Chapter 2

THIOL/ALKYLSULFONIC ACID-PAIRED CATALYSTS FOR THE SYNTHESIS OF BISPHENOL A

Abstract

The synthesis and characterization of heterogeneous catalysts containing surfaces functionalized with discrete pairs of sulfonic acid and thiol groups are reported. A catalyst having acid and thiol groups separated by three carbon atoms is ca. 3 times more active than a material containing randomly-distributed acid and thiol groups in the condensation of acetone and phenol to bisphenol A and 14 times more active in the condensation of cyclohexanone and phenol to bisphenol Z. Increasing the acid/thiol distance in the paired materials decreases both the activity and selectivity. This work clearly reveals the importance of nanoscale organization of two disparate functional groups on the surface of heterogeneous catalysts.

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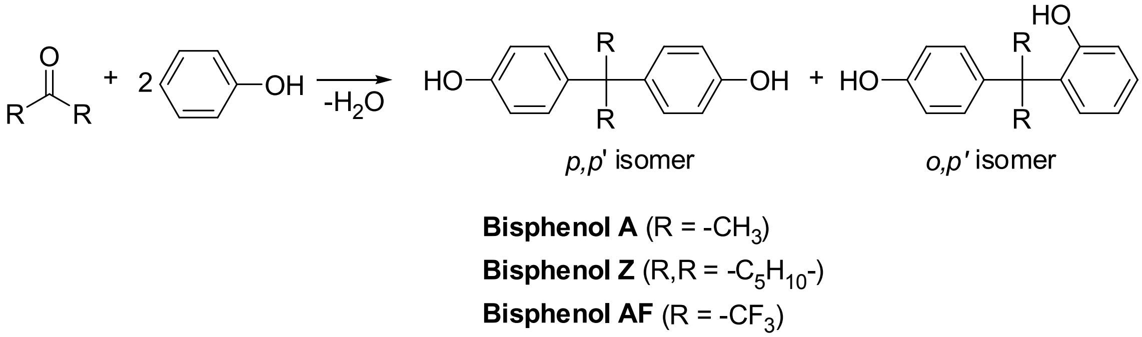
Introduction

There is growing interest in developing multifunctional catalyst systems where the different functional groups each play a distinctive role in the overall catalysis. Immobilization of two or more functional groups on a solid support allows for the possibility of spatial control of the different groups. They can be isolated from each other, which can be useful for sequential one-pot reactions,[1-4] or they can be intimately mixed such that direct interaction between the two groups is possible. In the latter case, the two groups can act in concert to provide activity greater than either could achieve alone (so-called cooperative catalysis).[5-10]

When seeking cooperative behavior between the functional groups, control of the distance between the reactive groups is essential in order to optimize the catalysis for a particular reaction. This is dramatically illustrated with enzymes that have multiple catalytic functional groups organized within a single active site. There have been several reports of the nanoscale arrangement of two or more *identical* functional groups on the surface of a silica catalyst,[11-15] but the arrangement of two *different* functional groups is more difficult. To our knowledge, there has been only one report of the organization of two disparate functional groups into pairs on a rigid support. Bass and Katz[16] synthesized a precursor containing carbamate and xanthate groups that was grafted onto silica and subsequently thermolyzed to generate pairs of amine and thiol groups. No catalytic results were reported from this bifunctional solid.

One reaction where cooperative, heterogeneous catalysis has been well established is the synthesis of bisphenol A from acetone and phenol. This reaction is catalyzed by strong acids, and promoted by thiols that have been shown to increase both the yield and selectivity of *p,p'* bisphenol A over the undesired *o,p'* isomer (Scheme 2.1). Industrial processes typically employ sulfonated polystyrene resins promoted by thiols such as cysteamine, bound to the resin by acid/base pairing[17, 18]. These resins have a random arrangement of acid and thiol groups, leading to a broad distribution of acid/thiol distances.



Scheme 2.1. Condensation of phenol with acetone, cyclohexanone, and hexafluoroacetone to form bisphenols

The mesoporous silica SBA-15[19] is well suited as a support for immobilizing organized functional groups. Its large, uniform pore diameter (~ 6 nm) provides ample room for reactant and product diffusion, and its thick walls provide hydrothermal stability. The rigidity of the silica matrix ensures that the bound functional groups do not change their positioning (unlike polymeric supports, that have the potential to shrink and swell in different solvent environments). Furthermore, SBA-15 can be easily functionalized with a wide variety of functional groups by grafting an appropriate organosilane onto surface silanol groups in order to form covalent bonds to the surface.

We have recently shown[20] that SBA-15 functionalized with randomly-distributed arylsulfonic acid and alkyl thiol groups is an effective catalyst for the synthesis of BPA.

We also demonstrated that the acid and thiol groups must be near each other to achieve high activity and selectivity: a physical mixture of acid-functionalized and thiol-functionalized SBA-15 materials exhibited only moderate activity, whereas when the two functionalities were randomly distributed on the surface of the same SBA-15 material at high loadings (at a total organic loading ~ 0.7–1.0 mmol/g) the activity was nearly fourfold higher and the isomer ratio was sixfold higher. We also showed that in this reaction the selectivity is essentially independent of conversion, which allows for the comparison of selectivities at different levels of conversion. We hypothesized that the thiol activates the protonated acetone molecule through formation of a propylidene sulfonium species that exhibits increased electrophilicity in addition to sterically disfavoring the *o,p'* isomer (Figure 2.1). If the acid and thiol groups are located near each other, the thiol can rapidly attack the protonated acetone molecule, generating the sulfonium species faster than if the groups are spatially isolated. Therefore we hypothesized that the catalytic activity should increase as the acid/thiol distance decreases.

Here, we report the synthesis of SBA-15 with alkylsulfonic acid and thiol groups organized into discrete pairs on the silica surface with varying distances between the acid and thiol groups. The distances are fixed by changing the nature of spacing groups between the acid and thiol functions, and the different spacers also provide the ability to tune both the acid/thiol distance and the electronic properties of the thiol. The resulting bifunctional catalysts give high activity and selectivity in the synthesis of bisphenol A. Pairing of the acid and thiol groups increases catalytic activity substantially compared to a randomly-bifunctionalized catalyst.

