 kcal mol^{-1}) but not pyruvic acid (ΔH_{acid} = 333.5 ± 2.9 kcal mol^{-1}); also, pyruvate deprotonates TADDOL, but perfluoro-*tert*-butoxide does not. We therefore bracket the acidity of TADDOL to be 333 ± 4 kcal mol^{-1}. The same acidity is obtained using the Cooks kinetic method (reference acids: 3,4,5-trichlorophenol (ΔH_{acid} = 330.8 ± 2.2 kcal mol^{-1}), perfluoro-*tert*-butanol (ΔH_{acid} = 331.6 ± 2.2 kcal mol^{-1}), 3-trifluoromethyl benzoic acid (ΔH_{acid} = 332.2 ± 2.1 kcal mol^{-1}), 4-hydroxybenzophenone (ΔH_{acid} = 332.9 ± 2.1 kcal mol^{-1}), and iodoacetic acid (ΔH_{acid} = 334.7 ± 2.2 kcal mol^{-1})).

*c. N,N-Diphenylthiourea (**12**).* Proton transfer occurs in both directions with perfluoro-*tert*-butanol (ΔH_{acid} = 331.6 ± 2.2 kcal mol^{-1}), yielding a bracketed ΔH_{acid} of 332 ± 3 kcal mol^{-1}. Using 3,4,5-trichlorophenol (ΔH_{acid} = 330.8 ± 2.2 kcal mol^{-1}), perfluoro-*tert*-butanol (ΔH_{acid} = 331.6 ± 2.2 kcal mol^{-1}), 3-trifluoromethyl benzoic acid (ΔH_{acid} = 332.2 ± 2.1 kcal mol^{-1}), 4-hydroxybenzophenone (ΔH_{acid} = 332.9 ± 2.1 kcal mol^{-1}), and iodoacetic acid (ΔH_{acid} = 334.7 ± 2.2 kcal mol^{-1}) as reference acids in the Cooks kinetic method, we obtain an acidity of 333 ± 3 kcal mol^{-1}.

*d. 2-[[3,5-Bis(trifluoromethyl)phenyl]thioureido]-N-benzyl-N,3,3-trimethylbutanamide (**13a**).* Bracketing experiments were prohibited by the paucity of volatile reference acids. The Cooks kinetic method was used, using heptafluorobutyric acid (ΔH_{acid} = 321.9 ± 2.2 kcal mol^{-1}), perfluorobenzoic acid (ΔH_{acid} = 323.6 ± 2.1 kcal mol^{-1}), and 3,5-bis(trifluoromethyl)-benzoic acid (ΔH_{acid} = 324.4 ± 2.1 kcal mol^{-1}). The acidity is measured to be 322 ± 3 kcal mol^{-1}.

DISCUSSION

All of the experimental data obtained in this study are summarized, along with corresponding computational values, in Figure 2. From these results, it can be seen that for the experimental data (in red) the acidity values obtained by the two experimental methods—bracketing and Cooks kinetic method—are comparable for any given species. Also, for the calculations, the higher computational level (B3LYP/6-311++G(2df,p); data in blue (b)) generally yields an acidity for these compounds that is closer to the experimental value than that at the lower level (B3LYP/6-31+G*).

This large number of experimental measurements therefore establish that calculations of silanol (and carbon analogue) acidity at B3LYP/6-311++G(2df,p) is reasonably accurate. A summary of the calculations conducted at this level is shown in Table 5.[28]

Overall, these results demonstrate the tunable acidities of organic silanols. The monosilanols vary in acidity from 348 to 359 kcal mol^{-1} (at B3LYP/6-311++G(2df,p)); silanediols, from 343 to 352 kcal mol^{-1}, and disiloxanediols from 333 to 339 kcal mol^{-1}.

