STUDY OF DIFFERENT ROUTES TO DEVELOP ASYMMETRIC DOUBLE DECKER SILSESQUIOXANE (DDSQ)

By

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ABSTRACT

STUDY OF DIFFERENT ROUTES TO DEVELOP ASYMMETRIC DOUBLE DECKER SILSESQUIOXANE (DDSQ)

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Silsesquioxane cages can be considered as well-defined nanosized molecules and have attracted widening interests due to their possible use as components of resourceful inorganic/organic hybrid materials,[1,2] as well as their applications in optics, catalysis, polymers and electronics. Double-decker silsesquioxane (DDSQ) nanoparticles have attracted much attention recently due to the ease of which these particles can be incorporated into polymeric materials and their unique capability to reinforce polymers.[3,4] These systems are of high interest to scientists, due to their unique chemical and physical properties.[5,6,7] For example, the United States Air Force and NASA use DDSQ incorporated polymers as thermoset material and flame retardants.

This thesis discussed mainly three projects. One project centered on the research to improve and optimize the synthetic routes for a large scale synthesis of DDSQ functionalized oligoimides. The second project discussed is on the synthesis of a novel **(**phenylethynyl)phenyl DDSQ oligomer that can be used for high temperature application. The main project was on studies of different routes to an asymmetric DDSQ cage. DDSQ molecules possess a higher symmetry. Breaking the symmetry and selective functionalization of the DDSQ molecule would be highly desirable to fine tune the physical properties. Different routes were studied to develop an asymmetric DDSQ cage.

ACKNOWLEDGEMENTS

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I would also like to thank the members of the committee Dr. M. Smith, Dr. X. Huang, Dr. J. Tepe for their continuous involvement in the project. I would like to thank the Department of Chemistry at Michigan State University for providing me the opportunity to complete my M.S degree thesis work, I would like to respectfully thank all the faculty members and staff in the Department of Chemistry at MSU. My sincere thanks goes to Dr. Holmes and Dr. Li for their help and suggestions related to NMR experiments.

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KEY TO ABBREVIATIONS

DDSQ = Double Decker Silsesquioxane

POSS = Polyhedral Oligomeric Silsesquioxane

PEPI = Phenylethynyl Pthalic Imide

PEPA = Phenylethynyl Pthalic Anhydride

SQ = Silsesquioxane

Tg = Glass transition temperature

Td = Decompostion Temperature

TGA = Thermo Gravimetric Analysis

CP = Cross Polarization

CHAPTER 1: INTRODUCTION

1.1 Background

The chemistry of organo-functionalized silsesquioxane has emerged as a fascinating new field of modern technology. Silsesquioxane materials are a class of organosilicon compound with the formula $(RSiO_{1.5})_n$, where 'n' is an integer and R can be an inert organic group or active functional group. Silsesquioxanes can have various geometrical structural orders, including random, ladder and cage structures; the latter are also known as polyhedral oligomeric silsesquioxanes (POSS).[1] The first synthesis of a POSS cage was developed in the 1946 when Scott[1] isolated the highly symmetric Me_8T_8. The most common POSS cage is the T_8 (e.g., Me_8T_8 in Figure 1.1), although other cages with well-defined geometries include n = 6, 10, 12, 14, 16 and 18.[2,3]

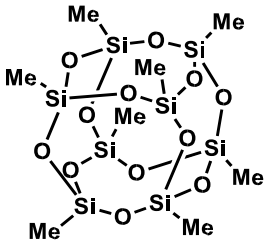


Figure 1.1 A common POSS material: a fully condensed cage with eight methyl groups (Me_8T_8).

These POSS cages can be considered as well-defined nanosized molecules (1-3 nm) and have attracted widening interest due to their possible use as components of resourceful inorganic/organic hybrid materials such as liquid crystals, porous materials and catalytic chemistry.[4,5] Okubo *et al*. developed hierarchial micro-mesoporus silica that has been synthesized by solid-phase conversion of molecular crystals of an alkoxy derivatives of cubic silsesquioxane as a molecular building unit.[5] Poly (L-lysine) dendrimers with POSS core were synthesize via Cu-catalyzed azidealkyne cycloaddition click chemistry by Gu *et al*.[5] It is a facile approach to prepare

peptide dendrimers with perfect architecture. He *et al.* designed POSS based thermo-responsive amphiphilic hybrid copolymers for thermally denatured protein protection applications.[5]

Organic–inorganic hybrid materials are attracting considerable interest because they offer the opportunity to develop high-performance materials that combine many desirable properties of conventional organic and inorganic components, such as thermal stability, solubility, lower dielectric property and processability.[6] The silica core confers rigidity and thermal stability that provides mechanical and thermal properties surpassing typical organic compounds.

POSS cages can be easily incorporated into polymeric matrices to prepare novel polymer hybrids with promising properties, such as thermal and flammability resistance, solubility, oxidation resistance, decreased viscosity and excellent dielectric properties.[7-11] In the literature, the POSS-containing thermosetting polymers such as polyimide,[12] polyurethane,[13] poly(methyl methacrylate),[14] polybenzoxazines[15] and poly(ethylene imine)[16] have been prepared by the use of POSS cages. The US Air Force has identified the thermal stability of POSS incorporated polymers and using as thermoset material. NASA is also researching their properties as flame retardants and atomic oxygen resistance materials and considering using these materials as film coatings for cabin items during space missions (POSS cages form a glassy, passivating SiO_2 layer that prevents further decay of the underlying polymer in the presence of atomic oxygen / Low Earth Orbit condition simulations).

The addition of POSS cages into organic monomers and polymers has been recognized to increase the decomposition temperature (T_d). During the degradation, the organic groups of POSS initially damage rapidly and form an active char-like coating on top of the Si-O cage, providing extra protection.[17] This is specifically useful in increasing the limiting oxygen intake (LOI), or the

volume fraction of oxygen necessary for a material to sustain combustion,[18] for flame retardant applications. Each silicon atom is covalently bonded to an organic peripheral group, which allows these molecules to interact with themselves or other organics in the medium. This property increases the solubility and processability of the polymer. These peripheral groups can be modified to make the Silsesquioxane (SQ) cage reactive.

One of the major focus of POSS/polymer research over the last two decades has been in the covalent incorporation of POSS moieties into a polymeric architecture, either during synthesis or network formation, with the goal of improving the thermal/thermo-oxidative performance of the resultant hybrid system. The core tenet of this approach is that the inclusion of well-defined nano-scale silica (in the form of a functional POSS) as a chain segment, pendant, or crosslinking moiety will impart a range of physical and chemical improvements to the polymeric system that will in turn, make the system more thermally and oxidatively resistant. SQ cages have been attached to polymers in three different ways; pendent-like, bead-like and beads on chain like structures.

1.2 Pendant-like structure

Pendant-like structures are synthesized by corner capping, which is the most common method for modifying one of the peripheral groups on a cage-like SQ. This structure is also known as a monofunctionalized SQ (Figure 1.2).

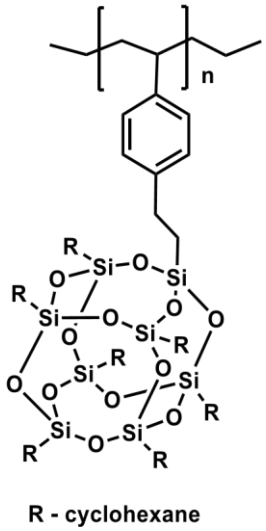


Figure 1.2. Example of monofunctionalized, corner-capped SQs.

1.3 Bead-like structure

To achieve a bead-like structure, two reactive moieties must be present on two silicon atoms. Difunctional SQs are mostly used for spacecraft applications. SQ cages incorporated into the polyimide Kapton® (Figure 1.3) provide additional protection in lower Earth orbit from atomic oxygen. Polymers based on SQs have demonstrated 10 times higher durability than neat Kapton®, which has the highest resistance of conventional polymers towards active atomic oxygen. Similar to thermal degradation, when these SQs are exposed to atomic oxygen, their organic groups degrade and a silica (SiO_2) layer is preserved, providing protection from degradation.[19] This silica layer protects the underlying polymer from further degradation. The erosion yield of the SQ-Kapton® is as low as ~ 0.01 that of neat Kapton®, depending on the weight % of SQ in the polymer.

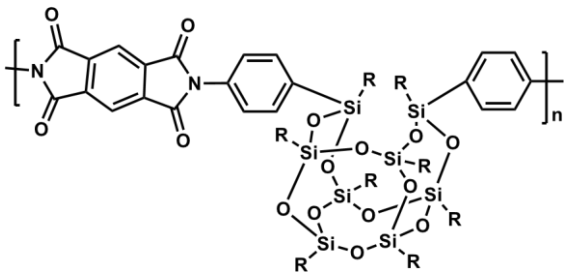


Figure 1.3. Example of a difunctionalized SQ from a disilanol (R= cyclopentyl) (POSSpolyimide copolymer).

1.4 Beads on a chain

Another approach to the synthesis of reactive SQ molecule is to create a "beads on a chain" type of structure, called double-decker silsesquioxane (DDSQ) cages (Figure 1.4).[20] DDSQ is composed of two "decks" of silsesquioxane, stacked on top of each other to form a cage-like structure. The only DDSQ molecule available to date has only phenyl (Ph) moieties attached to the tetrasilanol structure. Since its introduction in 2004, DDSQ has attracted researchers to explore the development of polymerizable SQ monomers with an architecture where the inorganic SQ cage can easily become part of the linear backbone of the resulting polymers.[21]

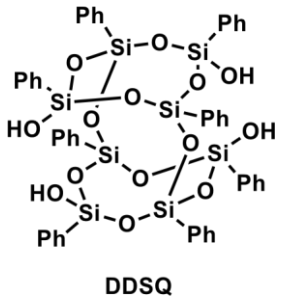
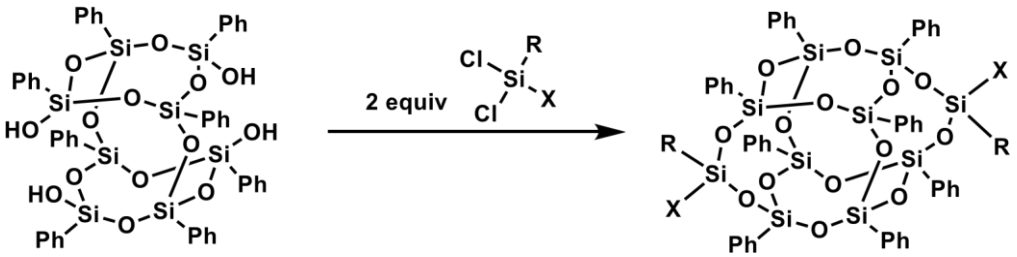


Figure 1.4. Double-Decker Silsesquioxane (DDSQ)



Scheme 1.5. Capping reaction of DDSQ molecule.

These DDSQ cages can be closed via a capping agent like aminophenyl (X) dichloroalkyl (R) silane (Scheme 1.5). During the capping reaction, DDSQ cages generate *cis* and *trans* isomers (Figure 1.6). These two isomers of DDSQ exhibit different physical properties, such as melting point and solubility.

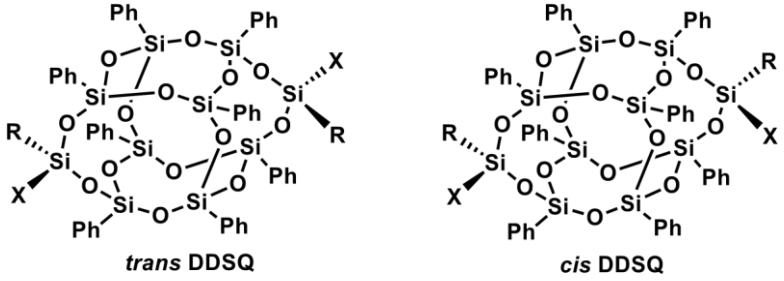


Figure 1.6. *cis* and *trans* isomers of DDSQ molecule.

Depending on the capping agent, different functionalized DDSQ compounds can be synthesized. This is particularly important in terms of reactive functional groups attached to a POSS core, e.g. vinyl, amino, epoxy, methacryloxy, and chloropropyl groups.[22] The development of new and efficient methods for DDSQ synthesis with various functional groups can open up new possible applications.

1.5 Objectives

DDSQ molecules exhibit a high symmetry. One of the major goals of the proposed work is to synthesize asymmetric DDSQ molecules that are scientifically innovative. It can be evisioned that functionality, and hopefully physical properties will be improved by attaching two different functional groups to the asymmetric sites of the DDSQ molecule. However, with the higher symmetry of the DDSQ molecule, asymmetric functional group manipulation is challenging.

Other than the above mentioned goal, synthesis of a novel DDSQ analog and optimization of the route to existing functionalized DDSQ oligoimides were carried out. The main objectives of the work carried out can be summarized as follows.

1. ***Study different routes to synthesize DDSQ functionalized oligoimides.***
2. ***Synthesis of novel phenyl ethynyl (phenyl) DDSQ oligomers***
3. ***Study different routes to synthesize asymmetric DDSQ molecules***

CHAPTER 2: ROUTES TOWARDS THE SYNTHESIS OF DDSQ FUNCTIONALIZED OLIGOIMDES

2.1 Introduction

Polyimides are among the most successful commercial thermoset (synthetic materials that strengthen when heated, but cannot successfully be remolded when reheated) polymers, due to their excellent thermal stability and mechanical properties. They are widely used as coatings for microelectronic devices, integrated circuit fabrication, and high-temperature materials for the aerospace industry. Despite their wide use, polyimides are not without shortcomings. Due to their higher viscosity properties, in order to process and fabricate the structural composites, disadvantageous higher pressures are required.

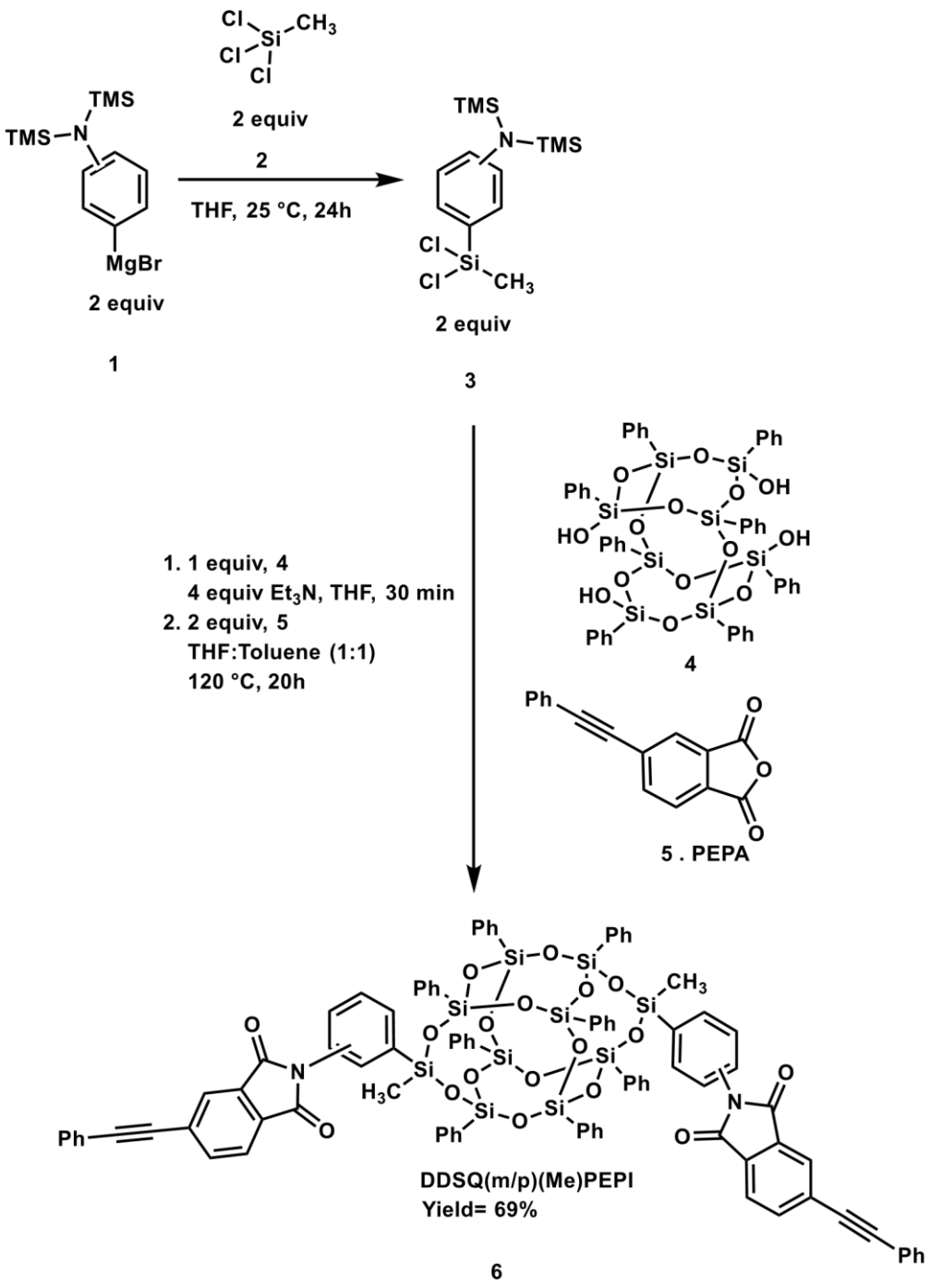
Therefore, research on polyimides is directed towards decreasing the viscosity without sacrificing desired characteristics. One method is to incorporate DDSQ as the backbone for these polyimides,[29,30,31] which interrupt the interlayer interactions of polymer layers that facilitate the reduction of the viscosity.

Another disadvantage of polyimides is the small processing window, as the solid to liquid phase transition (319-349 °C) of polyamides is so close to the curing reaction (350-371 °C) (toughening or hardening of a polymer material by cross-linking of polymer chains). Therefore, considerable efforts have been made to address these issues and to design polyimides with the desired properties. The incorporation of the DDSQ cages decreases the glass transition temperature (170 °C) (hard and relatively brittle state into a molten or rubber-like state) by breaking the interlayer interactions, while maintaining higher thermomechanical features of the polyimide.

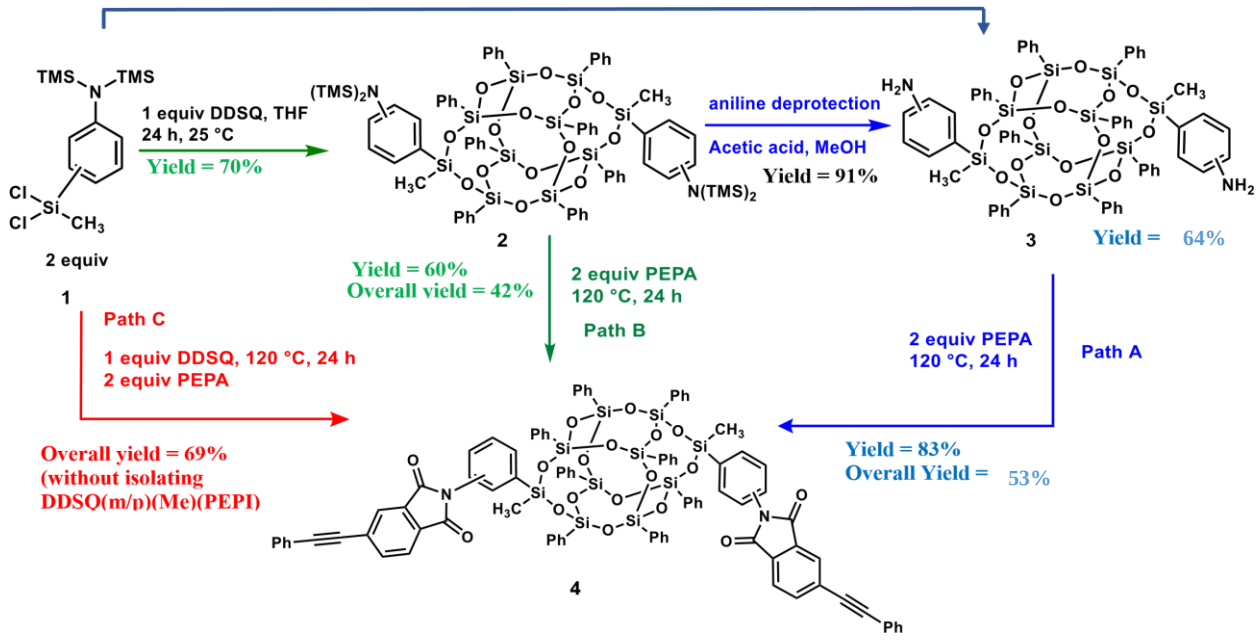
In order to overcome these issues and to improve the properties, our group previously attempted to synthesize a functionalized DDSQ with phenylethynylphthalic (PEPI) anhydride (PEPI-DDSQ oligoimides). According to the previous studies, mixtures of six-isomers of DDSQ(m/p)(Me)(PEPI), which includes the asymmetric mixture of stereo- (*cis* and *trans*) and regio- (para- and meta-) isomers, exhibit lower viscosity.

2.2 Optimization of synthetic routes

However the attempted synthesis possessed several disadvantages such as diminished yields and being time intensive. In this work, extensive research was carried out to overcome the above mentioned drawbacks by improving and optimizing the synthetic routes for a large scale synthesis. Scheme 2.1 shows the novel synthetic route of DDSQ(m/p)(Me)(PEPI) compound. The end product contains 6 isomers of DDSQ(m/p-PEPI)(Me) (*cis* and *trans* isomers of DDSQ(mPEPI)(Me), *cis* and *trans* isomers of DDSQ(p-PEPI)(Me) and (*cis* and *trans* isomers of DDSQ(m/p-PEPI)(Me)). As shown in the Scheme 2.1, DDSQ(m/p-PEPI)(Me) was synthesized using meta- and para-aminophenyl methyl dichlorosilane as the capping agent. First, the capping agent **3** was synthesized by reacting a 50:50 mixture of (3(bis(trimethylsilyl)amino)phenyl) magnesium bromide **1** (meta) and (4(bis(trimethylsilyl)amino)phenyl) magnesium bromide **1** (para) with methyl trichlorosilane **2**. Then capping agent **3** was reacted with DDSQ cage **4** and PEPA **5** to synthesize the DDSQ(m/p-PEPI)(Me) in 69% yield.



Scheme 2.1. Synthesis of DDSQ(m/p)(Me)(PEPI).



Scheme 2.2. Three different routes to synthesize DDSQ (m/p)(Me)(PEPI).

The novel synthetic route was revealed by doing a systematic study of the previous synthetic route. Scheme 2.2 summarizes the previous and current attempts that were made to synthesize DDSQ(m/p)(Me)(PEPI). According to **Path A (blue color route),** meta- and para-aminophenyl methyl dichlorosilane capping agents **1** were reacted with DDSQ and DDSQ(m/pAP)(Me) (protected amine) **2** was synthesized. Then the amine group of **2** was deprotected and DDSQ(m/p-AP)(Me) (deprotected amine) **3** was synthesized. After that, **3** was reacted with PEPA and DDSQ(m/p)(Me)(PEPI) **4** was obtained with 53% yield. According to **Path B (green color route),** meta- and para- aminophenyl methyl dichlorosilane capping agents **1** were reacted with DDSQ and DDSQ(m/p-AP)(Me) (protected amine) **2** was synthesized. Then **2** was directly reacted with PEPA and DDSQ(m/p)(Me)(PEPI) **4** was synthesized with 42% yield. The third route, **Path C (red color route)** was performed without isolating DDSQ(m/p-AP)(Me) **2** or **3**. According to **Path C (red color route),** meta- and para- aminophenyl methyl dichlorosilane

capping agents **1** were reacted with DDSQ and PEPA to synthesis DDSQ(m/p)(Me)(PEPI) **4** with 69% yield.

2.3 Conclusion

These studies concluded that **Path A**, the previously reported synthesis yielded about 50% of the desired compound, but also required seven days for the completion of the synthesis. In the novel synthetic route **Path B**, it was anticipated that the overall yield could be enhanced by avoiding the isolation of pure deprotected amine. Nevertheless, no such improvement was observed. Then the studies were directed towards the total one pot synthetic route **Path C**, which avoids the tedious separation of the intermediate analogs. To our delight, not only **Path C** avoid tedious isolations of intermediates, it also enhanced the overall yield to about 70%. Moreover, we were able to decrease the time required from seven days to three days in the overall synthetic process.

The novel improved synthetic route enabled us to efficiently synthesize about 50 g of the DDSQ(m/p-AP)(Me) molecule, which was sent to our collaborator as well as our funding source, the United State Air Force Research Institute, to explore further research avenues.

2.4 Experimental section

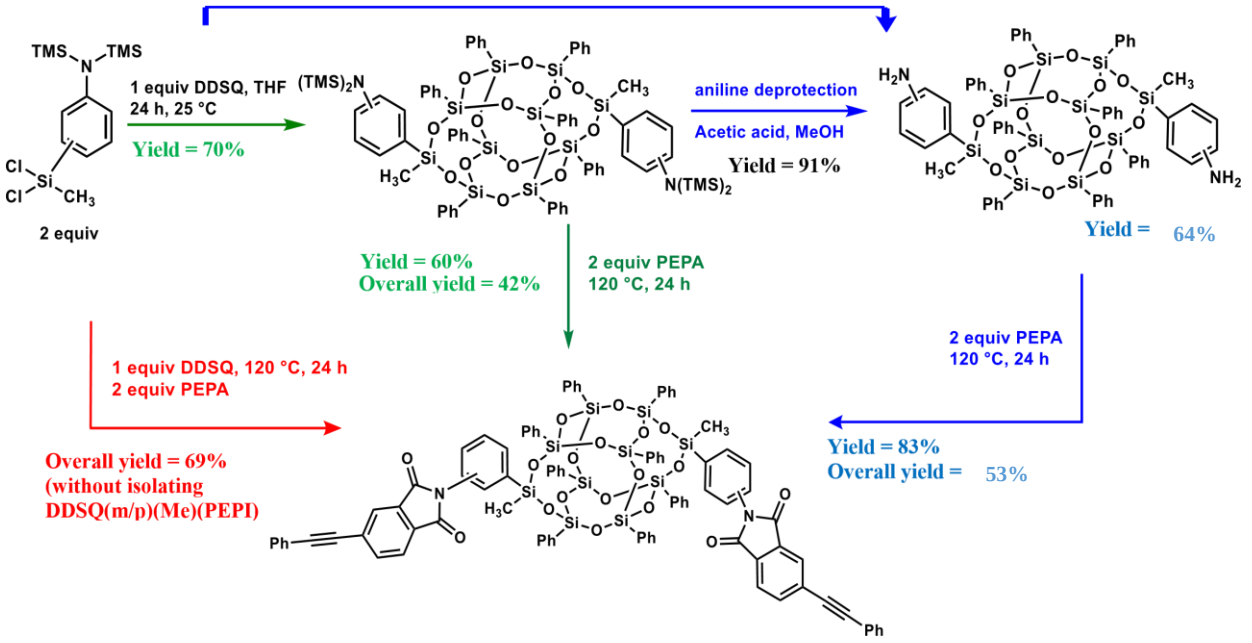
2.4.1 General materials and methods

Octaphenyl(Ph8tetrasilanol POSS) (DDSQ) was obtained from Hybrid Plastics (Hattiesburg, MS). Tetrahydrofuran (THF), hexanes, diethyl ether, magnesium turnings, triethylamine,trichloro methylsilane, 3-[bis (trimethylsilyl)amino]phenyl-magnesium chloride, and 4[bis(trimethylsilyl)amino]phenyl (bromo)magnesium were obtained from Sigma-Aldrich. Phenylethynylphthalic anhydride (PEPA) was obtained from Chriskev Company. The solvents were distilled under nitrogen and degassed using Freeze-Pump-Thaw methods. All reactions were carried out under an N_2 atmosphere, unless otherwise noted.

2.4.2 NMR spectroscopy

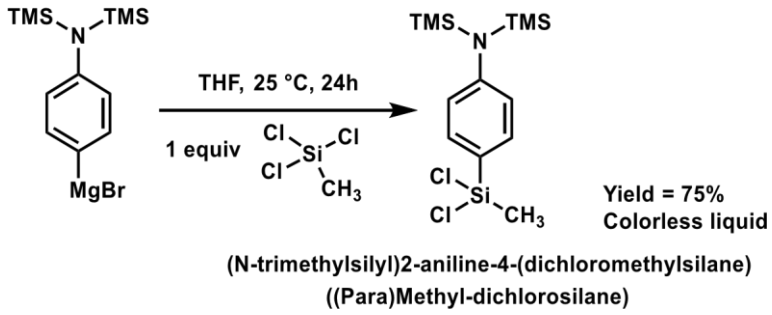
NMR spectra were recorded at 25 ºC on Agilent DDR2 500 MHz NMR spectrometer (500 MHz (^{1}H) and 100 MHz (^{29}Si)). ^{1}H NMR data were acquired using a recycle delay of 20 s and 32 scans. The ^{1}H NMR chemical shifts were referenced to that of residual protonated solvent in $CDCl_3$ (7.24 ppm). ^{29}Si NMR data were acquired using a recycle delay of 20 s. ^{29}Si NMR spectra were referenced against the lock solvent using vendor supplied lock referencing. ^{13}C NMR data were acquired using a recycle delay of 1 s and 256 scans.

2.4.3 Studies about different route to synthesize DDSQ functionalized oligoimides.



Scheme 2.3. Synthesis of DDSQ(m/p)(Me)(PEPI).

2.4.4 Synthesis of (Para)Methyl-dichlorosilane

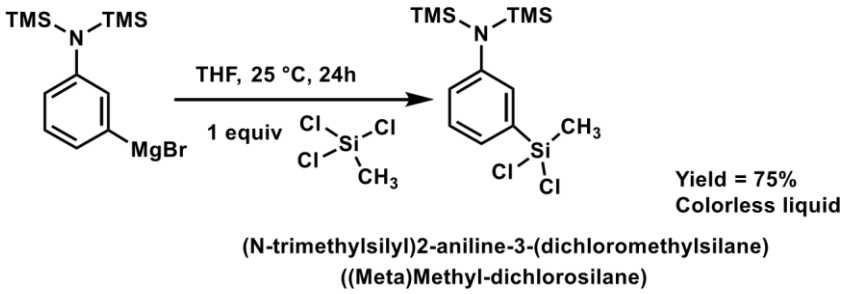


Scheme 2.4. Synthesis of (Para)Methyl-dichlorosilane capping agent.

Under a nitrogen atmosphere a solution of 0.5M (4(bis(trimethylsilyl)amino)phenyl) magnesium bromide (30 mL, 15 mmol) in THF was added dropwise to a stirred solution of trichloromethyl silane (2.12 g, 18 mmol) and THF (5 mL). The solution was stirred for 20 h at 25

°C and then purified by fractional distillation (120 °C, 0.1 Hgmm) to obtain (N-trimethylsilyl)2-aniline-4(dichloromethylsilane) (3.95 g, 11.26 mmol, 75 % yield) as a colorless liquid. ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 18.89 (1Si), 5.12 (2Si) (Figure S1). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.58 (2H, multiplet), 7.01 (2H, multiplet), 1.02 (3H, CH_3, singlet), 0.10 (18H, TMS, singlet) (Figure S2).

2.4.5 Synthesis of (Meta)Methyl-dichlorosilane



Scheme 2.5. Synthesis of (Meta)Methyl-dichlorosilane capping agent.

Under a nitrogen atmosphere a solution of 1M (3(bis(trimethylsilyl)amino)phenyl) magnesium bromide (15 mL, 15 mmol) in THF was added dropwise to a stirred solution of trichloromethylsilane (2.71 g, 18.5 mmol) and THF (5 mL). The solution was stirred for 20 h at 25 °C and then purified by fractional distillation (110 °C, 0.1 Hgmm) to obtain (N-trimethylsilyl)2-aniline-4(dichloromethylsilane) (3.85 g, 11.2 mmol, 75 % yield) as a colorless liquid. ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 18.41 (1Si), 5.19 (2Si) (Figure S3). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.44 (1H, doublet, J = 7.67 Hz), 7.33 (1H, triplet, J = 6.39 Hz), 7.27 (1H, singlet), 7.08 (1H, doublet, J = 8.95 Hz), 1.04 (6H, CH_3, singlet), 0.11 (18 H, TMS, singlet) (Figure S4).

2.4.6 Synthesis of DDSQ(m/p)(Me)(PEPI) using path A

A solution of (N-trimethylsilyl)2-aniline-3(dichloromethylsilane) (1.00 g, 2.85 mmol, 1equiv), (N-trimethyl silyl)2-aniline-4-(dichloromethylsilane) (1.00 g, 2.85 mmol, 1 equiv), and triethyl amine (1.16 g, 11.5 mmol, 4 equiv) in THF (14 mL) was added dropwise into a stirred solution of Ph8tetrasilanol-POSS (3.02f g, 2.82 mmol, 0.98 equiv) at 25 °C THF (40 mL). After 30 minutes, the $HNEt_3Cl$ (1.43g, 10.5 mmol) precipitate was separated by filtration, and the solvent was removed from the filtrate under vacuum. To the resultant residue diethyl ether (5 mL) was added followed by acidified methanol, which gave a white suspension that was stirred at 25 °C for 20 h. The heterogeneous mixture was filtered, and the precipitate was dried under nitrogen to yield compound DDSQ–diamine (de-protected), (2.20 g, 1.65 mmol, 58 % yield).

Under a nitrogen atmosphere, a well-stirred solution of DDSQ–diamine (deprotected) (2.20 g, 1.65 mmol) and PEPA (1.20 g, 4.83 mmol) in anhydrous THF (28 mL) and toluene (28 mL) was stirred at room temperature (25 °C) for 1 h. The solution was heated to 60 °C for 2 h and refluxed at 115 °C for 20 h. Solvent was removed under vacuum and subsequently washed and precipitated with methanol. The product (PEPI) was filtered and dried. (2.30 g, 1.30 mmol, 79 % yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: -31.20, -31.46, -77.34, - 77.92, -78.03, -78.63, -78.69, -78.75, -79.06, -79.17, -79.23, -79.35 (Figure S6). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09-7.03 (64H, overlapping multiplets), 0.58-0.56 (6H, overlapping singlets) (Figure S5).

2.4.7 Synthesis of DDSQ(m/p)(Me)(PEPI) using path B

A solution of (N-trimethylsilyl)2-aniline-3(dichloromethylsilane) (1.00 g, 2.85 mmol, 1equiv), (N-trimethyl silyl)2-aniline-4-(dichloromethylsilane) (1.00 g, 2.85 mmol, 1 equiv), and triethylamine (1.164 g, 11.5 mmol, 4 equiv) in THF (14 mL) was added dropwise into a stirred solution of Ph8tetrasilanol-POSS (3.02 g, 2.82 mmol, 0.98 equiv) at 25 °C THF (40 mL). After 30 minutes, the $HNEt_3Cl$ (1.42g, 10.4 mmol) precipitate was separated by filtration, and the solvent was removed from the filtrate under vacuum. To the resultant residue diethyl ether (5 mL) was added, which gave a white suspension that was stirred at 25 °C for 20 h. The heterogeneous mixture was filtered, and the precipitate was dried under nitrogen to yield compound DDSQ–diamine (protected), (2.65 g, 1.98 mmol, 70 % yield).

Under a nitrogen atmosphere, a well-stirred solution of DDSQ–diamine (protected) (2.20 g, 1.65 mmol) and PEPA (1.20 g, 4.83 mmol) in anhydrous THF (28 mL) and toluene (28 mL) was stirred at room temperature (25 °C) for 1 h. The solution was heated to 60 °C for 2 h and refluxed at 115 °C for 20 h. Solvent was removed under vacuum and subsequently washed and precipitated with methanol. The product (PEPI) was filtered and dried. (1.75 g, 0.97 mmol, 59 % yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: -31.08, -31.33, -77.21, - 77.79, -77.90, -78.49, -78.55, -78.61, -78.92, -79.03, -79.09, -79.21 (Figure S7). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09-7.22 (64H, overlapping multiplets), 0.57-0.56 (6H, overlapping singlets) (Figure S8).

2.4.8 Synthesis of DDSQ(m/p)(Me)(PEPI) using path C

A solution of (N-trimethylsilyl)2-aniline-3(dichloromethylsilane) (1.00 g, 2.85 mmol, 1equiv), (N-trimethyl silyl)2-aniline-4-(dichloromethylsilane) (1.00 g, 2.85 mmol, 1 equiv), and triethyla-

-mine (1.16 g, 11.5 mmol, 4 equiv) in THF (14 mL) was added dropwise into a stirred solution of Ph8tetrasilanol-POSS (3.02 g, 2.82 mmol, 0.98 equiv) at 25 °C THF (40 mL). After 30 minutes, the $HNEt_3Cl$ (1.43g, 10.50 mmol) precipitate was separated by filtration, and the solvent was removed from the filtrate under vacuum. To the resultant residue PEPA (1.2 g, 4.83 mmol), THF 28 mL and toluene 28 mL were added. Reaction mixture was stirred at room temperature (25 °C) for 1 h. The solution was heated to 60 °C for 2 h and refluxed at 115 °C for 20 h (under nitrogen atmosphere). Solvent was removed under vacuum and subsequently washed and precipitated with methanol. The product (PEPI) was filtered and dried (3.60 g, 2.00 mmol, 70 % yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: -31.28, -31.54, -77.38, - 77.96, -78.07, -78.67, -78.73, -78.82, -79.10, -79.21, -79.27, -79.39 (Figure S9). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.09-7.24 (64H, overlapping multiples), 0.57-0.56 (6H, overlapping singlets) (Figure S10).