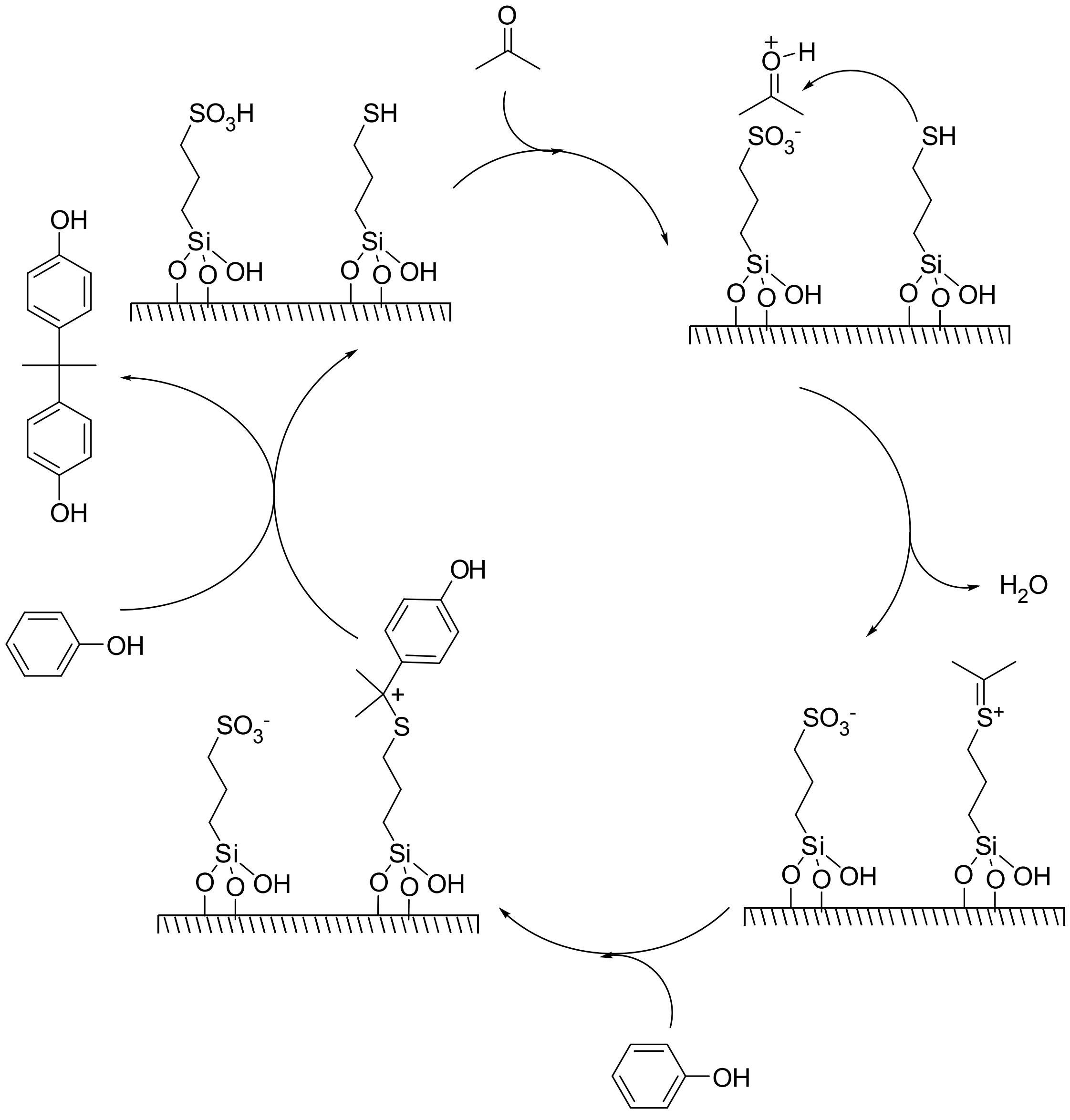


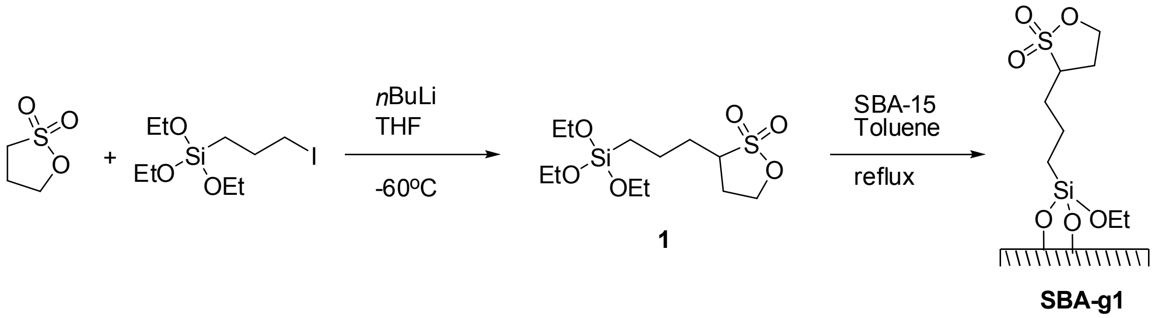
Figure 2.1. Proposed catalytic cycle for the synthesis of bisphenol A over a bifunctional acid/thiol catalyst. The propylidene sulfonium (bottom right) and carbocation (bottom left) intermediates are in close proximity to the pore wall, which provides the steric driving force that favors the formation of the *p*,*p*’ isomer of bisphenol A.

Results and Discussion

Alkylsulfonic acid-functionalized mesoporous silica has been prepared through an oxidative method where surface-bound propylthiol groups are oxidized with H_2O_2[14, 21-25] or HNO_3[26] to give propylsulfonic acid groups. Such an oxidative method is unsuitable for the preparation of bifunctional catalysts when the second functionality is also oxidizable. Furthermore, the oxidation is often incomplete and leads to disulfides and other partially oxidized species.[22, 25, 26] To circumvent this difficulty we utilized a different route to alkylsulfonic acid groups based on a sultone intermediate. This intermediate serves both as a sulfonic acid precursor and as a site for anchoring a second functionality. Reaction of the sultone ring with a thiol-containing nucleophile generates the acid/thiol pair.

Sultone rings have been opened by a wide variety of nucleophiles, including halides,[27-29] phosphines,[30, 31] thiolates,[32] sulfides,[32] alkoxides,[27, 33] and amines.[33-35] In particular, if the nucleophile contains a thiol group, then the resulting material will contain pairs of acid and thiol groups.

In order to functionalize a silica surface with sultone moieties, the organosilane **1** was synthesized from 1,3-propanesultone and 3-iodopropyltriethoxysilane using a modification of the sultone alkylation method of Durst and Du Manoir.[36] Grafting of this silane onto SBA-15 in refluxing toluene resulted in the intermediate material **SBA-g1** (Scheme 2.2). **SBA-g1** is a versatile intermediate for generating bifunctional catalysts containing a sulfonic acid group and another functional group without the need for thiol oxidation.



Scheme 2.2. Synthesis of silane **1** and grafting onto SBA-15 to form **SBA-g1**

SBA-g1 was characterized by cross-polarization magic angle spinning (CP/MAS) NMR, x-ray diffraction (XRD), nitrogen adsorption/desorption porosimetry, and elemental analysis. The ^{29}Si CP/MAS NMR spectrum (Figure 2.2) shows the incorporation of organosilanes, with most bonded by two bridging oxygen atoms (the T^2 peak in the spectrum) as well as some singly and triply bonded silanes (T^1 and T^3 peaks, respectively).[*] The ^{13}C CP/MAS NMR spectrum shows the same resonances as the molecular precursor **1** (Figure 2.3); thus, the sultone ring remains intact throughout the grafting process. The sulfur content of the materials (from elemental analysis) was used as a measure of the organic loading, and it was found that approximately 30–80% of the silane used in the grafting reaction ended up covalently bound to the surface. The XRD pattern of the functionalized material is identical to that of the parent SBA-15 and indicates that long-range ordering of the material is not affected by the grafting process (see Figure 2.4). Nitrogen adsorption/desorption porosimetry (Table 2.1, Figure 2.5)

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[*] Q denotes quaternary silicon species (four Si-O bonds) and T denotes tertiary silicon species (three Si-O bonds). The superscript number following the Q or T denotes the number of Si-O-Si bonds attached to the center.

shows that the SBA-15 surface area drops from 810 to 613 m^2/g upon grafting **1** at 0.2 mmol/g, but that the pore diameter remains constant at 6.1 nm.

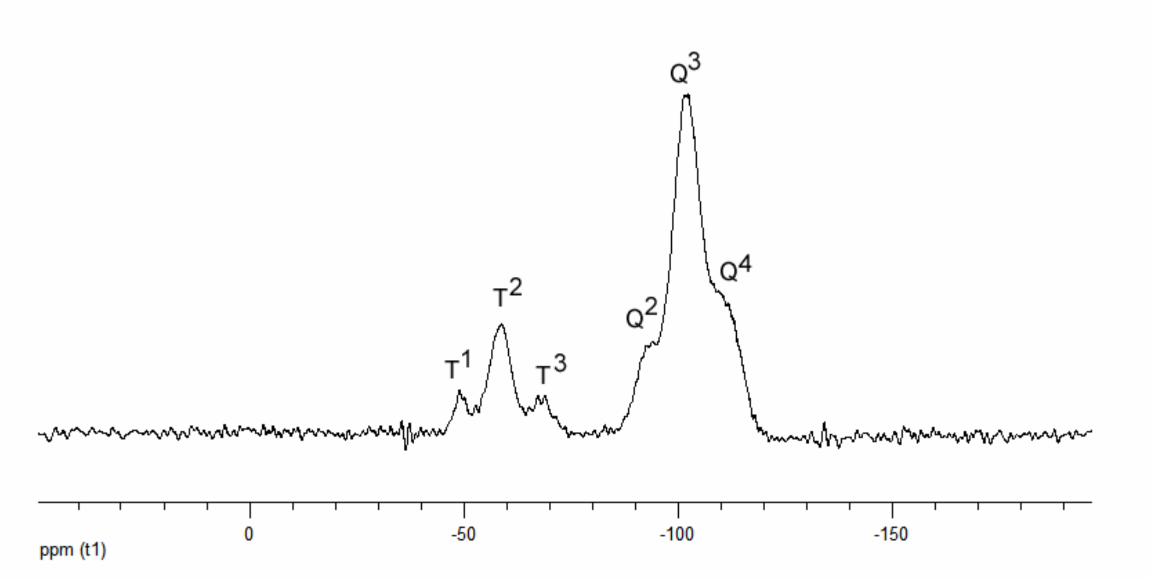


Figure 2.2. ^{29}Si{^{1}H} CP/MAS NMR spectrum of **SBA-g1** (loading = 0.7 mmol/g)

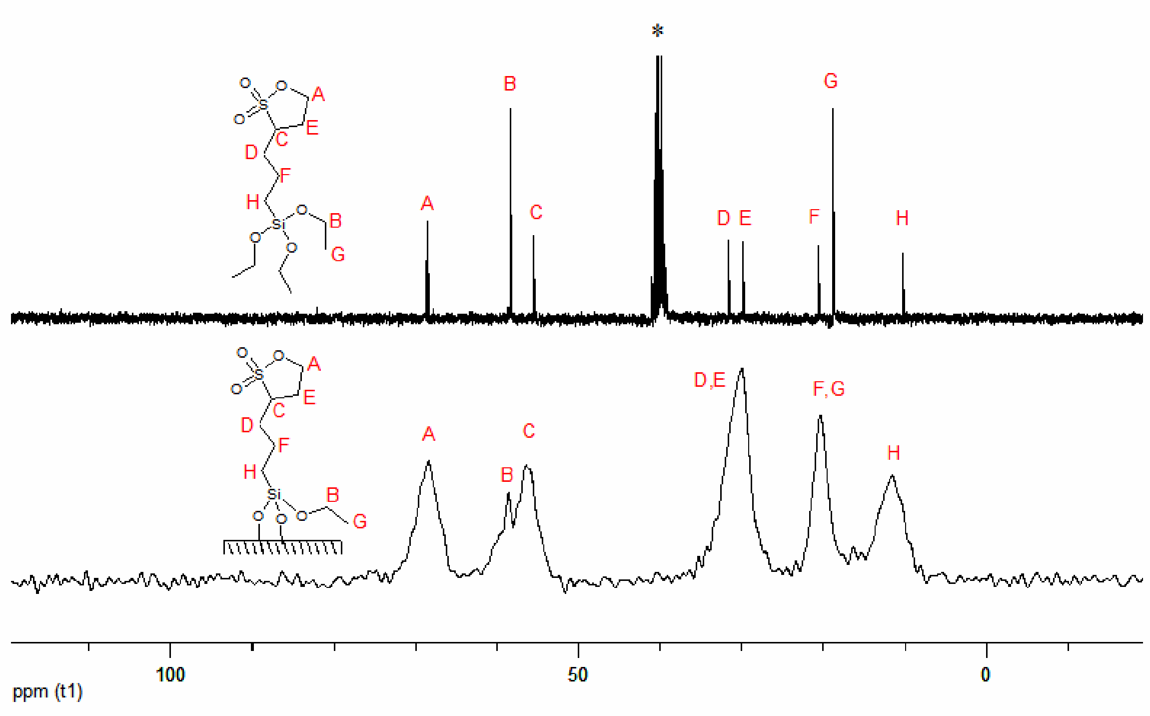


Figure 2.3. ^{13}C NMR (DMSO-d_6) of silane **1** (top) and ^{13}C{^{1}H} CP/MAS NMR of **SBA-g1** (bottom). * denotes solvent peak.