Comparison of Acidity: Silicon versus Carbon Analogues. In terms of monosilanols, Damrauer and co-workers examined a series of simple monosilanols in the gas phase and found that, for the species studied, the silanols had considerable enhanced acidity relative to the corresponding alcohols (carbon analogues).[14] This effect is also seen in solution and is attributed to the lower electronegativity (more positive character) of silicon versus carbon, which provides greater stabilization of the anionic oxygen.[14,30−32] Furthermore, Damrauer found that, while alkyl groups increase alcohol acidity in the gas phase, such groups had the opposite effect on silanol acidity. The explanation made for this focuses on the opposing effects of polarizability and induction. In the gas phase, for alcohols, the former prevails.[33−36] Therefore, *tert*-butanol is more acidic than methanol because of the increased polarizability of the *tert*-butyl groups. Polarizability effects have an r^{-4} distance dependence; induction effects vary as r^{-2}.[14,33,37,38] Since bonds involving silicon are longer than those involving carbon, induction should play a larger role in silanols than it does in alcohols. Since alkyl groups have an acid-weakening inductive effect, silanols with more alkyl substitution become progressively less acidic.

For our monosilanols (**1**−**3**, Table 5), the alcohol analogues (**1′**−**3′**) are all, as expected, less acidic. The ΔH_{acid} difference decreases as one moves from **1** to **3**. This too would be expected: phenyl groups are polarizable but weakly inductive.[14,37,39] Therefore, such groups would be expected to increase acidity more for

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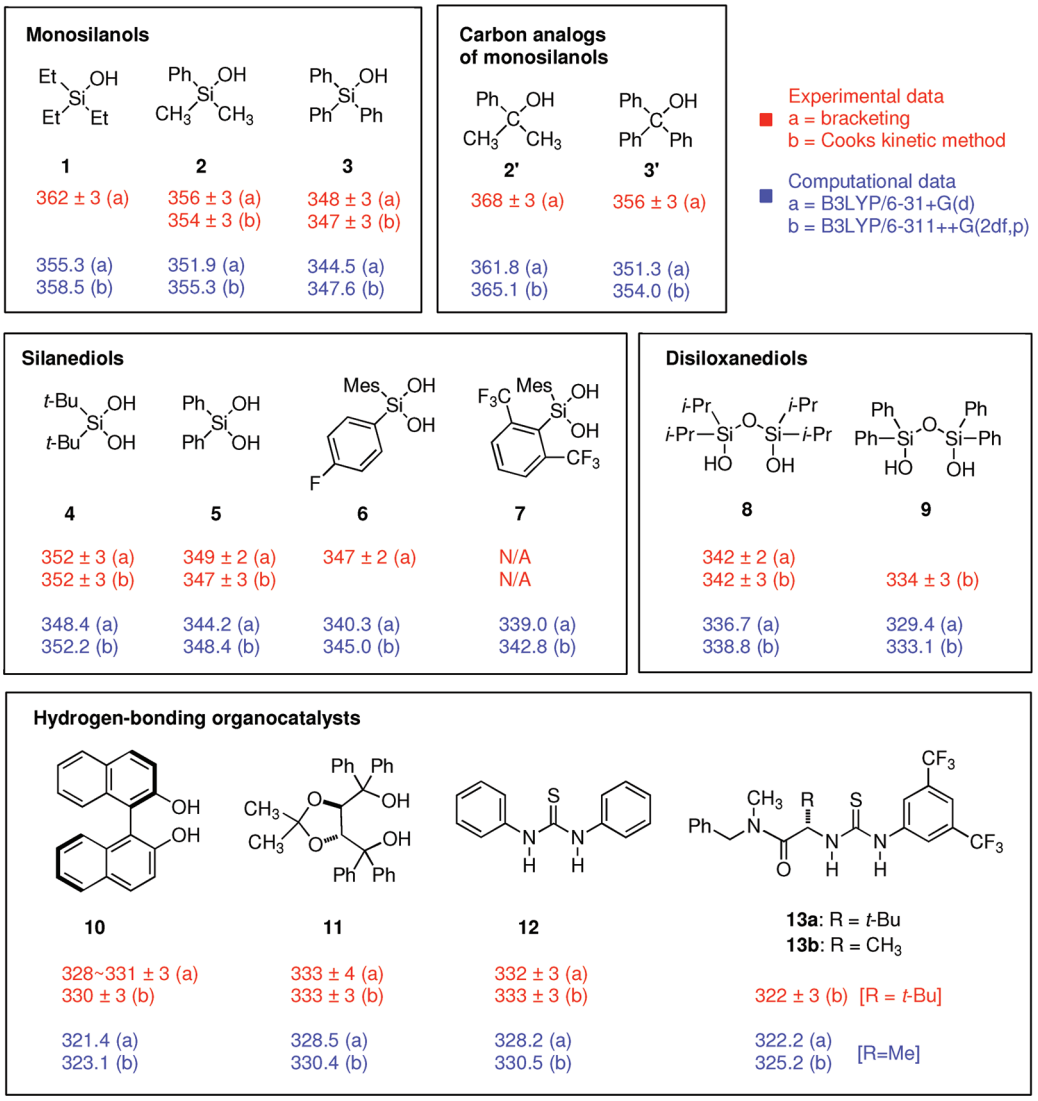