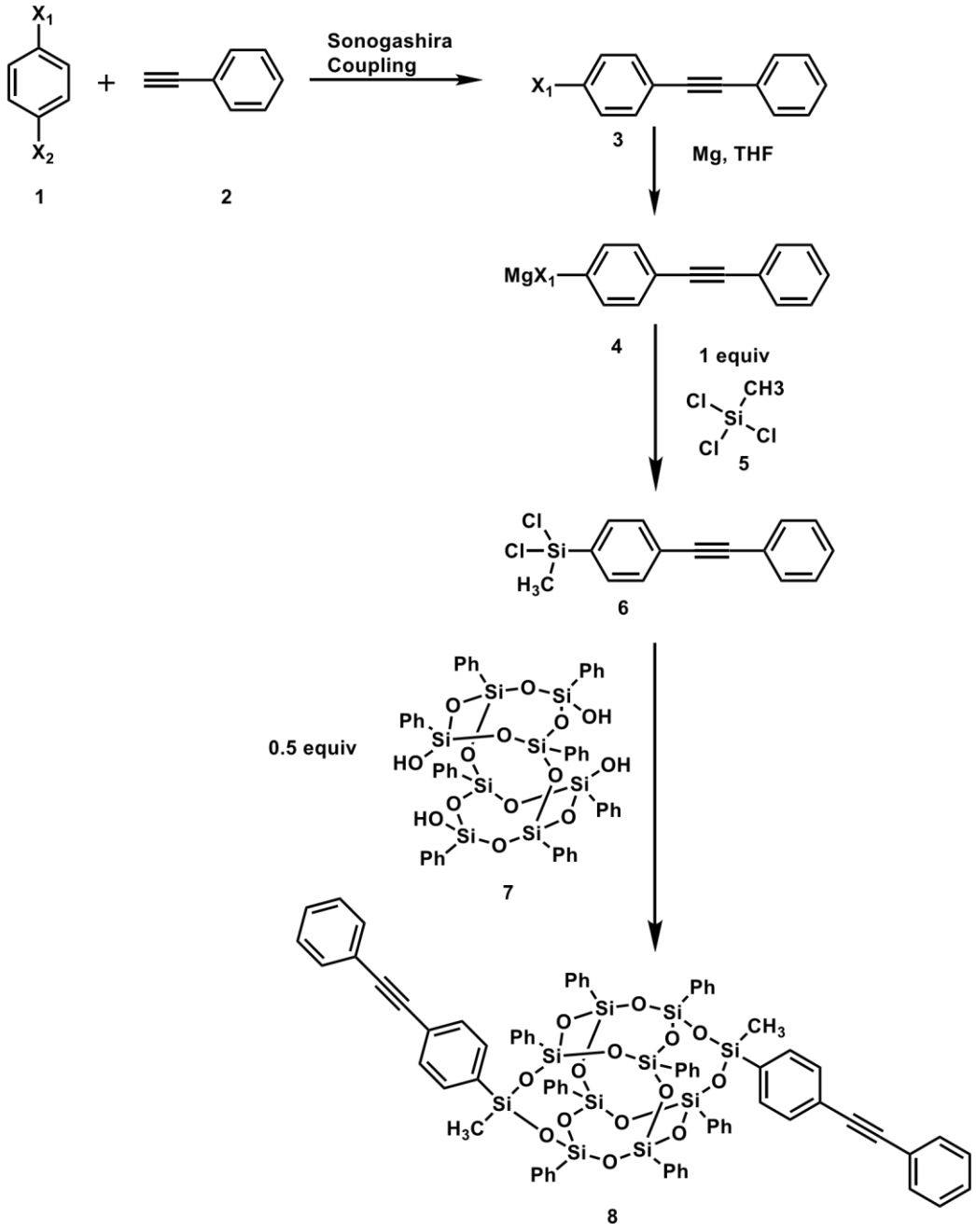
CHAPTER 3: SYNTHESIS OF NOVEL (PHENYLETHYNYL)PHENYL DDSQ OLIGOMERS

3.1 Introduction

Oligomers and polymers containing phenylethynyl groups have received considerable attention in high temperature applications. Upon thermal cure, the phenylethynyl group undergoes a complex reaction involving chain extension, branching and crosslinking to afford materials exhibiting a favorable combination of physical and mechanical properties.[40]

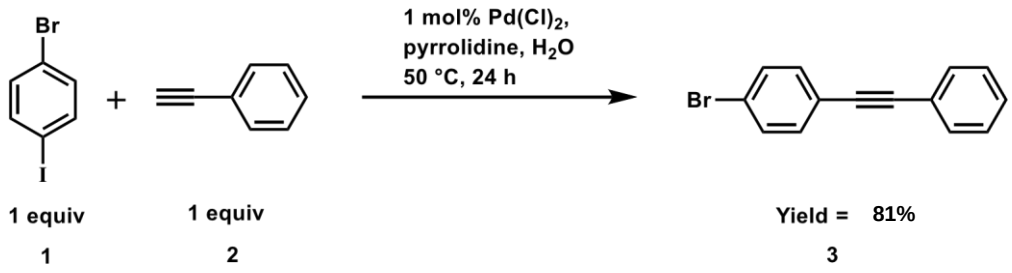
In the past, high temperature application has concentrated on silsesquioxane incorporated imide oligomers. In the present work, phenylethynyl functionality was considered and DDSQ incorporated phenylethynyl oligomers were synthesized. The development of (phenylethynyl)phenyl DDSQ novel molecule was illustrated in (Scheme 3.1).

As shown in Scheme 3.1, first di-halide benzene **1** was reacted with phenyl acetylene **2** to form halogen 4-(phenylethynyl) benzene **3** based on Sonogashira coupling. Then the Grignard reaction was performed to form **4**. The treatment of one equivalent of methyl trichlorosilane **5** with **4** caused the formation of dichloro(methyl)(4-(phenylethynyl)phenyl silane **6.** After that half an equivalent of DDSQ **7** was reacted with one equivalent of capping agent **6** to form the (phenylethynyl)phenyl DDSQ **8**.



Scheme 3.1. Synthesis of (phenylethynyl)phenyl DDSQ

3.2 Optimization of conditions to synthesize 1-bromo-4-(phenylethynyl)benzene

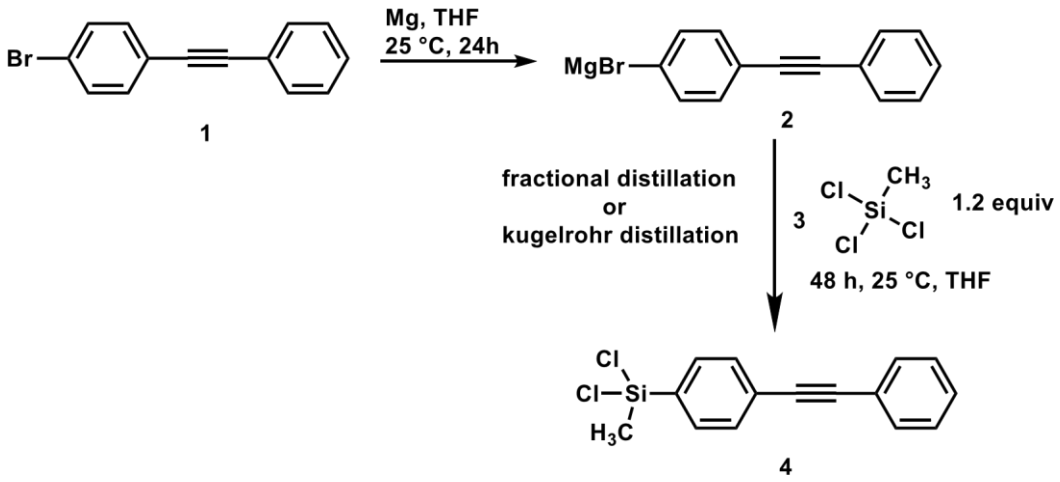


Scheme 3.2. Synthesis of 1-bromo-4-(phenylethynyl)benzene

The synthesis of halogen 4-(phenylethynyl) benzene **3** is depicted in Scheme 3.2. A mild protocol for the copper-free Sonogashira coupling of bromo-4-iodo benzene **1** with phenyl acetylene **2** in water under aerobic conditions has been used in this synthesis.[41] The use of 1 mol % $PdCl_2$ in the presence of pyrrolidine allows the coupling reaction to proceed at 50 °C with 81% yield.

3.3 Optimization of conditions to synthesize (phenylethynyl)phenyl dichlorosilane

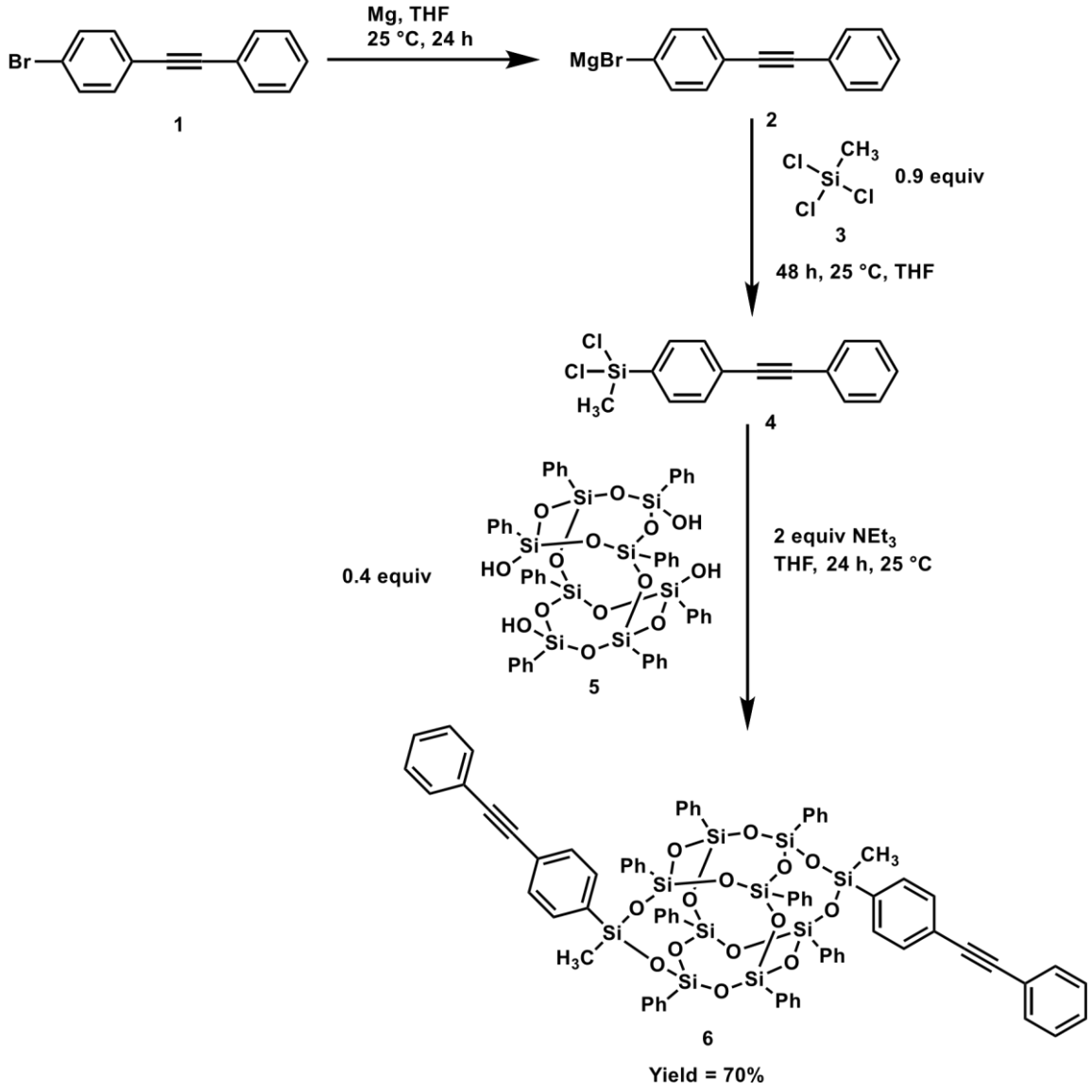
Then the synthesis of (phenylethynyl)phenyl dichlorosilane capping agent **2** was carried out as shown in Scheme 3.3. The fractional distillation and Kugelroher distillation were performed to obtain the purified dichlorosilane capping agent. According to NMR studies (Figure S31) the (phenylethynyl)phenyl dichlorosilane was observed in the distilled product with some byproducts. Further purification of the distilled product from those byproducts failed. These observation confirmed that purification of dichlorosilane capping agent was difficult.



Scheme 3.3. Synthesis of (phenylethynyl)phenyl dichlorosilane capping agent

3.4 Synthesis of phenylethynyl(phenyl) DDSQ – one pot route

In order to avoid the tedious purification steps in this synthetic procedure, attempts were made for a one pot synthesis. According to Scheme 3.4, the crude product of dichlorosilane capping agent **4** was introduced in to the DDSQ **5** under basic conditions. The desired product was not observed in the one pot synthesis even with the use of excess or one equivalent of methyltrichlorosilane. All these studies confirmed that, dichlorosilane capping agent should be purified to avoid other reactions. Otherwise trichlorosilane will react with DDSQ and disrupt the reaction. Therefore the one pot route was optimized by the use of 0.9 equivalents of methyltrichlorosilane and the dichlorosilane capping agent was obtained without any of the previously obtained undesired byproducts (Figure S29). Without any further purification the dichlorosilane capping agent was reacted with DDSQ for 24 h at room temperature. To our delight (phenylethynyl)phenyl DDSQ was synthesized through this one-pot route in 70% yield.

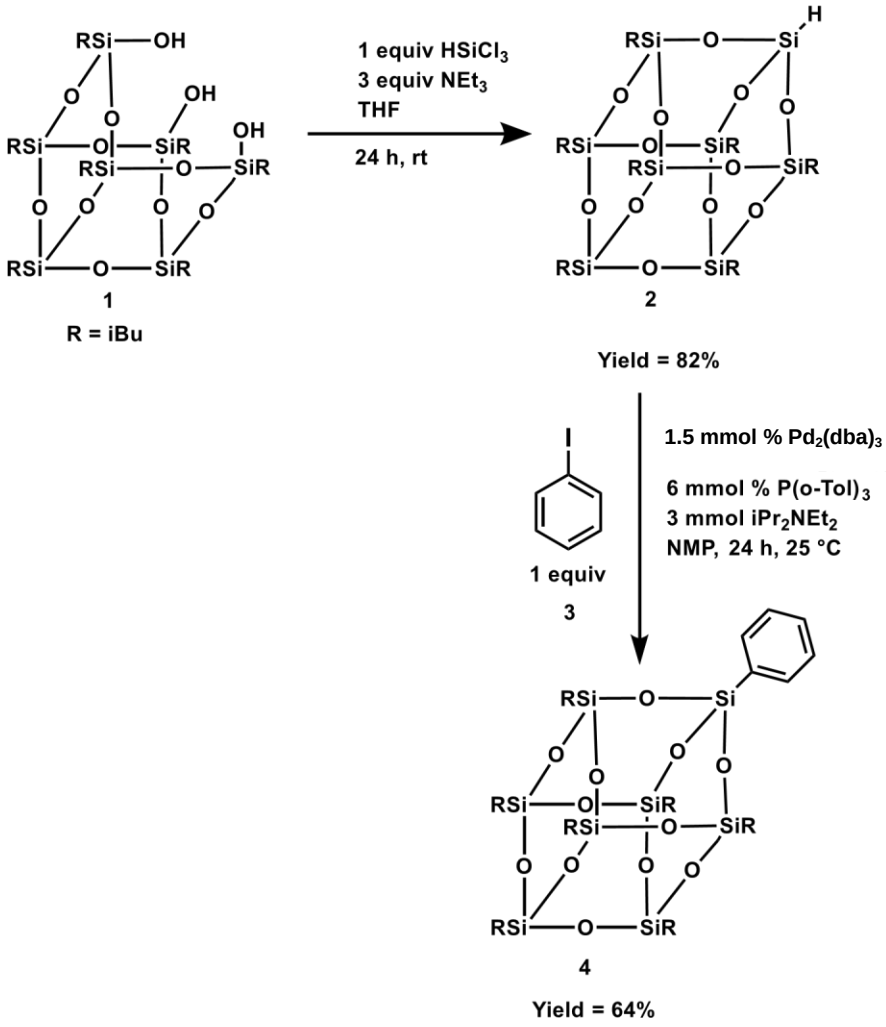


Scheme 3.4. Synthesis of phenylethynyl(phenyl) DDSQ – one pot route

3.5 Pd catalyzed silylation of aryl halides with dihydro DDSQ or T7(iBu) cage

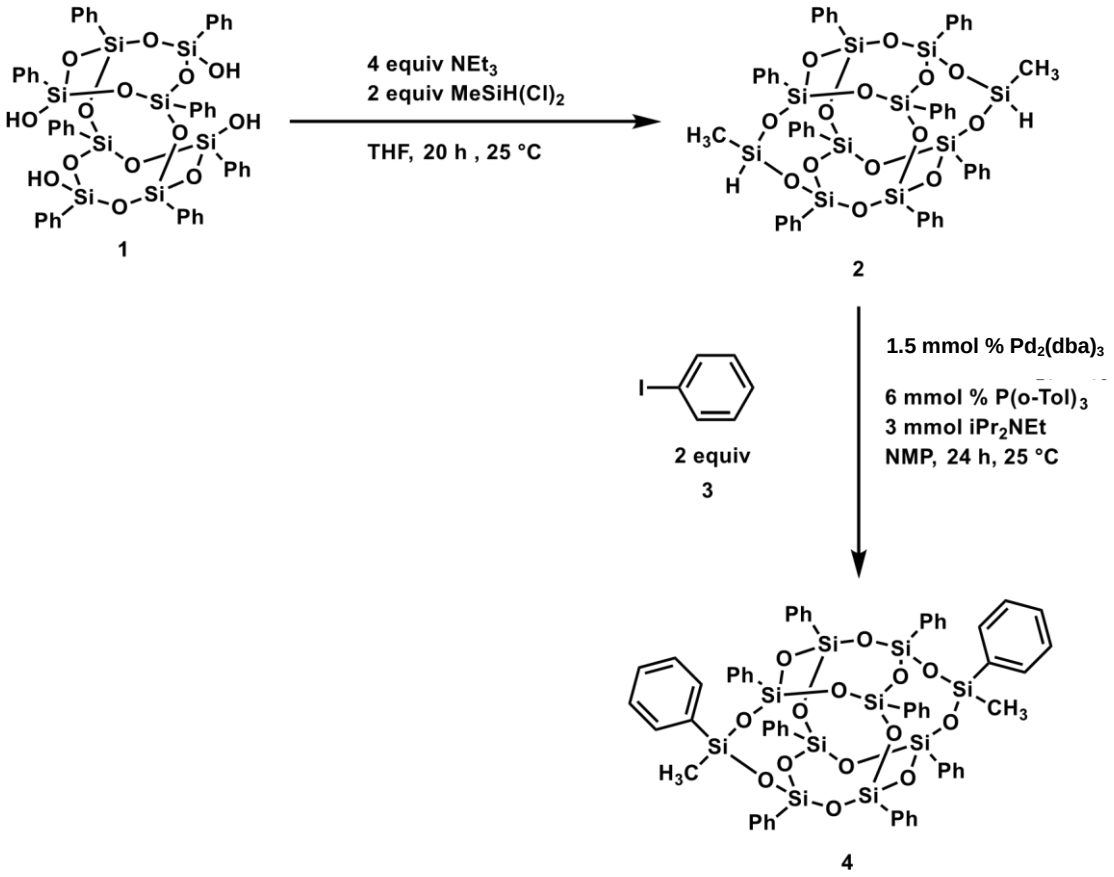
In our efforts to explore novel synthetic approaches towards the synthesis of (phenylethynyl)phenyl DDSQ oligomers, a new approach based on Pd catalyzed silylation of aryl halides was carried out. Organosilicon reagents have played an increasingly important role in Pd(0)-catalyzed cross couplings with organohalides. To the best of our knowledge, Pd catalyzed silylation has been developed for DDSQ molecules and we were interested in doing as well as the synthesis of (phenylethynly)phenyl DDSQ molecule through such a novel route. For the preliminary studies, corner capped T7-iBu POSS cage was selected.

First, Pd catalyzed silylation chemistry was tested with the simple structure skeleton corner capped T7-iBu cage. According to the Scheme 3.5, first T7-iBu cage **1** was reacted with trichlorosilane ($HSiCl_3$) to obtain the hydrogen substituted closed T8 cage **2** in 82% yield. Then Pd catalyzed reaction was performed between aryl halide **3** and T8 cage **2**. Phenyl substituted T8 cage **4** was obtained in 64% yield. With these positive data and inferences in hand we elaborated our work towards the complex DDSQ molecule.



Scheme 3.5. Pd catalyzed silylation of aryl halides with T7(iBu) cage.

As shown in Scheme 3.6, the reaction between DDSQ **1** and methyldichlorosilane can was carried out to prepare the DDSQ(Me)(H) **2**. Then two equivalents of iodobenzene **3** were reacted with DDSQ(Me)(H) **2** using Pd catalyst**.** Even though this chemistry worked for T7(iBu) cage, it was not applicable to the DDSQ-H cage. The major products were iodobenzene and decomposed DDSQ cage.



Scheme 3.6. Pd catalyzed silylation of aryl halides with DDSQ-H cage.

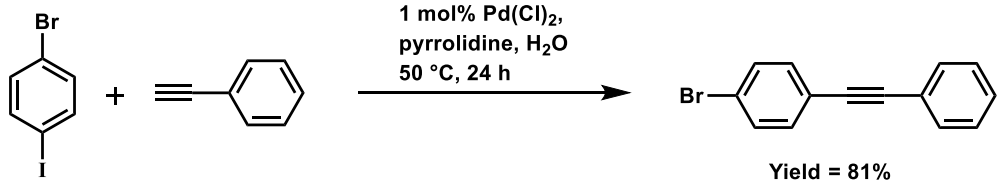
3.6 Conclusion

The novel **(**phenylethynyl)phenyl DDSQ oligomer was successfully synthesized through a one pot route with 70% yield. This synthesis avoids the tedious separation techniques, fractional distillation or kugelroher distillation. This novel oligomer will be characterized using TGA (Thermal gravimetric Analysis) and DSC (Differential Scanning Calorimetry) for future studies.

A new approach based on Pd catalyzed silylation of aryl halide was carried out to develop (phenylethynyl)phenyl DDSQ oligomer. Even though Pd catalyzed silylation of aryl halides was successful for T7(iBu) cage, this chemistry was not applicable for DDSQ-H cage as it showed decomposition during the reaction.

3.7 Experimental Section

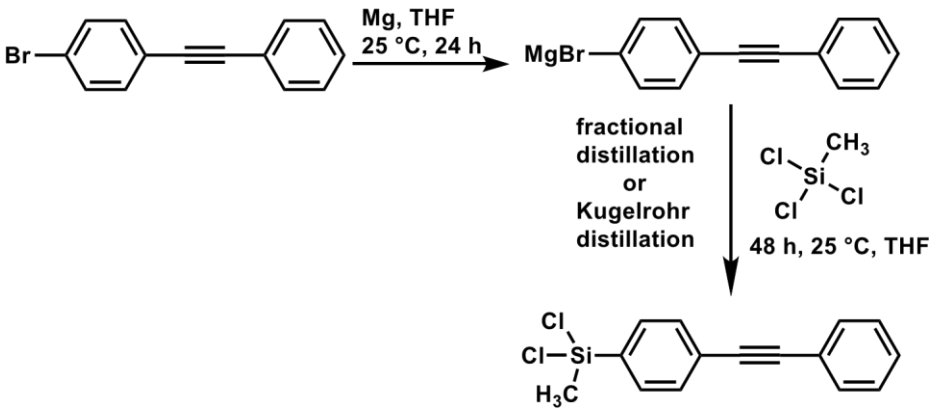
3.7.1 Synthesis of bromo-4-(phenylethynyl)benzene



Scheme 3.7. Synthesis of bromo-4-(phenylethynyl)benzene.

$Pd(Cl)_2$ (0.1 mmol, 0.02 g), bromo-4-iodobenzene (10 mmol, 2.83 g), water (12.50 mL) and pyrrolidine (50 mmol, 4.15 mL) were charged into a flask equipped with a stir bar. The reaction mixture was heated at 50 °C for 5 min. Afterward phenylactylene (12 mmol, 1.30 mL) was added and the mixture stirred at 50 °C for 24 h. After vigorous stirring, the reaction mixture was extracted with ethyl acetate (3 X 10 mL). The extracted solution was dried over anhydrous sodium sulfate (Na_2SO_4). The solvent was removed under vaccum and the residue was purified by flash chromatography on silica gel (hexane) give the product as a white solid (7.20 mmol, 2.40 g, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.53 – 7.47 (4H, multiples), 7.39 - 7.34 (5H, multiplet) (Figure S26) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ: 133.0, 131.5, 128.5, 128.3, 122.8, 122.5, 122.2, 90.4, 88.3 ppm (m.p 83-85 °C) (Figure 25).

3.7.2 Synthesis of dichloro(methyl)(4-(phenylethynyl)phenyl) silane



Scheme 3.8. Synthesis of dichloro(methyl)(4-(phenylethynyl)phenyl) silane.

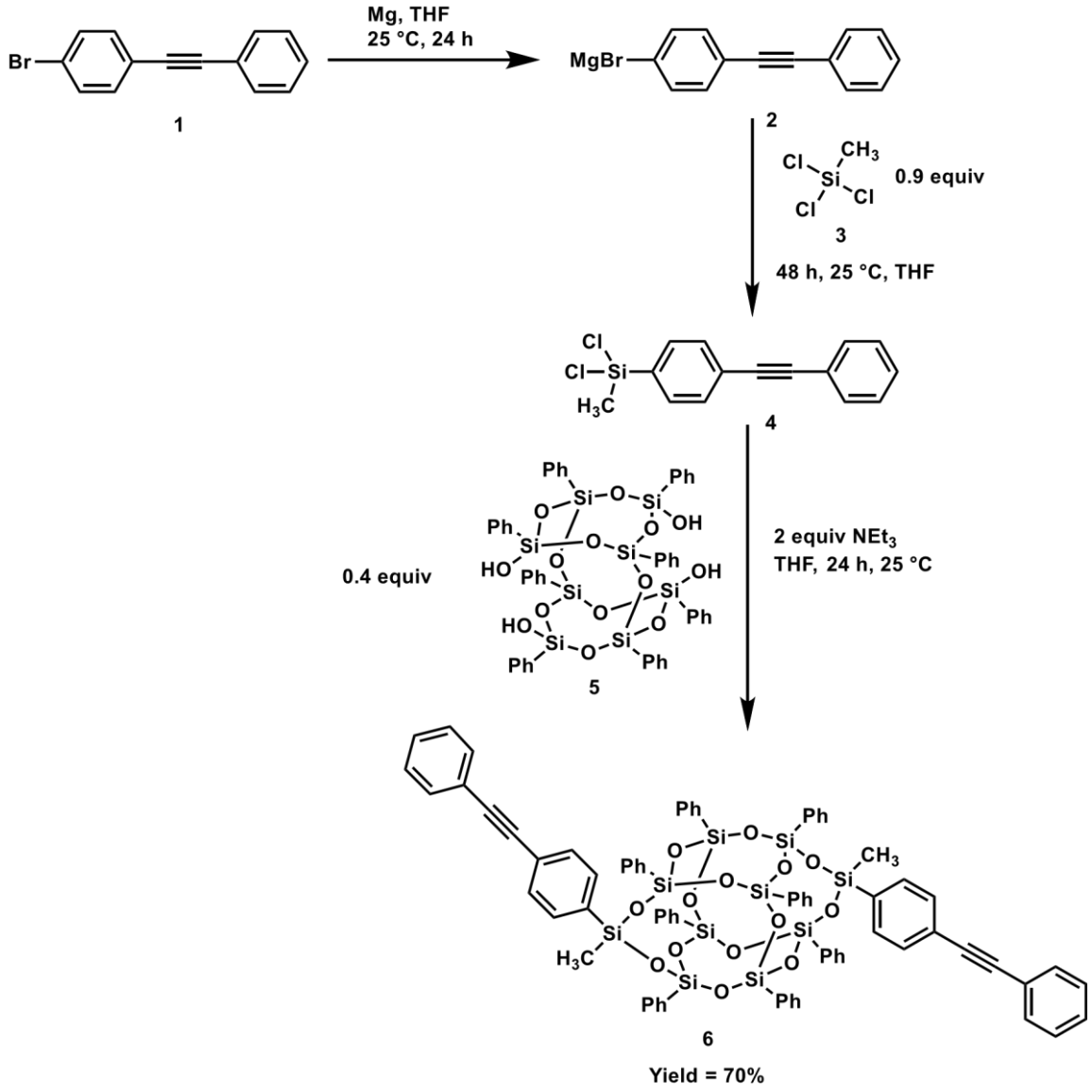
Bromo-4-(phenylethynyl)benzene (10 mmol, 2.56 g) was charged into a flask equipped with a stir bar, Mg turnings (12 mmol, 0.26 g) and THF (5 mL). Reaction was carried out at 25 °C for 24 h under a nitrogen environment. After the Grignard reaction, the crude product was charged into a flask equipped with a stir bar, methyl trichlorosilane (12 mmol, 1.4 mL) and THF (5 mL). The reaction was performed at 25 °C for 48 h under a nitrogen environment. The product was purified by fractional distillation or Kugelrohr distillation (Figure S29).

3.7.3 Synthesis of phenylethynyl(phenyl) DDSQ – one-pot route

Bromo-4-(phenylethynyl)benzene (10 mmol, 2.56 g) was charged into a flask equipped with a stir bar, Mg turnings (12 mmol, 0.26 g) and THF (5 mL). Reaction was carried out at 25 °C for 24 h under a nitrogen environment. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.46 – 7.44 (4H, multiplet), 7.00 – 6.99 (5H, multiplet) ppm (Figure S27). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 131.5, 128.2, 123.4, 109.6, 92.4, 89.6 ppm (Figure S28).

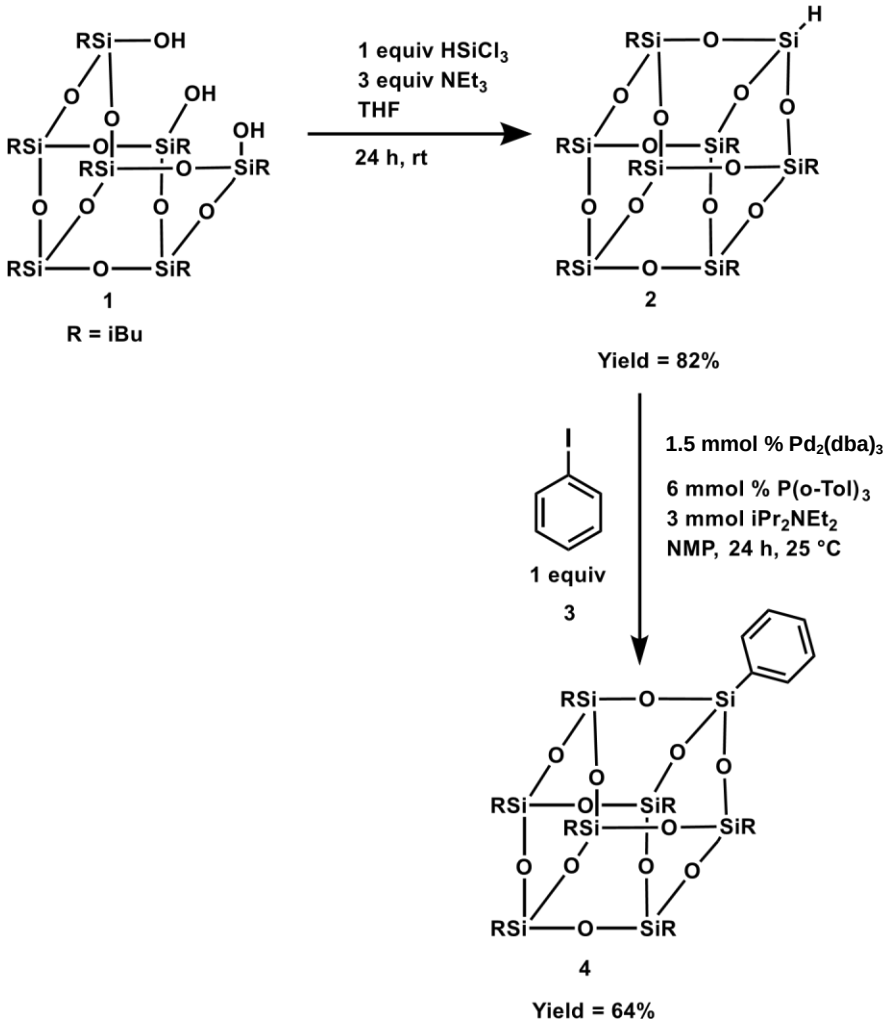
After the Grignard reaction, the crude product was charged to the flask equipped with a stir bar, methyl trichlorosilane (12 mmol, 1.4 mL) and THF ((5 mL). The reaction was performed at 25 °C for 48 h under a nitrogen environment. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.24 (4H, multiplet), 7.08 – 7.05 (5H, multiplet) ppm (Figure S30). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 18.66, 12.79 ppm (Figure S29).

Dichloro(methyl)(4-(phenylethynyl)phenyl) silane was charged into a flask equipped with a stirbar, DDSQ (5 mmol, 5.30 g), THF (20 mL) and triethylamine (NEt_3) (20 mmol, 2.02 mL). The reaction was performed at 25 °C for 24 h under a nitrogen environment. After 24 h, the $HNEt_3Cl$ precipitate was separated by filtration, and the solvent was removed from the filtrate under vacuum. The residue was purified by flash chromatography on silica gel (hexane: dichloromethane 80:20). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.65 – 7.20 (58H, multiplet), 0.55 (5H, singlet) ppm (Figure S35). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: -32.40, -78.59, -79.34, -79.65, -79.88 ppm (Figure S33) (dichloro-DDSQ). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 136.51, 134.20, 134.10, 130.86, 128.34, 127.87, 127.71, 127.62, 124.87, 123.24, 90.22, 89.44 ppm (Figure S34) (diphenylethyne).



Scheme 3.9. Synthesis of phenylethynyl(phenyl) DDSQ – one-pot route.

3.7.4 Pd catalyzed silylation of aryl halides with T7(iBu) cage



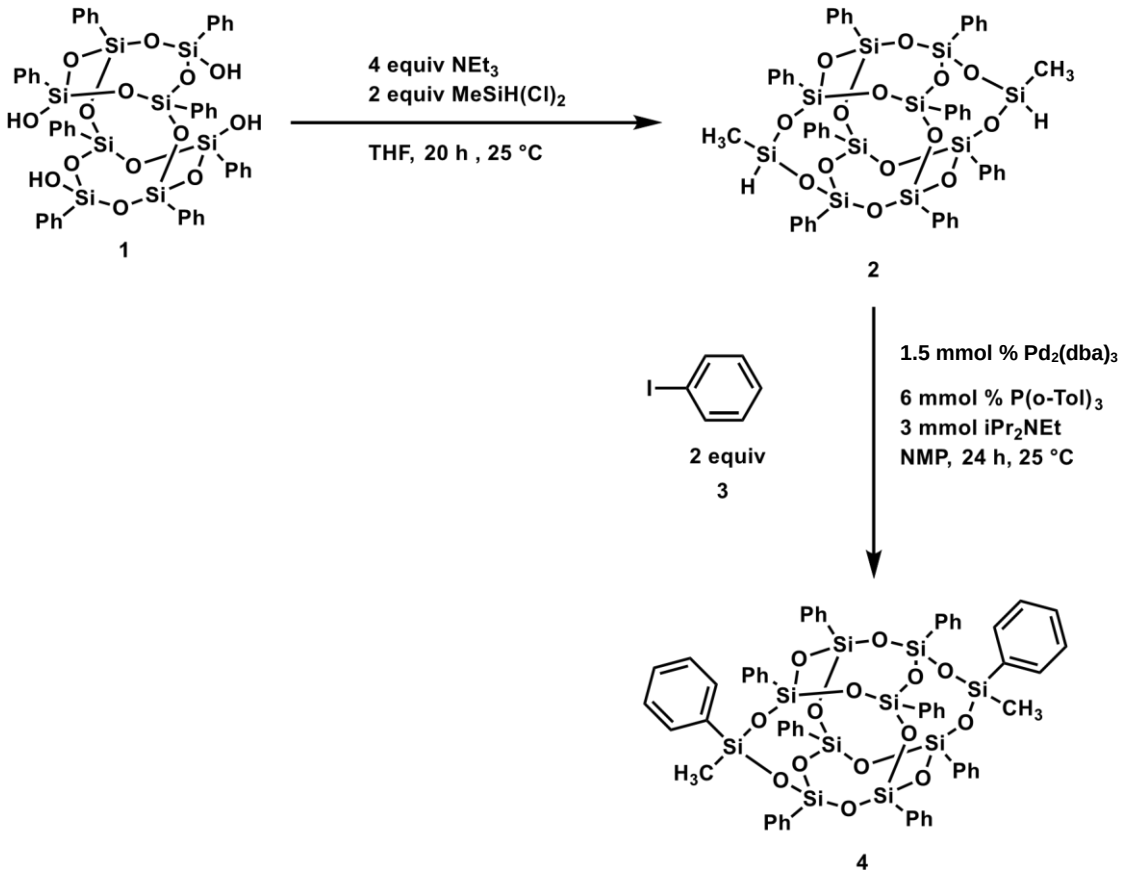
Scheme 3.10. Pd catalyzed silylation of aryl halides with T7(iBu) cage.

$Pd_2(dba)_3$ (0.015 mmol, 0.013 g) and P(o-tol)$_3$ (0.06 mmol, 0.018 g) were placed in a round bottom flask capped with a rubber septum. The flask was flushed with nitrogen and then charged with NMP (4 mL). Iodobenzene (1.00 mmol, 0.10 mL), i-Pr_2NEt (3.00 mmol, 0.54 mL), and T7(iBu) **1** (1.50 mmol, 1.05 g) were added successively. The reaction mixture was then stirred at r.t. for 24 h. When the reaction was complete, Et_2O (10 mL) was added; the organic phase was washed with H_2O (3 × 15 mL) to remove NMP and dried over Na_2SO_4. The solvent was removed

under reduced pressure and the residue was purified by flash column chromatography (hexane–CH_2Cl_2, 3:1) to give the desired product with 67% yield (0.67 mmol, 0.70 g) ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.73 – 7.71 (2H, multiplet), 7.34 (1H, multiplet), 7.12 – 7.10 (2H, multiplet), 1.9-1.87 (1H, multiplet), 1- 0.98 (38H, multiplet), 0.67- 0.62 (13H, multiplet) ppm (Figure S38). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: -66.74, -67.85, -67.87 ppm (Figure S39)

.

3.7.5 Pd catalyzed silylation of aryl halides with DDSQ(Me)(H) cage



Scheme 3.11. Pd catalyzed silylation of aryl halides with DDSQ(Me)(H) cage.

$Pd_2(dba)_3$ (0.015 mmol, 0.013 g) and $P(o\text{-}tol)_3$ (0.06 mmol, 0.018 g) were placed in a round bottom flask capped with a rubber septum. The flask was flushed with nitrogen and then charged with NMP (4 mL). Iodobenzene (2.00 mmol, 0.20 mL), i-Pr_2NEt (3.00 mmol, 0.54 mL), and DDSQ(Me)(H) (1.00 mmol, 1.54 g) were added successively. The reaction mixture was then stirred at r.t. for 24 h. When the reaction was complete, Et_2O (10 mL) was added; the organic phase was washed with H_2O (3 × 15 mL) to remove NMP and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (hexane– CH_2Cl_2, 3:1).

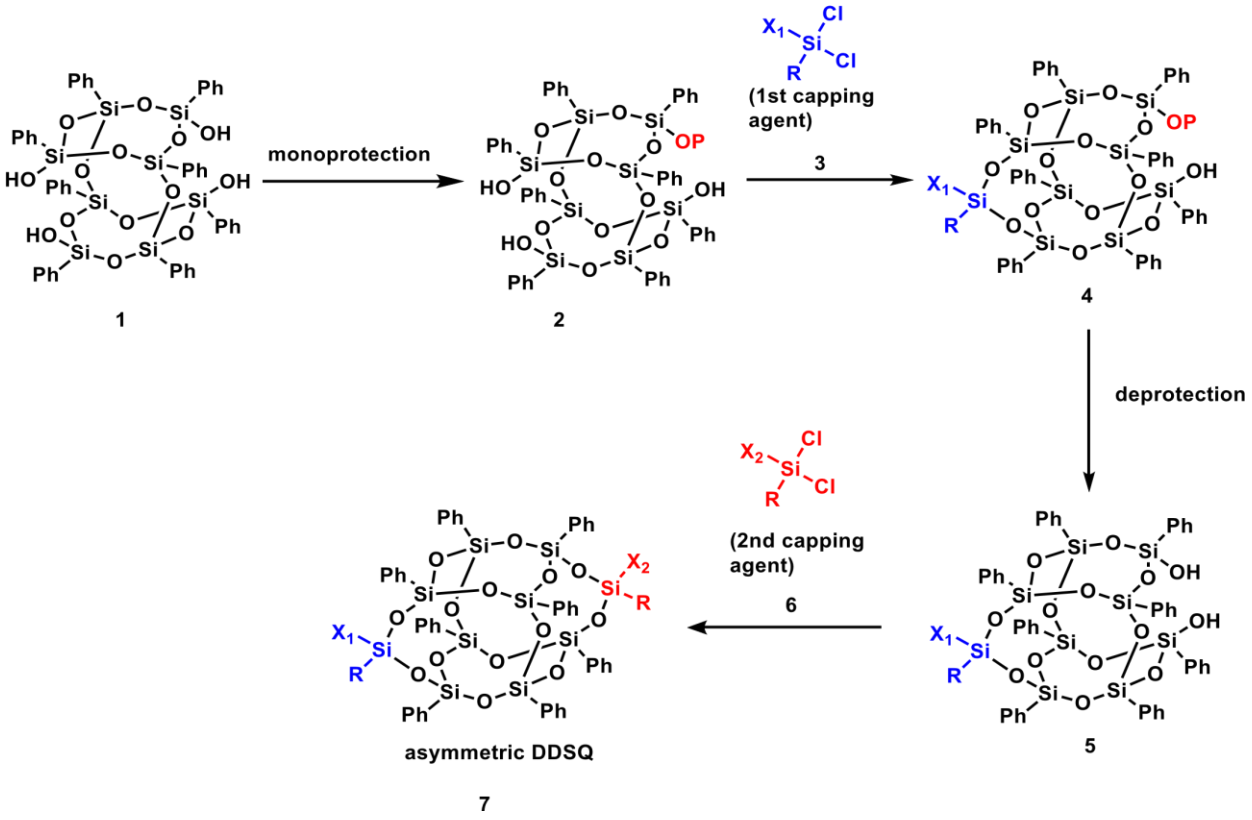
CHAPTER 4: DEVELOPMENT OF ASYMMETRIC DDSQ MOLECULE BY MONOPROTECTING HYDROXYL GROUP

4.1. Introduction

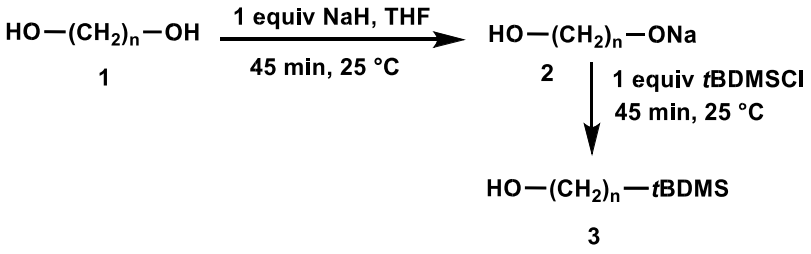
As stated earlier, DDSQ molecules possess a higher symmetry. Breaking the symmetry and selective functionalization of the DDSQ molecule will be highly desirable to fine tune the physical properties.