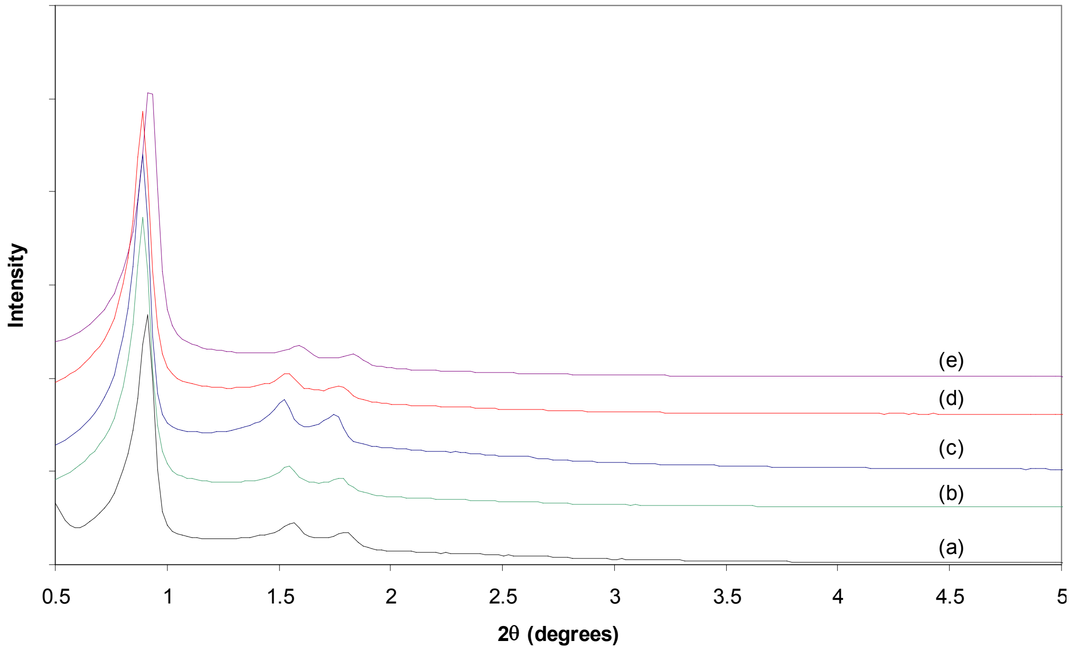


Figure 2.4. X-ray diffraction patterns of functionalized SBA-15 materials. (a) **SBA-15** (b) **SBA-g1** (c) **SBA-a** (d) **SBA-at-p** (e) **SBA-at-s5**

Sultone Ring-Opening. The sultone ring in **SBA-g1** can be hydrolyzed or thiolyzed to produce different surface groups (Scheme 2.3). Hydrolysis of the sultone in neutral water produces a solid that was used as a control catalyst because it contains acid groups but no thiols (**SBA-a**). Ring-opening with sodium hydrosulfide produces acid/thiol pairs separated by three carbon atoms (**SBA-at-p**). ^{13}C CP/MAS NMR (Figure 2.6) shows complete ring-opening of the sultone in both cases as evidenced by the disappearance of the carbon resonance at 68 ppm. The acid loadings of these materials were measured by ion-exchange with NaCl followed by filtration and titration of the resulting HCl with NaOH.[20] The sulfur content of **SBA-at-p** was found to be twice as high as the acid content measured by titration, confirming the 1:1 ratio of acid to thiol groups. The catalyst characterization data are summarized in Table 2.1.

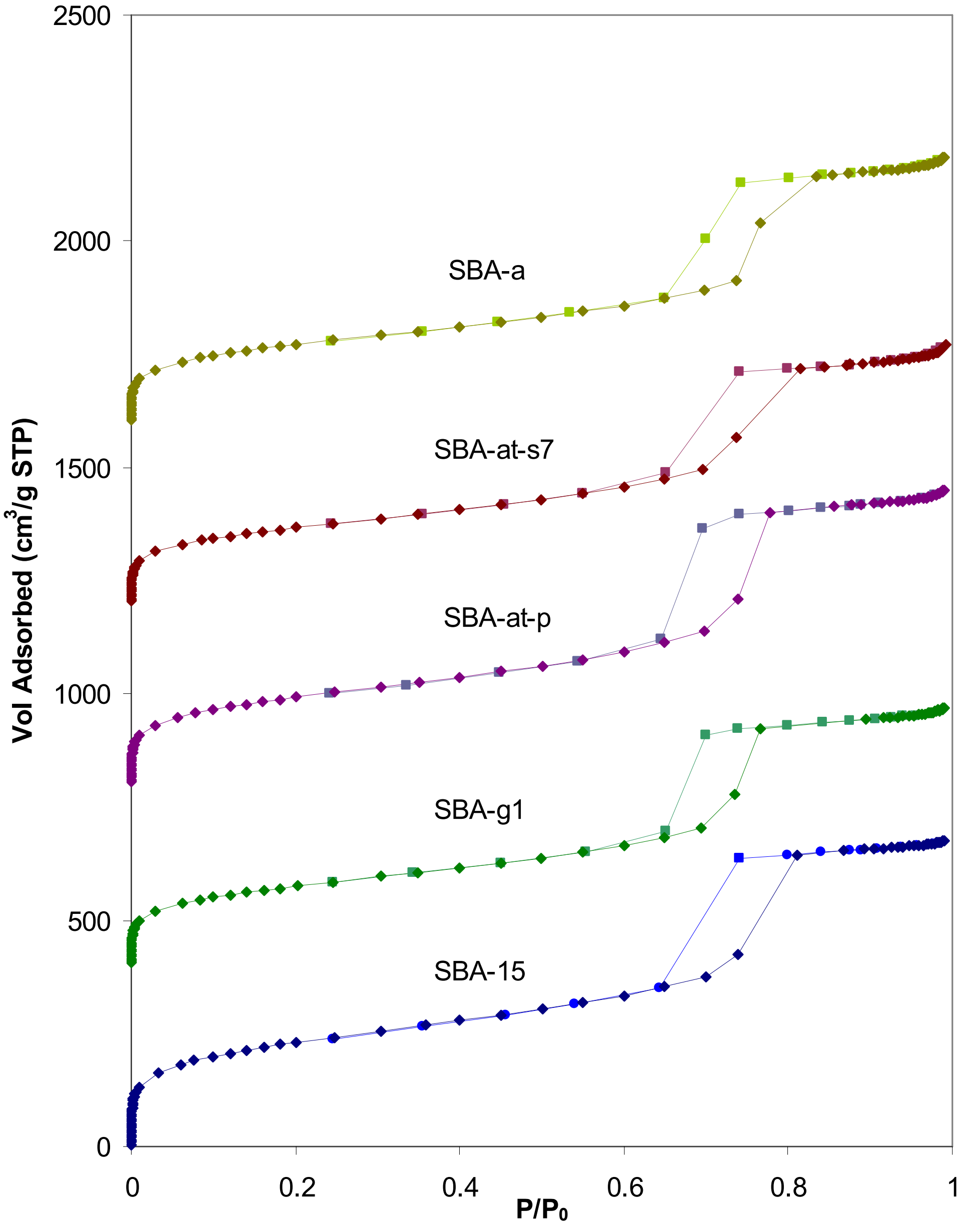


Figure 2.5. Nitrogen adsorption/desorption isotherms for various SBA-15 materials. Diamonds correspond to adsorption, squares to desorption. Data have been offset vertically by 400 units for clarity. The organic loading of each functionalized material is ~ 0.2 mmol/g.

Entry	Material	d^a (nm)	$S_{BET}{}^b$ (m^2/g)	$D_p{}^c$ (nm)	H^{+d} (mmol/g)	S^e (mmol/g)	S/H^+ (expected)	S/H^+ (found)
1	**SBA-15**	11.3	810	6.1	N/A	N/A	N/A	N/A
2	**SBA-g1**	11.5	613	6.1	N/A	0.26	N/A	N/A
3	**SBA-a**	11.6	603	6.5	0.17	0.26	1	1.5
4	**SBA-as-p**				0.38	0.81	2	2.1
5	**SBA-at-p**	11.5	676	6.2	0.18	0.4	2	2.2
6	**SBA-at-r**				0.18	1.04	N/A	5.8
7	**SBA-at-s1**				0.22	0.54	3	2.5
8	**SBA-at-s2**				0.18			
9	**SBA-at-s3**				0.21			
10	**SBA-at-s4**				0.17			
11	**SBA-at-s5**	11.1			0.2			
12	**SBA-at-s6**[f]				0.16			
13	**SBA-at-s7**		585	6.3	0.2	0.5	3	2.5
14	**SBA-at-s8**				0.21	0.56	3	2.7
15	**SBA-at-s9**[f]				0.18			

Table 2.1. Catalyst characterization data

[a] unit cell parameter, from x-ray diffraction data

[b] Surface area, calculated from adsorption branch of N_2 isotherm using the BET method

[c] pore diameter from BJH analysis of desorption branch of N_2 isotherm

[d] from titration

[e] total sulfur content, from elemental analysis (performed by QTI, Whitehouse, NJ)

[f] **SBA-at-s6** and **SBA-at-s9** turned pink upon acidification due to a trace amount of organic byproduct resulting from the decomposition of the monosodium salt of the *o*-xylyl or *o*-durenyl dithiol.