Figure 2. Summary of data for substrates examined in this study. Values are ΔH_{acid}, in kcal mol^{-1}, at 298 K.

Table 5. B3LYP/6-311++G(2df,p) Calculated ΔH_{acid} Values for Silanols X and Carbon Analogues X′

	ΔH_{acid}, kcal mol^{-1} B3LYP/6-311++G(2df, p)		
compound	silanol	carbon analogue[a]	$\Delta H_{acid}(X) - \Delta H_{acid}(X')$
triethylsilanol (**1**; carbon analogue is **1′**)	358.5	370.3	−11.8
dimethylphenylsilanol (**2**)	355.3	365.1	−9.8
triphenylsilanol (**3**)	347.6	354.0	−6.4
di-*tert*-butylsilanediol (**4**)	352.2	351.9	+0.3
diphenylsilanediol (**5**)	348.4	350.8	−2.4
(4-fluorophenyl)(mesityl)silanediol (**6**)	345.0	343.1	+1.9
(2,6-bis(trifluoromethyl)phenyl)(mesityl)silanediol (**7**)	342.8	338.5	+4.3
1,1,3,3-tetraisopropyldisiloxane-1,3-diol (**8**)	338.8	342.3	−3.5
1,1,3,3-tetraphenyldisiloxane-1,3-diol (**9**)	333.1	334.6	−1.5

[a] From ref 29.

alcohols than for silanols, and the difference in acidity between the two is lessened.

The silanediols have not heretofore been studied and are intriguing because there are no stable carbon analogues for these geminal-diol silicon species in solution. In solution, carbon analogues of the silanediols and disiloxanediols favor dehydration to form the corresponding carbonyl compound; this is one of the reasons that silanediols are of great

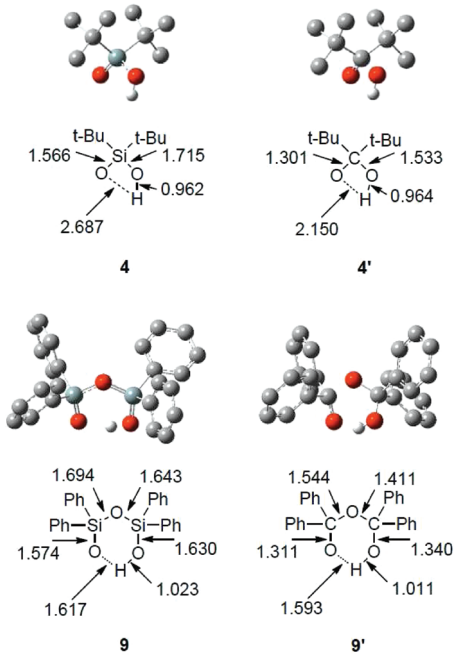


Figure 3. Deprotonated diol structures, calculated at B3LYP/6-311++G(2df, p).