DDSQ molecules possess four symmetrical hydroxyl groups at each corner. One of the approaches to achieve an asymmetric DDSQ molecule **7** is the protection of one hydroxyl group and subsequently closing the DDSQ cage **2** with the first capping agent **3** (Scheme 4.1). Then the hydroxyl group of **4** can be deprotected and a different second capping agent **6** can be incorporated to close the DDSQ molecule **5**.

As shown in Scheme 4.2, McDougal and coworkers studied the monoprotection of diol systems. This was anticipated to incorporate in the current asymmetric synthesis of DDSQ molecules.[32] The source of this selectivity may reside in the properties of the monosodium salt **2** of the diol **1**. Treatment of the diol **1** with 1 equivalent of NaH causes the formation of a voluminous precipitate. They observed that the solubility of the monosodium salt of the diol **2** was considerably less soluble in this solvent system. Upon the addition of silylating agent (*t*BDMSCl), the small amount of dissolved monosodium salt **2** was silylated. As more salt slowly was going into solution, the rate of silylation of salt was faster than the backward reaction.

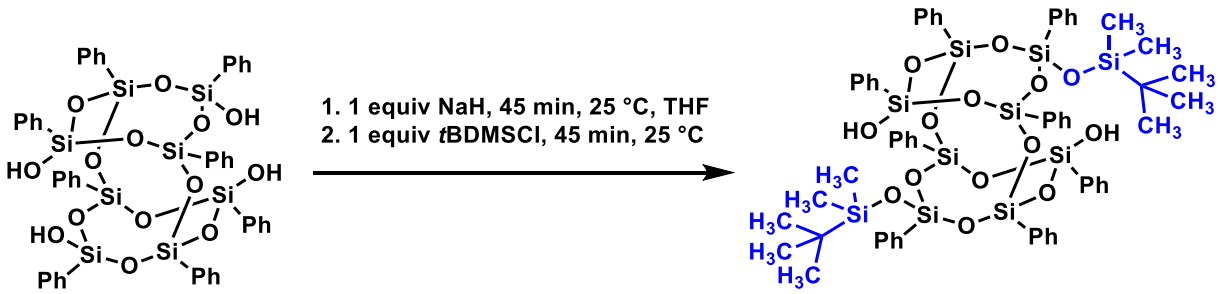


Scheme 4.1. Asymmetric DDSQ synthesis by using monoprotection.



Scheme 4.2. The chemistry developed by McDougal and coworkers to monoprotect the symmetric diol

4.2 Monoprotection of DDSQ

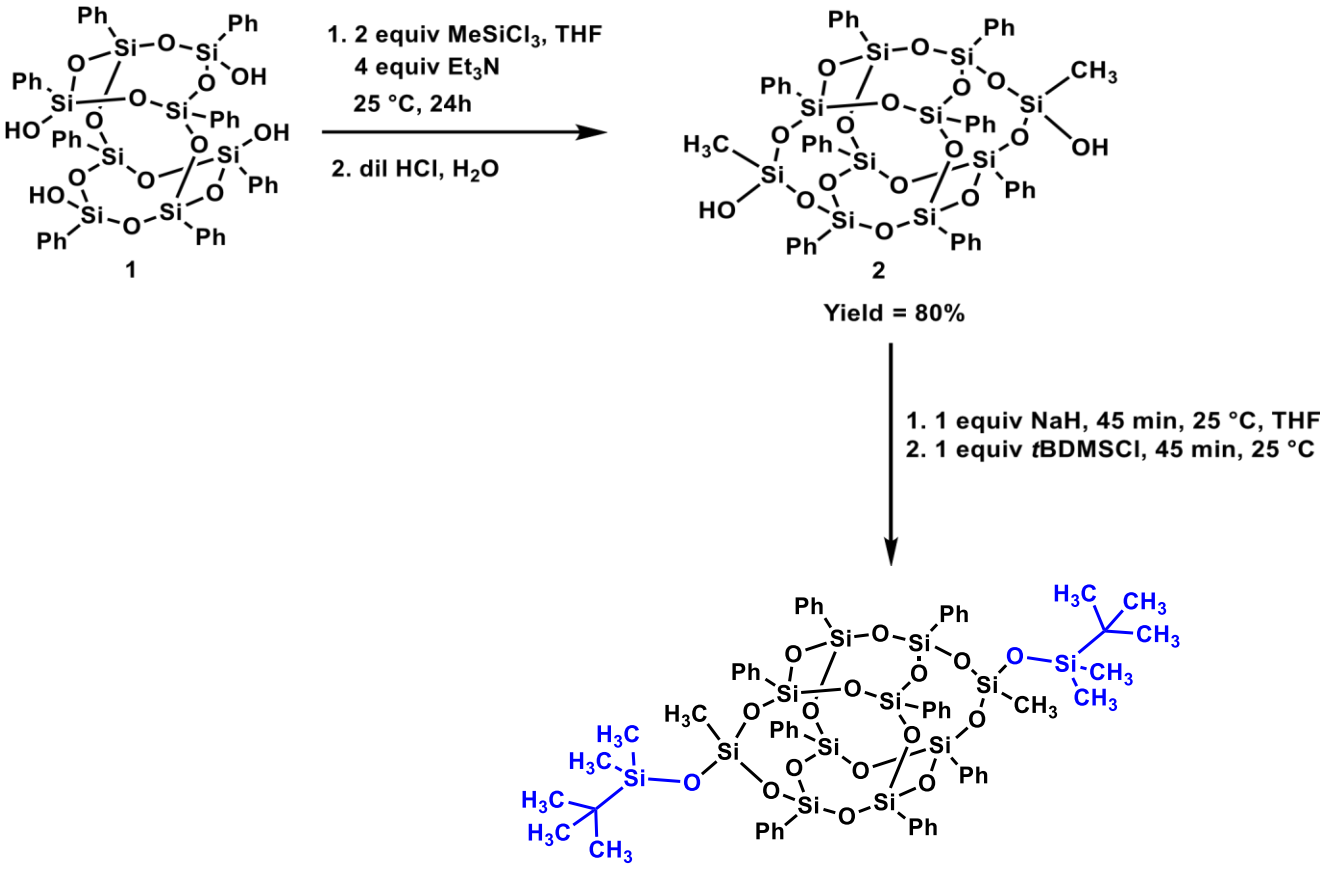


Scheme 4.3. Monoprotection of symmetric DDSQ.

As shown in Scheme 4.3, the McDougal chemistry was applied to DDSQ in an attempt to synthesize a monoprotected cage. Though we expected to achieve the monoprotected DDSQ molecule with the use of the chemistry developed by McDougal and coworkers, the desired product was not observed. According to the NMR analysis (Figure S11 and S12) and mass spectrum, the major product was the diprotected hydroxyl group containing DDSQ molecule. Though various reaction conditions like variable temperatures, reaction time, and base were tested to get the expected monoprotected DDSQ molecule, all efforts were unsuccessful.

4.3 Synthesis of DDSQ(Me)(OH) and Monoprotection

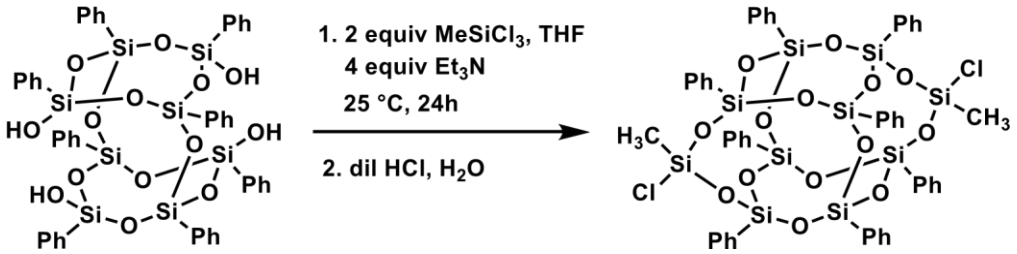
As it was challenging to achieve the monoprotection of this tetrasilanol system, a simplified diol system was synthesized by using the capping agent as shown in Scheme 4.4 These capping agents have two hydroxyl groups and now the DDSQ molecule is turned into a simplified diol structure. As shown in Scheme 4.4, the DDSQ(Me)(OH) **2** was synthesized by reacting with $MeSiCl_3$ and DDSQ **1** followed by hydrolysis in 80% yield. Then, the monoprotection conditions were applied for this diol **2**.



Scheme 4.4. Monoprotection of symmetric DDSQ(Me)(OH).

Even in the simplified diol DDSQ system, desired monoprotection of the hydroxyl group was not observed. NMR studies (Figure S15 and S16) concluded, that the reaction conditions provided the diprotected DDSQ(Me)(OH) molecule.

According to the literature, the DDSQ cage is closed using dichlorosilane as the capping agent. During this project a novel approach was discovered to close the DDSQ cage. I found that DDSQ cages can be closed using trichlorosilane and then the remaining Cl atom can be converted to a stable functional group (Scheme 4.5).

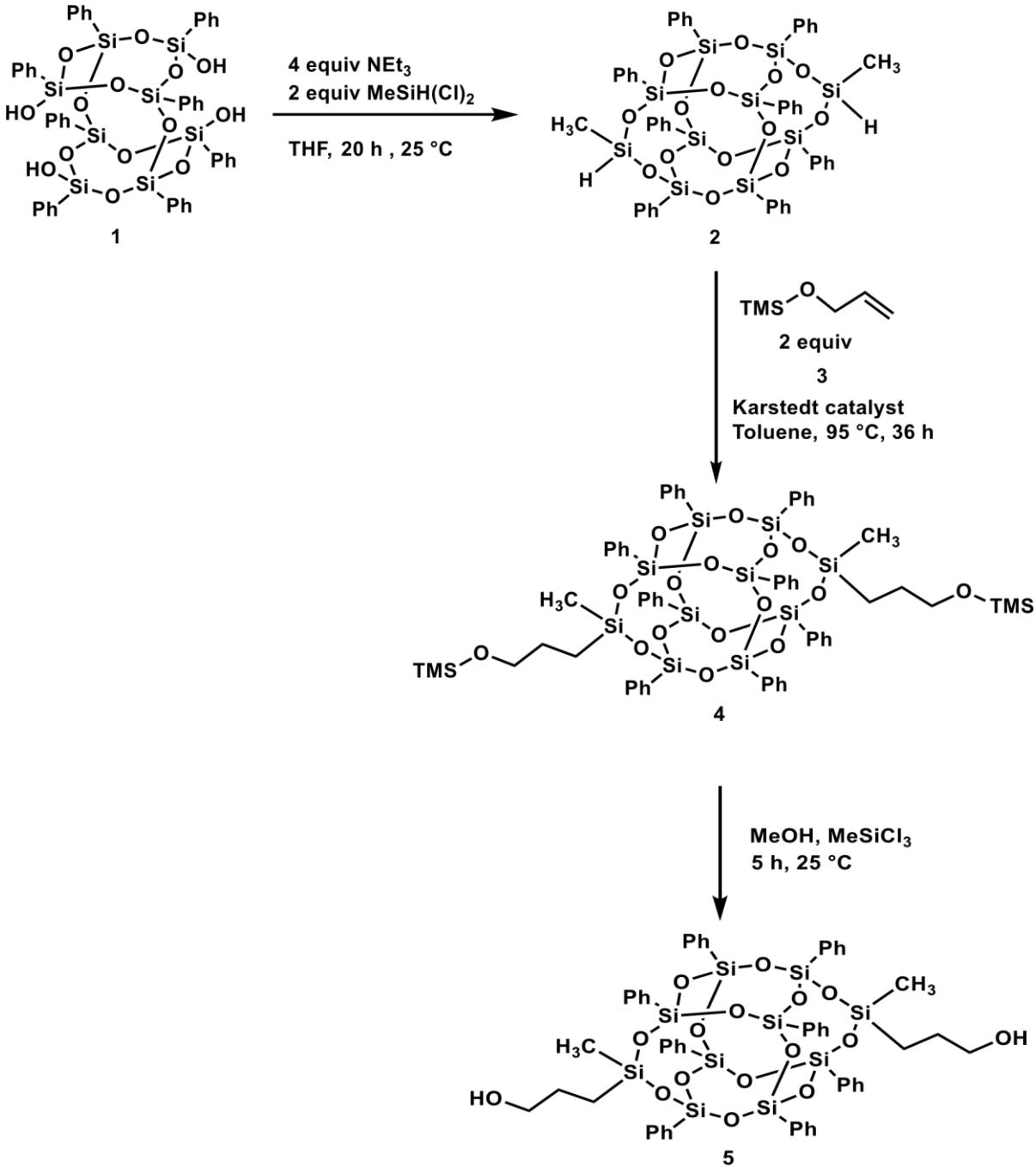


Scheme 4.5. Closing of DDSQ cage using trichlorosilane capping agent

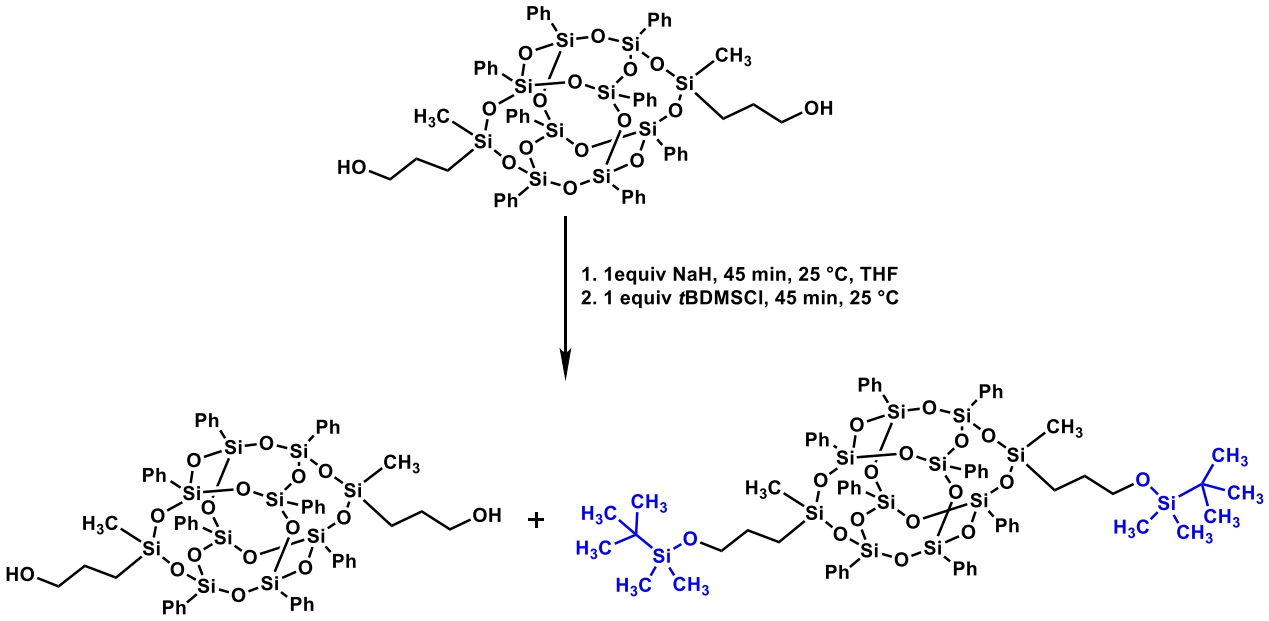
According to the literature,[32] McDougal's chemistry was applied always for carbinol system without any issue. Nevertheless, for silanol, this chemistry was not applicable the same way. Therefore, the DDSQ cage was closed with a capping agent that had a hydroxyl group on the carbon atom.

4.4 Synthesis of DDSQ(Me)(Hydroxopropyl) and Monoprotection

DDSQ(Me)(Hydroxopropyl) was synthesized using hydrosilation chemistry.[33] As shown in Scheme 4.6, the silylation reaction between DDSQ **1** and methyldichlorosilane was carried out to prepare the DDSQ(Me)(H) **2**. The hydrosilylation reaction between **2** and allyloxytrimethylsilane **3** was performed to afford DDSQ(Me)((trimethylsilyl)oxypropyl) **4**. The deprotection reaction of **4** with MeOH and $MeSiCl_3$ was carried out to afford DDSQ(Me)(Hydroxypropyl) **5** in 36% yield. After that, monoprotection of DDSQ(Me)(Hydroxypropyl) was performed using McDougal's chemistry.



Scheme 4.6. Synthesis of DDSQ(Me)(Hydroxopropyl)



Scheme 4.7. Monoprotection of DDSQ(Me)(Hydroxopropyl).

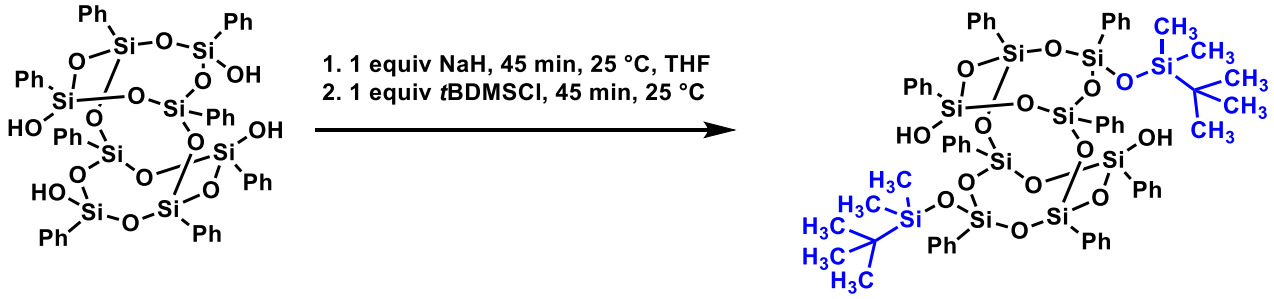
Based on ^{29}Si NMR and ^{1}H NMR, (Figure S23 and S24) two different proton environments can be observed. If DDSQ(Me)(Hydroxopropyl) was monoprotected, two different proton environments should be present in the NMR. A high resolution mass spectrum was acquired for further confirmation. Even though NMR showed two different proton environments, desired monoprotection of the hydroxyl group was not observed in mass spectrum. According to the mass spectrum, diprotected product and starting material were present. Two different proton environments were observed due to starting material and diprotected material. The monoprotection conditions were not successfully applicable for this carbinol system.

4.5 Conclusion

Monoprotection of diols were studied to develop a route to an asymmetric DDSQ molecule. The possibility of monoprotection among the four hydroxyl groups was difficult. Therefore the structure was simplified using a closed DDSQ cage with two hydroxyl groups that was tested to do monoprotection. However, the diol monoprotection conditions were not successfully applicable for our disilanol system. Therefore, monoprotection was tested for the DDSQ(Me)(Hydroxoprop-yl) (carbinol system). Nevertheless the monoprotection conditions were not successfully applicable for the carbinol system. Possibly the MacDougal chemistry was not applicable for bulky skeleton molecules. Therefore future studies will be focused on development of a different route to synthesize an asymmetric DDSQ cages.

4.6 Experimental Section

4.6.1 Monoprotecton using NaH

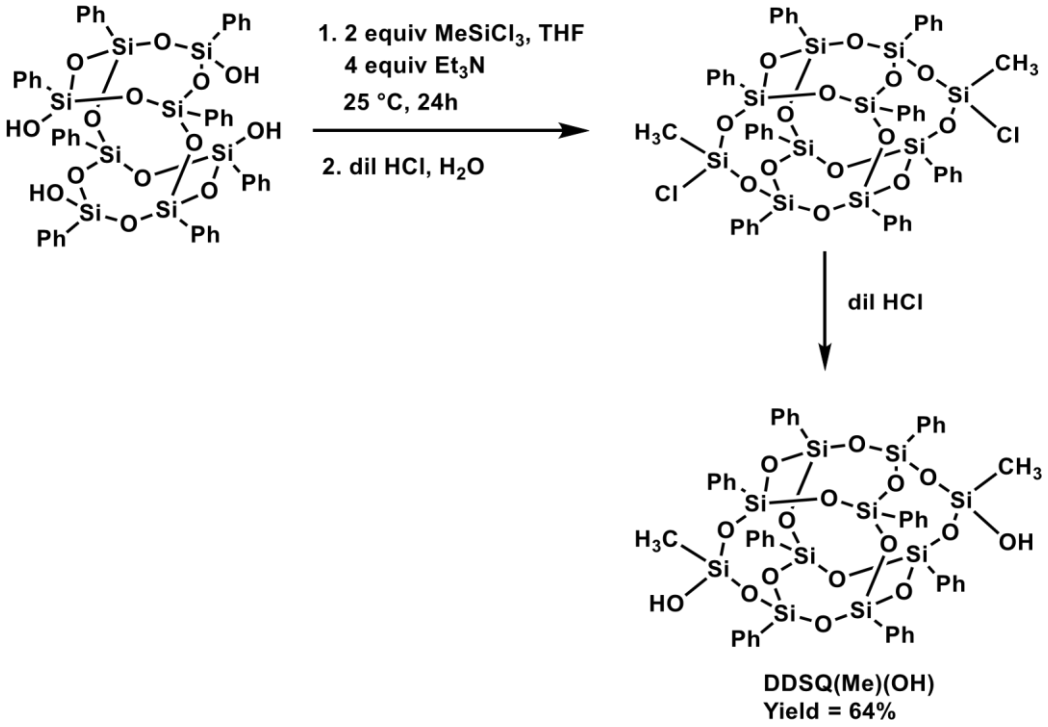


Scheme 4.8. Monoprotection of symmetric DDSQ.

Sodium hydride (NaH 60% dispersion in mineral oil) was washed with hexane and suspended in THF (0.27 g, 6.75 mmol, 1.20 equiv) was suspended in THF (11 mL) after being washed with hexane. The Ph8tetrasilanol-POSS (5.98 g, 5.6 mmol, 1 equiv) was added to this

reaction solution at room temperature and the mixture stirred for 45 min. The *tert*-butyldimethylsilyl chloride (*t*BDMSCl) (0.84 g, 5.60 mmol, 1 equiv) was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (100 mL), washed with 10% aqueous K_2CO_3 (10 mL) and brine solution (10 mL), dried using anhydrous Na_2SO_4 and concentrated in vacuo (3.00 g, 2.53 mmol, 45 % yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 20.54 (2Si), -77.34 (2Si), - 78.42 (2Si), -78.92 (2Si), -79.12 (2Si) (Figure S12). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75-7.09 (40H, overlapping multiplets), 0.90 (15H, singlet), 0.08 (10H, singlet) (Figure S11).

4.6.2 Synthesis of DDSQ(Me)(OH)

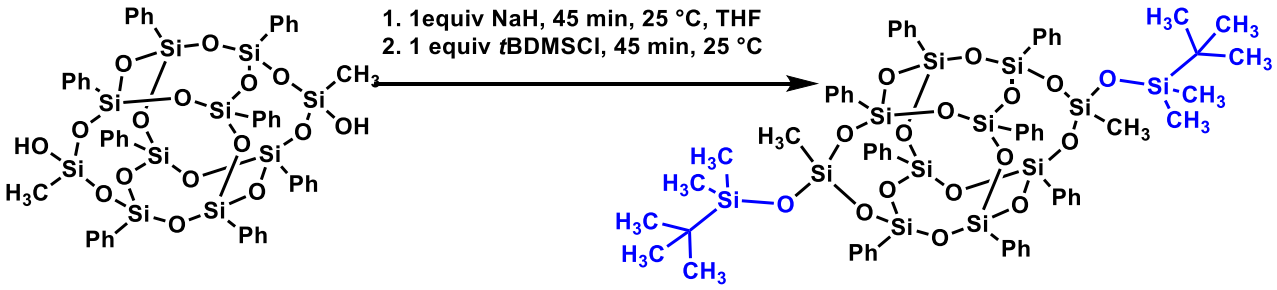


Scheme 4.9. Synthesis of DDSQ(Me)(OH)

A mixture containing Ph8tetrasilanol-POSS (2.65 g, 2.48 mmol, 1 equiv) and trimethylamine (Et_3N) (1.14g, 11.26 mmol, 4.5 equiv) and 100 mL of THF was placed under an Ar atmosphere in a Schlenk bomb flask fitted with a plug valve. Then flask was placed in an ice bath and methyltrichlorosilane ($MeSiCl_3$) (0.74 g, 4.96 mmol, 2equiv) was added drop wise. The suspension was stirred for 24 h at room temperature and filtered through a glass frit (of triethylammonium chloride salt). The precipitate was washed with THF (3 × 5 mL) and solvent evaporated.

The crude condensation product (DDSQ(Me)(Cl)), was dissolved in THF (1.5 mL) and chloroform (4 mL), water (4 mL) and diluted HCl (0.5 mL) over a 90 min period. The aqueous layer was separated and extracted twice with chloroform. The combined organic layers were extracted with water first, then with diluted HCl, water, saturated brine and then dried with $MgSO_4$. After filtration, the solvent was removed under vacuum to obtain the product (DDSQ(Me)(OH)), in the form of a white residue. (1.80 g, 1.60 mmol, 64 % yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 53.99 (2Si), -78.57 (4Si), - 79.03 (1Si), -79.13 (2Si), -79.23 (1Si) (Figure S13). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.57-7.19 (40H, overlapping multiplet), 0.35 (6H, singlet) (Figure S14).

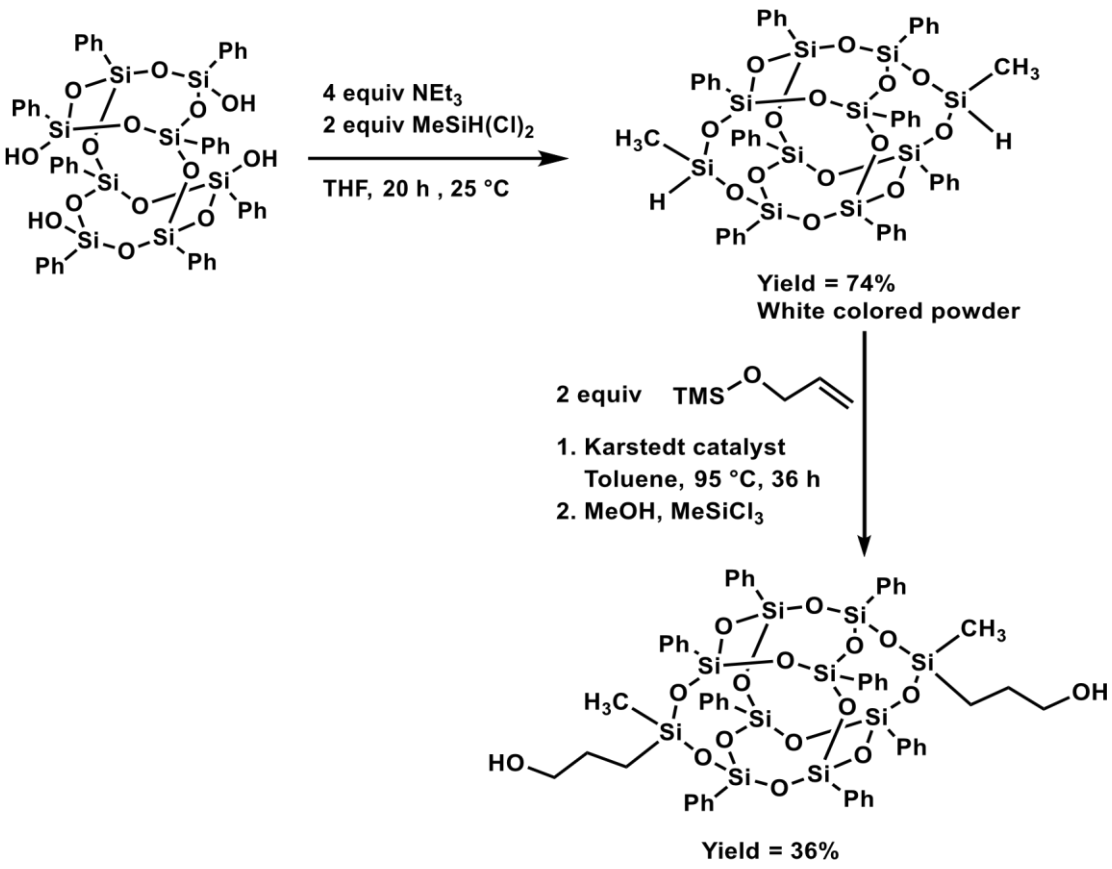
4.6.3 Monoprotection of DDSQ(Me)(OH) using NaH



Scheme 4.10. Monoprotection of DDSQ(Me)(OH) using NaH

Sodium hydride (NaH 60% dispersion in mineral oil) was washed with hexane and suspended in THF (32.00 mg, 0.80 mmol, 1 equiv) was suspended in THF (1 mL) after being washed with hexane. The DDSQ(Me)(OH) (1.00 g, 0.80 mmol, 1 equiv) was added to this reaction solution at room temperature and stirred for 45 min. The *tert*-Butyldimethylsilyl chloride (*t*BDMS) (0.13 g, 5.60 mmol, 1 equiv) was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (20 mL), washed with 10% aqueous K_2CO_3 (10 mL) and brine solution (10 mL), dried using anhydrous Na_2SO_4 and concentrated in vacuo to afford (0.03g, 0.35 mmol, 44%). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 20.55 (2Si), -54.13 (2Si) -78.64 (4Si), - 78.79 (1Si), -79.18 (2Si), -79.39 (1Si) (Figure S15). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.60-7.22 (40H, overlapping multiplets), 0.94 (15H, singlet), 0.38 (6H, singlet), 0.12 (10H, singlet) (Figure S16).

4.6.4 Synthesis of DDSQ(Me)(Hydroxopropyl)



Scheme 4.11. Synthesis of DDSQ(Me)(Hydroxopropyl)

Ph8tetrasilanol-POSS (11.60 g, 10.0 mmol) and triethylamine (4.13 mL, 41.2 mmol) were charged to a flask equipped with a magnetic stirrer, 100 mL of anhydrous tetrahydrofuran were added with vigorous stirring. The flask was immersed in an ice-water bath and purged with highly pure nitrogen for one hour. After that, methyldichlorosilane (3.45 g, 30.0 mmol) dissolved in 10 mL tetrahydrofuran were added dropwise within 30 min. The reaction was performed at 0 °C for 4 hours and at room temperature for 20 hours. The insoluble solids were removed by a filtration and the solvents together with other volatile compounds were eliminated via rotary evaporation to afford the white solids. The solids were washed with 100 mL of methanol thrice and dried in vacuo

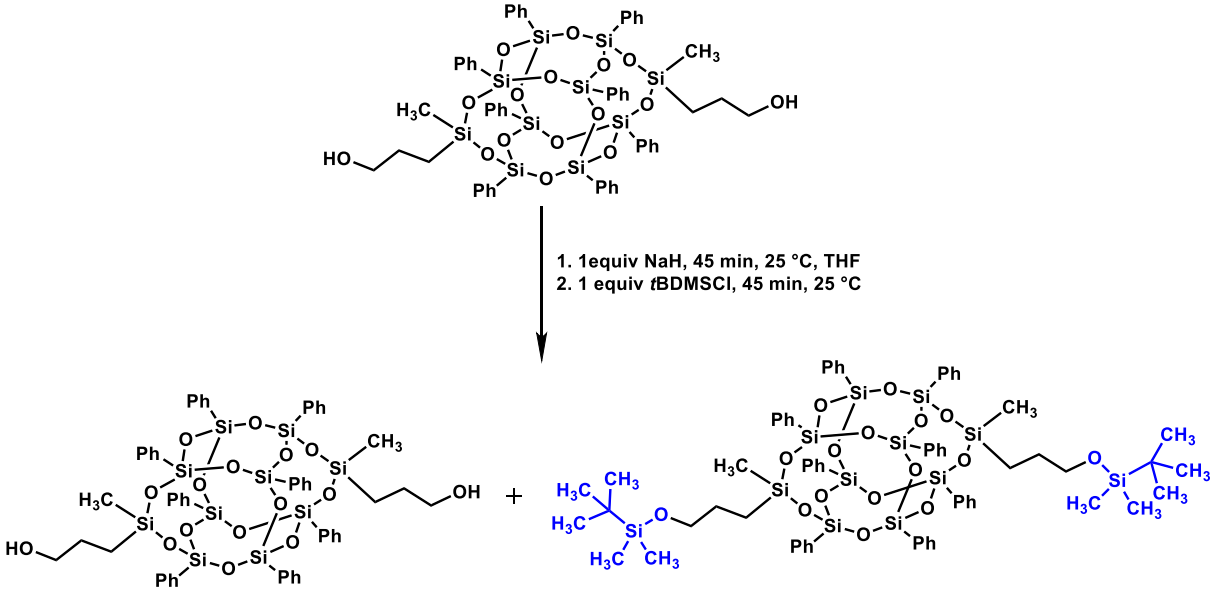
at 40 °C for 24 hours; the product (DDSQ (Me)(H)) (8.50 g, 7.36 mmol) was obtained with 74% yield. ^{29}Si NMR (100 MHz, $CDCl_3$) δ: −32.76 (2Si), −77.79 (4Si), −79.07 (1Si), −79.28 (2Si) and −79.47 (1Si) (Figure S18). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.57–7.16 (40H, multiplet), 4.99 (2H, singlet), 0.37 (6H, singlet) (Figure S17).

To a flask equipped with a magnetic stirrer, DDSQ(Me)(H)) (1.55 g, 1.34 mmol), anhydrous toluene (7 mL) and allyloxytrimethylsilane (2.35 g, 14.47 mmol) were charged. The flask was connected to a Schlenk line to degas with a repeated exhausting-refilling process with highly pure nitrogen and then Karstedt catalyst [Pt] (two drops) was added with vigorous stirring. The hydrosilylation was performed at 95 °C for 36 hours to ensure that the reaction went onto completion. The solvent and excess allyloxytrimethylsilane were removed via rotary evaporation to afford the solids with 90% yield (1.70 g, 1.20 mmol). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 17.00 (2Si), −17.12 (2Si), −78.61 (4Si), −79.51 (1Si), −79.55 (2Si) and −79.59 (1Si) (Figure S19). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.60–7.23 (40H, multiplet), 3.50 (4H, triplet, J = 6.71 Hz), 1.68 (4H, multiplet), 0.78 (4H, triplet, J = 5.48 Hz), 0.36 (6H, singlet) 0.06 (19H, singlet) (Figure S20).

To a flask equipped with a magnetic stirrer, DDSQ(Me)(trimethylsilyl)oxypropyl) (6.00 g, 4.24 mmol) and dichloromethane (90 mL) were charged and then 90 mL of methanol was added with vigorous stirring. Thereafter, methyltrichlorosilane (1.360 g, 12.52 mmol) was added dropwise within 30 min using a syringe. The reaction was performed at room temperature for 5 hours. The solvents and the excess methyltrichlorosilane were removed via rotary evaporation. The resulting product was obtained via recrystallization from the mixture of THF with hexane (50/50 by vol.). After being dried in a vacuum oven at 40 °C for 24 hours, the product (2.10 g, 1.67 mmol) was obtained with 39% yield (overall yield = 36%). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: −17.51 (2Si), −78.54 (4Si), −79.44 (1Si), −79.52 (2Si) and −79.61 (1Si) (Figure 22). ^{1}H NMR (500

MHz, $CDCl_3$) δ: 7.57–7.22 (40H, multiplet) 3.48 (4H, triplet, *J* = 6.51 Hz), 1.68 (4H, multiplet), 0.78 (4H, triplet, *J* = 5.72), 0.35 (6H, singlet) (Figure S21).

4.6.5 Monoprotection of DDSQ(Me)(Hydroxopropyl) using NaH



Scheme 4.12. Monoprotection of symmetric DDSQ.