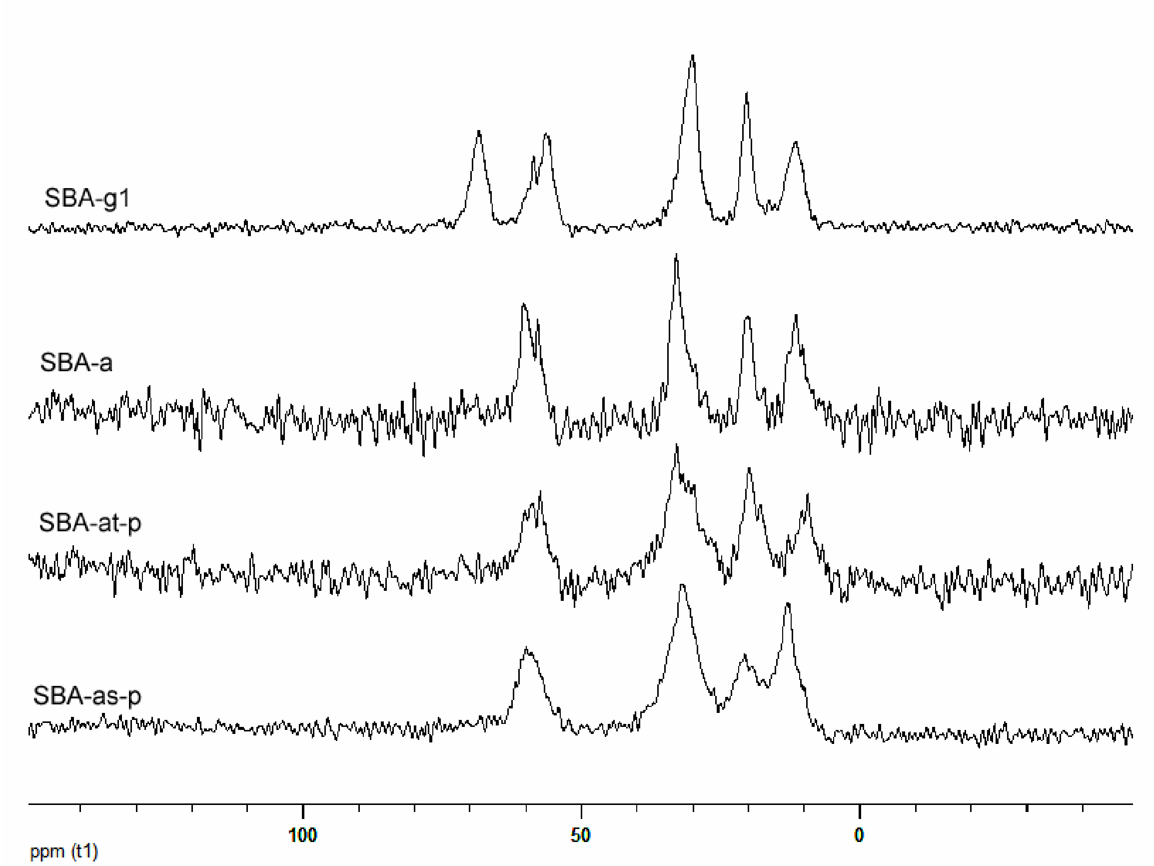
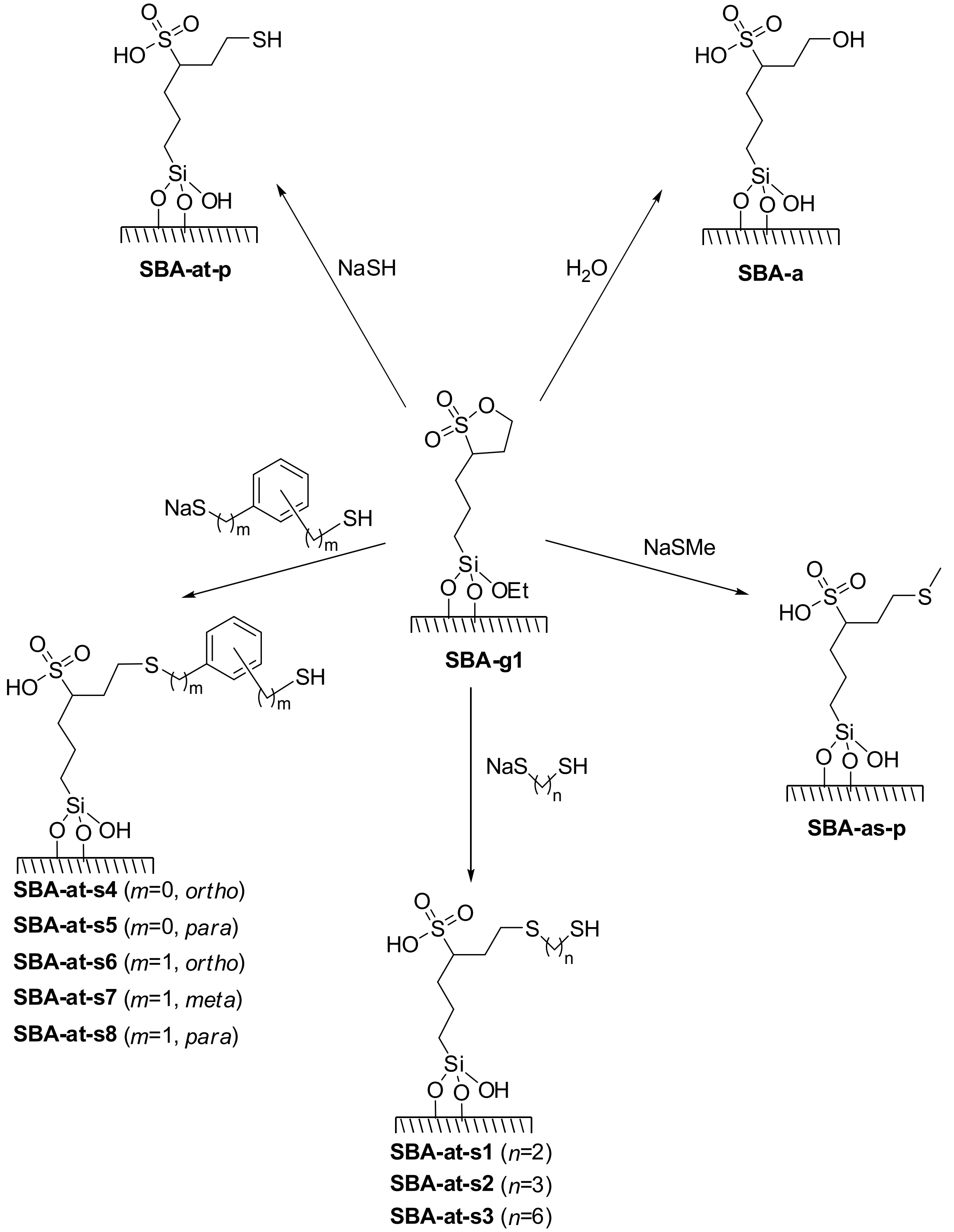


Figure 2.6. Comparison of $^{13}C\{^1H\}$ CP/MAS NMR spectra of **SBA-g1** (top) and sulfonic-acid-containing SBA-15 materials. The complete disappearance of the sultone peak at 68 ppm indicates complete ring-opening of the sultone.



Scheme 2.3. Ring-opening of surface-bound sultone to form sulfonic acid-containing materials

Catalytic Reactions. The catalysts were used in the synthesis of bisphenol A. Surface loadings were purposely maintained low (~ 0.2 mmol/g) in order to keep the resulting catalytic sites sufficiently isolated to observe the effects of discrete acid/thiol pairing. The results are given in Table 2.2. **SBA-a** gives a very low per-site yield (PSY = 3.1, defined as mmol total products / mmol H^+) and selectivity (1.8, defined as *p,p'*/*o,p'* product ratio) due to the lack of thiol. Addition of homogeneous thiol improves both the yield and selectivity, though both are still only modest (10 and 8.4 respectively). **SBA-at-p** is a highly active catalyst, and gives a per-site yield of 83 and a selectivity of 14. Addition of homogeneous thiol to this material decreases the per-site yield to 74, and the selectivity is slightly increased to 15. Another catalyst was prepared via sultone thiolysis with sodium methanesulfide. This material contains pairs of acid and methyl sulfide groups, and is denoted **SBA-as-p**. In the bisphenol A reaction **SBA-as-p** is only slightly better than **SBA-a** (Table 2.2, Entry 5). These results confirm that the thiol functionality is necessary for high catalytic activity, and also indicates that sulfide linkages can be used to tether other groups without substantially affecting catalysis (*vide infra*).