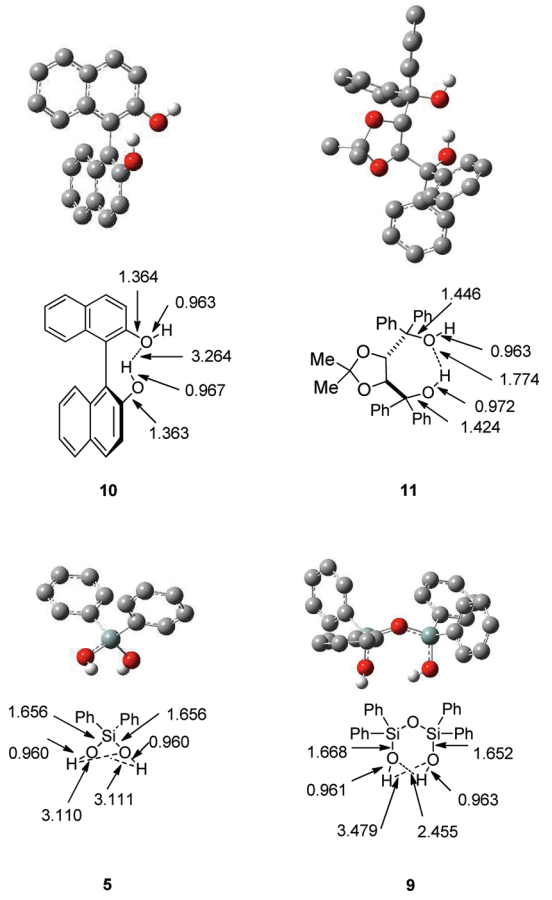


Figure 4. Organocatalyst and organosilicon neutral diol structures, calculated at B3LYP/6-311++G(2df,p).

interest because they are often stable where the carbon analogue is not.

In the comparison of silanediols with the theoretical carbon analogues, a different trend is observed than for the monosilanols. The acidities of the silanediols (**4**−**9**) and carbon analogues (**4′**−**9′**) are quite close, and in some cases (**4**, **6**, and **7**), unlike with the monosilanols, the carbon analogue is actually *more* acidic than the corresponding silanol (Table 5). For silanediols **4**, **5**, **6**, and **7**, this effect is probably due to two factors. First, the high polarizability of the *tert*-butyl and phenyl groups would, as previously discussed, enhance the acidity of the carbon analogue more than the silicon. Second, deprotonation of the diol results in an anionic oxide, which can potentially hydrogen bond with the remaining "OH" moiety.[40] For these species, the hydrogen bond is significantly longer for the deprotonated silanediol than for the corresponding deprotonated carbon analogue (Figure 3, shown for **4** and **4′**). The deprotonated product is therefore quite stabilized for the carbon analogue, which greatly increases the acidity of the corresponding neutral one. The greater enhanced acidity of the carbon analogues brings the difference in acidity between the silanediols and carbon analogues much closer: for **4**, **6**, and **7**, to the point where the carbon analogue is actually more acidic.

Substrates **8** and **9** are slightly different in that the internal hydrogen bond in the deprotonated species is more comparable for the Si and C compounds (Figure 3, shown for deprotonated **9** and **9′**). Therefore, both the deprotonated silicon and carbon analogues should get a similar benefit from the internal hydrogen bond. The influence of the four highly polarizable groups (isopropyl for **8** and phenyl for **9**) must be again enhancing the acidity of the carbon analogue more than that of the silicon analogue (due to the distance dependence discussed earlier), so that the difference in acidity between the two is attenuated.