Sodium hydride (NaH 60% dispersion in mineral oil) was washed with hexane and suspended in THF (11.20 mg, 0.28 mmol, 1 equiv) was suspended in THF (1 mL) after being washed with hexane. The DDSQ(Me)(Hydroxypropyl) (0.35 g, 0.28 mmol, 1 equiv) was added to this reaction solution at room temperature and stirred for 45 min. The *tert*Butyldimethylsilyl chloride (*t*BDMSCl) (0.04 g, 0.28 mmol, 1 equiv) was then added, and vigorous stirring was continued for 45 min. The mixture was poured into ether (20 mL), washed with 10% aqueous K_2CO_3 (10 mL) and brine solution (10 mL), dried using anhydrous Na_2SO_4 and concentrated in vacuo to afford (0.14 g, 0.11 mmol, 39% yield). ^{29}Si NMR (100 MHz, $CDCl_3$) δ: 20.35 (1Si), -

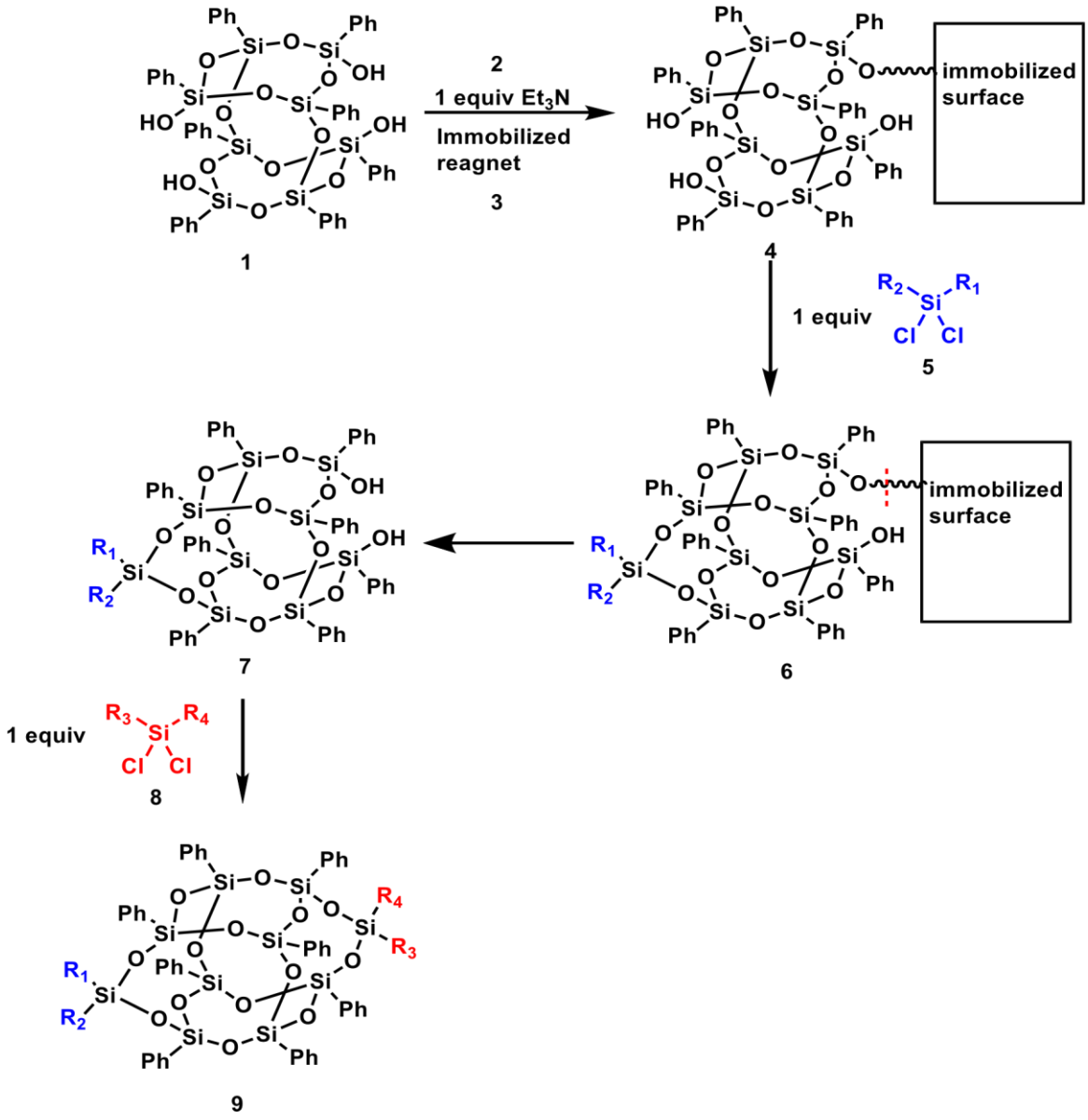
17.57 (1Si), -17.65 (1Si), -78.17 (1Si) -78.54 (1Si), -78.90 (1Si), -79.23 (2Si), -79.36 (1Si), -79.46 (2Si) (Figure S24). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.59-7.20 (40H, overlapping multiplets), 3.41 (2H, triplet, *J* = 7.21 Hz) 3.35 (2H, triplet, *J* = 6.56 Hz), 1.61 (2H, multiplet), 1.48 (2H, multiplet), 0.89 (8H, singlet), 0.72 (2H, triplet, *J* = 6.91), 0.59 (2H, triplet, *J* = 6.42), 0.31 (3H, singlet), 0.19 (3H, singlet), 0.07 (6H, singlet) (Figure S23).

CHAPTER 5: DEVELOPMENT OF ASYMMETRIC DDSQ MOLECULE BY USING IMMOBILIZED SURFACE

5.1 Introduction

Another approach to synthesize asymmetric DDSQ can be proposed using surfacesupported or immobilized reagents. According to the Scheme 5.1 one side of the DDSQ cage can be blocked using the immobilized reagent **3**. DDSQ cage can be anchored to the immobilized surface with the use of a linkage (structure **4**). The formerly open side of the DDSQ cage **4** can be closed using 1 equivalence of alkyl/aryl dichlorosilane **5**. Afterward the one side closed DDSQ cage **6** can be cleaved from the immobilized surface to synthesize DDSQ cage **7**. By adding another 1 equivalence of a different alkyl/aryl dichloro silane capping agent **8** can close the open side of the DDSQ cage **7** to synthesize an asymmetric DDSQ cage **9**.

Different surface immobilized reagents such as "Red-Sil" (Reducing Silica) and Merrifield resin were analyzed in this project as screening surfaces. As the first screening “Red Sil” immobilized reagent was explored.

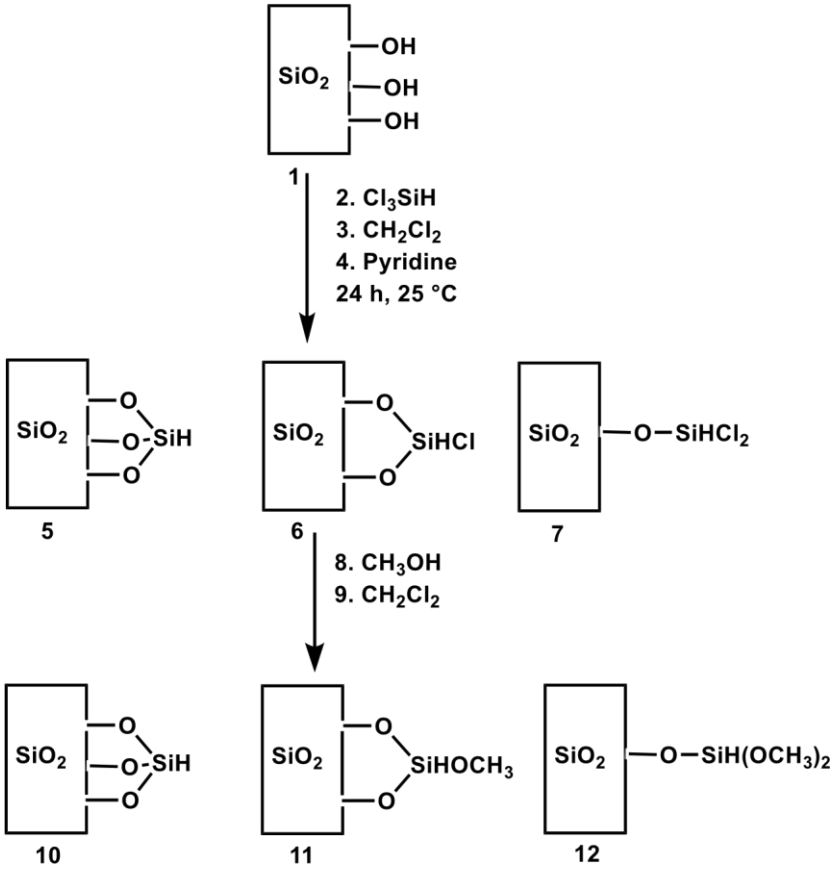


Scheme 5.1. Synthesis of asymmetric DDSQ cage using immobilized reagents.

5.2 Development of asymmetric DDSQ using Red-Sil immobilized surface

Red-Sil surface synthesized by modifying the surface of silica gel using trichlorosilane (Scheme 5.2). First the dried silica gel **1** was treated with trichlorosilane in methylene chloride with pyridine to remove the hydrogen chloride formed. There are three different surface modifications that can be formed during this reaction. Those can be represented as surface **5**, **6** and

7. After washing with methanol and dichloromethane Red-Sil surfaces were modified as surface **10**, **11** and **12**. ^{29}Si cross polarization (CP) solid state NMR was used to identify the nature of SiH functional group on the surface of the resulting product.



Scheme 5.2. Synthesis of Red-Sil.

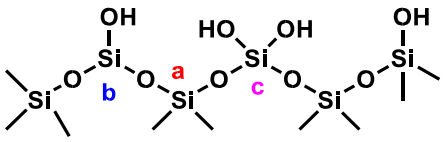


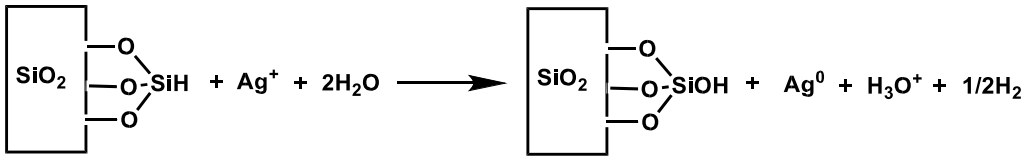
Figure 5.3. Structure of silica gel.

The ^{29}Si solid-state CP NMR spectrum of the original and unreacted silica gel showed the three different types of Si atoms (a-c) present in the silica gel (Figure 5.3). The ^{29}Si CP NMR

spectrum of the Red-Sil (Figure S44) showed the presence of two new signals at δ -77 and -87 ppm in addition to the signals from the silicon atoms already present in the backbone of silica gel. The signal related to silicon atom **c** (Figure 5.3) had disappeared after treatment, and the intensity of the signal related to silicon atom **b** was sharply reduced. This is indicative of the reaction of the trichlorosilane with the pendant hydroxyl groups present on the silica gel. As shown in Scheme 5.2 there can be three different modes of attachment of trichlorosilane to the surface of the silica gel, giving rise to species A-C. The two new peaks at δ -77 and -87 ppm in the ^{29}Si NMR spectrum belong to Si atoms bearing hydrogen -SiH and -Si$(OCH_3)_n$H groups respectively.

5.2.1 Quantitative estimation of Si-H on the surface of Red-Sil

For any surface-immobilized reagent to be synthetically useful, it is essential to know the amount of the active species or functional groups present on the surface of the supporting material. Silver ions (Ag^+) reduction by silyl hydrides, used as the quantitative method for determination the concentration of immobilized silyl hydrides (Scheme 5.4).[38] The stoichiometry of the reduction of silver ions by Si-H was confirmed by the reaction of a known amount of trimethoxysilane with a known excess of aqueous silver nitrate solution. It was found that 1 equivalent of silver nitrate was needed to oxidize 1 equivalent of trimethoxysilane.[38] The excess of silver ions can be quantitatively recovered as AgCl precipitate by using diluted HCl solution. This confirmed the one electron nature of this reduction reaction. The following relationships were used to calculate the concertation of active surface-immobilized SiH functions on the sample.



Scheme 5.4. Ag^{+} reduction by silyl hydrides

Moles of AgCl **(1.39 mmol)** = Moles of unchanged $AgNO_3$

Moles of original AgNO **(3.75 mmol)** - Moles of unchanged $AgNO_3$ **(1.39 mmol)**
= Moles of $AgNO_3$ consumed **(2.35 mmol)**

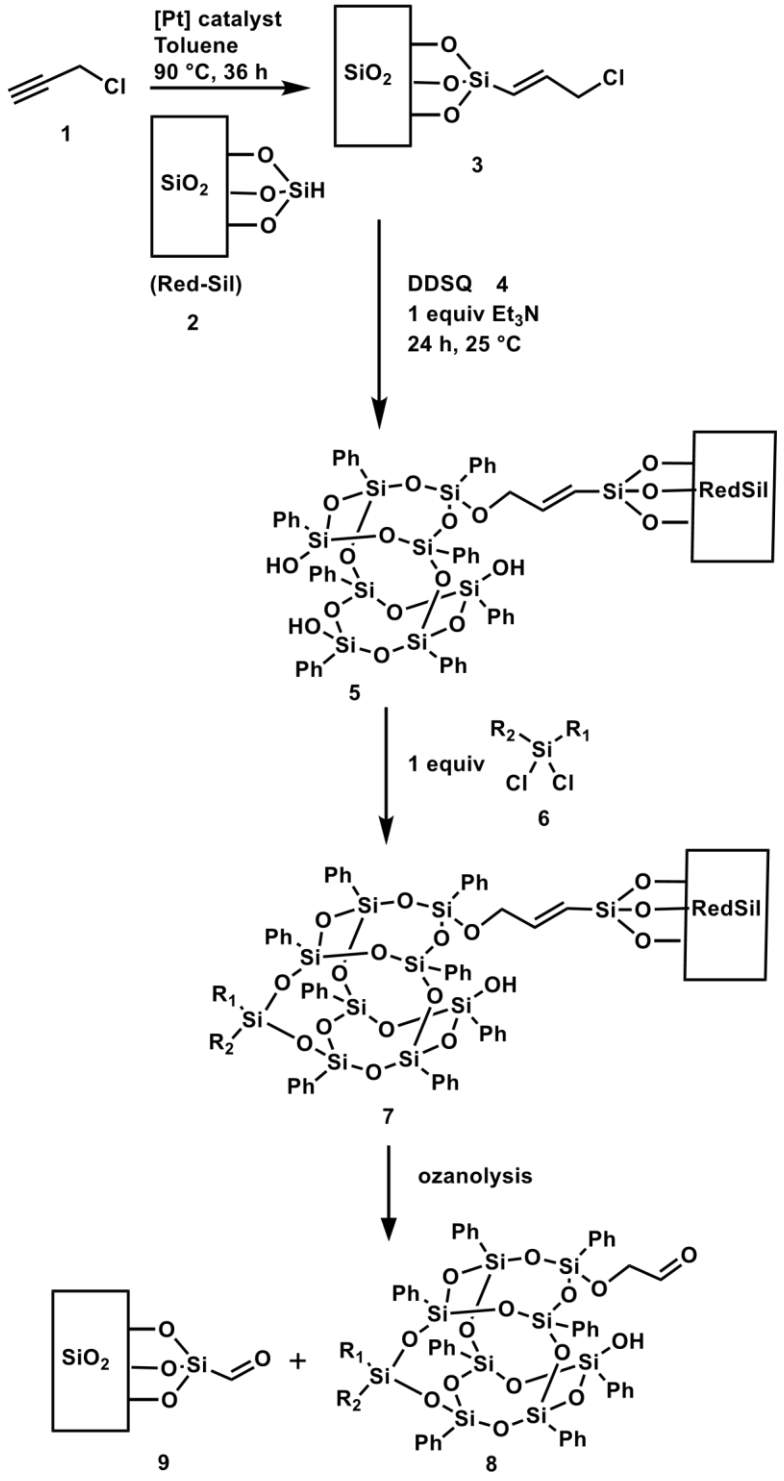
Moles of $AgNO_3$ consumed = Moles of SiH present **(2.35 mmol)**

1g of Red-Sil = **2.35** mmol of Si-H

Repeated analyses of material obtained by using the same amount of silica gel and trichlorosilane consistently yielded 2.35 mmol of SiH/g of silica gel product.

5.2.2 Studies of different routes to attach the DDSQ cage to the Red-Sil surface

A reagent can be anchored onto a solid surface either by covalent bonding or through ionic interaction between the surface functional groups and reagent.[39] Various methods were tested to attach the DDSQ cage to the Red-Sil surface.

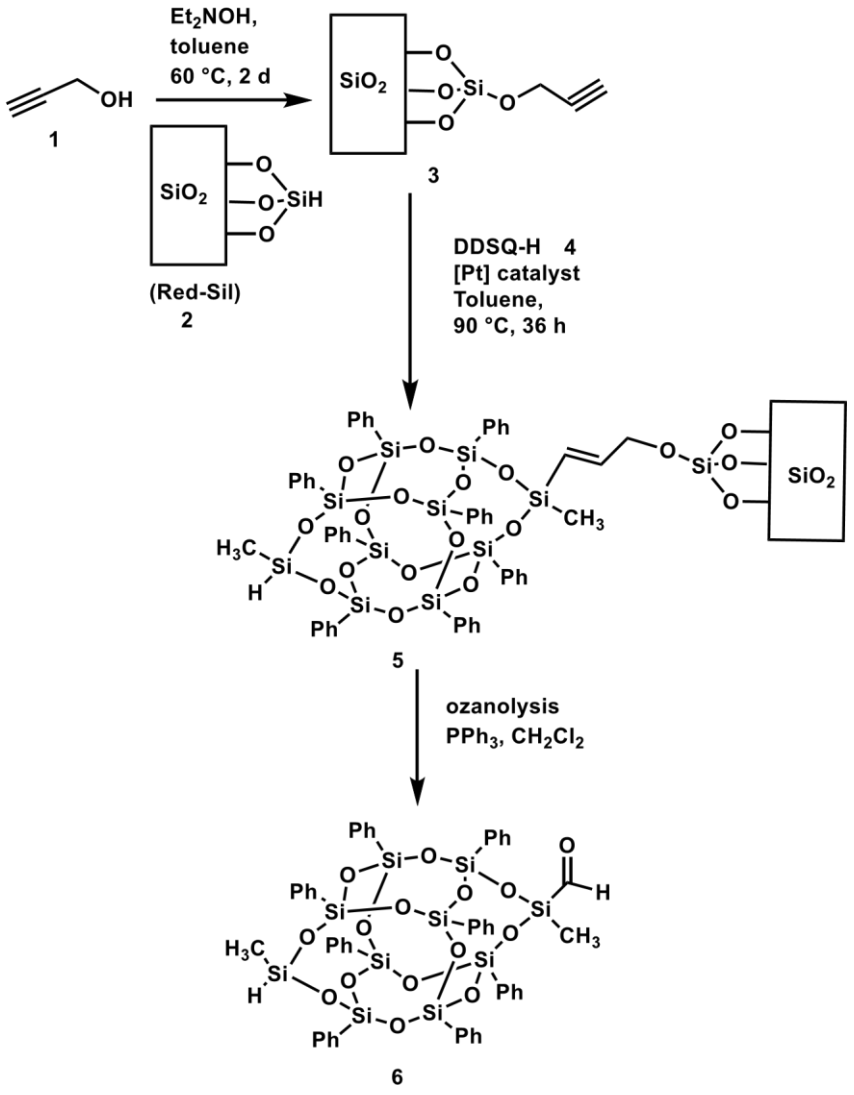


Scheme 5.5. Development of asymmetric DDSQ – Method A

One route, method A is described in Scheme 5.5. Red-Sil surface **2** undergoes hydrosilylation with propargylic chloride **1** to modify the Red-Sil surface to structure **3**. The surface reaction of this reagent **3** with the DDSQ **4** would be expected to react at only one of the silanols and formed structure **5**. Afterward the open side of the DDSQ cage **5** can be closed using 1 equivalence of alkyl/aryl dichloro silane **6**. One side closed DDSQ cage **7** can be cleaved from the immobilized surface to synthesize DDSQ cage **8**. Adding another 1 equivalence of a different alkyl/aryl dichloro silane capping agent can close the open side of the DDSQ cage **8** to synthesize an asymmetric DDSQ cage.

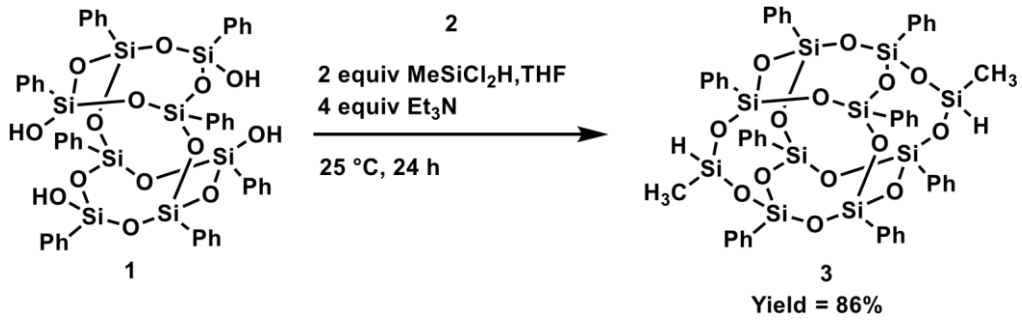
Solid state ^{29}Si CP NMR and ^{13}C CP NMR were studied for the method A. ^{29}Si CP NMR (Figure S46) of DDSQ attached Red-Sil surface (Scheme 5.5) indicated a new signal at δ -77.9 ppm in addition to the signals from the silicon atoms already present in the backbone of silica gel (δ -103 and -112 ppm) and Red-Sil Si peaks (δ -70.4 and -83.5 ppm). The new peak at δ -77.9 ppm was due to Si atoms of DDSQ cage.

Another route (Method B) is described in Scheme 5.6. "Red-Sil" **2** could be made to undergo dehydrogenation of a propargyl hydroxide **1** with diethyl hydroxylamine (Et_2NOH). The surface reaction of this reagent **3** with the dihydro DDSQ (DDSQ(Me)(H)) **4** would be expected to react at only one side (synthesis of DDSQ(Me)(H) will be described in Scheme 5.7) Then DDSQ(Me)(H) **4** will be immobilized and site isolated. Afterward, the DDSQ(Me)(H) cage **5** would be cleaved by ozonolysis from the Red-Sil to synthesize an asymmetric DDSQ cage **6**.



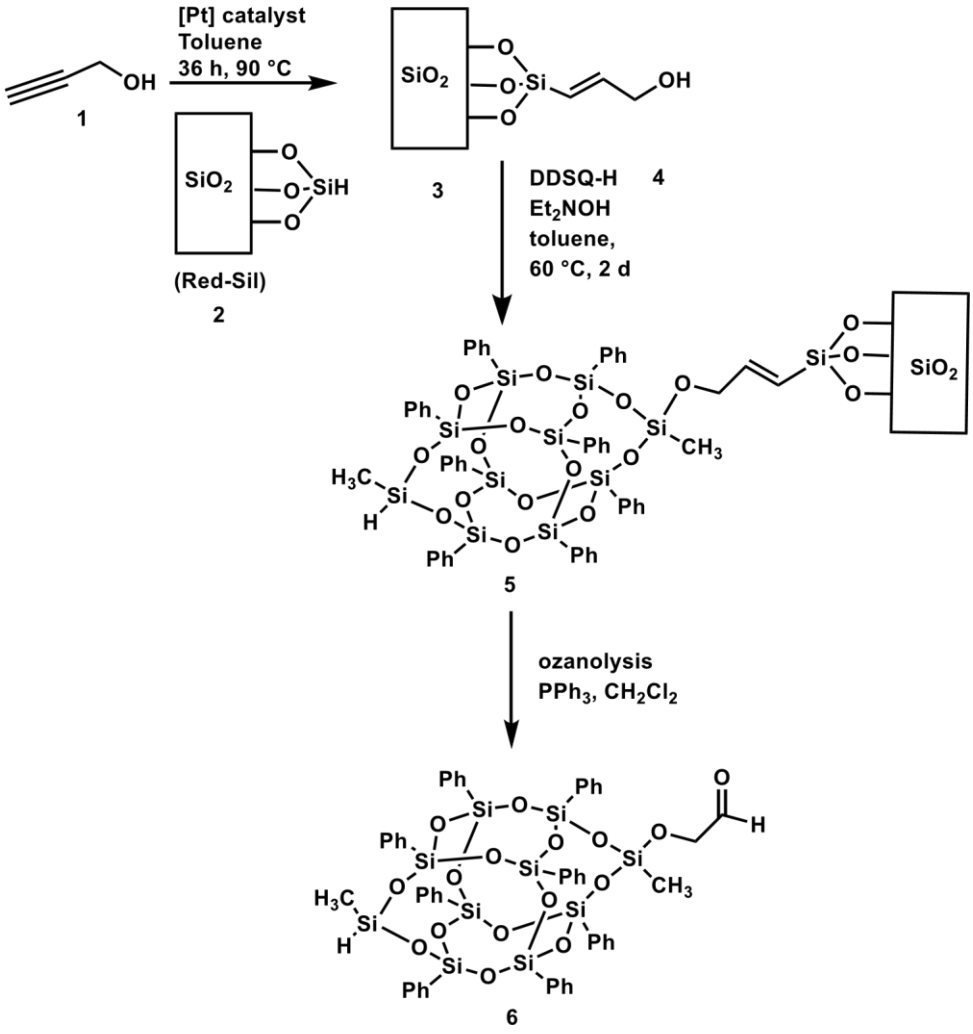
Scheme 5.6. Development of asymmetric DDSQ – Method B

DDSQ(Me)(H) **3** was synthesized by reacting DDSQ **1** with methyl dichlorosilane ($MeSiCl_2H$) capping agent **2** (Scheme 5.7).



Scheme 5.7. Synthesis of DDSQ(Me)(H)

Solid state ^{29}Si CP NMR and ^{13}C CP NMR were studied for the method B. ^{29}Si CP NMR (Figure S47) of DDSQ attached Red-Sil surface (Scheme 5.6) indicated a new signal at δ -80.8 ppm in addition to the signals from the silicon atoms already present in the backbone of silica gel (δ -103 and -112 ppm). The new peak at δ -80.8 ppm was due to Si atoms of DDSQ(Me)(H) cage. The peak of DDSQ(Me)(H) had low intensity when compared with peaks intensities of method A. It was concluded that DDSQ(Me)(H) attachment to the Red-Sil surface was not efficient in method B.



Scheme 5.8. Development of asymmetric DDSQ – Method C

Another attempt of attachment of DDSQ cage in to the Red-Sil surface is illustrated in Scheme 5.8. In method B, hydrosilylation was performed first to connect the propargylic alcohol **1** in to the Red-Sil surface **2**. As shown in the Scheme 5.8, DDSQ(Me)(H) **4** can be anchored onto the modified Red-Sil surface **3** via dehydrogenation. According to the solid state ^{29}Si CP NMR (Figure S48) the DDSQ(Me)(H) attachment to the Red-Sil surface was more effective when compared with method A and method B. The peak around -80 ppm was more intense compared with other two methods.

Solid state CP NMR studies confirmed the attachment of propargylic alcohol to the Red-Sil surface (Scheme 5.8). Solid state ^{29}Si CP NMR (Figure S49) showed a less intense for peak at –77 and -87 ppm compared with the (Figure S44) unmodified Red-Sil surface. The peaks were less intense due to removal of hydrogen of the Si-H group of Red-Sil surface. Generally solid-state NMR of dilute nuclei, such as ^{13}C, ^{29}Si, and ^{15}N (isotopic abundance of 1.1%, 4.7%, and 0.03%, respectively), suffers from low sensitivity. Cross-polarization (CP) overcomes this common problem in the NMR of solids. Cross polarization from abundant nuclei like ^{1}H, ^{19}F and ^{31}P can be transferred to dilute or rare nuclei like ^{13}C, ^{15}N, ^{29}Si in order to enhance signal to noise ratio. Cross polarization can be reduced due to loss of hydrogen from the Si-H fragment. Therefore the intensity will be reduced. This is indicative of the reaction of the propargylic chloride with the pendant Si-H groups present on the Red-Sil surface. Solid state CP ^{13}C NMR (Figure S50) exhibits the allylic carbon peaks at δ 144 and 137 ppm. The route of method C (Scheme 5.8) was improved the efficiency of DDSQ cage attachment to the modified Red-Sil surface. The higher peak intensity of DDSQ cage in solid state ^{29}Si CP NMR (Figure S48) was concluded the efficiency of DDSQ cage attachment compared to the methods A and B. According to these comparison studies, method C provides a better route to attach the DDSQ onto the Red-Sil surface.

The challenging part is detachment of the DDSQ cage from the Red-Sil surface. Ozonolysis was carried out to detach the DDSQ cage. Before the ozonolysis, DDSQ cage stability was checked under an ozone environment. DDSQ cage was stable after ozone purging, but the detachment was not successful by ozononlysis. Maybe the reductive workup of the ozonolysis was really slow or ozonolysis did not occur. Therefore another approach for the detachment will be considered in future.

5.2.3 Conclusion

According to the solid state NMR studies significantly DDSQ was attached through the method C when compared with methods A and B. Nevertheless the challenging part of detachment was not successful through the ozonolysis. Therefore in the future, other approaches will be considered for the detachment.

5.2.4 Future studies

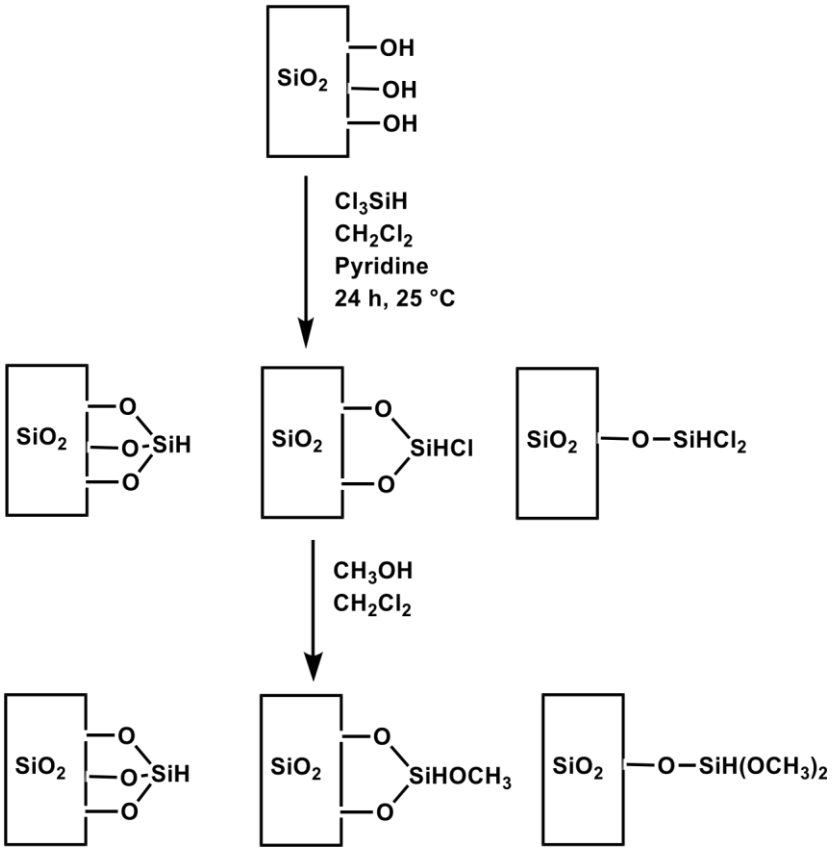
Cross metathesis was considered for the detachment of the DDSQ cage from the Red-Sil surface. According to the literature, the Grubbs catalyst generation 1 (G1) $(Pcy_3)_2(Cl)_2Ru{=}CHPh$ is using for cross metathesis of vinyl silane.[42] We were interested about using this chemistry in our situation to detach the DDSQ cage from the Red-Sil surface. Future studies will be focused on cross metathesis to detach the DDSQ cage from the immobilized surface.

5.2.5 Experimental section

5.2.5.1 Synthesis of "Red-Sil"

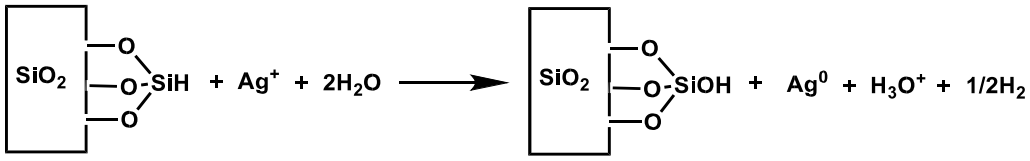
Dried silica gel (8.00 g) was transferred into a three-necked 500 mL flask equipped with an addition funnel. Freshly distilled trichlorosilane (25 mL, 0.24 mol) in 160 mL of dry CH_2Cl_2 was added to silica gel under an argon atmosphere. The reaction mixture was cooled to -78 °C with dry ice and acetone. Pyridine (60 mL, 0.74 mol) was added slowly dropwise from an additional funnel to the reaction mixture at -78 °C with intermittent stirring. A thick precipitate of pyridinium chloride formed in the reaction flask. An additional (80 mL) portion of dry CH_2Cl_2 was added to the reaction mixture, and the mixture was stirred at room temperature under argon for 24 h. The reaction mixture was then again cooled to -78 °C, and dry methanol (80 mL) was added to slowly to the mixture dropwise. The reaction mixture filtered on a Buchner funnel, and

the silica gel was washed further with 200 mL of dry methanol to dissolve and remove the pyridinium chloride precipitate. Finally, the silica gel was washed with CH_2Cl_2 (125 mL). This modified silica gel product was product was dried to afford ^{29}Si NMR (CP) (79 MHz, $CDCl_3$) δ:- 77.0 (SiH), -87.0 (SiH(OCH_3), -103.7, and -112.9 ppm. ^{13}C NMR (CP) (100 MHz, $CDCl_3$) δ:- 48.2 ppm.



Scheme 5.9. Synthesis of "Red-Sil".

5.2.5.2 Quantitative estimation of Si-H on the surface of Red-Sil



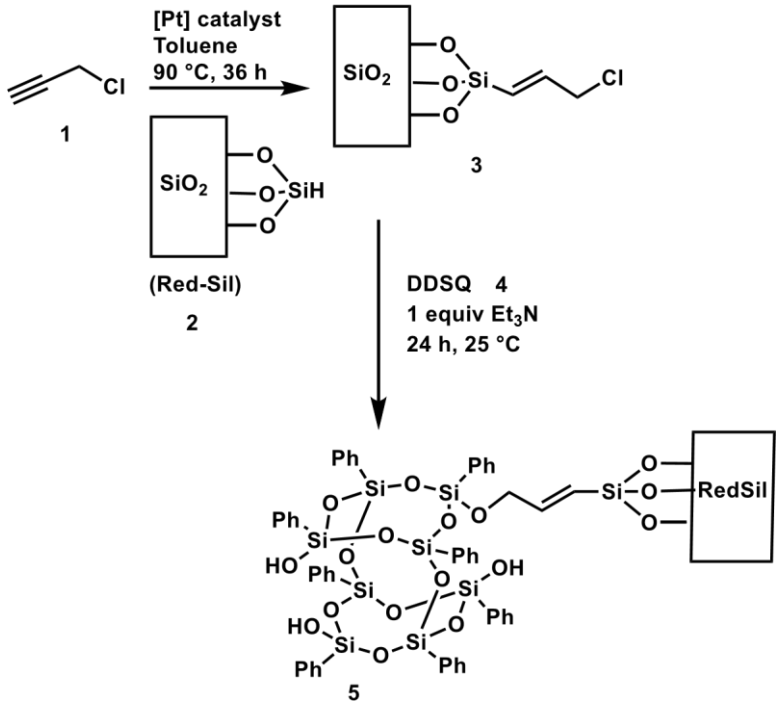
Scheme 5.10. Ag^{+} reduction by silyl hydride.

The following procedure for the estimation of silyl hydirdes on the surface of silica gel is representative. Silver nitrate (3.75 mmol, 0.64 g) was dissolved in distilled water (50 mL) in a volumetric flask. Silica gel immoblized silyl hydride (1.00 g) was placed in a 250 mL round-bottom flask. The silver nitrate solution made as above was added to the silica gel. The volumetric flask was rinsed with distilled water (20 mL), and the washings were added to the silica gel. An immediate black precipitate was observed after the addition of silver nitrate solution to the silica gel immobilized silyl hydirde. The solution was covered to exclude light and stirred with a magnetic stirrer for 24 h, and the solution was then filtered through a Buchner funnel. The silica gel was washed with distilled water (50 mL) to remove traces of unchanged silver nitrate. Five drops of 1% HNO_3 solution were added to the filtrate. The solution was then warmed to 50-60 °C. Silver chloride was precipitated out by adding 0.2 M aqueous HCl solution dropwise to the filtrate (unchanged silver nitrate solution). During the precipitation the temperature was kept at around 50-60 °C. The precipitate was allowed to settle in the flask in a dark place for 2 h at room temperature. The supernatant liquid was tested for further precipitation with aqueous HCl solution. The precipitate was allowed to settle in the flask in a dark place overnight. The silver chloride precipitate was filtered and washed with 1% HNO_3 (20-25 mL) solution. This was followed by washing with distilled water (100 mL). The precipitate was dried and then weighed. Silver ion analysis showed 2.35 mmol of SiH/g of silica gel.

5.2.5.3 Development of asymmetric DDSQ – Method A

Hydrosilylation, was carried out in an argon environment. Propargylic chloride (3.00 mmol, 0.23 mL) and Red-Sil (1.00 g) were charged to a flask with toluene (20.00 mL) and Karstedt catalyst (Pt catalyst) (two drops). The reaction was performed at 90 °C for 36 h. After vigorous stirring, the solvent was removed using filtration. Then propargylic alcohol attached Red-Sil (species 3) solid powder was dried and weighed (1.21 g). ^{29}Si NMR (CP) (79 MHz, $CDCl_3$) -75.6 (SiH), -86.3 (SiH(OCH_3), -102.7, and -112.0 ppm. ^{13}C NMR (CP) (100 MHz, $CDCl_3$) δ 137.3, 127.4 (allylic C), 59.3 (C-Cl), 43.1 (OCH_3) ppm.

Propagylic chloride attached Red-Sil solid powder was charged into a flask equipped with a stir bar, DDSQ (3 mmol, 3.15 g), triethylamine (NEt_3) (3 mmol, 0.30 mL) and CH_2Cl_2 (35.00 mL). The reaction was performed at 25 °C for 24 h. After vigoruos stirring, the solvent was removed using filtration. Then DDSQ attached Red-Sil (species 3) solid powder was dried and weighed (1.73 g). ^{29}Si NMR (CP) (80 MHz, $CDCl_3$) δ -78.9 (DDSQ-Si), -102.9, and -112.7 ppm.



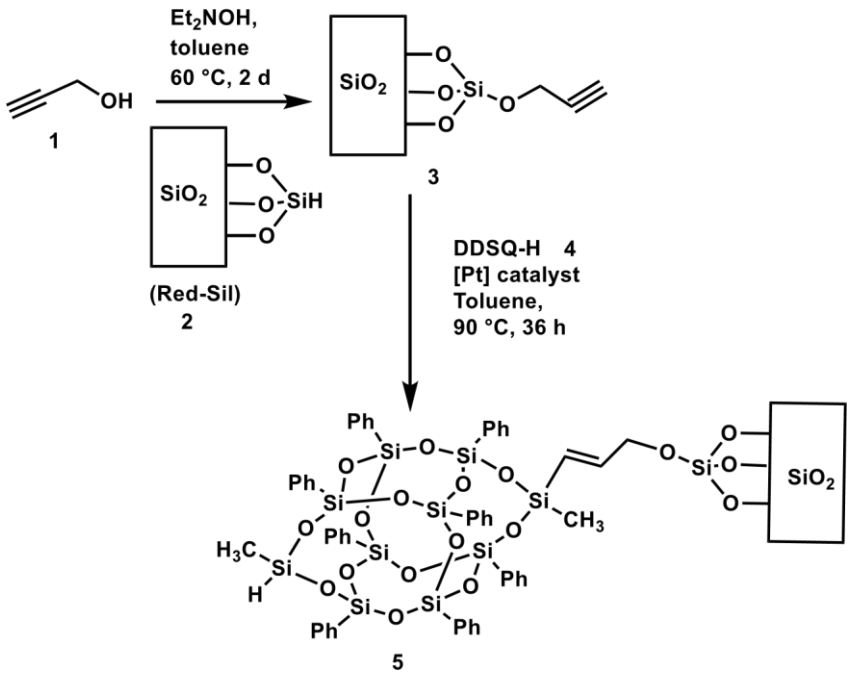
Scheme 5.11. Development of asymmetric DDSQ – Method A.

5.2.5.4 Development of asymmetric DDSQ – Method B

First step of this method B was dehydrogenation. The experiment was carried out in a nitrogen environment. Propargylic alcohol (3.00 mmol, 0.17 mL) and Red-Sil (1.00 g) were added to toluene (5.00 mL) and the mixture was heated at 60 °C. A solution of diethylhydroxyl amine (Et_2NOH) (10 µL) in toluene (10.00 mL) was added as the catalyst. Partial geletation was occurred in the flask while the mixture was heated at 60 °C. After vigoruos stirring for two days, the solvent was removed using filtration. Then propargylic alcohol attached Red-Sil (species 3) solid powder was dried and weighed (1.13 g).

Then hydrosilylation was carried out in an argon environment. Propargylic alcohol attached Red-Sil solid powder was charged into a flask equipped with a stir bar, dihydro DDSQ

(DDSQ-H) (3 mmol, 5.40 g), Karstedt catalsyt (Pt catalsyt) (two drops) and toluene (20 mL). The reaction was performed at 90 °C for 36 h. Solvent was eliminated via filtration. DDSQ-H attached Red-Sil solid powder was dried and weighed (1.38 g). ^{29}Si NMR (CP) (79 MHz, $CDCl_3$) δ -80.8 (DDSQ-H-Si), -93.3, -103.1, and -112.4 ppm.



Scheme 5.12. Development of asymmetric DDSQ-H – Method B.