SBA-at-p materials were prepared with varying loadings of surface site pairs. It was found that as the surface density of sites increases, the activity of the catalyst decreases, but selectivity increases (Figure 2.7). These data suggest that even at the moderately low loadings used here, the paired sites are not completely isolated from each other and neighboring-site interactions affect catalysis in a significant way. At higher loadings, the paired sites are less isolated from one another, leading to greater steric interactions between pairs and between reacting acetone/phenol/bisphenol molecules and adjacent surface sites. This greater steric clash leads to lower reaction rates but enhances the product selectivity. It is also possible that there is an effect of the greater number of surface silanols present at lower organic loadings; however, the highest loading used here was only 0.54 mmol/g, which is still low enough to leave a high silanol density (unmodified SBA-15 has a silanol density of ~ 3–5 mmol/g).[37]

Entry	Heterogeneous Catalyst	Homogeneous Catalyst	PSY[a]	Isomer Ratio[b]
1	SBA-a	none	3.1	1.8
2	SBA-a	PrSH	10	8.4
3	SBA-at-p	none	83	14
4	SBA-at-p	PrSH	74	15
5	SBA-as-p	none	8.1	2.7
6	none	$PrSO_3H$	8.1	1.5
7	none	$HOPrSO_3H$	10	1.7
8	none	$HSPrSO_3H$	113	11

Table 2.2. Catalysis data in bisphenol A synthesis for heterogeneous and homogeneous catalysts. Reaction conditions: 0.02 mmol H^+, 0 or 0.02 mmol propanethiol, 6 mmol acetone, 24 mmol phenol, 90°C, 24 hrs

[a] Per-site yield (mmol total product / mmol H^+)
[b] *p,p'/o,p'*

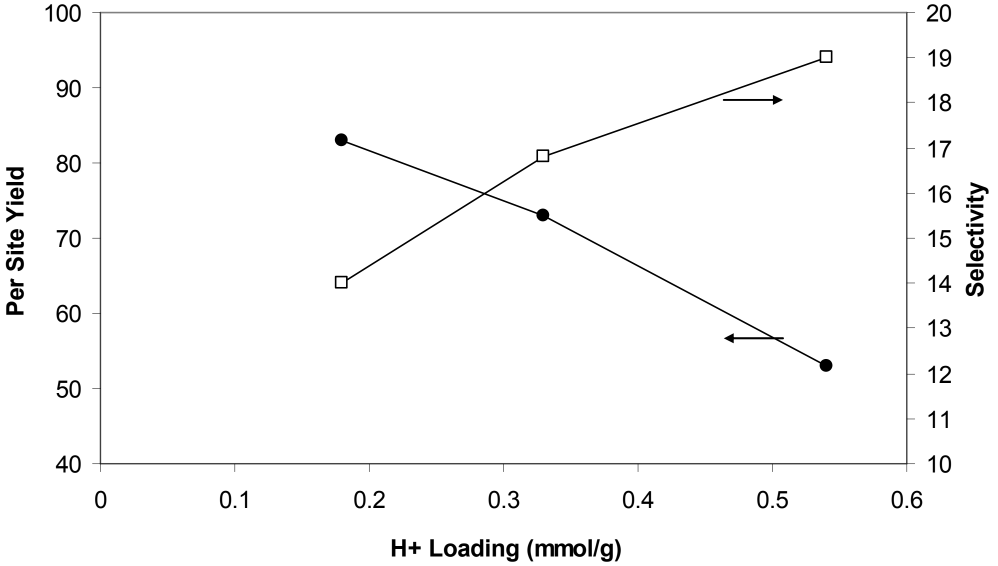


Figure 2.7. Effect of site density on total per-site yield (●) and selectivity (*p,p*'/*o,p*' ratio, □) of **SBA-at-p** catalysts in bisphenol A synthesis

Homogeneous analogues of **SBA-a** and **SBA-at-p** were also tested (Table 2.2, Entries 6–8). 1-Propanesulfonic acid and 3-hydroxy-1-propanesulfonic acid gave nearly identical catalytic results. This suggests that the adjacent hydroxyl group in **SBA-a** is not responsible for the poor catalytic activity of this material. The selectivity of these catalysts was similar to that of **SBA-a**, at a somewhat higher yield. 3-Mercapto-1-propanesulfonic acid also showed higher activity compared to its heterogeneous counterpart **SBA-at-p**, but somewhat lower selectivity. The reduced activity of the heterogeneous catalysts may be due to mass-transfer limitations, as the reagents must diffuse into the 1-D cylindrical pores of the SBA-15.

To investigate the possibility that the catalytic activity of **SBA-at-p** was due to surface species leaching into solution, a hot-filtration test was performed. The solid catalyst was removed after 8 hours, and no additional conversion was detected after an additional 9 or 16 hours at 90°C (see Figure 2.8). This result, along with the observation that unfunctionalized SBA-15 exhibits no catalytic activity towards bisphenol A, suggests that the catalytic activity of **SBA-at-p** is entirely due to its surface-bound acid/thiol pairs, rather than to the silica support or leached organic species.

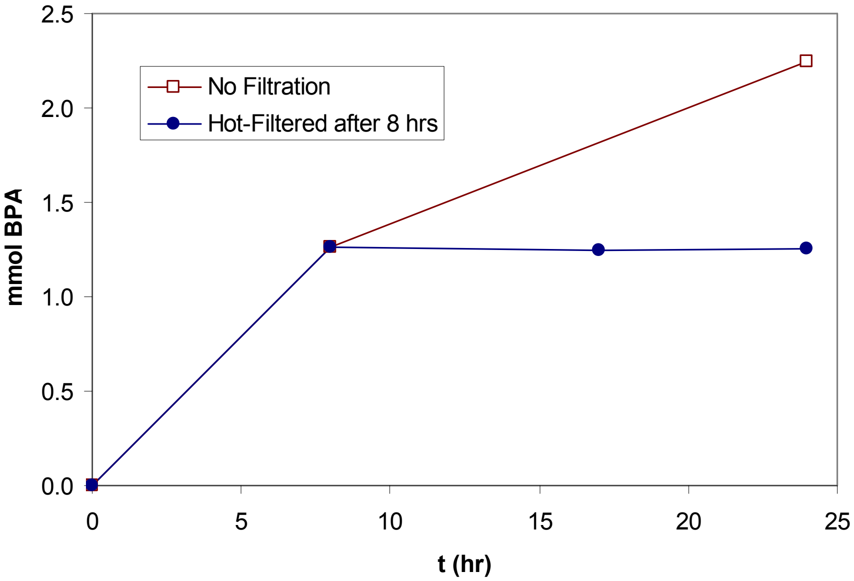


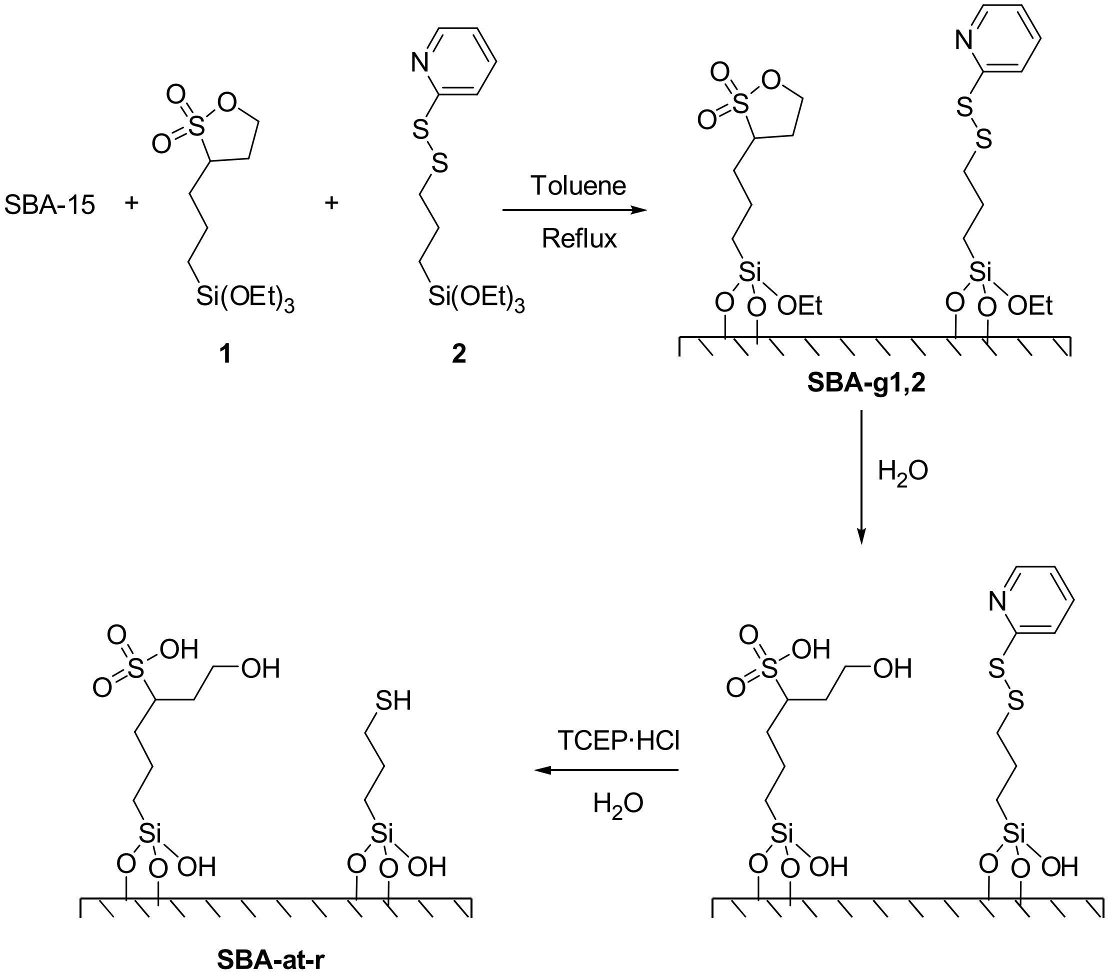
Figure 2.8. Hot-filtration test results with **SBA-at-p**. Reaction conditions: 0.02 mmol H^+, 6 mmol acetone, 24 mmol phenol, 90°C. Catalyst was removed after 8 hours and filtrate was heated at 90°C for another 16 hours.

Randomly-Distributed Acid/Thiol Catalysts. To test the effect of site organization, a catalyst containing randomly-distributed alkylsulfonic acid and propylthiol groups was synthesized via the simultaneous grafting of two organosilanes. Silane **1** was again used as a source of alkylsulfonic acid groups since it allows for a nonoxidative synthesis. Since sultone rings can be opened by thiols at elevated temperatures, silane **2** was used as a source of disulfide-protected thiols. **1** and **2** were grafted onto SBA-15, followed by sultone hydrolysis and disulfide reduction (Scheme 2.4). The resulting randomly-distributed acid/thiol material is denoted **SBA-at-r**. Due to the differential grafting efficiency of the two silanes, the acid/thiol ratio could not be controlled precisely at 1:1; elemental analysis showed that there were in fact nearly 5 times more thiol groups than acid groups. **SBA-at-r** exhibited good selectivity in the synthesis of BPA, but with a nearly threefold reduction in per-site yield compared to the paired material **SBA-at-p** (Table 2.3, Entries 2–3).