Single versus Double-Point Hydrogen Bonding. A diol structure could, hypothetically, participates in either single-point or double-point hydrogen-bonding activation of an electrophile.[16] *N,N*-Diphenylthiourea (**12**) and BINOL (**10**) have been proposed to act as double-point hydrogen-bonding catalysts, while TADDOL (**11**) organocatalysts have cooperative hydrogen bonding (i.e., an intramolecular hydrogen bond) that leads to single-point activation for carbonyl electrophiles (Figure 4).[41−43] The calculated structures for the aryl-containing silanediol and disiloxanediol are shown in Figure 4 for comparison (note that Figure 3, which pertains to the acidity discussion, shows deprotonated molecules; Figure 4, which pertains to the intermolecular hydrogen bonding of diols with electrophiles, shows neutral diols). With intramolecular H−O distances greater than 3.0 Å, the diphenylsilanediol **5** is more likely to provide double-point hydrogen-bonding activation, in analogy to BINOL. The disiloxanediol **9** has a fairly weak intramolecular hydrogen bond (2.5 Å), which may possibly lead to single-point hydrogen-bonding activation of electrophiles, like TADDOL.[44] Most of the silicon structures we examined do not have short (less than 3.0 Å) hydrogen bonds, with the exception of **8** and **9** (the two disiloxanediols) and silanediol **7** (structures in Supporting Information). Therefore, these three structures might be more prone to activating electrophiles via single-point hydrogen bonding.

Gas Phase versus Solution. These particular silanediols and disiloxanediols discussed herein are under development as hosts and catalysts based on their acidity and hydrogen-bonding abilities.[15a,45,46] Many reactions that are catalyzed by noncovalent hydrogen-bonding organocatalysts are conducted in

Table 6. Comparison of Catalytic Activation of Carbonyl Compounds in a Diels−Alder Reaction Using Various Silanols and Alcohols

catalyst	ΔH_{acid}, kcal mol^{-1}, B3LYP/6-311++G(2df,p)	yield at −72 °C (%)[a]
2	355.3	47
2′	365.1	5
3	347.6	53
3′	354.0	17
6	345.0	40
7	342.8	55
9	333.1	55
10	323.1	63
11	330.4	30[b]

[a] The reaction temperature of −72 °C was selected to provide data that are more representative of intrinsic activating abilities. When reactions are performed at −65 °C, higher yields are observed overall, but we believe this is due, in part, to an increase in the background rate. [b] Yield based on literature values taken from ref 48 and this work.

nonpolar solvents to enhance molecular recognition and substrate activation.[16] Since the gas phase is the "ultimate" nonpolar medium, gas-phase acidity values can help assess the strength of hydrogen bonding in these reactions, especially for cases where experimental pK_a values and binding affinities may not be available.

To date, catalytic studies (of carbonyl activation by **2**, **3**, **6**, **7**, and **9** in a Diels−Alder reaction of methacrolein and Rawal's diene) were conducted in a nonpolar solvent (toluene), so the gas-phase studies herein could be relevant.[15a,47] The observed catalysis, within a class (e.g., monosilanol, silanediol, and disiloxanediol), does track with acidity (Table 6): the more acidic monosilanol **3** is a better catalyst than **2**. The more acidic silanediol **7** is, likewise, a better catalyst than **6**. The disiloxanediol **9** is the most acidic silicon substrate (somewhat comparable to commercial catalysts in gas-phase acidity); catalytic activation by **9** was found to be quite high (55%, Table 6).

The somewhat high yields for the monosilanols **2** and **3** (relative to their acidities) have been attributed (in a recent study of ours) to these species having less of a propensity to self-associate than the silanediols **6** and **7** because monosilanols have one less hydroxyl and more steric bulk around that hydroxyl.[15a] Likewise, the yield of disiloxanediol **9** is similar to that of monosilanol **3** despite the higher acidity of **9** because **9** has two hydroxy groups that will be prone to strong self-association.