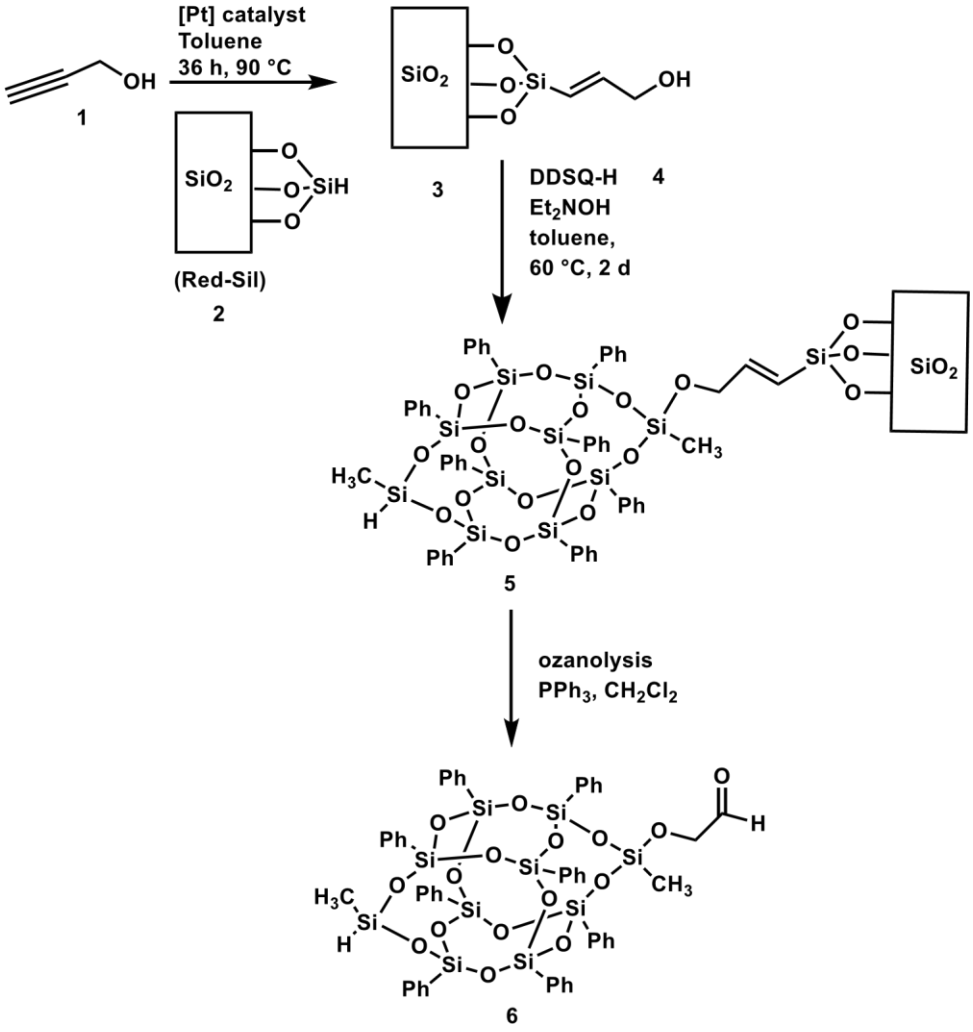
5.2.5.5 Development of asymmetric DDSQ – Method C

Hydrosilylation, was carried out in an argon environment. Propargylic alcohol (3.00 mmol, 0.17 mL) and Red-Sil (1.00 g) were charged into a flask with toluene (20.00 mL) and Karstedt catalyst (Pt catalyst) (two drops). The reaction was performed at 90 °C for 36 h. After vigorous

stirring, the solvent was removed using filtration. Then propargylic alcohol attached Red-Sil (species 3) solid powder was dried and weighed (1.18 g).

The second step, dehydrogenation was carried out in a nitrogen environment. Propargylic chloride attached Red-Sil solid powder (1.00 g) was charged into a flask equipped with a stir bar, and DDSQ-H (3 mmol, 5.40 g), and toluene (5.00 mL). A solution of diethylhydroxyl amine (Et_2NOH) (10 µL) in toluene (10.00 mL) was added as the catalyst. Partial gelation occurred in the flask while the mixture was heated at 60 °C. After vigorous stirring for two days, the solvent was removed using filtration. Then DDSQ-H attached Red-Sil (species 3) solid powder was dried and weighed (1.33 g). ^{29}Si NMR (CP) (79 MHz, $CDCl_3$) δ -66.3, -72.8, -73.7, -80.0 (DDSQ-H-Si), 103.1, and -112.5 ppm.

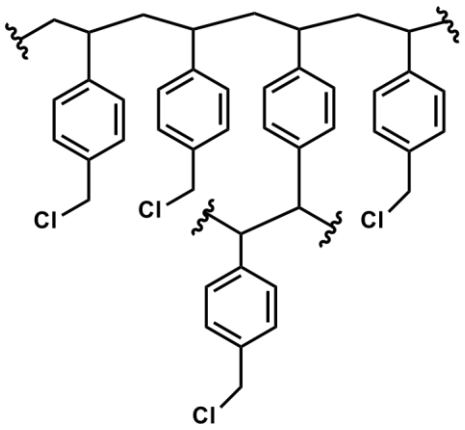
The final step ozonolysis was performed to cleave the linkage between Red-Sil and DDSQ cage. The solid powder (species 4) (1.80 g) was charged into a flask equipped with a stir bar and anhydrous CH_2Cl_2 (10.00 mL). Ozone was bubbled through the solution at -78 °C until the blue color persisted. Then solution was purged with oxygen for 10 min and triphenyl phosphine (PPh_3) (0.63 g) was added. The reaction was allowed to warm to room temperature and stirred overnight. After filtration, filtrate was concentrated through the vacuum rotavap.



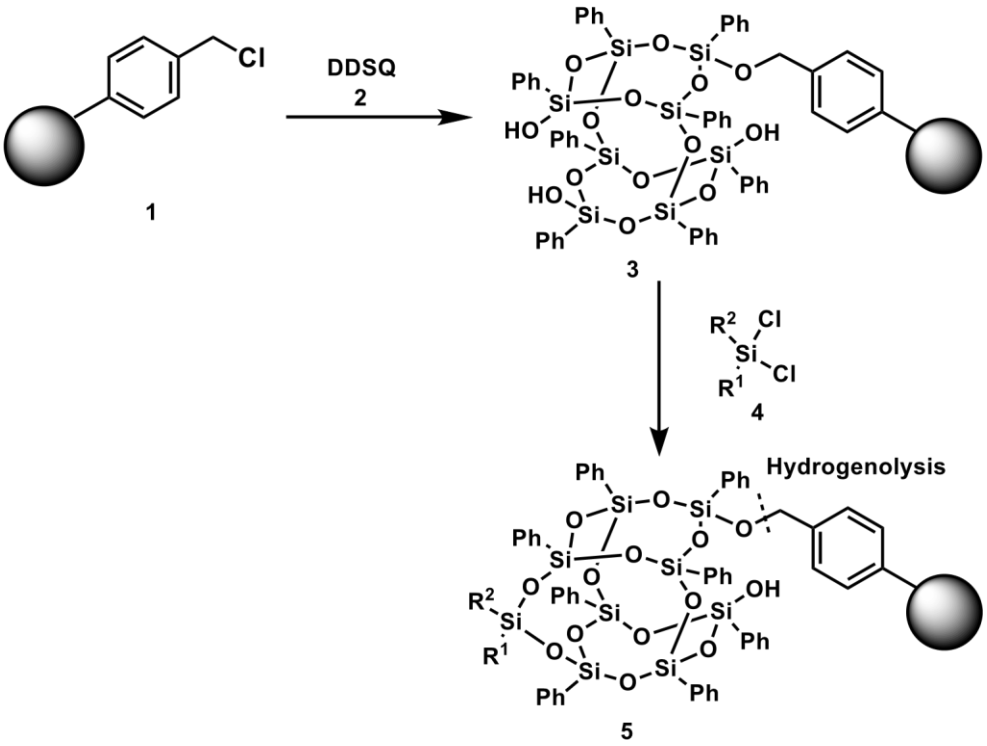
Scheme 5.13. Development of asymmetric DDSQ-H – Method C.

5.3 Development of asymmetric DDSQ using Merrifield resin.

In future studies another immobilized surface will be studied. Merrifield resin, which was originally extensively investigated for peptide and other oligomer synthesis. Merrifield resin is a polystyrene resin based on a copolymer of styrene and chloromethylstyrene, which is also crosslinked with divinylbenzene.[40] Merrifield resin, which was originally extensively investigated for peptide synthesis.



Scheme 5.14. Merrifield Resin



Scheme 5.15. Synthesis of asymmetric DDSQ cage using immobilized reagents.

As shown in Scheme 5.15, DDSQ cage **2** can be anchored into the Merrifield resin **1** through the chloromethylated bond. The advantage over the Red-Sil surface is, DDSQ cage can be anchored directly to the solid surface without any linkage. After the attachment, the open side of DDSQ cage **3** can be closed using a capping agent **4**. Through the hydrogenolysis the DDSQ cage can be detach from the immobilized surface. The future studies will be focused on this route to develop asymmetric DDSQ molecule.