Entry	Heterogeneous Catalyst	Bisphenol Product	PSY[a]	Isomer Ratio[b]
1	SBA-A	A	3.1	1.8
2	SBA-AT-p	A	83	14
3	SBA-AT-r	A	29	22
4	SBA-A	Z	0.3	N/A[c]
5	SBA-AT-p	Z	14	14
6	SBA-AT-r	Z	1.0	N/A[c]
7	SBA-A	AF	8.4	N/A[c]
8	SBA-AT-p	AF	15	N/A[c]

Table 2.3. Catalysis data for heterogeneous catalysts in synthesis of various bisphenols. Reaction conditions: 0.02 mmol H^+, 6 mmol ketone, 24 mmol phenol, 90°C, 24 hrs. Catalyst loading ~ 0.2 mmol H^+/g

[a] Per-site yield (mmol total product / mmol H^+)
[b] *p,p*'/*o,p*'
[c] *o,p*' isomer below detection limit



Scheme 2.4. Simultaneous grafting of silanes **1** and **2** to form randomly-bifunctionalized sultone/disulfide material **SBA-g1,2** and subsequent deprotection to form random acid/thiol material **SBA-at-r**

To investigate the substrate scope of the heterogeneous catalysts, the ketone was varied to produce other bisphenol products. Using the more sterically hindered cyclohexanone as reactant (to produce bisphenol Z), the effect of pairing is even more pronounced (Table 2.3, Entries 4–6). Thiol-free **SBA-a** gives low activity, the randomly-bifunctionalized material gives only a small improvement, and the acid/thiol-paired catalyst has a much higher activity (14 times higher than for the randomly-distributed catalyst). When hexafluoroacetone is used (to produce bisphenol AF), the effect of thiol promotion is greatly reduced, probably due to the greater reactivity of the fluorinated reactant (Table 2.3, Entries 7–8). The increase in activity from **SBA-a** to **SBA-at-p** is less than twofold. Thus we conclude that the improvement in catalytic activity gained by pairing acid and thiol groups varies for different condensation reactions, and is more pronounced for less-reactive ketones.

Varying Acid/Thiol Distance. The acid/thiol distance was varied to investigate what effects separation distance has on activity and selectivity in catalyzing the synthesis of BPA. By opening the sultone ring with the monosodium salt of a dithiol, a thiol group is tethered to the acid via a sulfide linkage. In this way it is possible to tune both the length of the acid/thiol spacer and the electronic properties of the thiol (*i.e.*, alkyl vs. phenyl vs. benzyl; see Scheme 2.3). ^{13}C CP/MAS NMR showed quantitative conversion of the sultone moieties to sulfonic acids for these products (Figures 2.11, 2.12). Elemental analysis revealed sulfur loadings to be approximately three times the acid loading (Table 2.1, Entries 7, 13, 14), corresponding to the expected 1:1 acid/thiol ratio, and the surface area, pore size, and long-range ordering were maintained. The resulting materials with various alkyl and aryl spacers (denoted **SBA-at-s1** through **SBA-at-s9**) were used to catalyze the BPA reaction (Table 2.4). Catalysts **SBA-at-s1**, **-s2**, and **-s3** (ring-opened by 1,2-ethanedithiol, 1,3-propanedithiol, and 1,6-hexanedithiol, respectively) showed reduced activity and selectivity compared to **SBA-at-p**, where the acid and thiol groups are in closer proximity (Table 2.4, Entries 1–4). The activity decrease with distance is quite dramatic, as increasing the length of the acid/thiol spacer by three atoms (**SBA-at-s1** vs. **SBA-at-p**) decreases the yield by a factor of two.

Additional increase in the spacer length by one atom (**SBA-at-s2**) reduces yield by another factor of two, down to a level similar to that of **SBA-at-r** (Table 2.4, Entry 3). **SBA-at-s3** exhibits similar activity to **SBA-at-s2** (Table 2.4, Entry 4).

Entry	Heterogeneous Catalyst	Spacer Type	PSY[a]	Isomer Ratio[b]
1	SBA-at-p	none	83	14
2	SBA-at-s1	alkyl, *n* =2	42	12
3	SBA-at-s2	alkyl, *n* =3	20	6.5
4	SBA-at-s3	alkyl, *n* =6	22	6.8
5	SBA-at-s4	aryl, *m* =0, *ortho*	5.2	1.9
6	SBA-at-s5	aryl, *m* =0, *para*	21	4.3
7	SBA-at-s6	aryl, *m* =1, *ortho*	64	9.6
8	SBA-at-s7	aryl, *m* =1, *meta*	37	7.9
9	SBA-at-s8	aryl, *m* =1, *para*	47	7.9
10	SBA-at-s9	aryl, *durenyl*	56	10

Table 2.4. Catalysis data in bisphenol A synthesis for heterogeneous acid/thiol spacer catalysts. Reaction conditions: 0.02 mmol H^+, 6 mmol acetone, 24 mmol phenol, 90°C, 24 hrs. Catalyst loading ~ 0.2 mmol H^+/g

[a] Per-site yield (mmol total product / mmol H^+)
[b] *p,p*'/*o,p*'

Catalysts **SBA-at-s4** and **-s5**, containing *ortho*- and *para*-phenylthiol groups, respectively, are both poor catalysts (Table 2.4, Entries 5–6). In particular, the *ortho* variant shows activity no better than the thiol-free material **SBA-a**. The poor activity of this material could be due to steric hindrance between the adjacent sulfide and thiol groups that could prevent the thiol from reacting with acetone. The reduced nucleophilicity of phenyl thiols vs. alkyl thiols is also likely responsible for some of the lower activity of these two catalysts.

Catalysts **SBA-at-s6**, **-s7**, and **-s8** (derived from *ortho*-, *meta*-, and *para*-xylyl dithiols, respectively) contain benzyl thiols. These materials generally show greater activity than those containing alkyl and phenyl spacers (Table 2.4, Entries 7–9). The catalyst **SBA-at-s6**, containing an *ortho*-benzyl spacer is the most active of all the spacer materials investigated here. We believe this is because the thiol is positioned such that it can point directly at the acid group and shortens the acid/thiol distance (see Figure 2.9).

A variant of the *ortho*-xylyl catalyst bearing two additional methyl groups was synthesized using the commercially available durene-α_1,α_2-dithiol. This catalyst (denoted **SBA-at-s9**; see Figure 2.10) exhibited slightly poorer activity than **SBA-AT-s6** (Table 2.4, Entry 10) with similar selectivity.

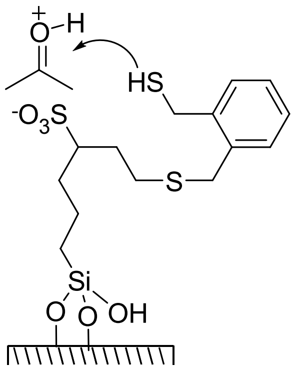
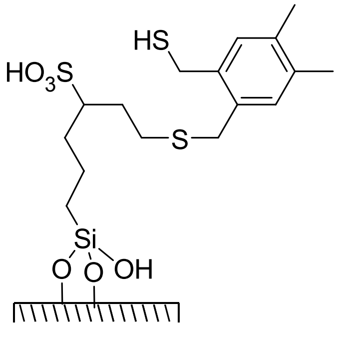


Figure 2.9. One possible conformation of **SBA-at-s6**, in which the thiol group is pointing directly toward the acid site, which allows for rapid attack of the thiol on the protonated acetone species.



SBA-at-s9

Figure 2.10. *Ortho*-durenyl spacer catalyst **SBA-at-s9**

Conclusions

The distance between the acid and thiol group in a series of heterogeneous catalysts was shown to have a profound influence on the catalytic behavior in the synthesis of bisphenols. These data highlight the importance of the spatial positioning of functional groups in the development of heterogeneous catalysts, and also reveal how the nanoscale organization of catalytic surfaces can be tuned to provide a level of reactivity control unachievable through traditional random functionalization approaches.

In the case of acid and thiol groups, it was found that the catalytic activity for bisphenol synthesis is highest when the two groups are as close as possible. It may be that for other pairs of groups, such as mutually destructive ones, that the activity vs. distance behavior could be qualitatively different.

The sultone-containing silica **SBA-g1** was used here to generate acid/thiol pairs. By the reaction of this intermediate with other nucleophiles, it is possible to create a wide array of surface-paired materials.

Experimental

Materials. Tetrahydrofuran (THF) and toluene were distilled over sodium immediately before use. All other solvents were analytical grade and used as received. 3-iodopropyltriethoxysilane was prepared from 3-chloropropyltriethoxysilane (Gelest) and sodium iodide according to the literature procedure.[38] Organosilane **2** was synthesized from 3-mercaptopropyltriethoxysilane and 2,2'-dipyridyldisulfide according to the literature procedure[14] followed by purification by chromatography on silica gel. Anhydrous sodium hydrosulfide was purchased from Alfa Aesar. Durene-α1,α2-dithiol was purchased from Acros Organics. All other chemicals were purchased from Aldrich and used as received. All reactions were performed under an argon atmosphere.