The carbon analogues **2′** and **3′** are less acidic than the corresponding silanols and do in fact show less catalysis, as would be expected. The organocatalysts **10** and **11** are very acidic; **10** is more acidic than **11** and has an accordingly higher yield.

The gas-phase acidities therefore can be correlated to activity, though the correlation is certainly not quantitative. However, examination of gas-phase properties is valuable since, when activity differs from acidity, the provenance must be solvation effects, whether self-association or other influences.[15a]

In polar solvents, catalytic activity may not track with the gas-phase acidity. In general, solvation tends to decrease the difference in the acidities observed in the gas phase. In polar solution, induction may prevail even more (this is why alcohol acidity decreases with increasing alkyl substitution in solution, but the opposite is true in the gas phase).[14,33−36] Therefore, in terms of catalyst design, catalysts with aryl groups are likely to be more versatile in a variety of solvents than those with alkyl groups since the latter have acid-weakening inductive effects that are stronger in polar solvents than in nonpolar media.[49,50]

Future studies will focus on designing molecules that will allow us to test our hypotheses concerning single- versus double-point hydrogen bonding, self-association, and other possible solvent effects on silanol properties.

CONCLUSIONS

Much experimental work has been undertaken to characterize a series of novel silanols. Experimental gas-phase acidity values for a variety of dual hydrogen-bonding silanols and organocatalysts have been measured, and the computational methods have been optimized to B3LYP/6-311++G(2df,p). With established theory and basis set, we have found that the acidities of organic silanols are fairly tunable: monosilanol (348−359 kcal mol^{-1}), silanediol (343−352 kcal mol^{-1}), and disiloxanediol (333−339 kcal mol^{-1}).

Although it is generally said that silanols are more acidic than their carbon counterparts, we have found that the diol analogues show a reversal of this trend, depending on substitution and structure. Polarizability and induction have opposing effects on acidity, which differ in importance when the medium is nonpolar versus polar. Our studies have some interesting implications for these compounds as participants in molecular recognition, as transition state analogues, and in catalysis.[9−12] Preliminary studies show that carbonyl activation in a Diels−Alder reaction generally correlates with the acidities of the various silanol and carbon analogues studied herein. The correlation is not quantitative due to effects that may dominate in solution, such as self-association.

EXPERIMENTAL SECTION

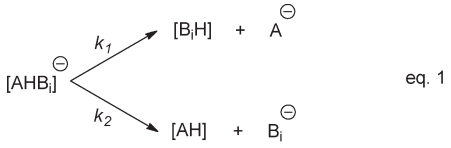
Silanols **3**, **4**, **6**, **7**, **8**, and **9** were synthesized as previously described.[15] Purity was established using ^{1}H NMR and ^{29}Si NMR spectroscopy for all; compounds **6** and **7** were also analyzed using ^{19}F NMR spectroscopy. Furthermore, the m/z ratios of the deprotonated silanols in both our high-resolution Fourier transform mass spectrometer and our quadrupole ion trap mass spectrometer are consistent with the expected structures. All other silanols (**1**, **2**, **5**), hydrogen-bonding catalysts (**10**, **11**, **12**, **13**), and reference acids are commercially available and were used as received.

Bracketing Method. Acidity bracketing measurements were conducted using a Fourier transform ion cyclotron resonance mass spectrometer (FTMS) with a dual cell setup, which has been described previously.[51−53] In our FTMS, two adjoining 1 in. cubic cells are positioned collinearly with the magnetic field produced by a 3.3 T superconducting magnet. The pressure of the dual cell is pumped down to less than 1×10^{-9} Torr. Solids are introduced into the cells via a heatable solids probe. Liquids are introduced via a batch inlet system or a leak valve. Ions are generated via reaction with HO^-. Ions can be transferred from one cell to the second cell via a 2 mm hole in the center of the central trapping plate. Transferred ions are cooled by a pulse of argon that raises the cell pressure to 10^{-5} Torr. Experiments are conducted at ambient temperature. Briefly, hydroxide ions are generated first by pulsing water into the FTMS cell and sending an electron beam (8 eV, 6 A, beam time 0.5 s) through the center of the cell. The hydroxide ions deprotonate neutral molecules "M" (either silanol or reference acid) to yield the $[M - H]^-$ ions. The $[M - H]^-$ ion is allowed to react with the neutral silanol or reference acid. The occurrence of proton transfer is regarded as evidence that the reaction is exothermic ("+" in tables).