APPENDIX

Figure S1 (Para) Methyl-di-chloro silane - ^{29}Si NMR

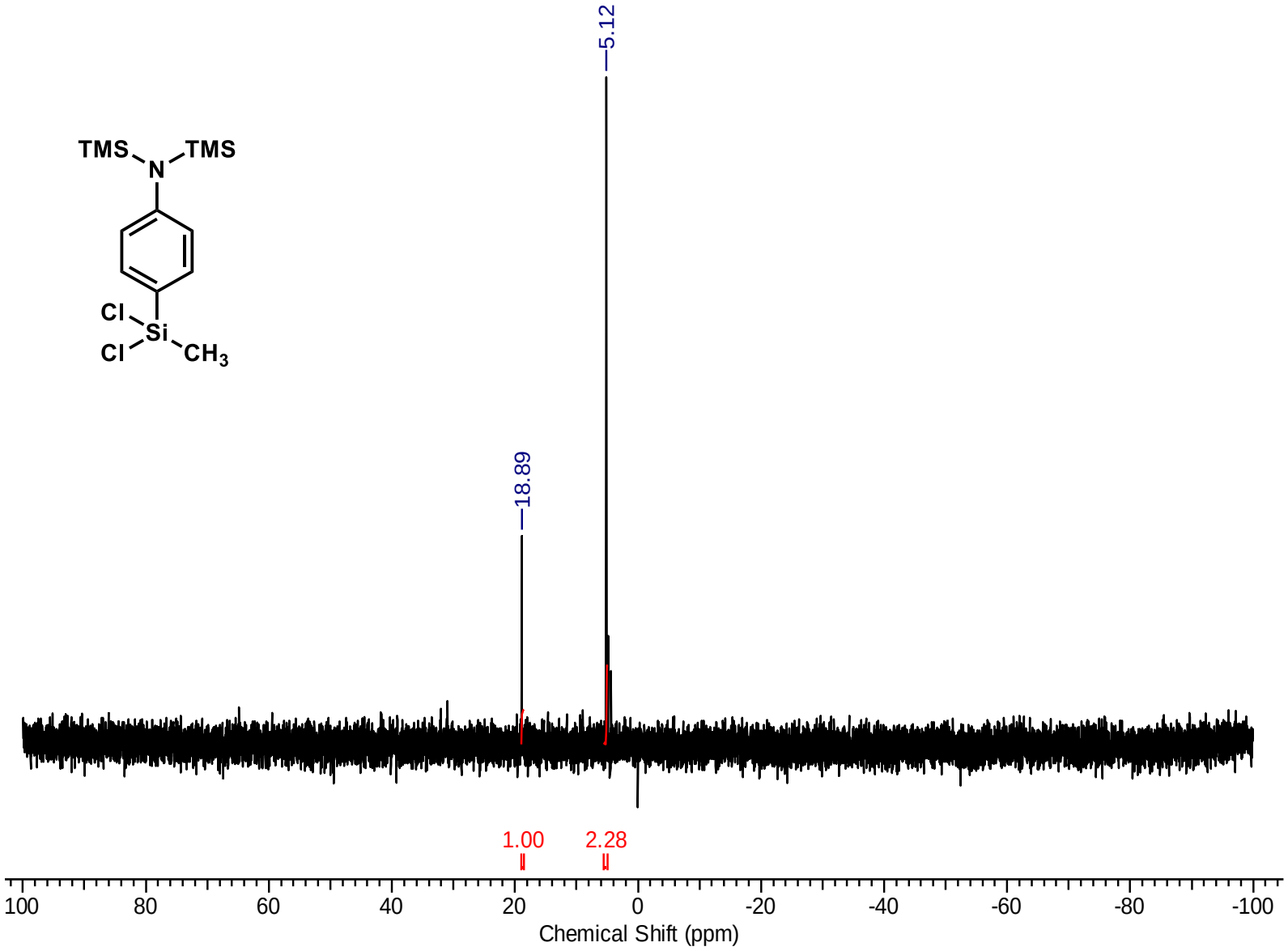


Figure S2 (Para) Methyl-di-chloro silane – ^{1}H NMR

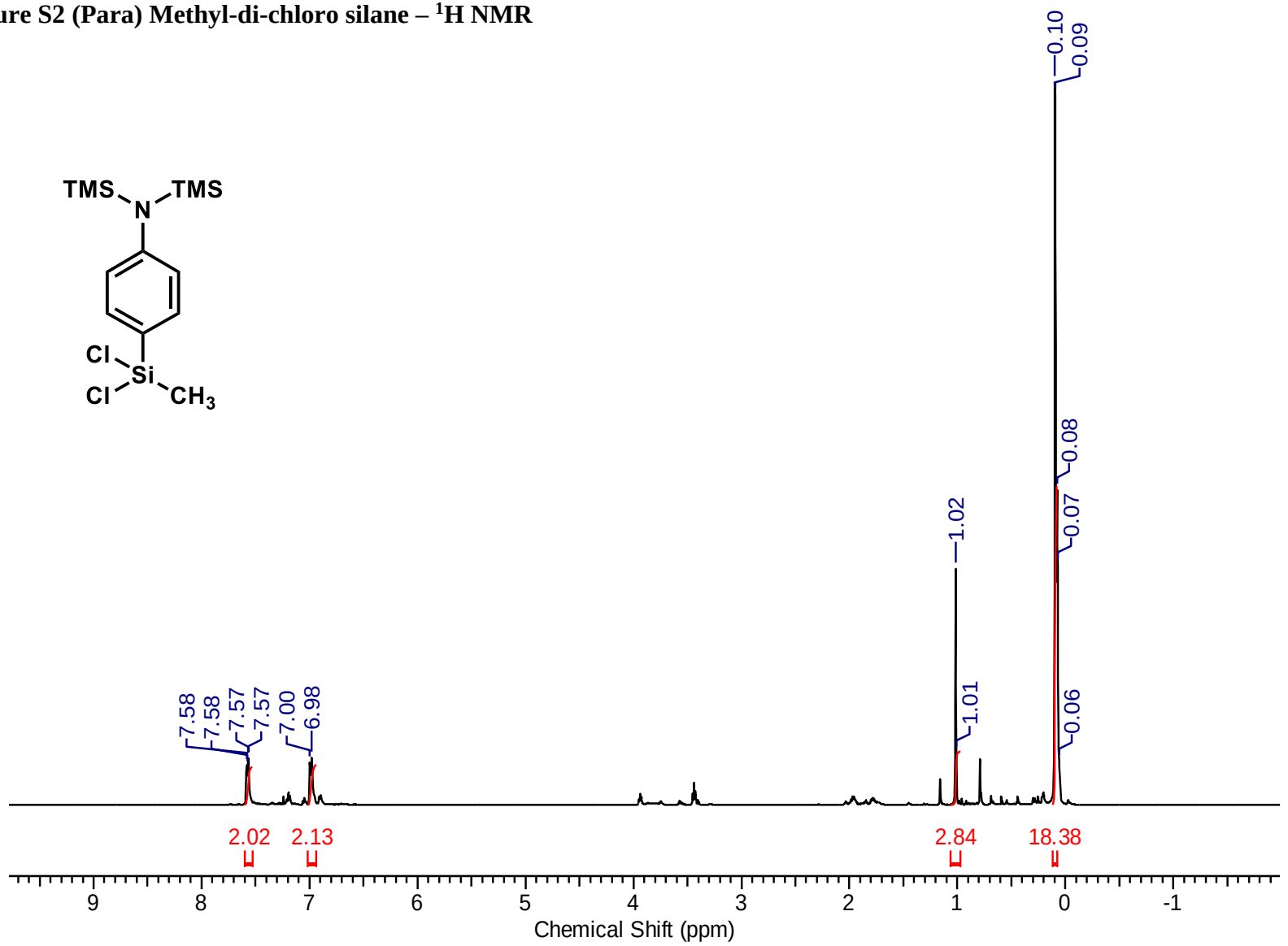


Figure S3 (Meta) Methyl-di-chloro silane - ^{29}Si NMR

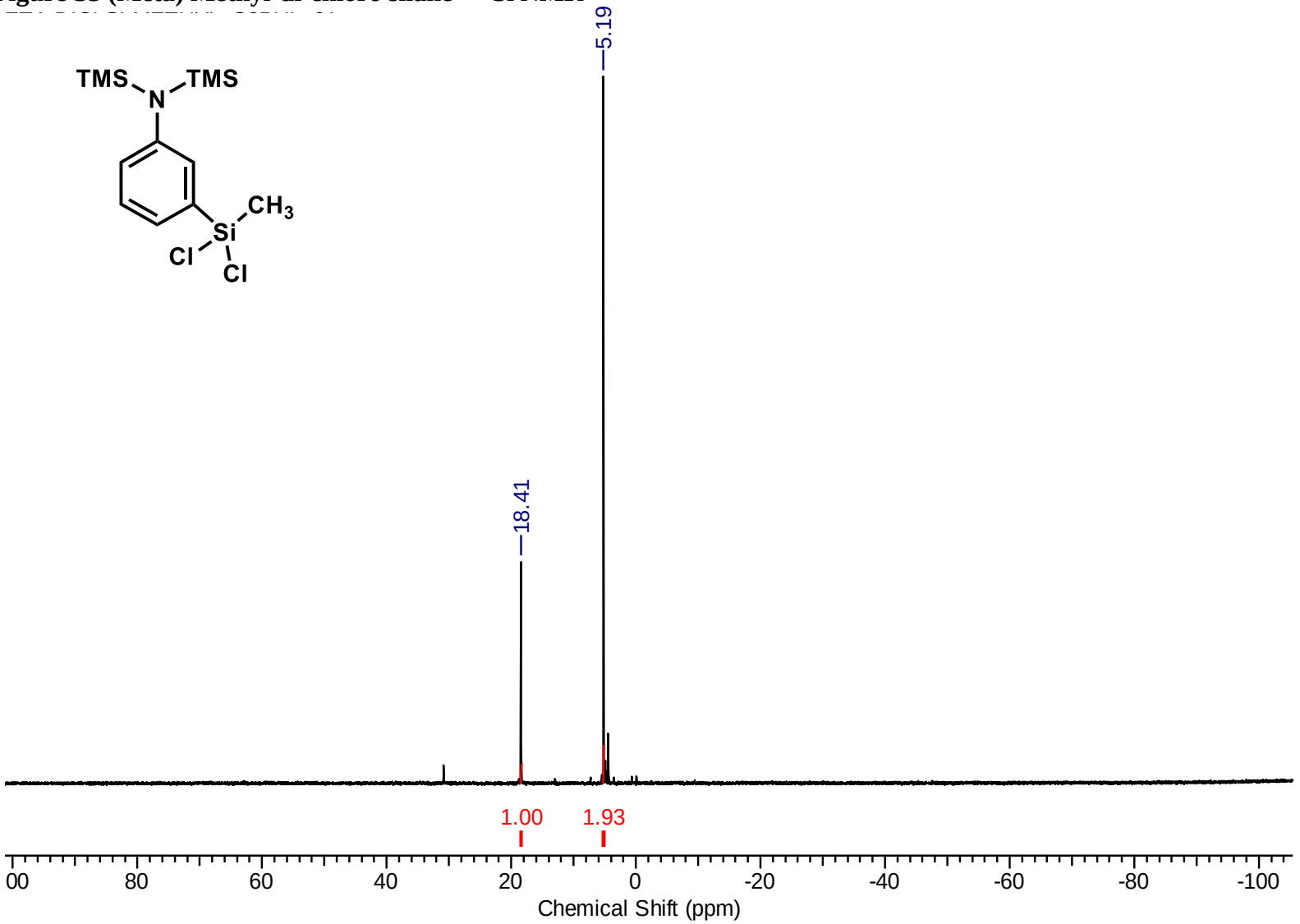


Figure S4 (Meta) Methyl-di-chloro silane – ^{1}H NMR

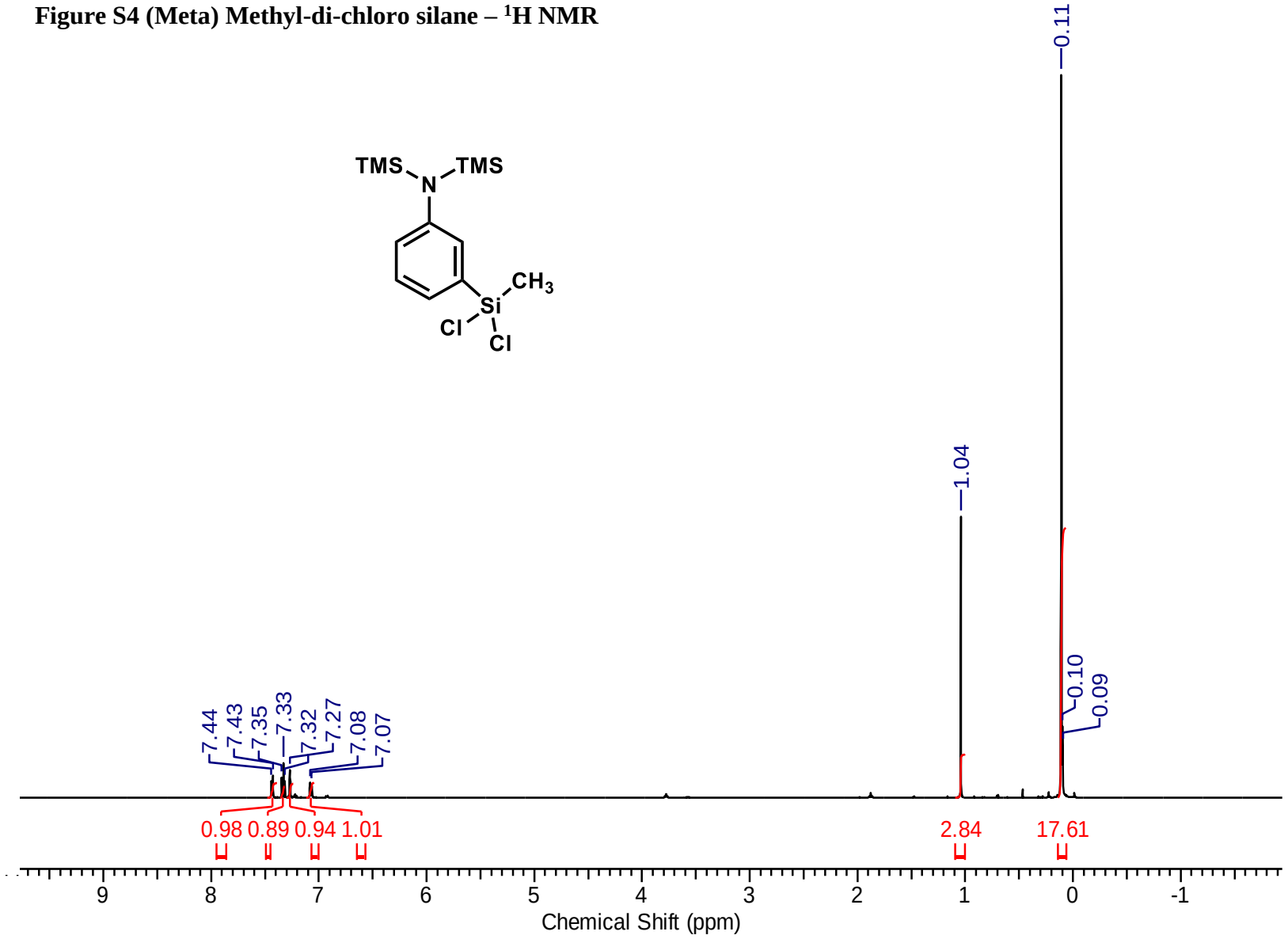


Figure S5 DDSQ(m/p)(Me)(PEPI) (Path A) – ^{1}H NMR

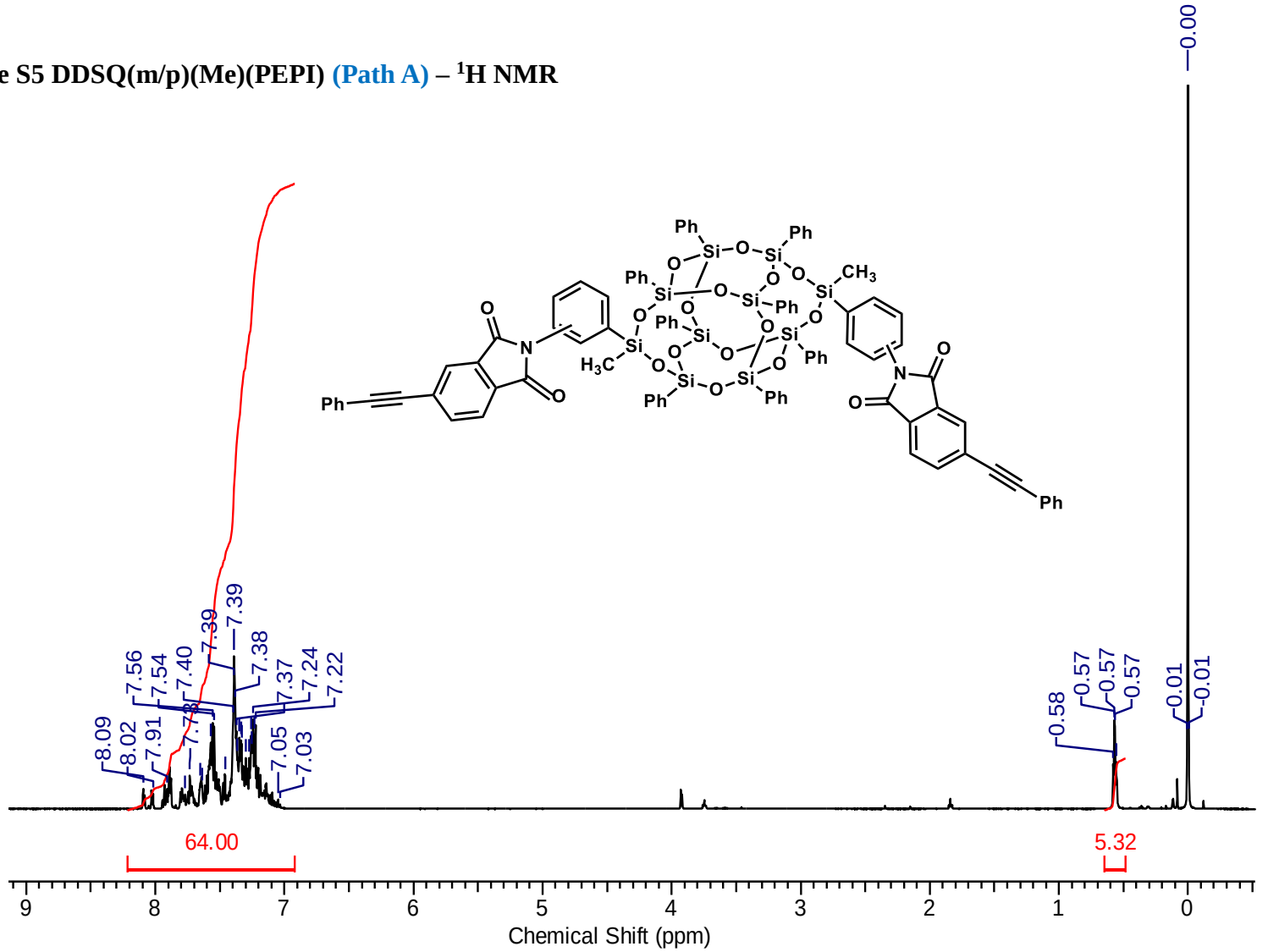


Figure S6 DDSQ(m/p)(Me)(PEPI) (Path A) – ^{29}Si NMR

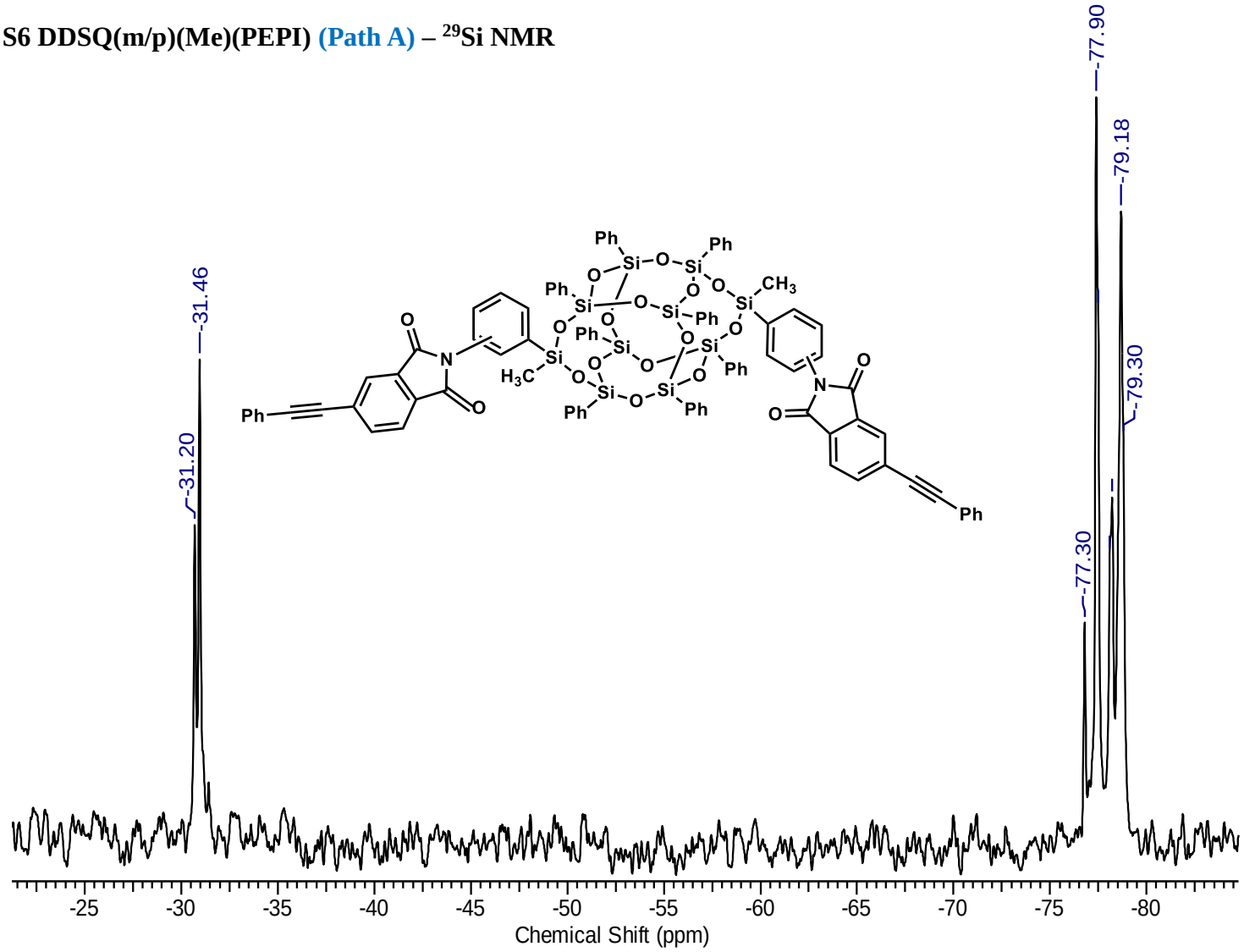


Figure S7 DDSQ(m/p)(Me)(PEPI) (Path B) – ^{29}Si NMR

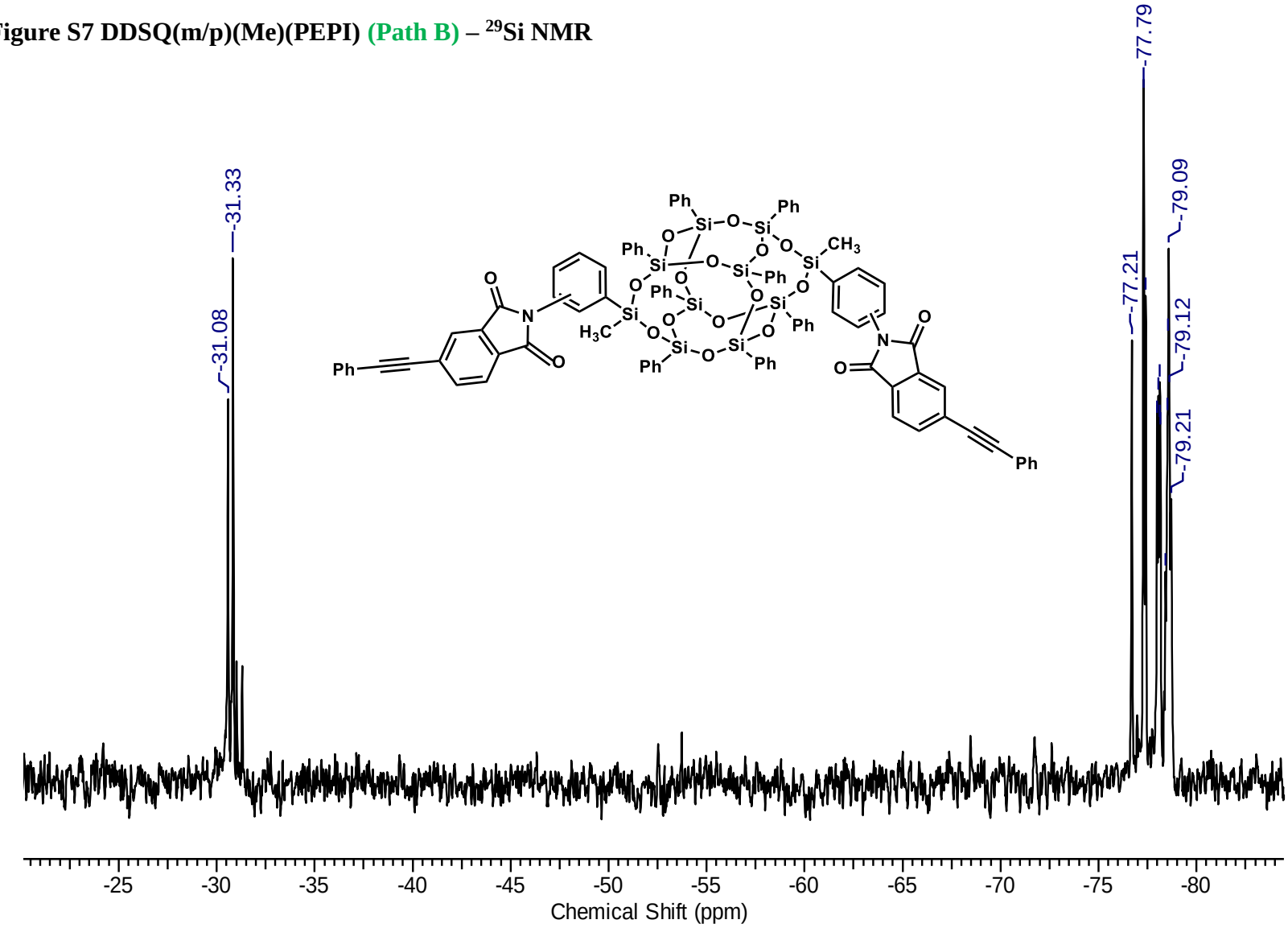


Figure S8 DDSQ(m/p)(Me)(PEPI) (Path B) – ^{1}H NMR

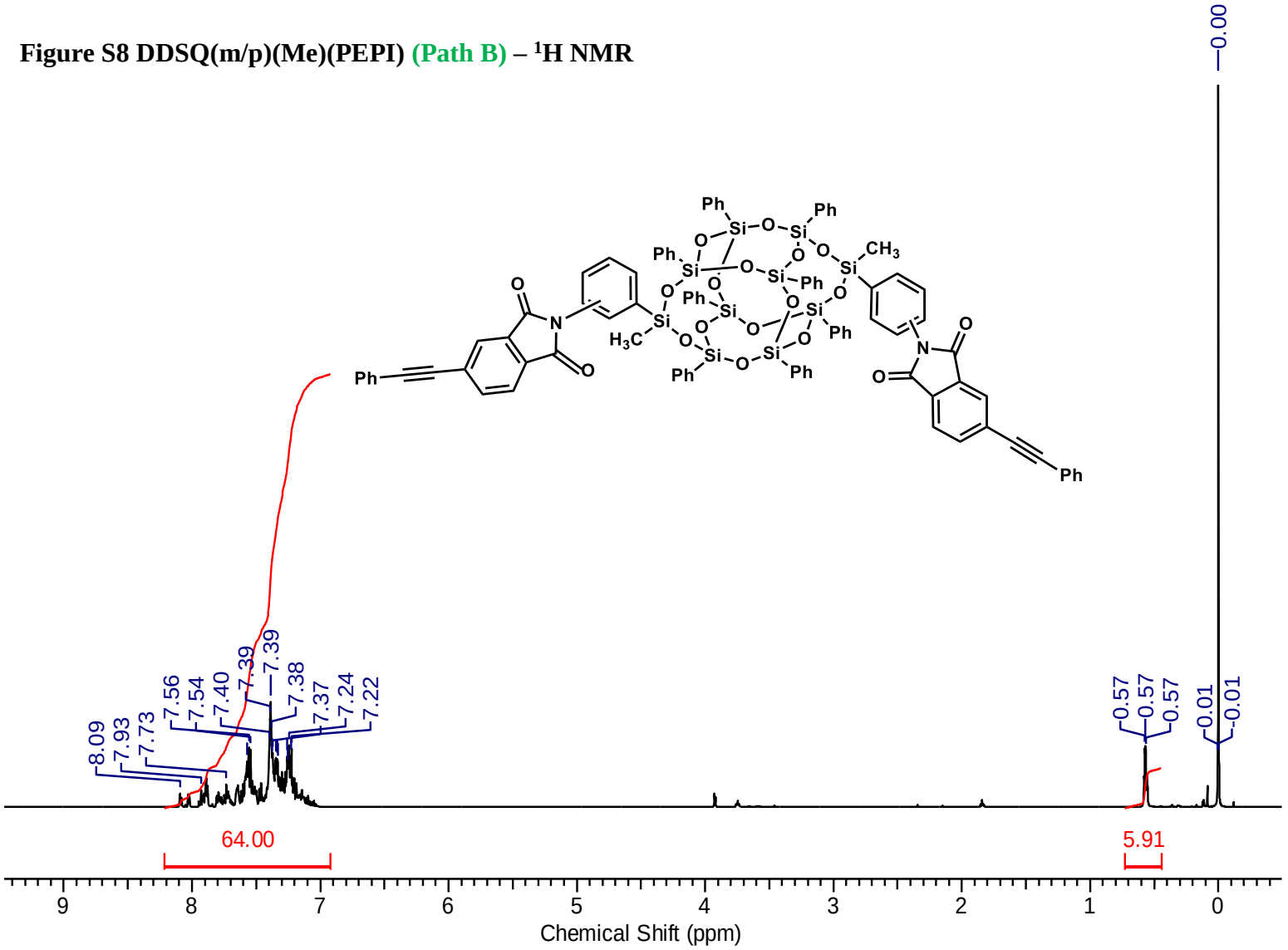


Figure S9 DDSQ(m/p)(Me)(PEPI) (Path C) – ^{29}Si NMR

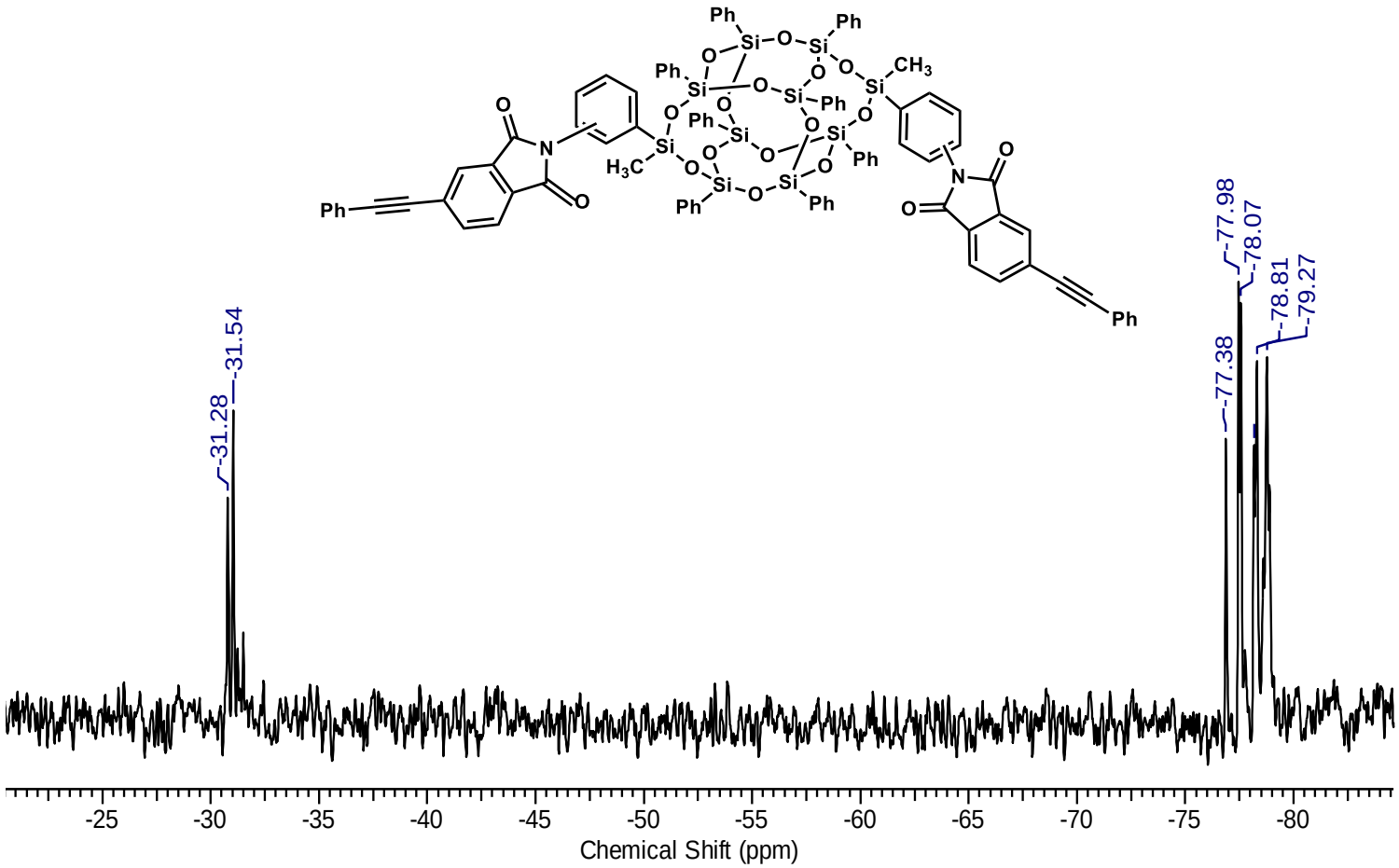


Figure S10 DDSQ(m/p)(Me)(PEPI) (Path C) – ^{1}H NMR

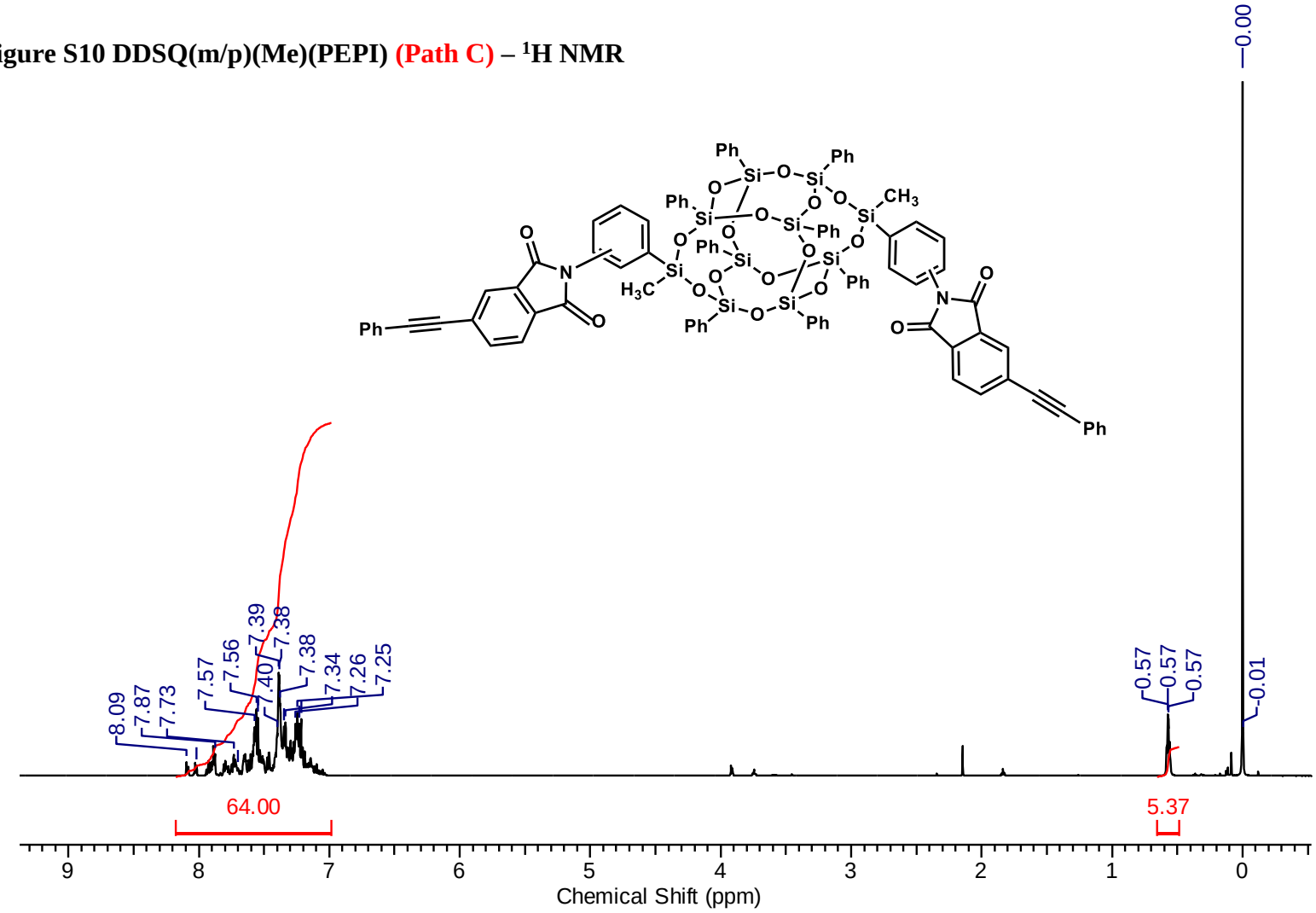


Figure S11 Mono-protection of DDSQ using NaH– ^{1}H NMR

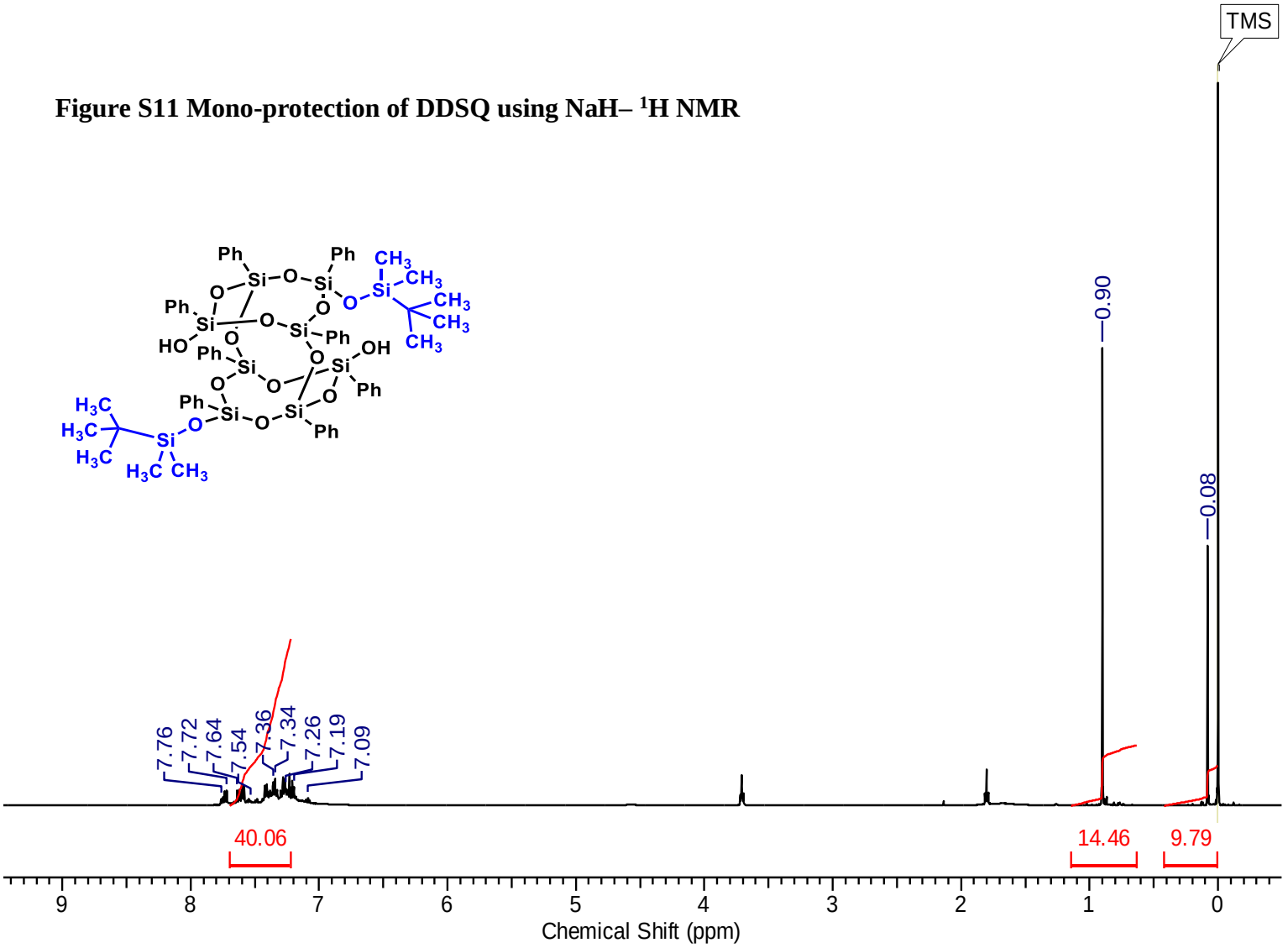


Figure S12 Mono-protection of DDSQ using NaH– ^{29}Si NMR

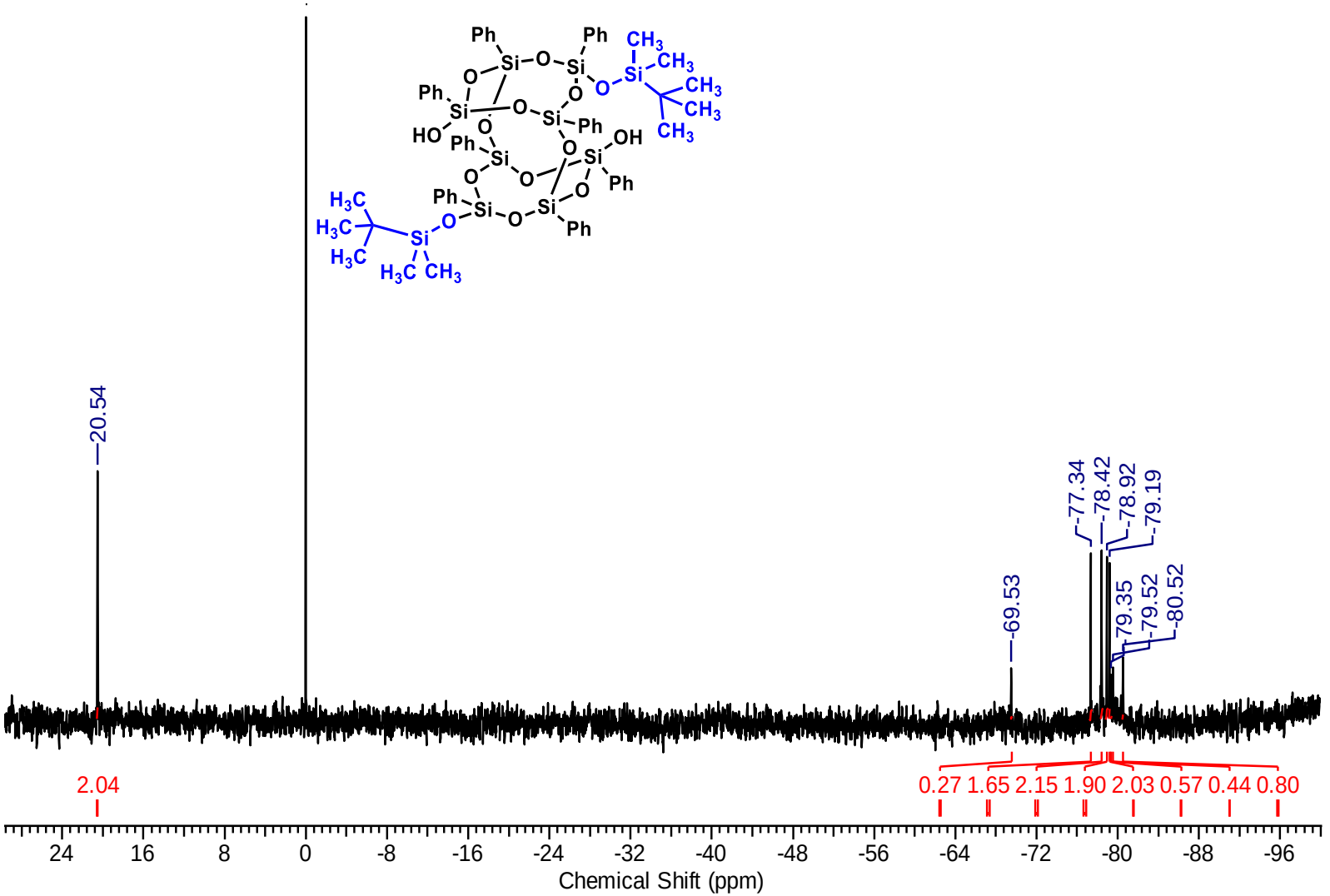


Figure S12 (cont'd)

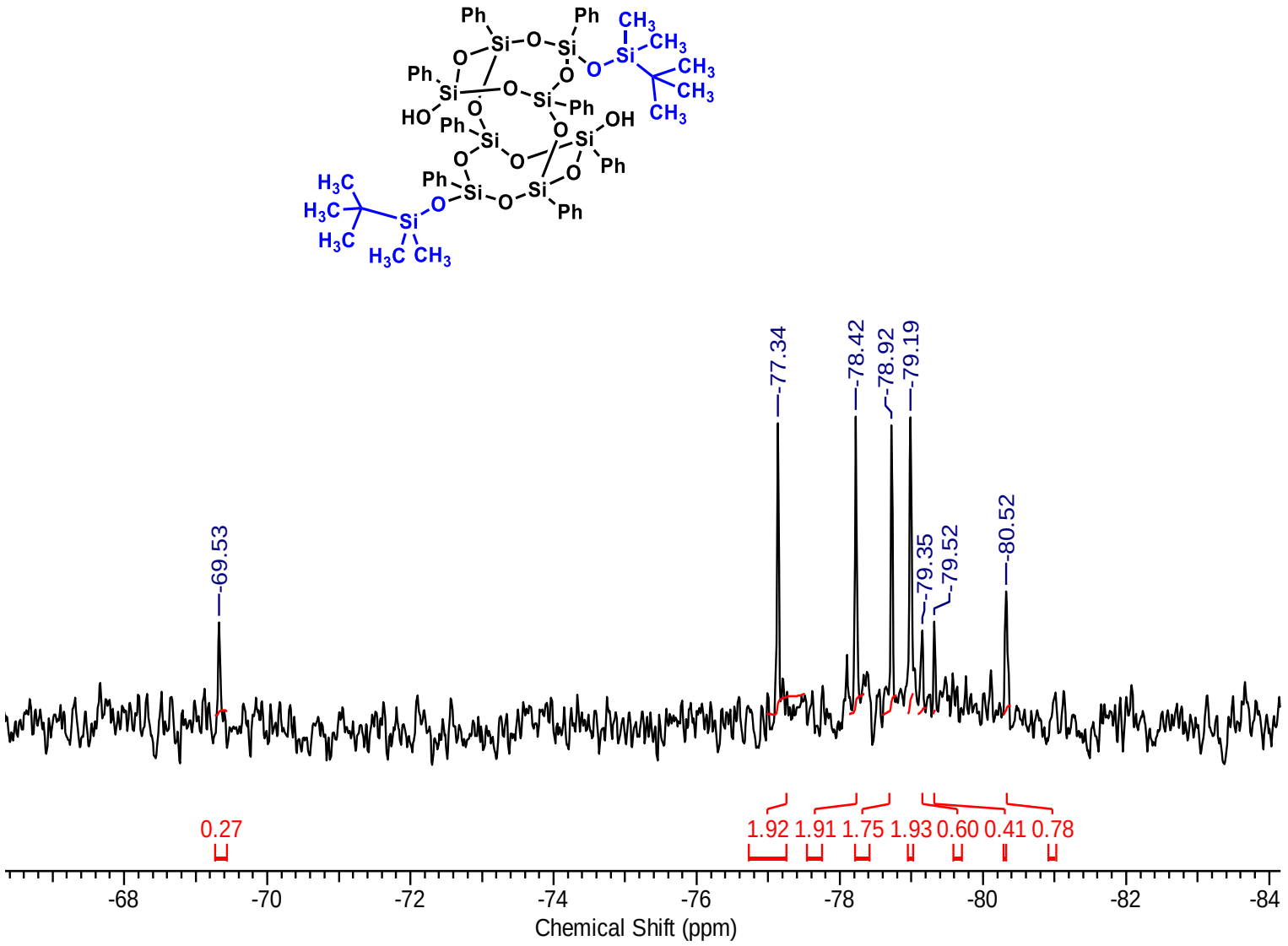


Figure S13 DDSQ (Me)(OH) – ^{29}Si NMR

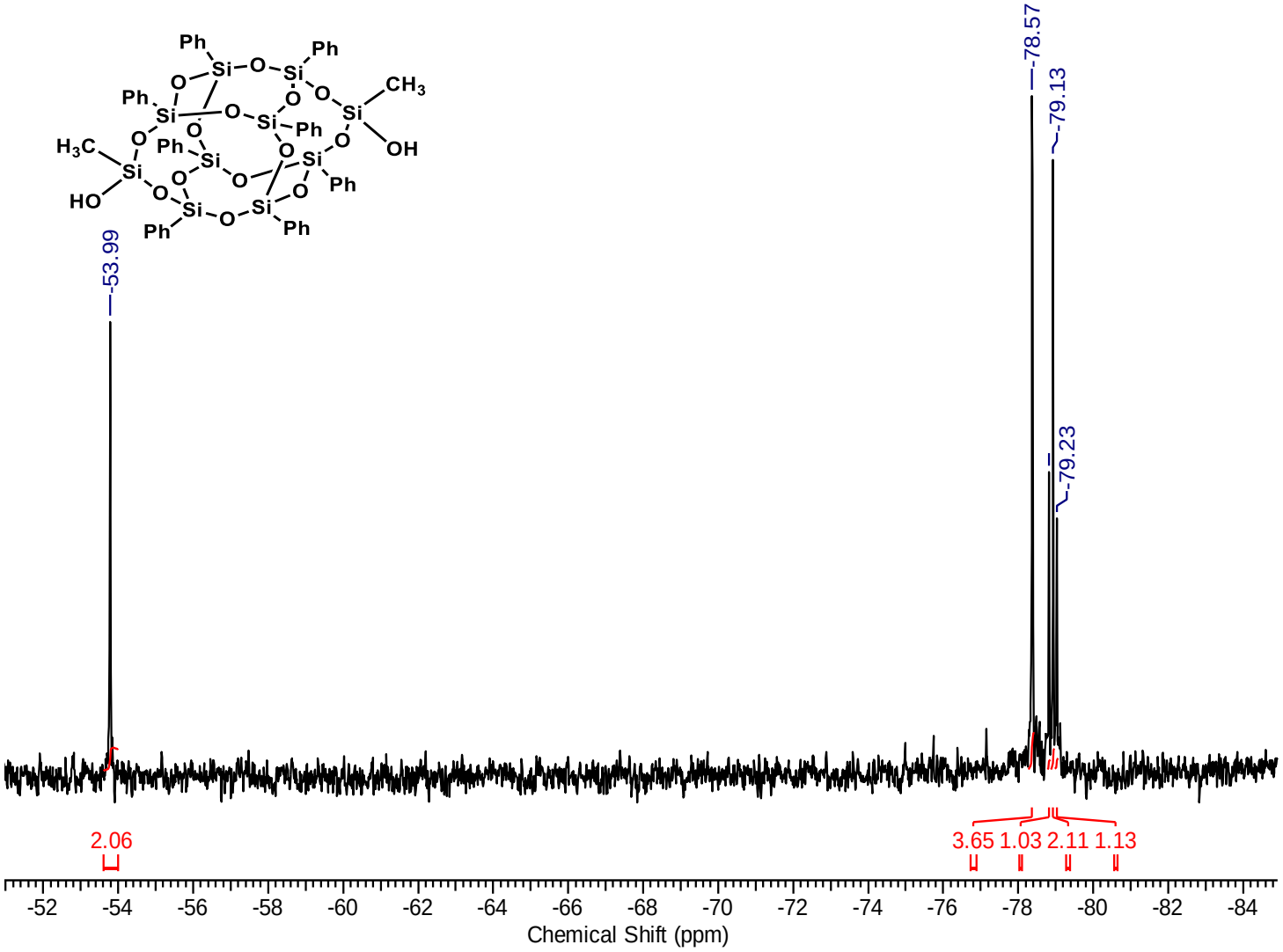


Figure S13 (cont'd)

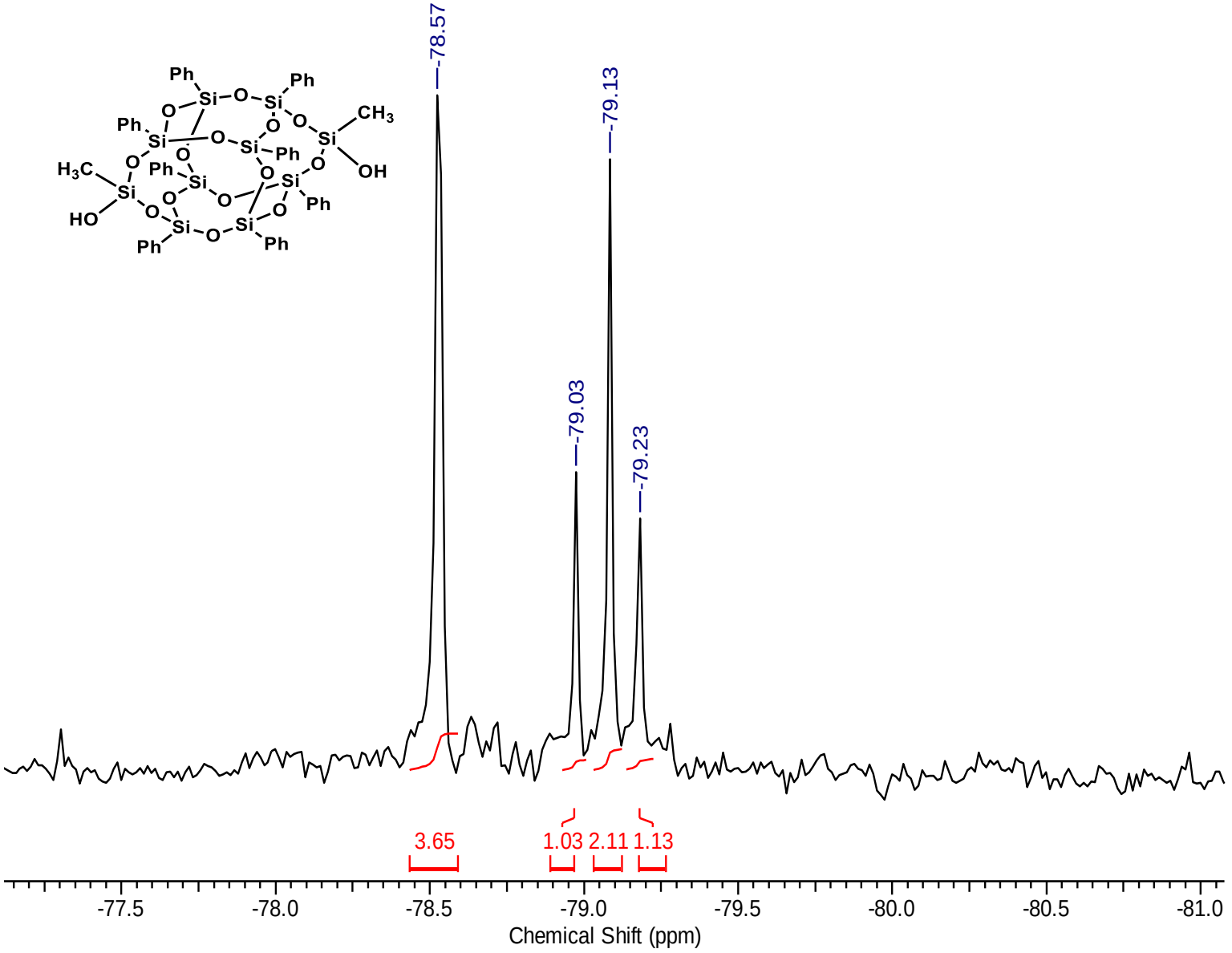


Figure S14 DDSQ (Me)(OH) – ^{1}H NMR

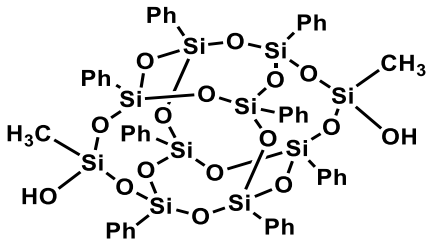


Figure S15 Mono-protection of DDSQ (Me)(OH) – ^{29}Si NMR

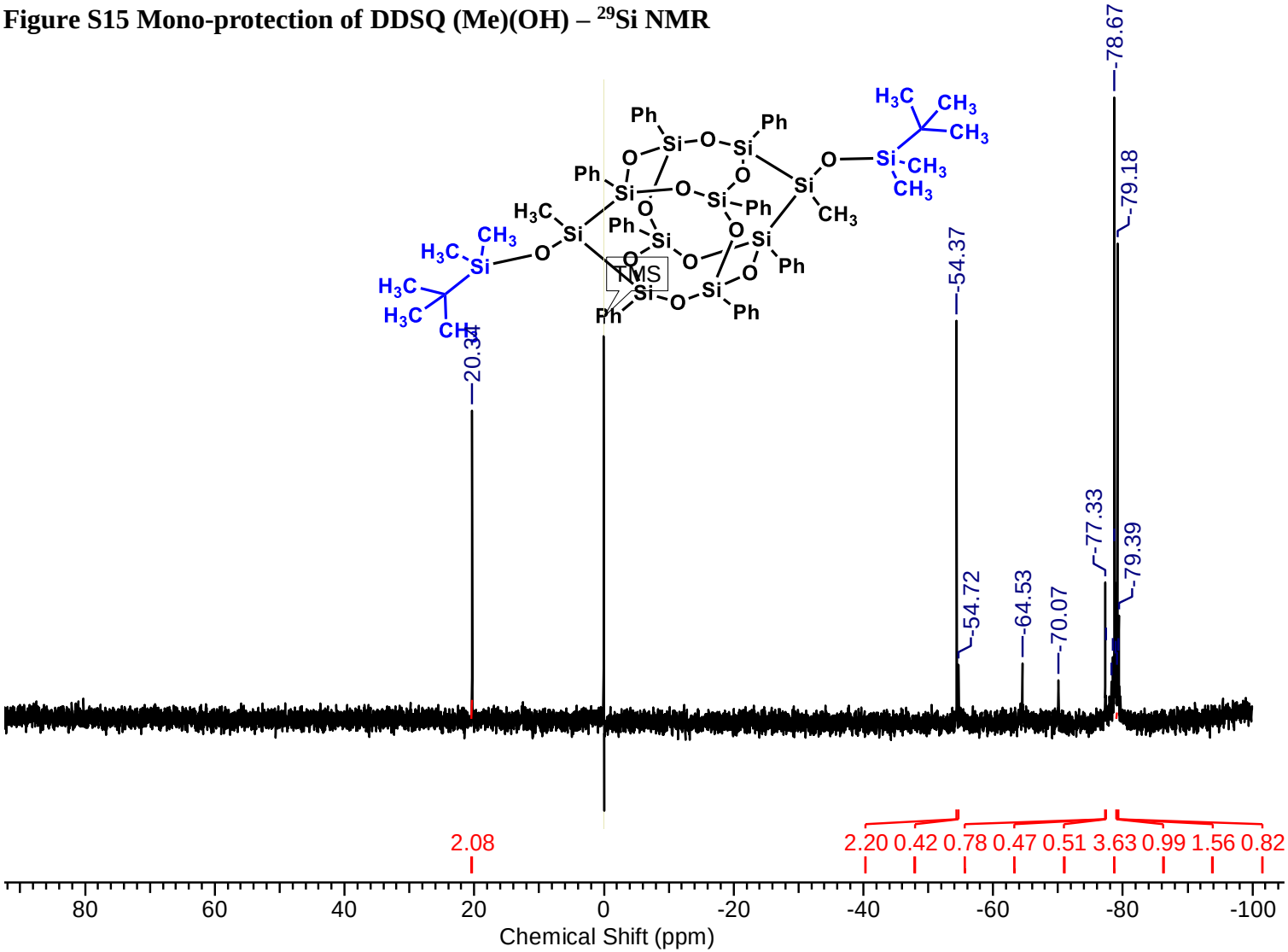


Figure S16 Mono-protection of DDSQ (Me)(OH) – ^{1}H NMR

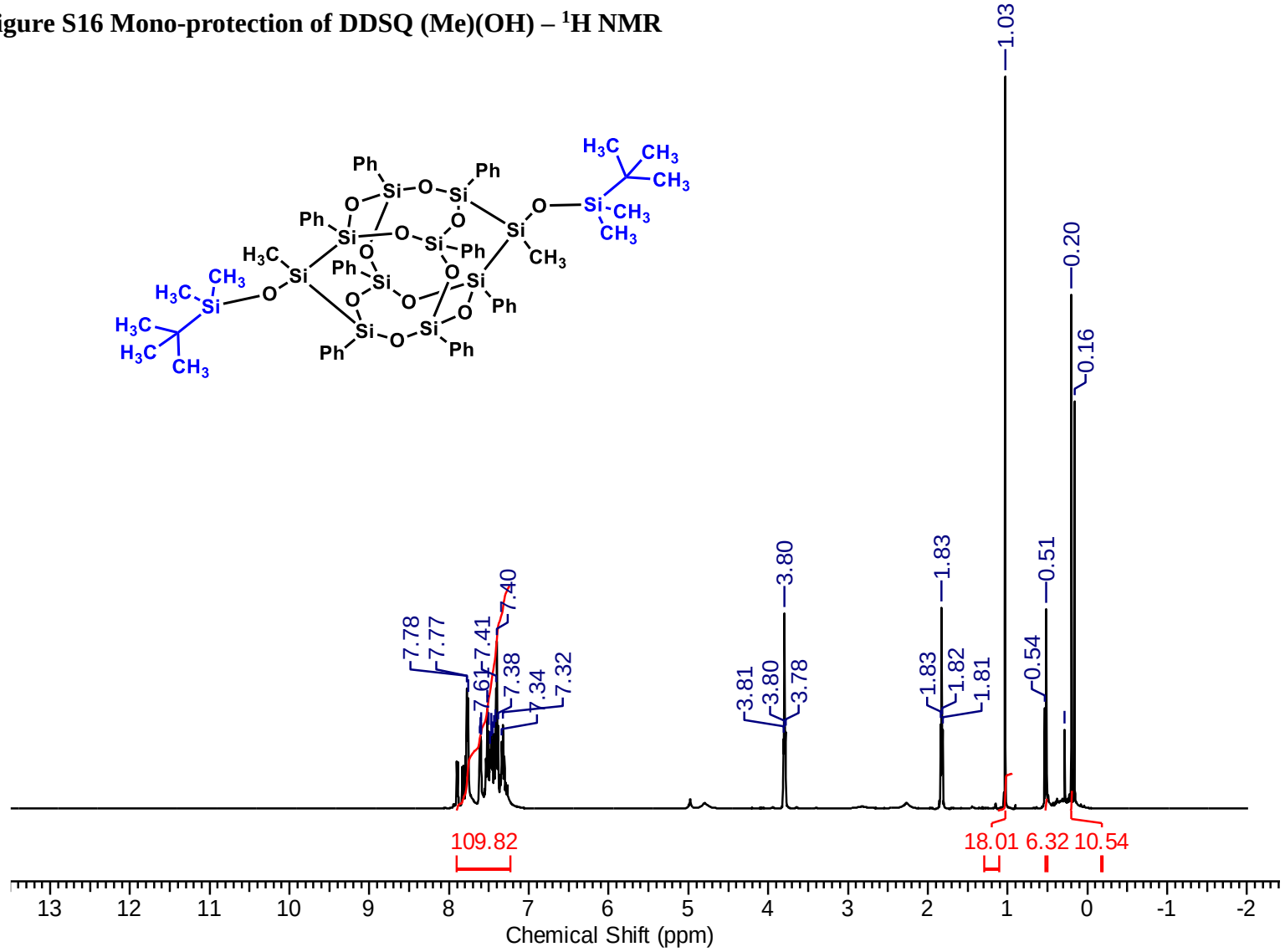


Figure S17 DDSQ (Me)(H) – ^{1}H NMR

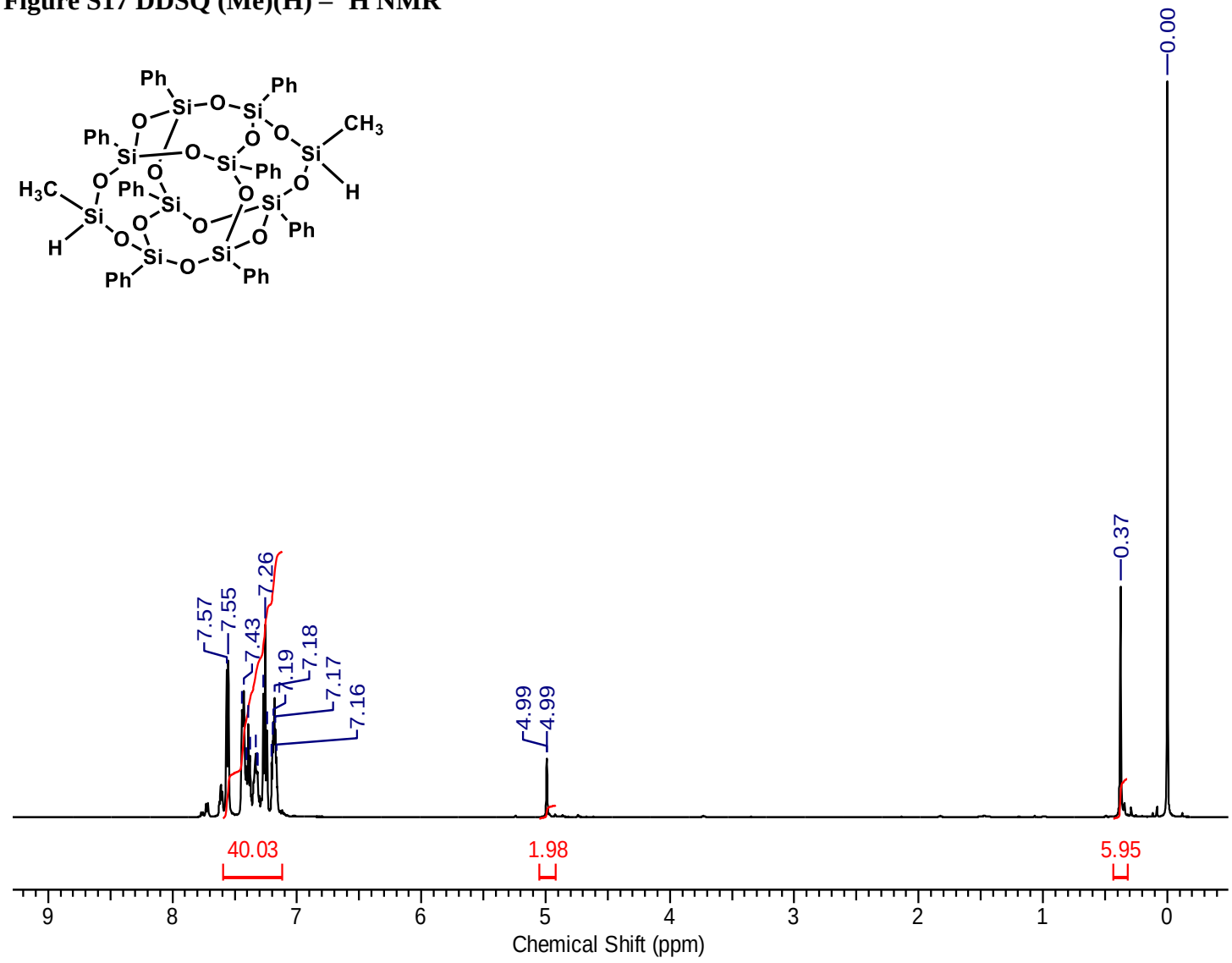


Figure S18 DDSQ (Me)(H) – ^{29}Si NMR

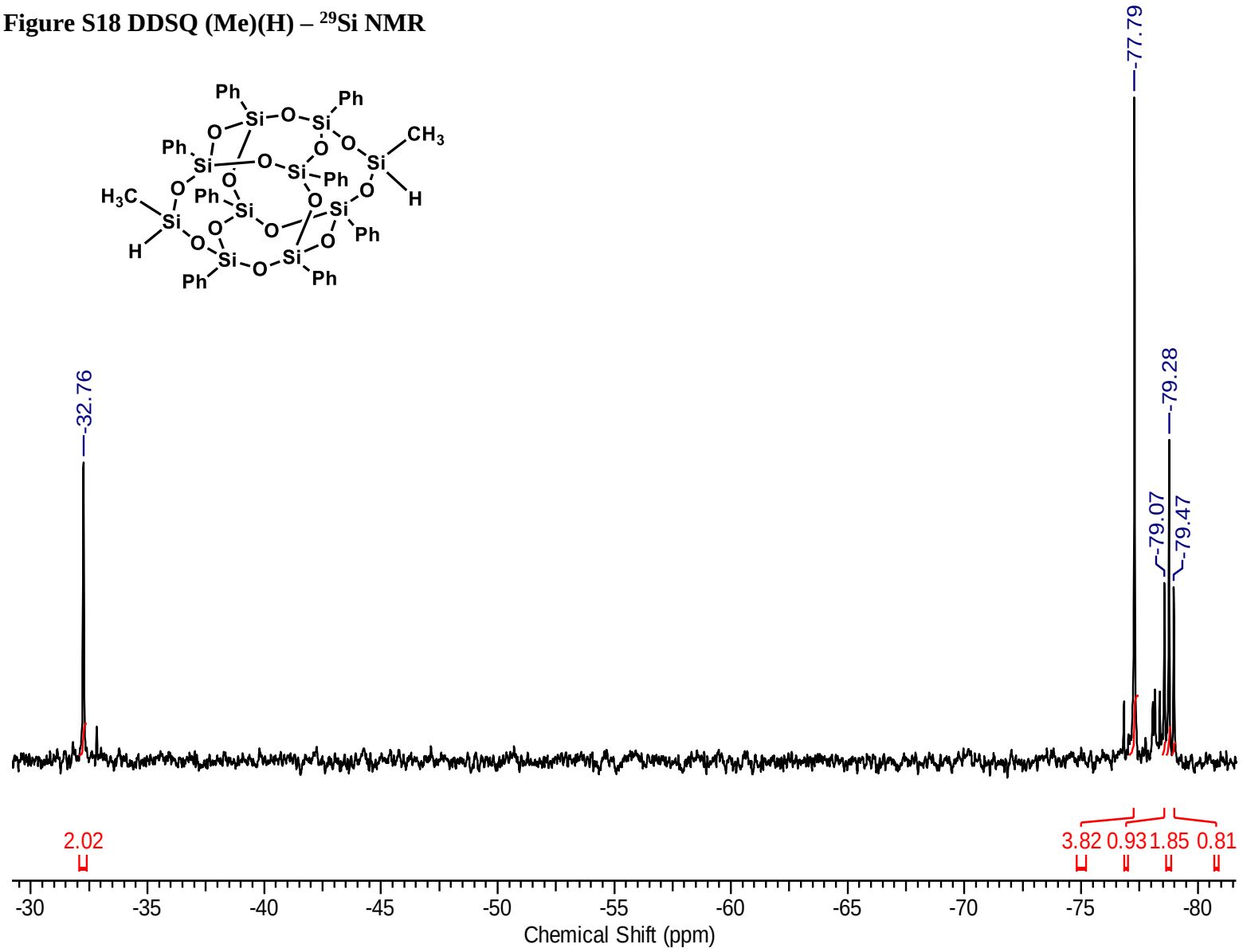


Figure S18 (cont'd)