3-(3-triethoxysilylpropyl)-[1,2]-oxathiolane 2,2-dioxide (Organosilane 1). 1,3-propanesultone (2.7 g, 22 mmol) was dissolved in dry THF (50 mL). The solution was cooled to -78°C and *n*-butyllithium (1.6 M in hexanes, 14 mL, 22 mmol) was added slowly over 10 minutes. After stirring for another 10 minutes, 3-iodopropyltriethoxysilane (3.3 g, 10 mmol) was added slowly over 5 minutes. After stirring for 15 minutes, the temperature was raised to -60°C. After stirring for 9 hours, the temperature was raised to 0°C and water (50 mL) was added and the mixture was transferred to a separatory funnel. The aqueous layer was removed and the organic layer was washed with saturated NaCl solution (50 mL) and dried over anhydrous $MgSO_4$. After the solvent was removed *in vacuo*, chromatography on silica gel (3:2 hexanes/ethyl acetate, $R_f = 0.3$) afforded **1** (0.61 g, 19%) as a colorless liquid. ^1H NMR (300 MHz, DMSO-d_6) δ 4.38 (m, 2H), 3.73 (q, $J = 7$ Hz, 6H), 3.48 (m, 1H), 2.58 (m, 1H), 2.13 (m, 1H), 1.70 (m, 2H), 1.46 (m, 2H), 1.13 (t, $J = 7$ Hz, 9H), 0.61 (t, $J = 8$ Hz, 2H). ^{13}C NMR

(300 MHz, DMSO-d_6) δ 68.6, 58.4, 55.5, 31.6, 29.9, 20.6, 18.9, 10.3. Anal. Calcd. for $C_{12}H_{26}O_6SSi$: C, 44.15; H, 8.03; S, 9.82. Found: C, 43.05; H, 7.46; S, 9.85. HRMS (FAB+): *m/z* (M + H^+) ($C_{12}H_{27}SiSO_6$) Calcd, 327.1298; Found, 327.1302.

SBA-g1 (Sultone-functionalized silica). SBA-15 (1.0 g, synthesized according to the literature procedure[39]) was dried under flowing argon at 170°C for 4 hours. After cooling, dry toluene (50 mL) was added via syringe and the mixture was stirred vigorously to form a uniform suspension. An appropriate amount of **1** (typically ~ 0.7 mmol) was added dropwise via syringe. The suspension was stirred for 45 minutes at room temperature, then refluxed for 16 hours. After cooling to room temperature, the solids were filtered and washed with toluene and dichloromethane (3 x 20 mL each). The solids were Soxhlet extracted with dichloromethane overnight, then dried under vacuum and stored under an argon atmosphere in a drybox until further use.

SBA-a (Thiol-free sulfonic acid catalyst). SBA-g1 (0.5 g) was added to water (40 mL) and the resulting suspension was stirred at 40°C for 2 days. Then the solids were filtered, washed with water (3 x 30 mL), 0.5 N HCl (3 x 30 mL), and water (4 x 30 mL) and dried under high vacuum overnight.

SBA-at-p (Acid/thiol-paired catalyst). SBA-g1 (0.5 g) was suspended in anhydrous DMF (15 mL). Anhydrous sodium hydrosulfide (86 mg, 1.5 mmol) was dissolved in anhydrous DMF (10 mL) and the resulting blue solution was added dropwise to the stirred silica suspension. After stirring for 24 hours at room temperature, the solids were filtered, washed with DMF (3 x 30 mL) and water (5 x 30 mL), and then suspended in 0.5 N HCl (30 mL) to acidify. After stirring for 3 hours the white solids were filtered and washed with 0.5 N HCl (3 x 30 mL) and water (5 x 30 mL) and dried under high vacuum overnight. **SBA-as-p** was prepared with the same procedure, except that sodium methanesulfide was used in place of sodium hydrosulfide.

SBA-at-r (Random acid/thiol catalyst). SBA-15 (0.5 g) was grafted with **1** (0.16 g, 0.5 mmol) and **2** (0.17 g, 0.5 mmol) according to the procedure above for **SBA-g1**. The two organosilanes were added dropwise simultaneously. After Soxhlet extraction the solids were dried to afford **SBA-g1,2** as a pale beige solid. **SBA-g1,2** (0.5 g) was suspended in water (50 mL) and stirred at 40°C for 2 days. The solids were filtered, washed with water (2 x 30 mL) and 0.5 N HCl (3 x 30 mL), and suspended in an aqueous solution of tris(2-carboxyethyl)phosphine hydrochloride (0.015 M, 50 mL). This suspension was stirred at 55°C for 2 days, and then the solids were filtered, washed with water and methanol (4 x 30 mL each), and dried under high-vacuum overnight to yield **SBA-at-r** as a nearly white powder.

SBA-at-s (Acid/thiol spacer catalysts). Dithiol (15 mmol) was dissolved in anhydrous DMF (10 mL) and sodium hydride (60 wt% in mineral oil, 5 mmol) was added. This mixture was stirred until all solids had dissolved and then was added slowly to a suspension of **SBA-g1** (0.5g) in anhydrous DMF (10 mL). After stirring for 24 hours at room temperature, the solids were filtered, washed, and acidified as described for **SBA-at-p**.

Acid Titration. To the silica material to be analyzed (~ 30 mg) was added aqueous NaCl (2N, 4 mL) and the suspension was stirred for 24 hours. The solids were removed by filtration, washed with water (4 x 2 mL), and the combined filtrate was titrated with 0.01 N NaOH using phenol red as indicator.

Catalytic Reaction—Condensation of Phenol and Ketone. An amount of catalyst corresponding to 0.02 mmol H^+ (~ 100 mg) was added to a vial and dried under high vacuum at 80°C overnight. Phenol (2.2 g, 24 mmol) and ketone (6 mmol) were added and the vial was sealed under argon and stirred at 90°C for 24 hours. The catalyst was removed by filtration and washed with acetonitrile to a total filtrate volume of 25 mL, and the products were quantified by HPLC. Per-site yield was calculated on the basis of the number of acid sites present and selectivity was defined as the ratio of bisphenol isomers (*p,p*'/*o,p*').

Acknowledgements

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Additional Figures—Selected NMR Spectra

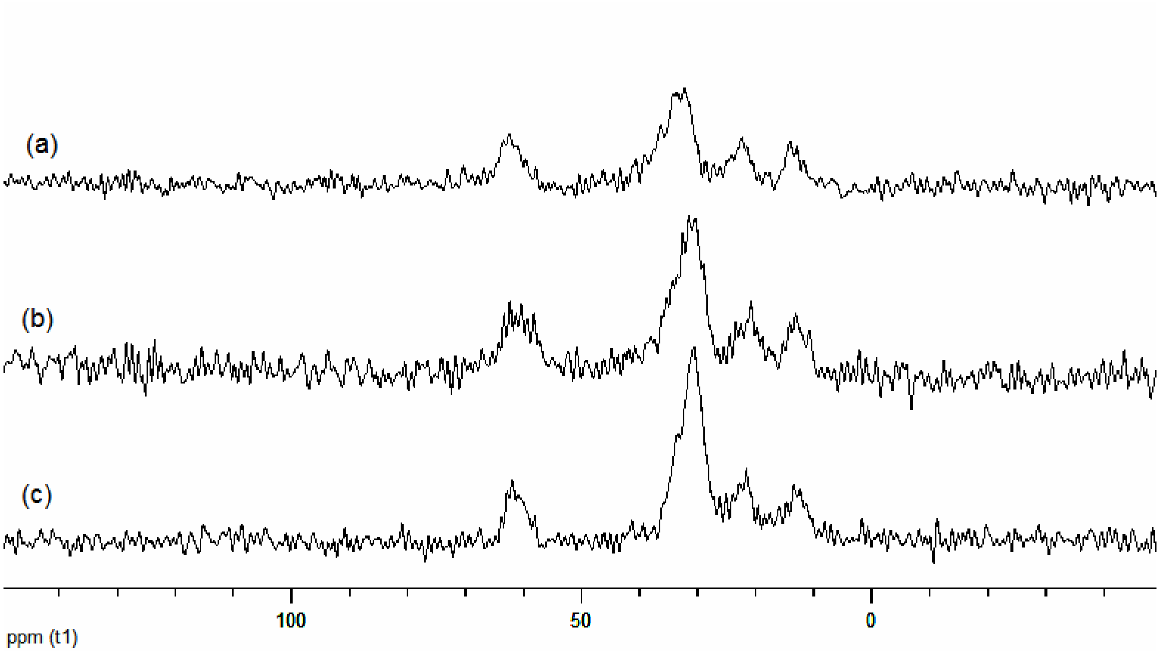

Figure 2.11. $^{13}C\{^1H\}$ CP/MAS NMR spectra of alkyl spacer materials. (a) **SBA-at-s1** (b) **SBA-at-s2** (c) **SBA-at-s3**