We run these bimolecular reactions under pseudo-first-order conditions, where the amount of the neutral substrate is in excess relative to the reactant ions. Reading the pressure from an ion gauge is often unreliable because of both the gauge's remote location as well as varying sensitivity for different substrates.[54,55] We therefore "calculate" the neutral pressure from a control reaction. Briefly, we obtain the pseudo-first-order rate constant for the reaction of hydroxide and the neutral substrate. Because hydroxide is very basic, we assume this reaction proceeds at the theoretical collision rate.[56,57] We can then use the calculated collisional rate constant to "back out" the neutral pressure.[58−61]

Cooks Kinetic Method. We also used the Cooks kinetic method in a Finnigan quadrupole ion trap (LCQ) mass spectrometer[21−25] to measure the acidities of silanols. The proton-bound complex ions are generated by electrospray (ESI).[62] For each experiment, a solution of the silanol and reference acid is prepared (10^{-3} to 10^{-4} M solutions in methanol). An electrospray needle voltage of ~4.5 kV was used. The flow rate is 25 μL/min. The proton-bound complex ions were isolated and then dissociated by applying collision-induced dissociation (CID); the complexes were activated for about 30 ms. Finally, the dissociation product ions are detected to give the ratio of the deprotonated analyte and deprotonated reference acid. A total of 40 scans was averaged for the product ions.

The Cooks kinetic method involves the formation of a proton bound complex, or dimer, of the unknown AH and a reference acid B_iH of known acidity (eq 1).



eq. 1

$$\ln (k_1/k_2) = (1/RT_{eff})(\Delta H_{BiH} - \Delta H_{AH}) \qquad \text{eq. 2}$$

The proton-bound dimer $[AHB_i]^-$ is dissociated via CID. The rate constants k_1 and k_2 are for the two different dissociation pathways. The relationship of these rate constants to ΔH_{acid} is shown in eq 2. R is the gas constant, and T_{eff} is the effective temperature[63] of the activated dimer.[21−25] The ratio of the amounts (intensities) of the two deprotonated products yields the relative acidity of the two compounds of interest, assuming the dissociation has no reverse activation energy barrier and that the dissociation transition structure is late and therefore indicative of the stability of the two deprotonated products. These assumptions are generally true for proton-bound systems. In order to obtain the acidity of compound AH, the natural logarithm of the relative intensity ratios is plotted versus the acidities for a series of reference acids, where the slope is $(1/RT_{eff})$ and the y-intercept is $(-\Delta H_{AH}/RT_{eff})$. The T_{eff} is obtained from the slope. The acidity of compound AH (ΔH_{AH}) is calculated from either eq 2 or the y-intercept.

Calculations. Calculations were conducted at B3LYP/6-31+G(d)//B3LYP/6-31+G(d) and B3LYP/6-311++G(2df,p)//B3LYP/6-311++G(2df,p) using Gaussian03 and Gaussian09; the geometries were fully optimized, and frequencies were calculated.[64−68] All the values reported are at 298 K; ΔH_{acid} values include the enthalpy of the proton at 298 K (1.5 kcal mol^{-1}). No scaling factor was applied.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Cartesian coordinates for all calculated species, experimental data, and full citations for references with greater than 16 authors are available. This material is available free of charge via the Internet at http://pubs.acs.org.

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