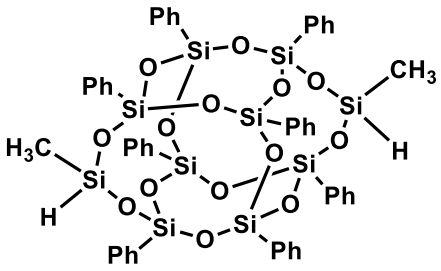


Figure S19 DSQ (Me)(di(trimethylsilyl)oxypropyl) – ^{1}H NMR

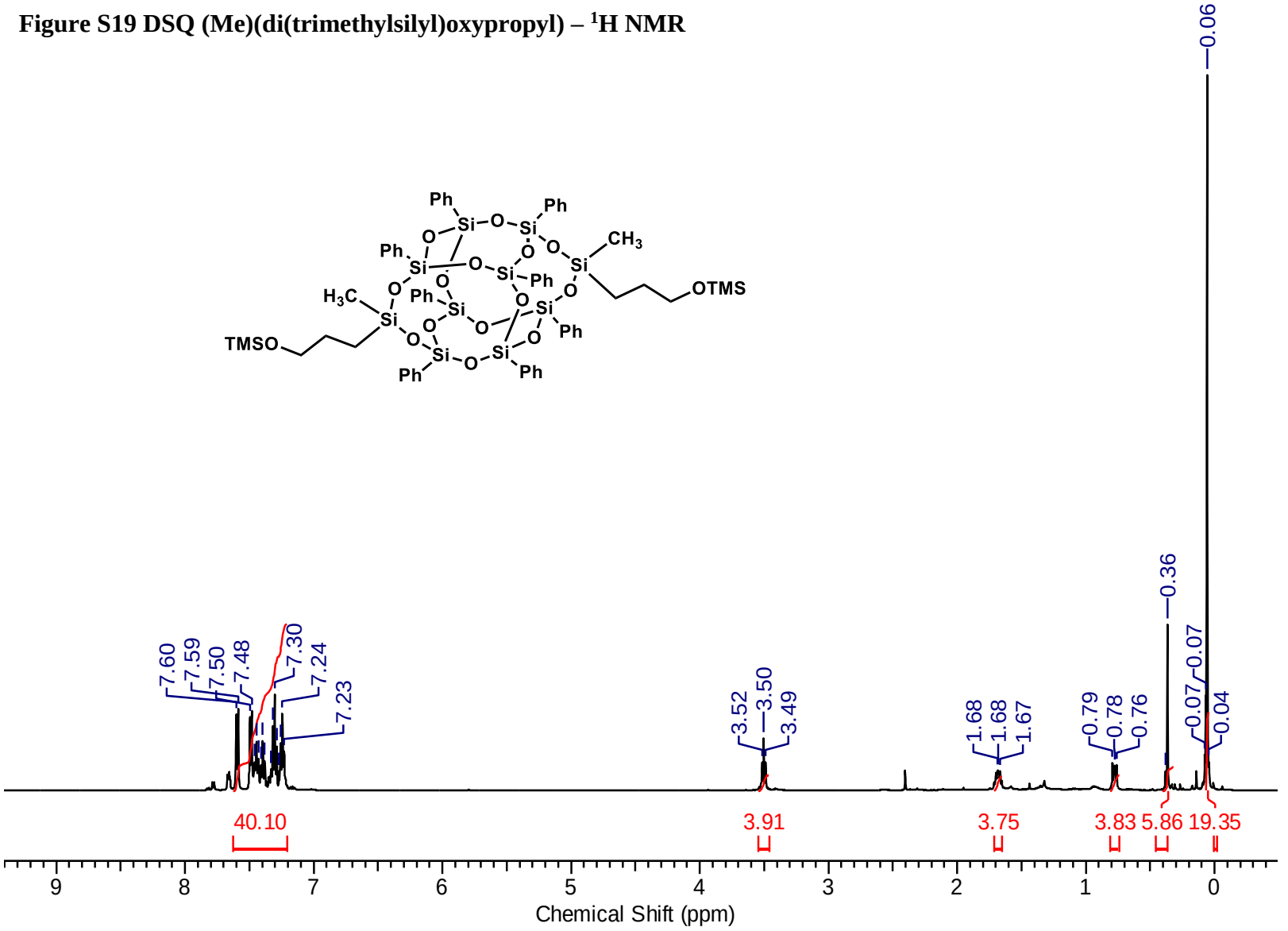


Figure S20 DDSQ (Me)(di(trimethylsilyl)oxypropyl) – ^{29}Si NMR

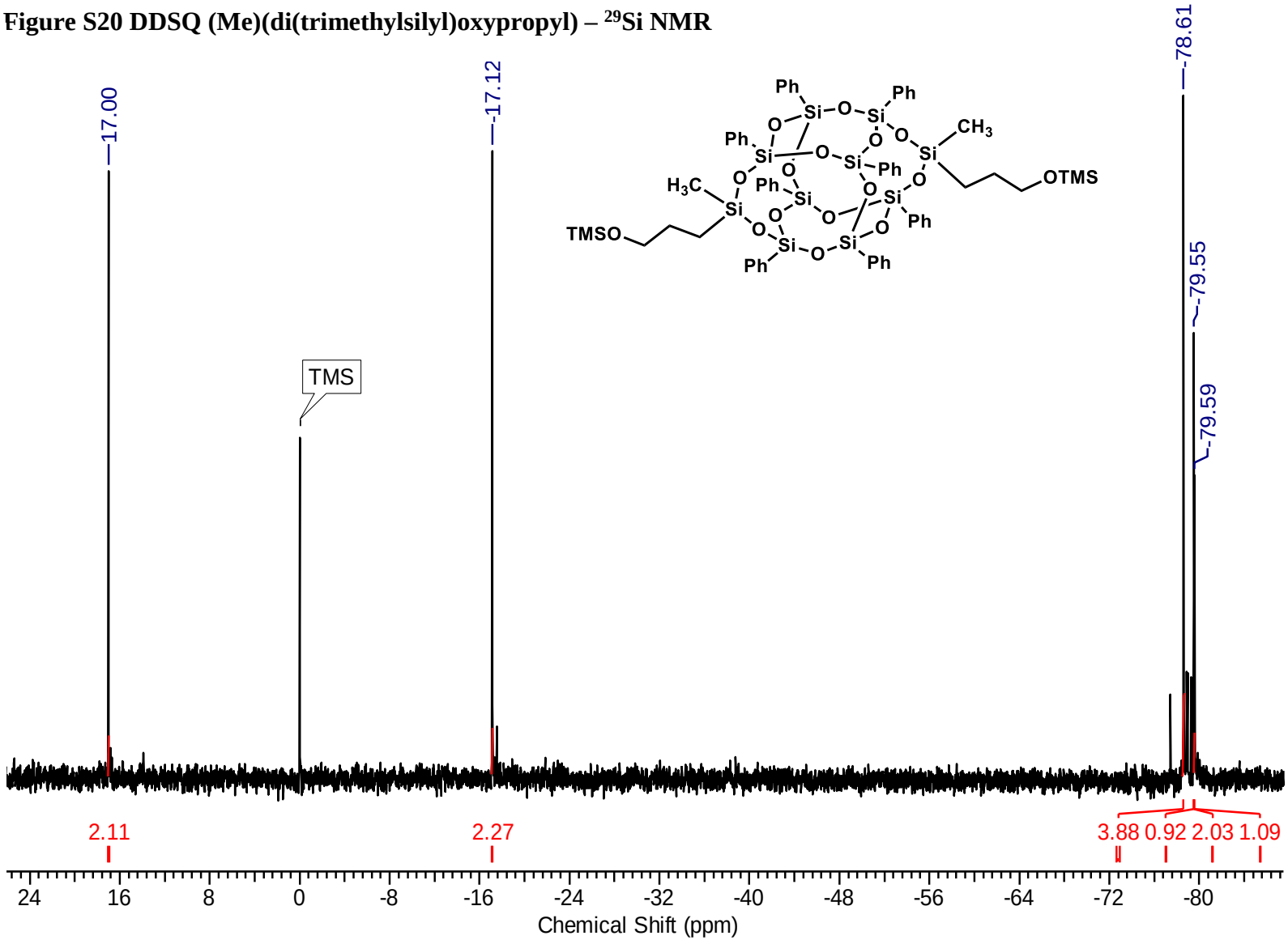


Figure S20 (cont'd)

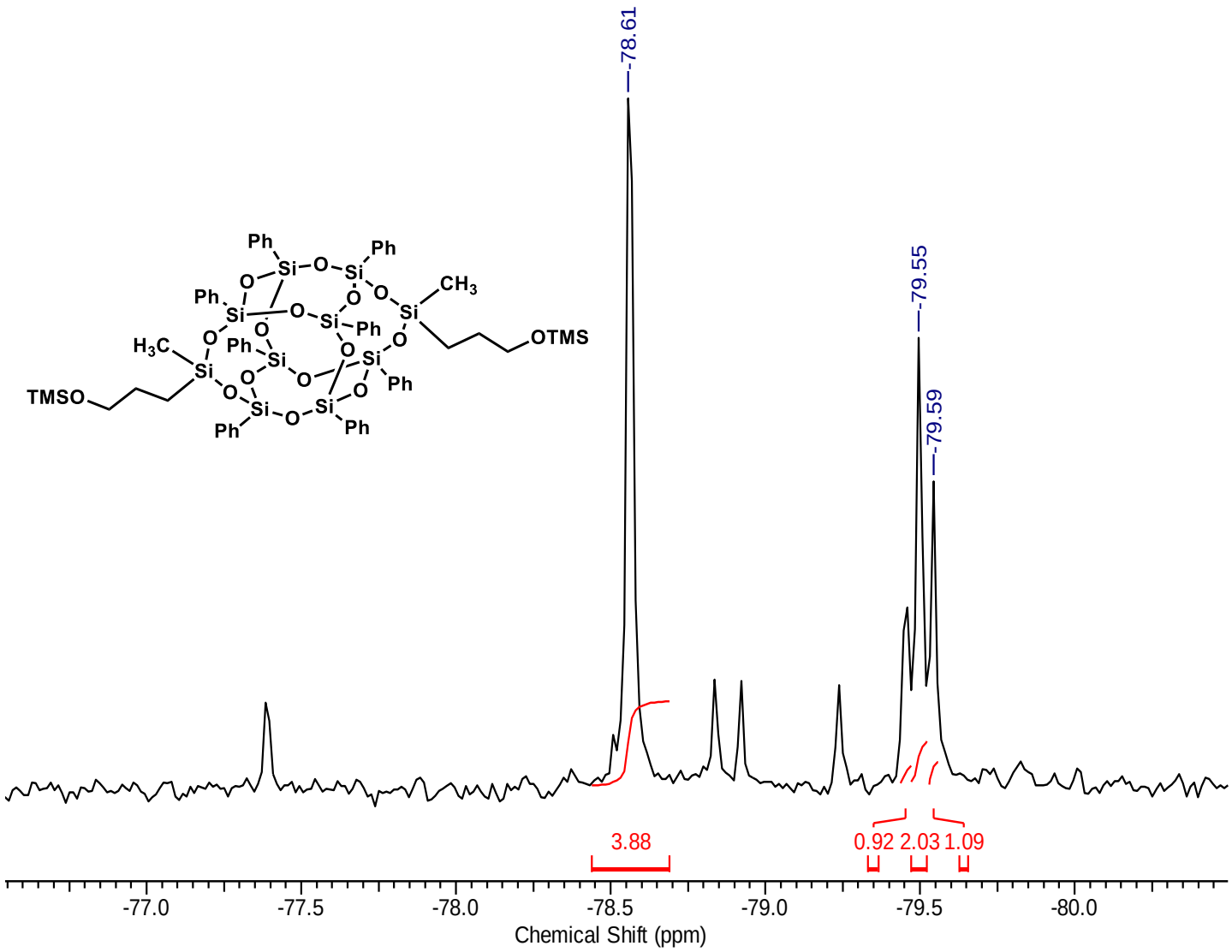


Figure S21 DDSQ (Me)(Hydroxopropyl) – ^{1}H NMR

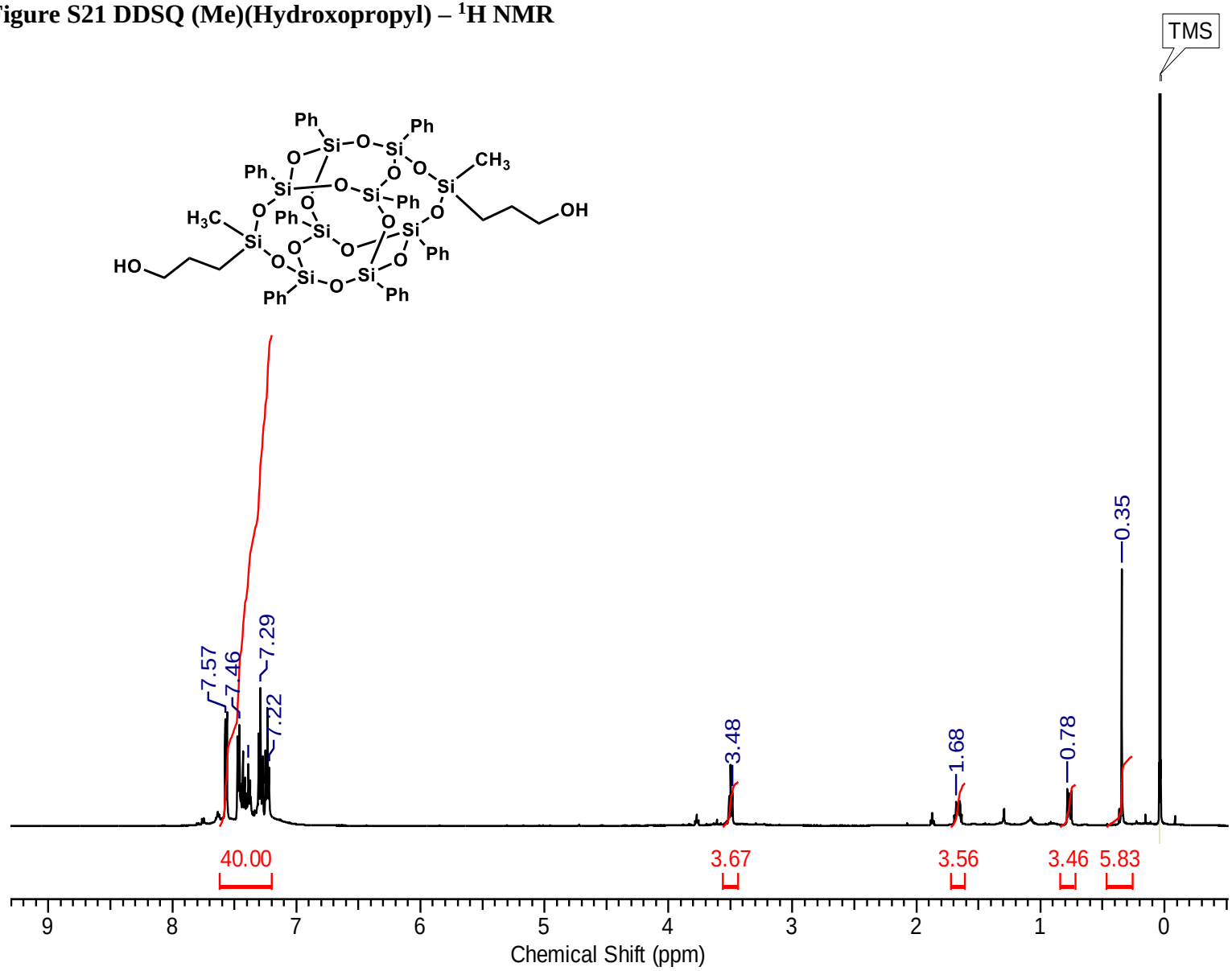


Figure S22 DDSQ (Me)(Hydroxopropyl) – ^{29}Si NMR

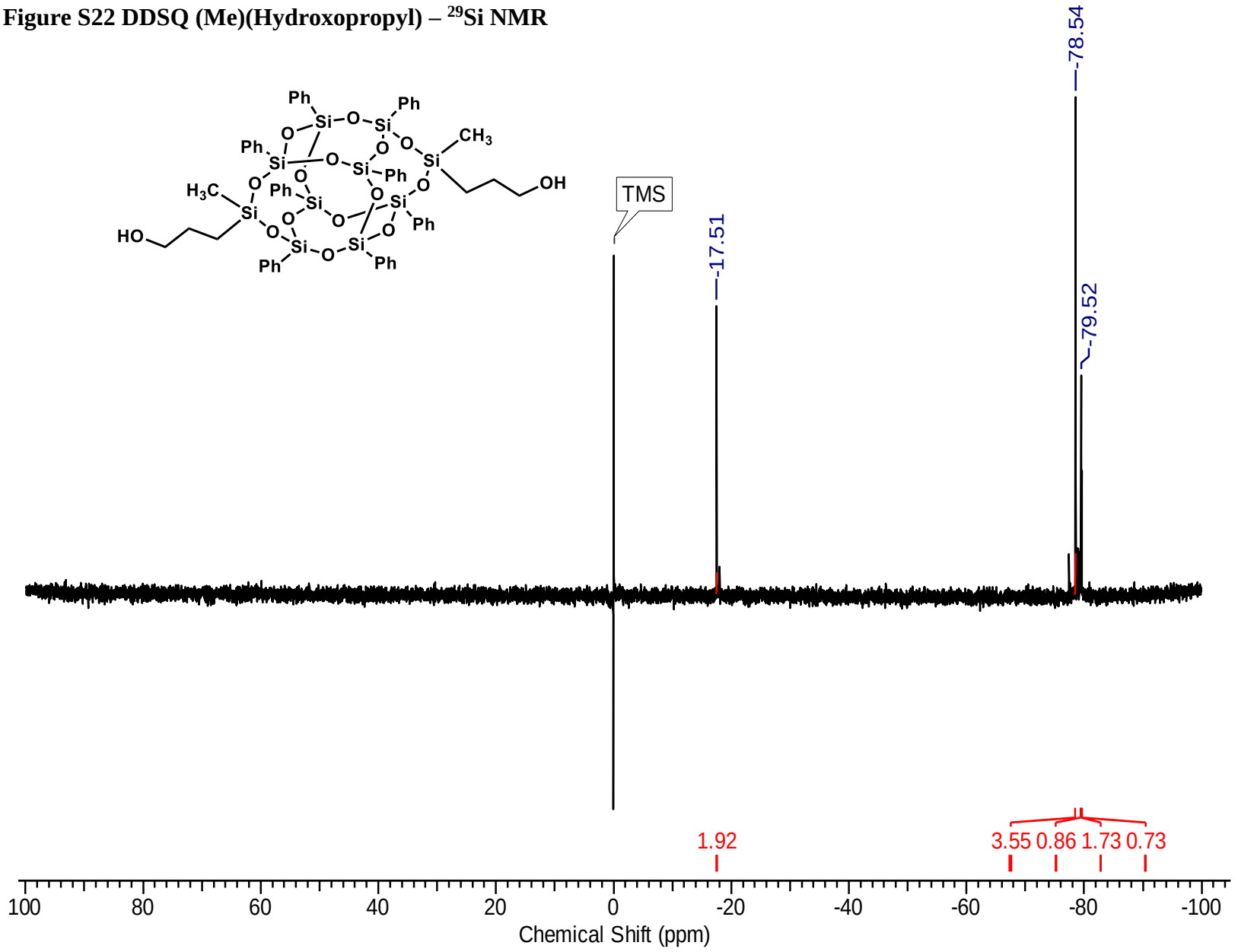


Figure S22 (cont'd)

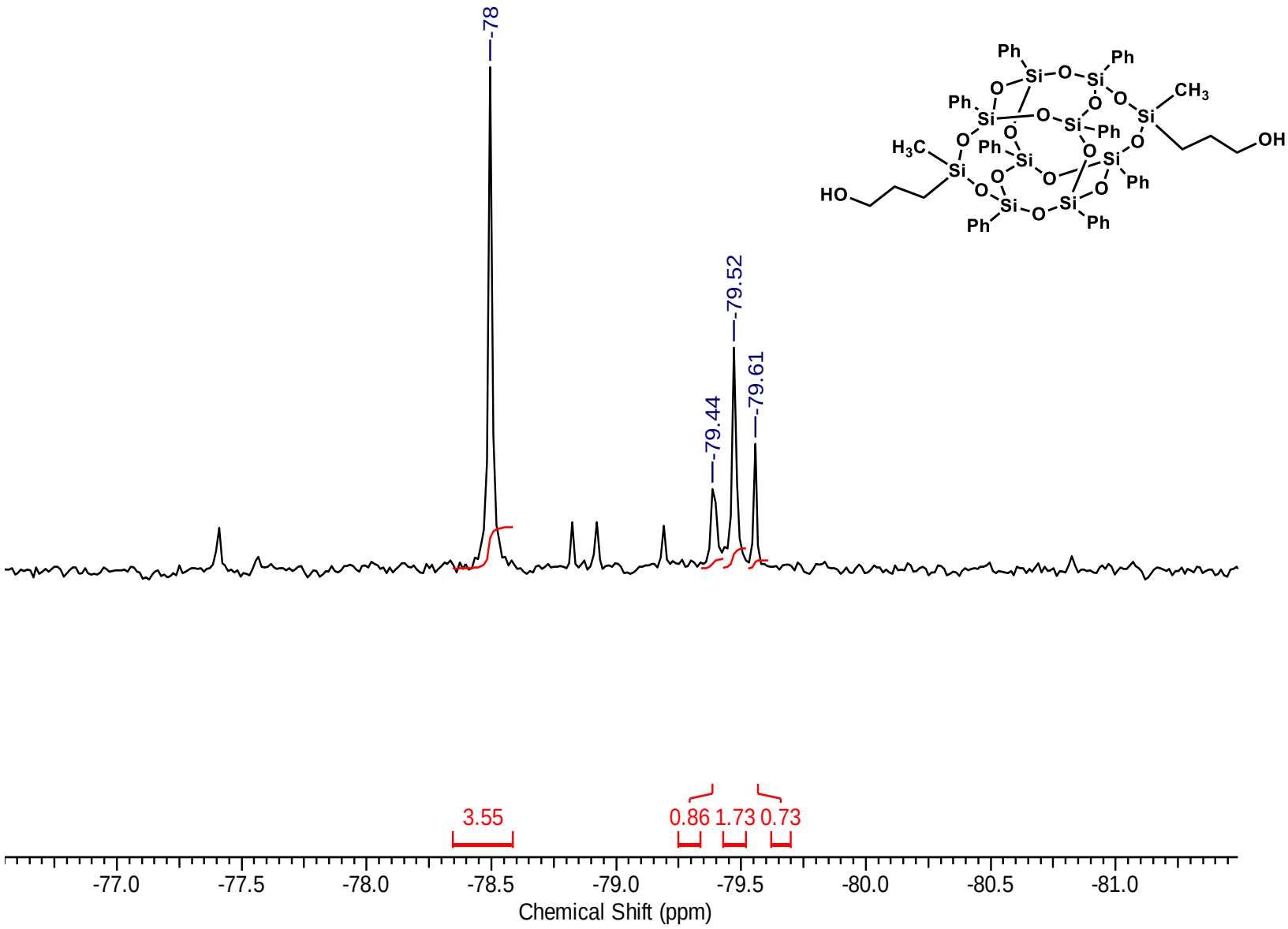


Figure S23 Mono-protection of DDSQ (Me)(Hydroxopropyl) – ^{1}H NMR

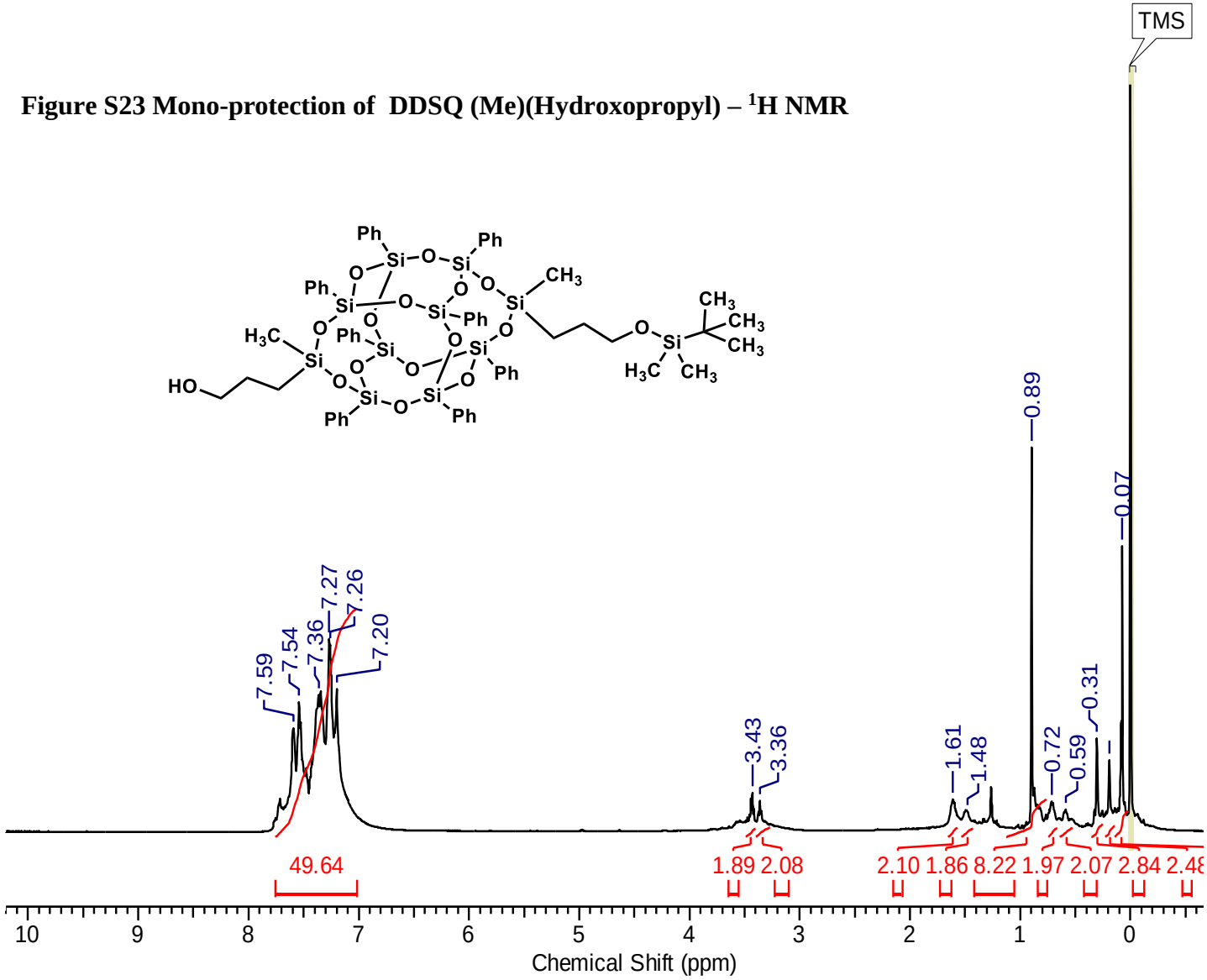


Figure S24 Mono-protection of DDSQ (Me)(Hydroxopropyl) – ^{29}Si NMR

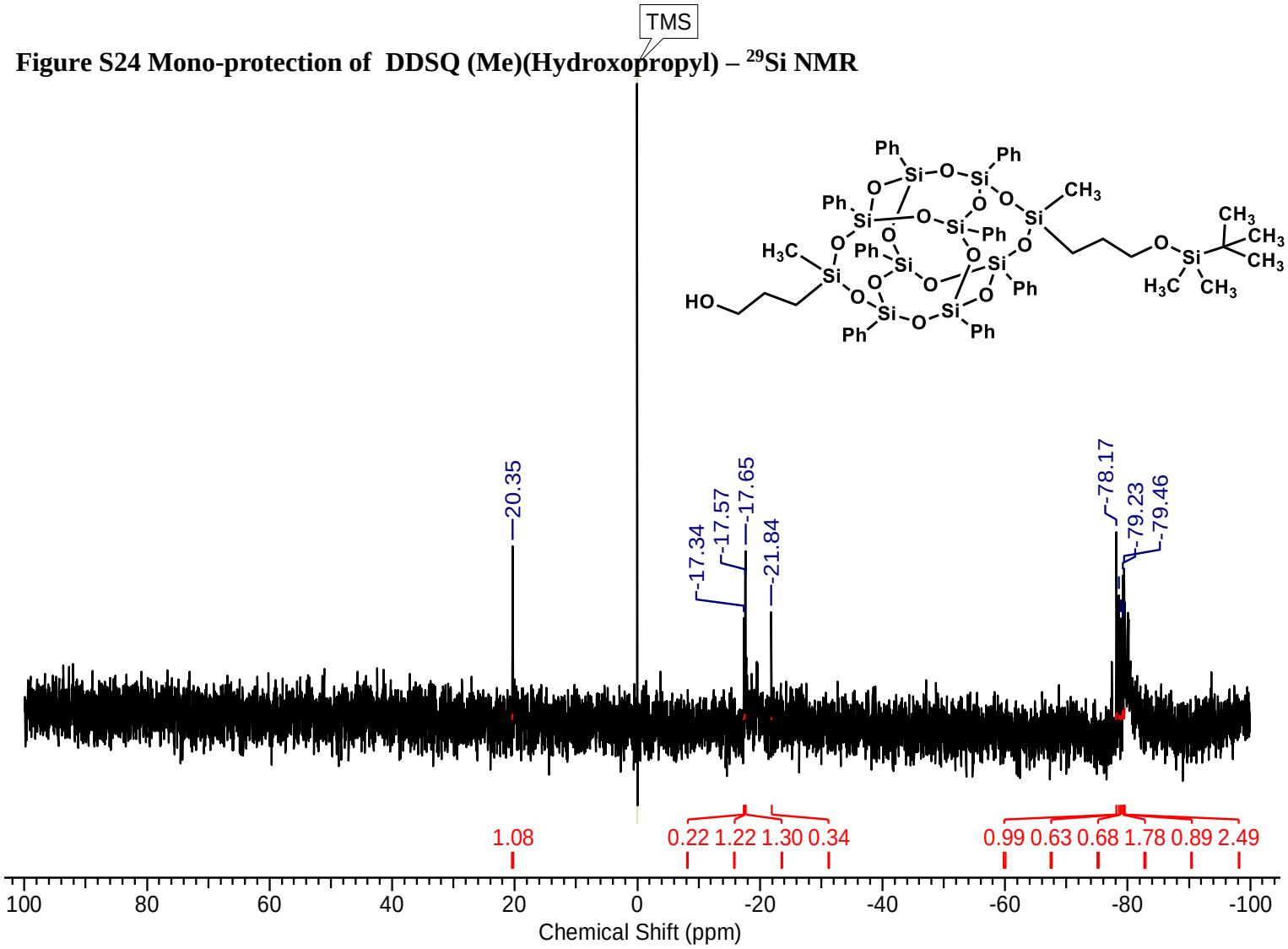
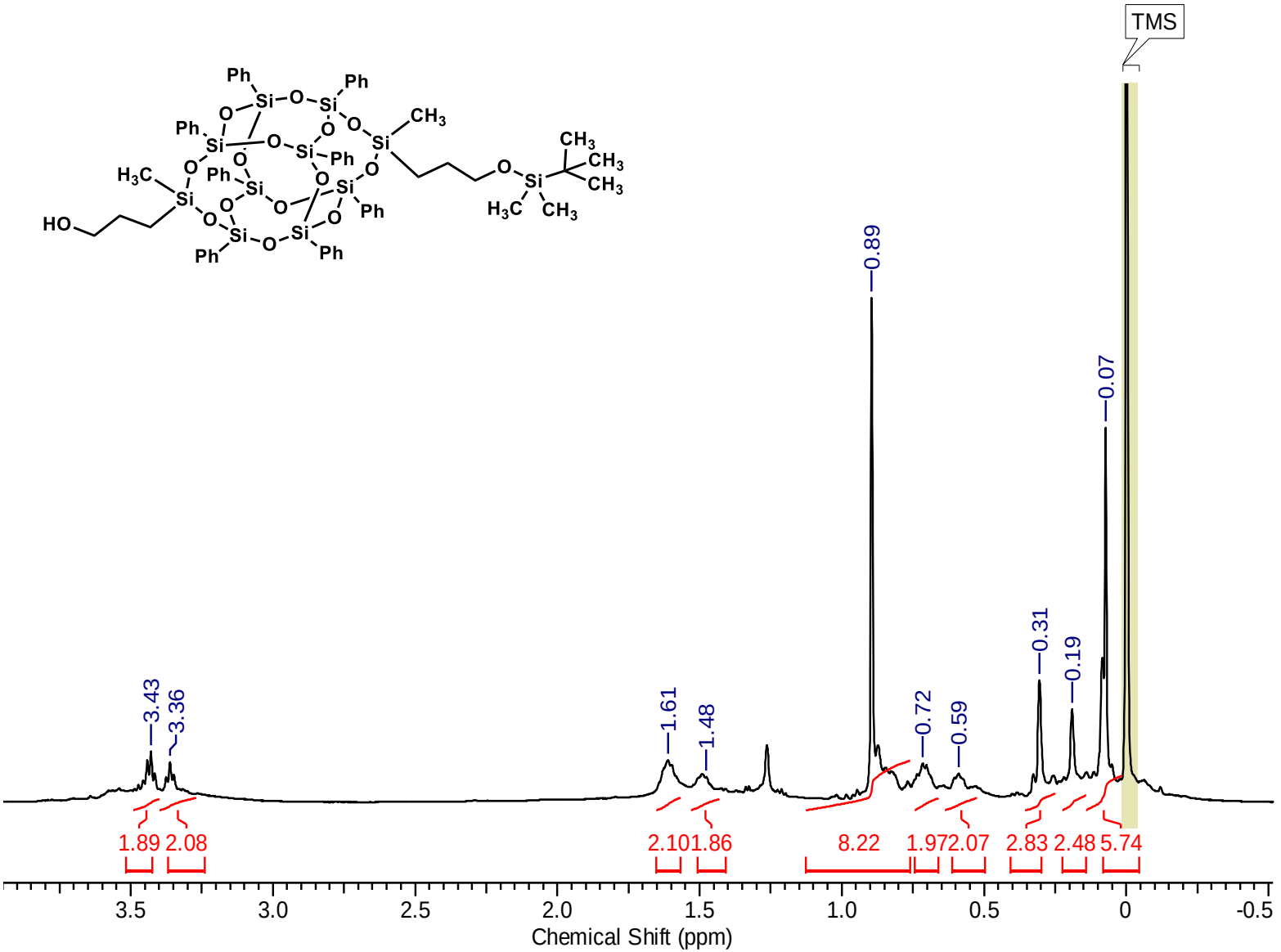


Figure S24 (cont'd)



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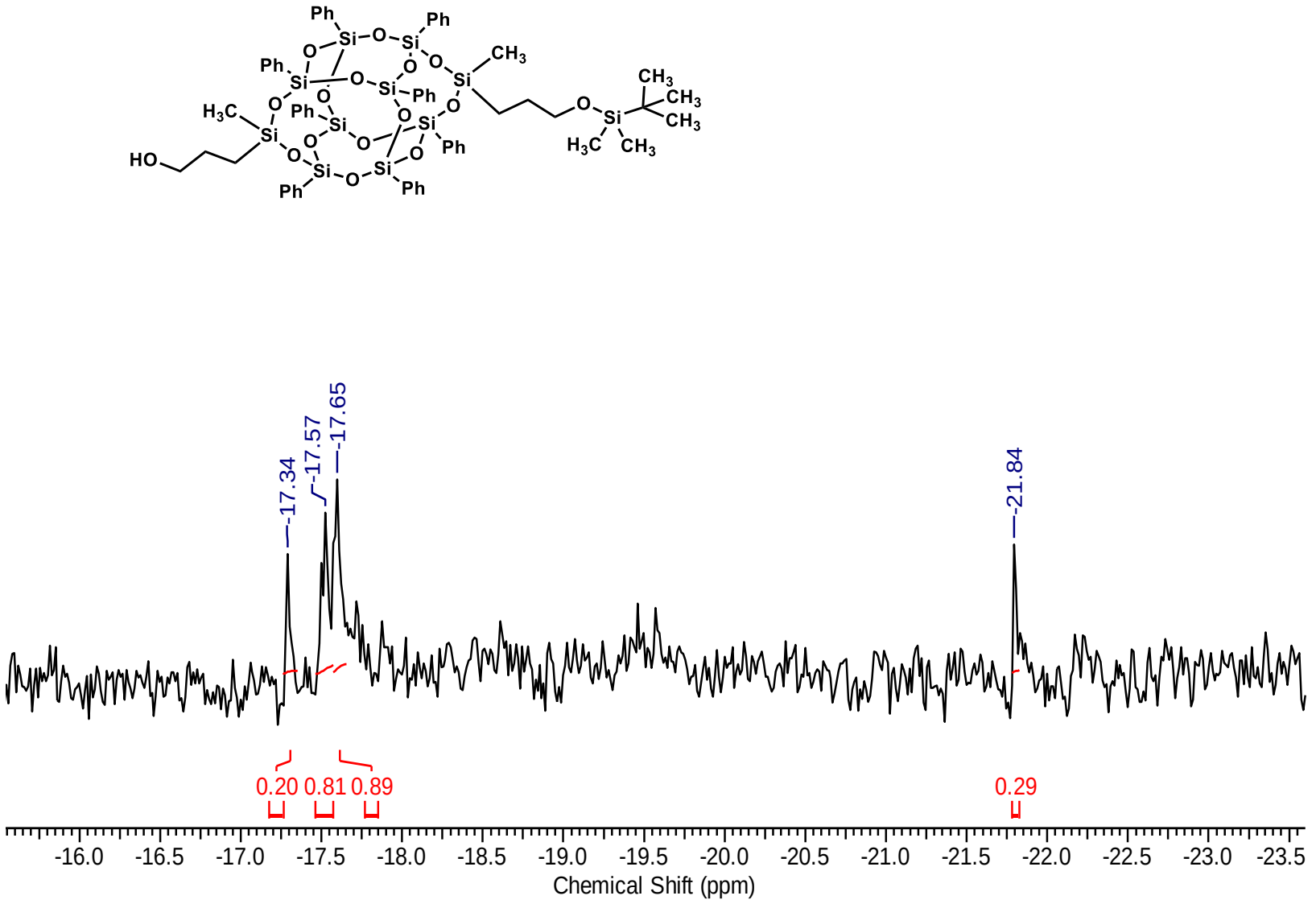