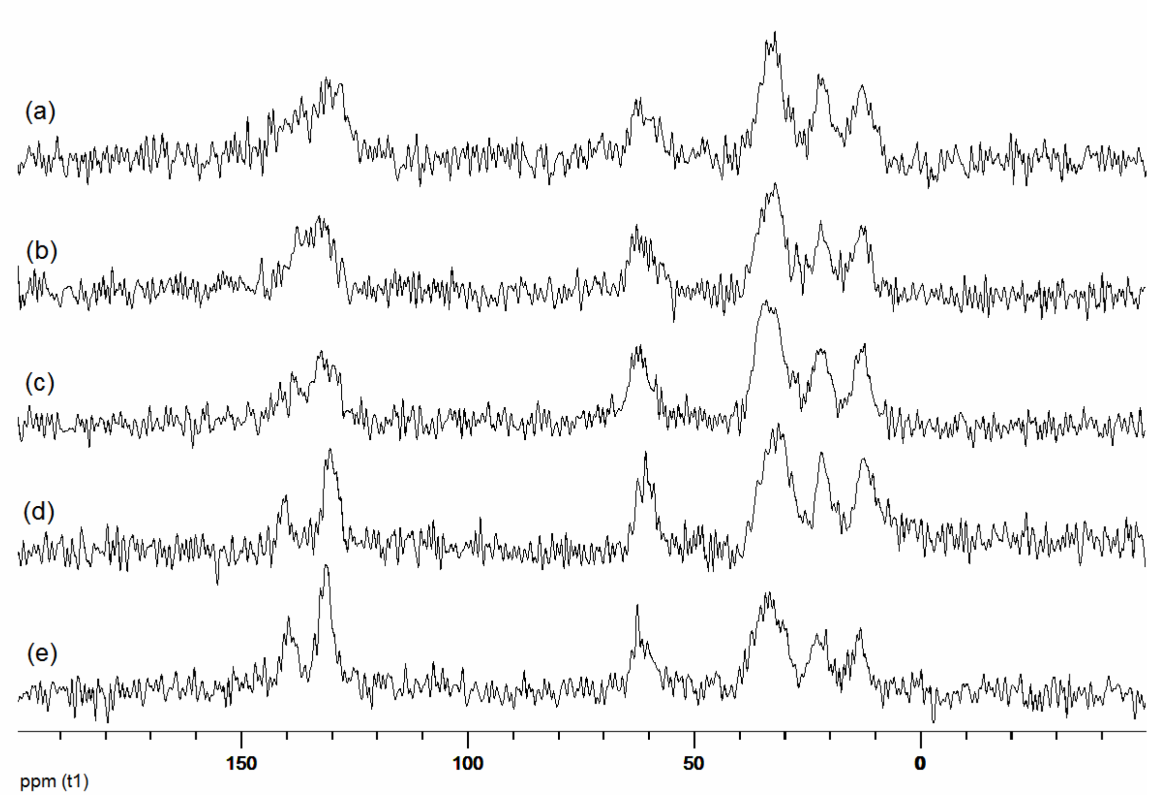

Figure 2.12. $^{13}C\{^1H\}$ CP/MAS NMR spectra of aryl spacer materials. (a) **SBA-at-s4** (b) **SBA-at-s5** (c) **SBA-at-s6** (d) **SBA-at-s7** (e) **SBA-at-s8**

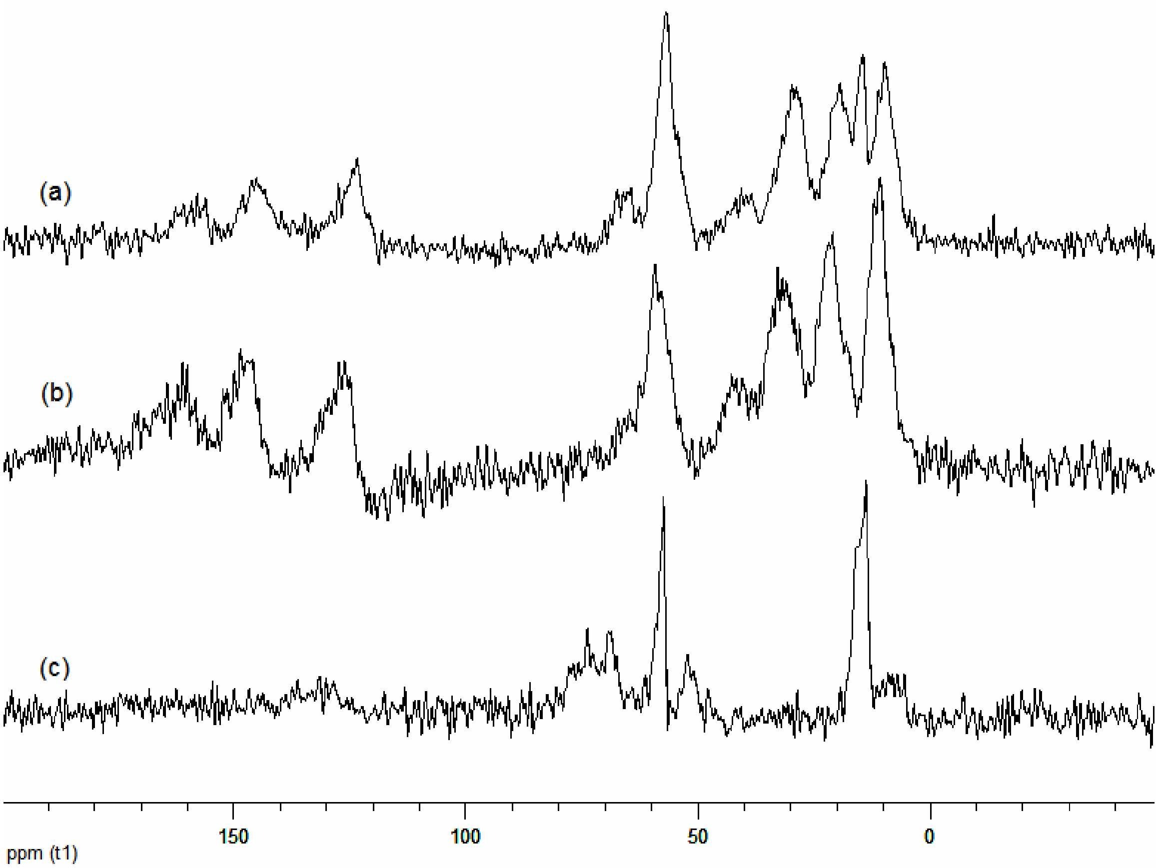

Figure 2.13. $^{13}C\{^{1}H\}$ CP/MAS NMR spectra of randomly-grafted materials

(a) **SBA-g1,2**

(b) after hydrolysis

(c) after disulfide reduction (**SBA-AT-r**). The disappearance of the peak at 67 ppm is due to hydrolysis of the sultone ring, and the disappearance of the aromatic peaks (125–155 ppm) indicates complete reduction of the disulfide.

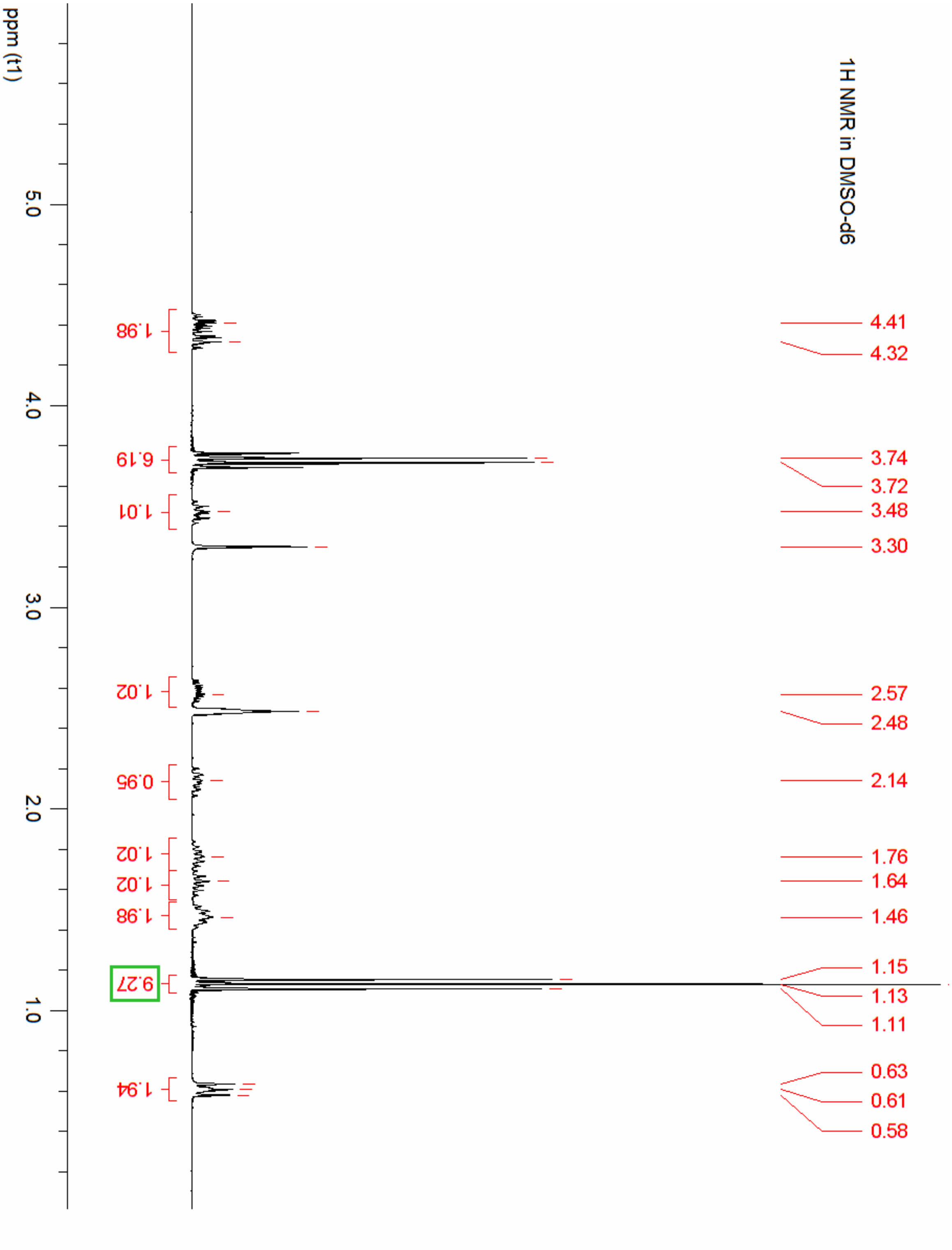

Figure 2.14. ^{1}H NMR spectrum of silane **1**. Peaks at 3.30 and 2.48 ppm correspond to H_2O and DMSO, respectively.