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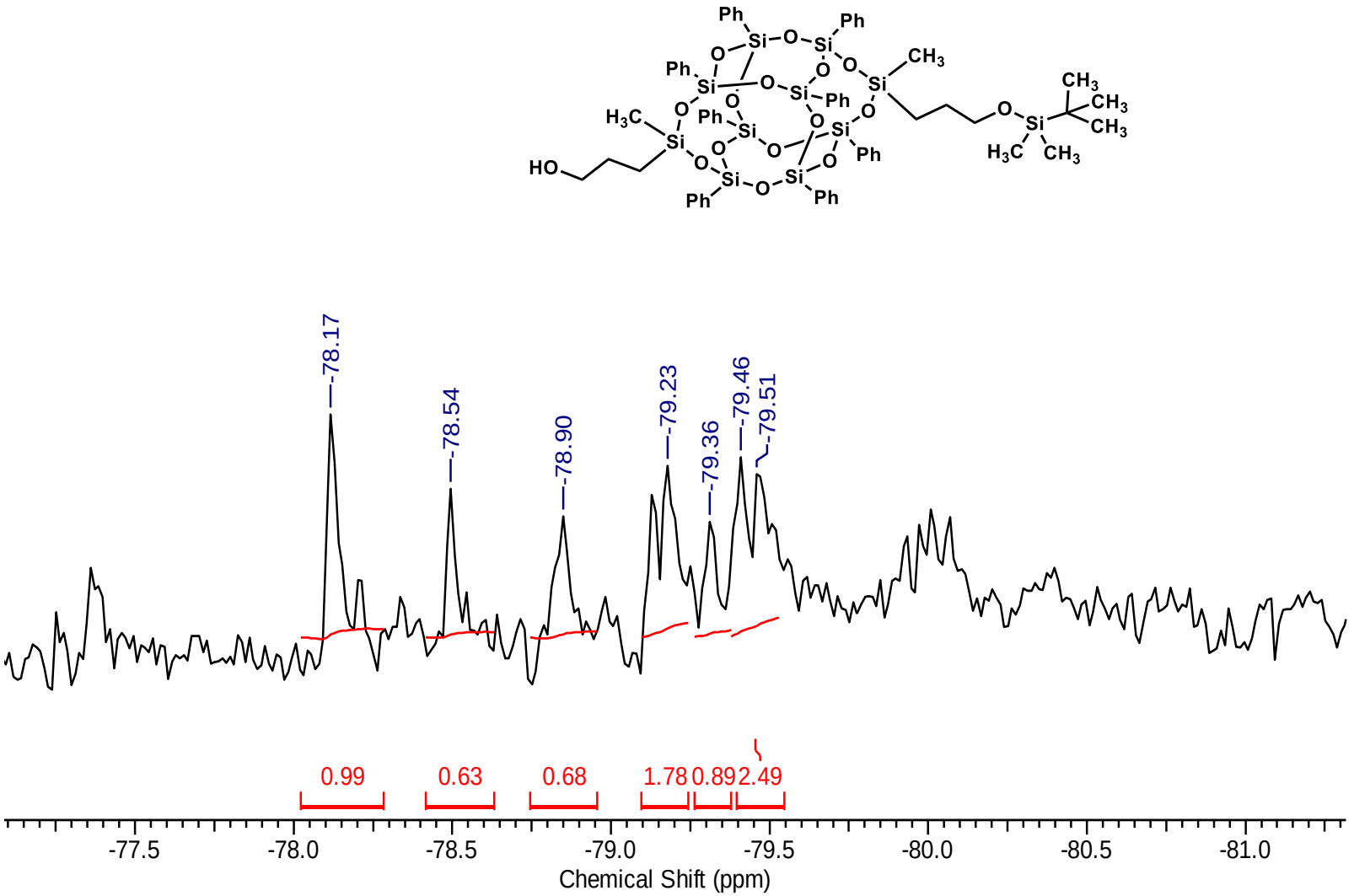


Figure S25 Phenylethynyl(phenyl) bromide – ^{13}C NMR

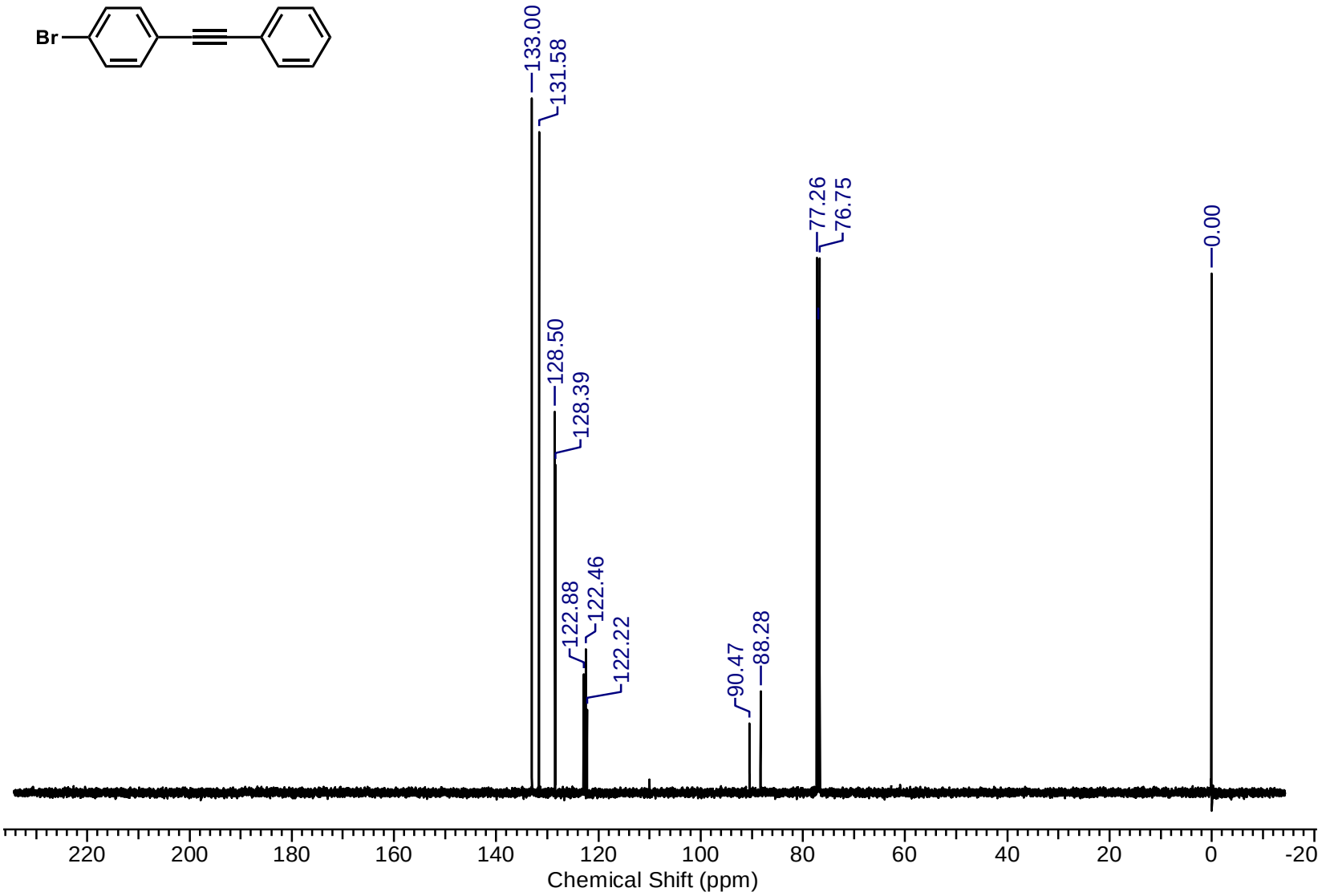


Figure S26 Phenylethynyl(phenyl) bromide – ^{1}H NMR

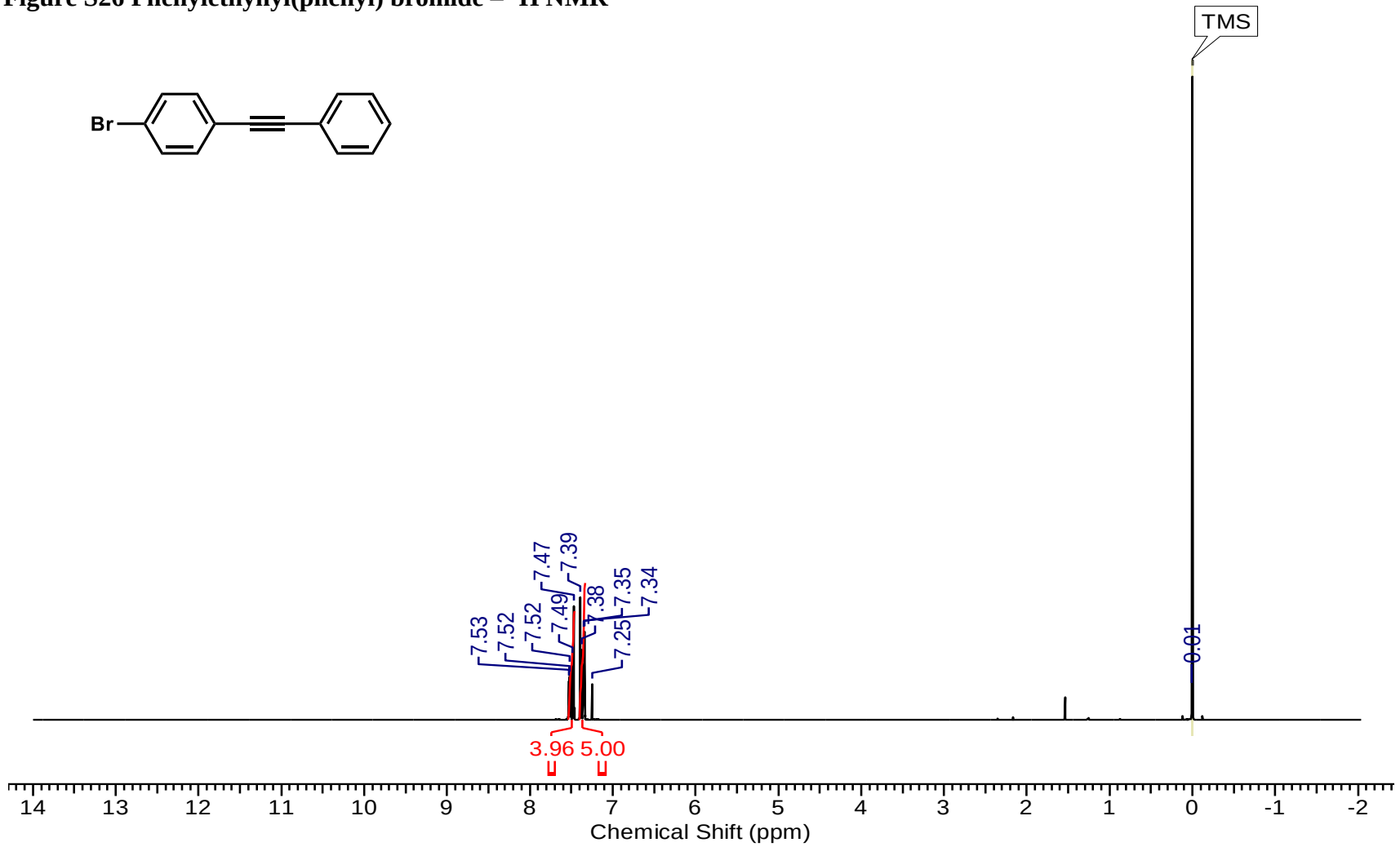


Figure S27 Phenylethynyl(phenyl) Grignard bromide – ^{1}H NMR

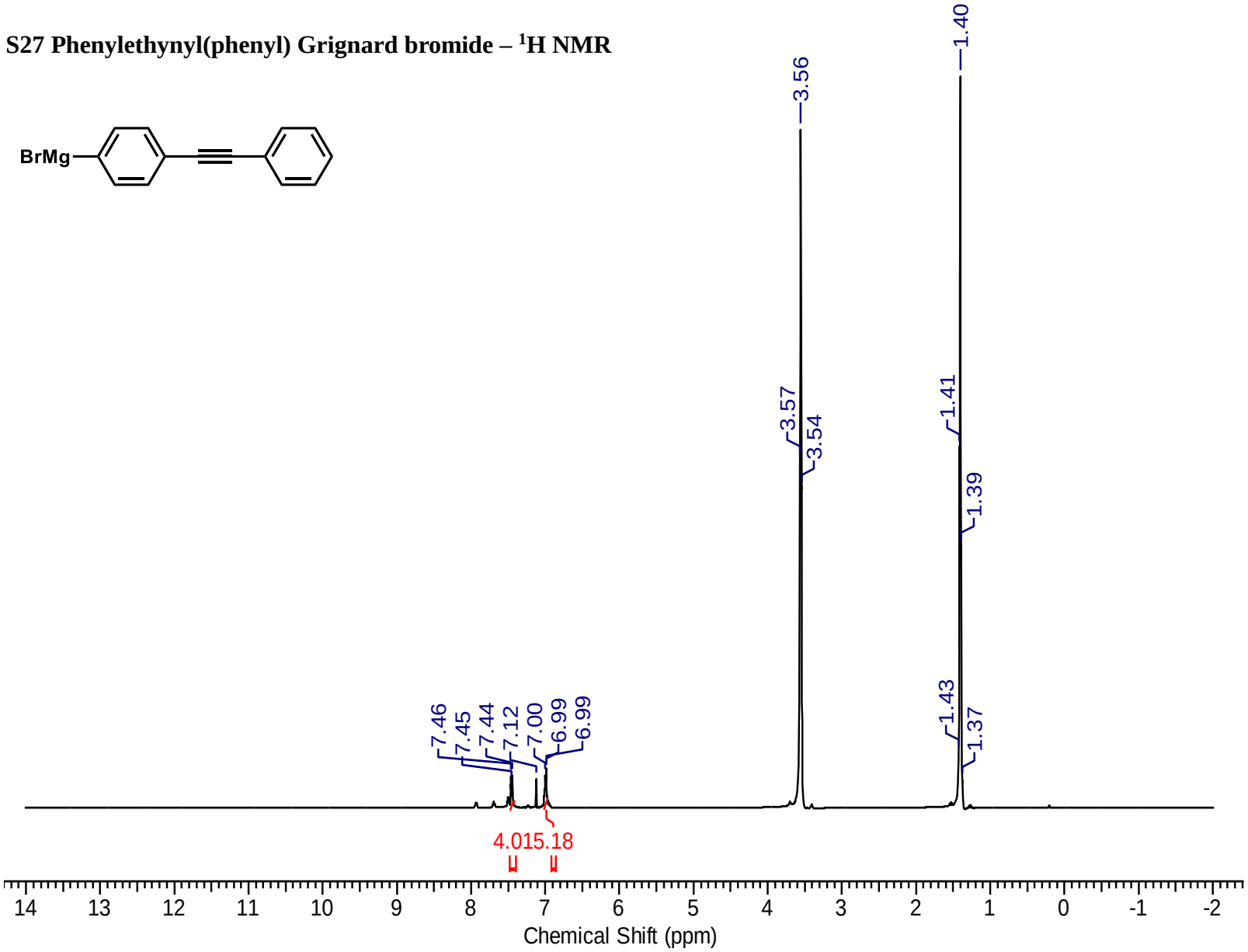


Figure S28 Phenylethynyl(phenyl) Grignard bromide – ^{13}C NMR

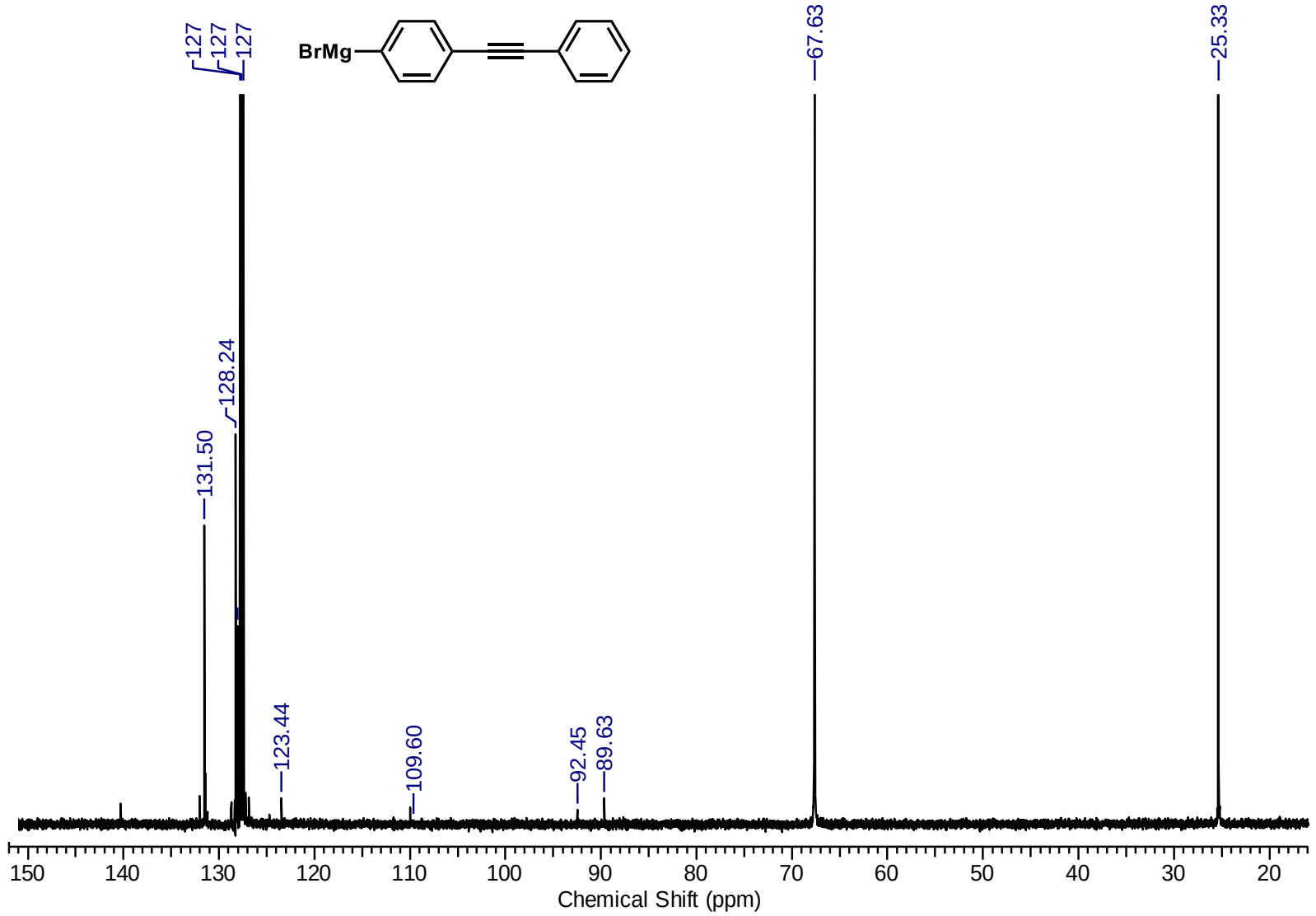


Figure S29 Phenylethynyl(phenyl) (methyl) dichloro silane before distillation – ^{1}H NMR

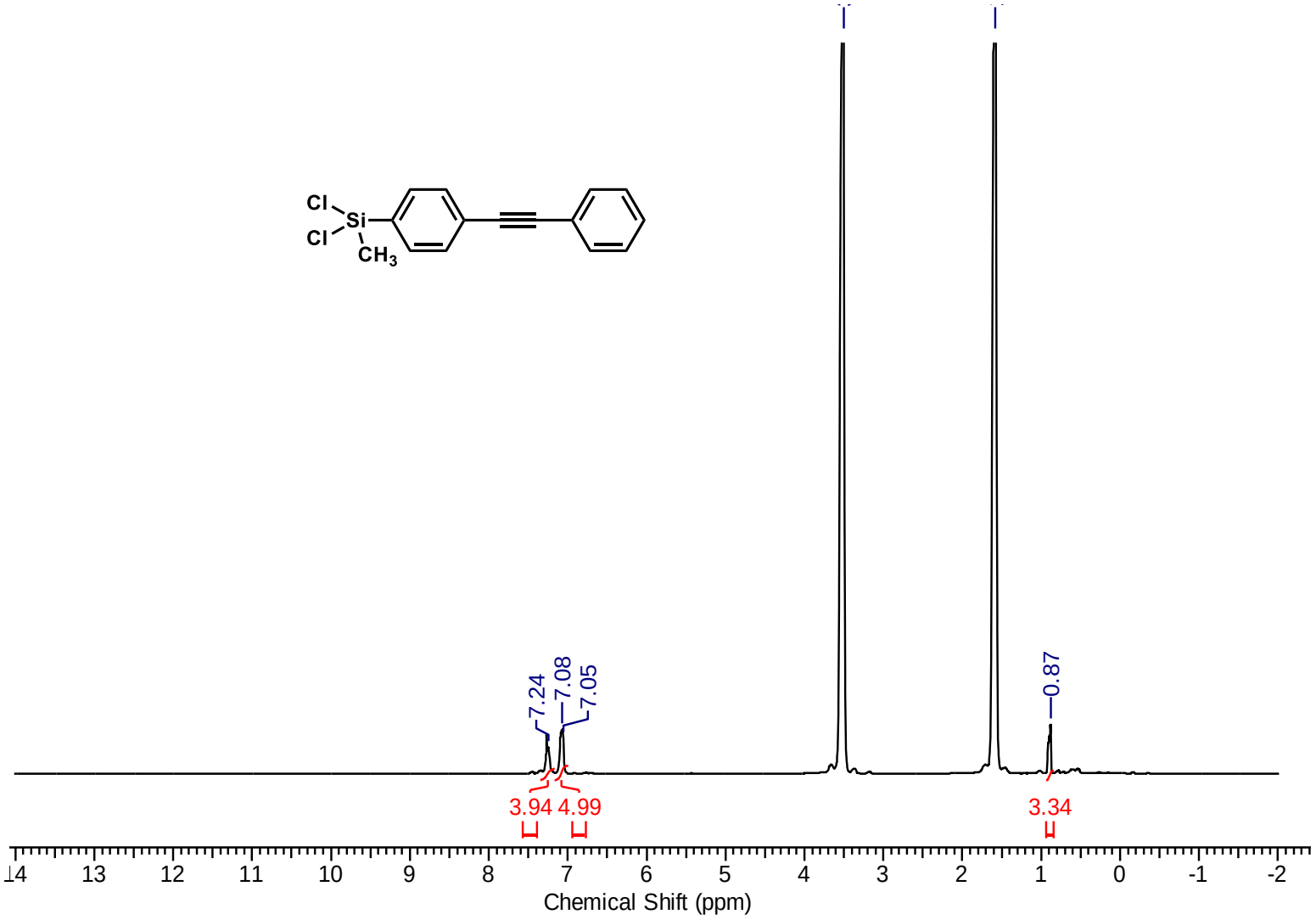


Figure S30 Phenylethynyl(phenyl) (methyl) dichloro silane before distillation – ^{29}Si NMR

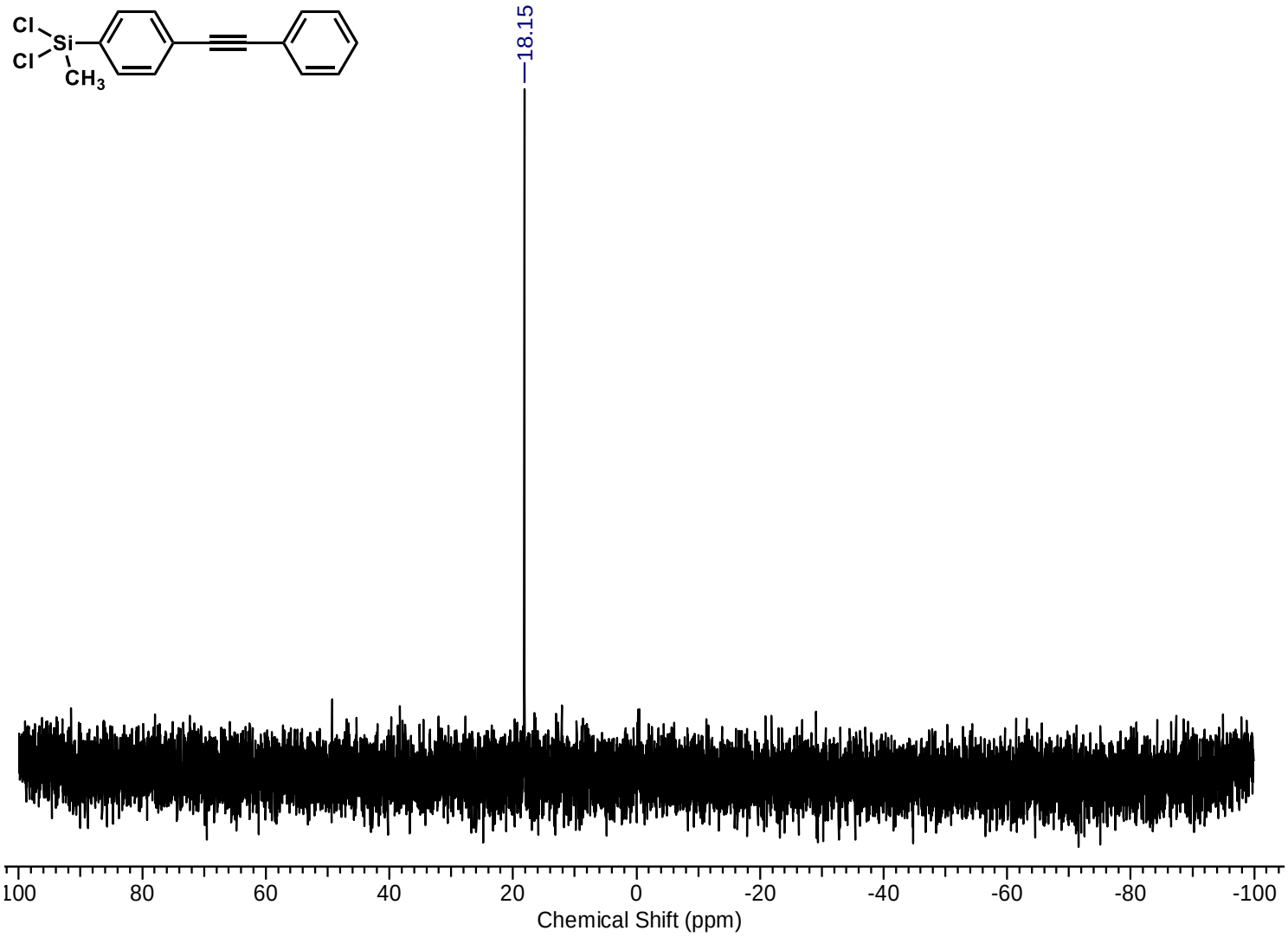


Figure S31 distilled product by Kugelrohr distillation – ^{1}H NMR

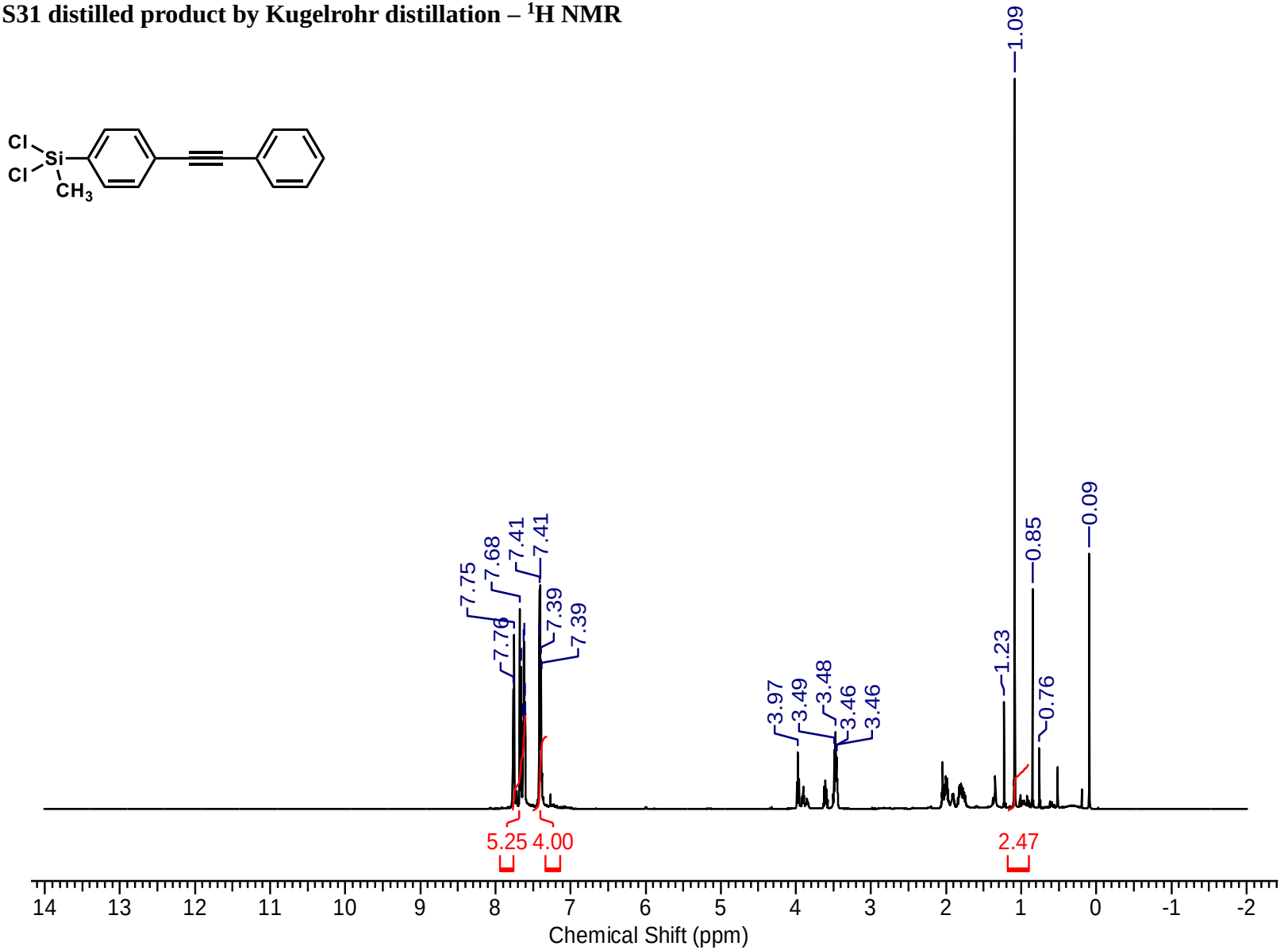


Figure S32 distilled product by Kugelrohr distillation – ^{29}Si NMR

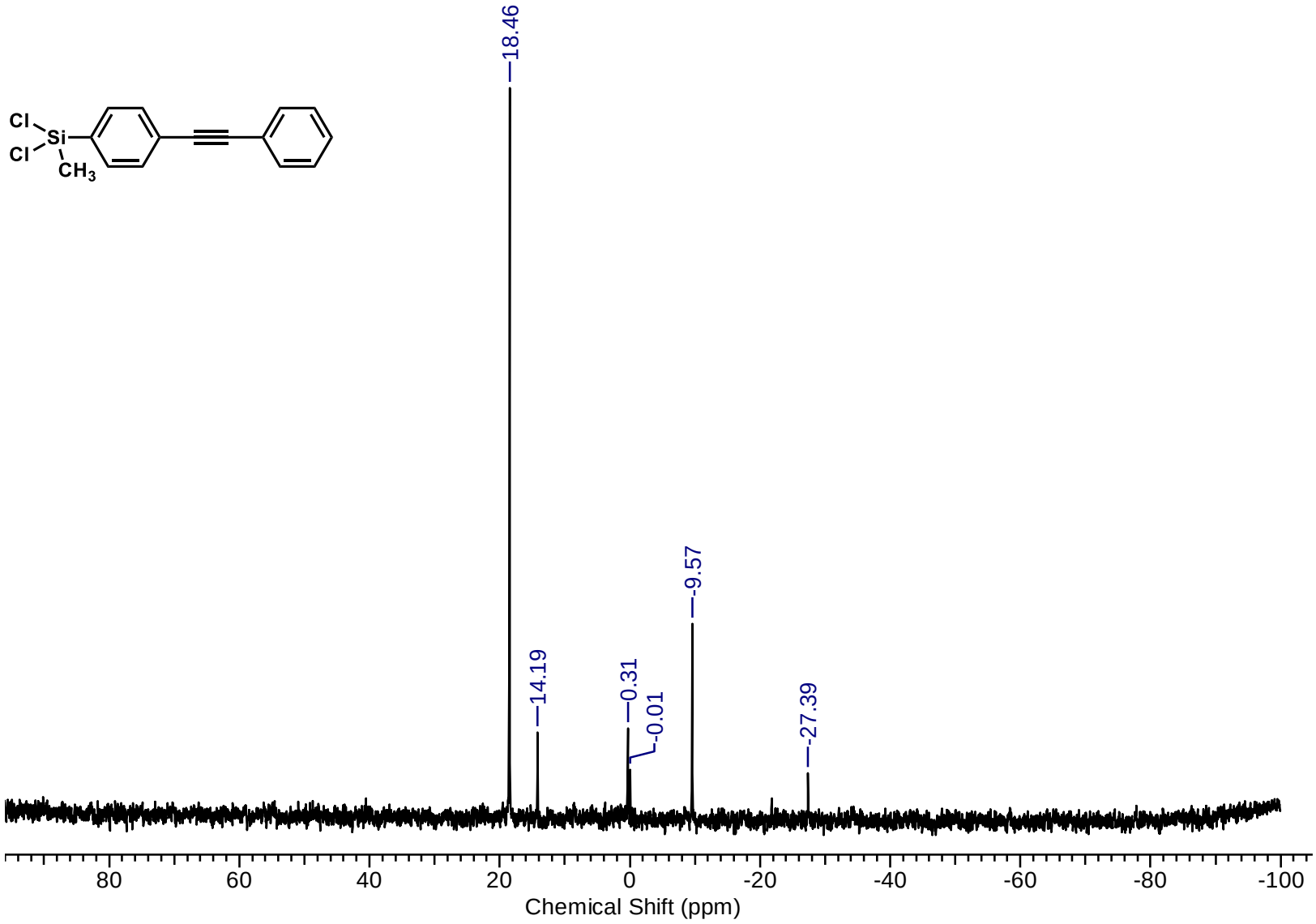


Figure S33 (phenylacetylene)phenyl DDSQ oligomer– ^{1}H NMR

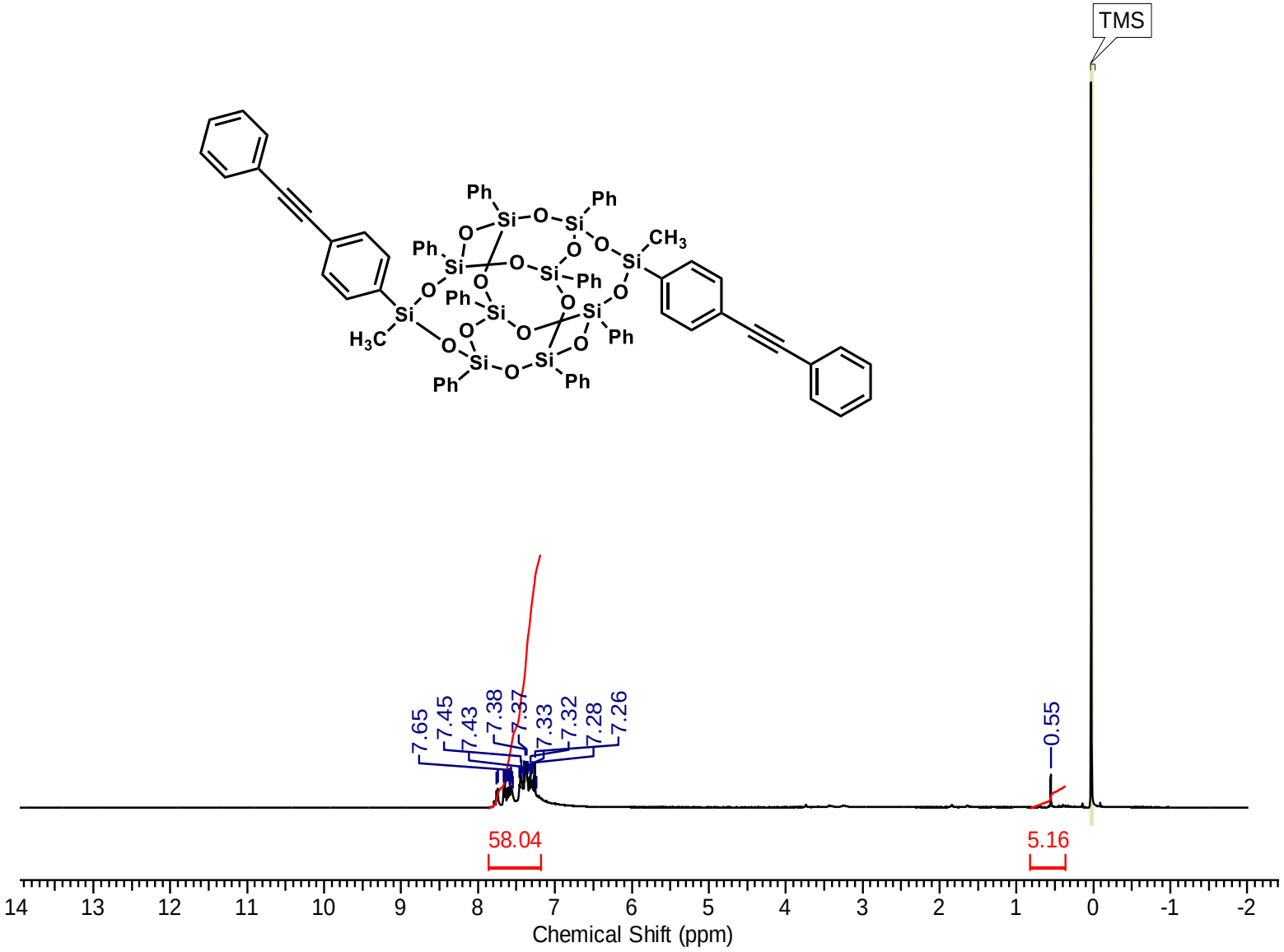


Figure S34 (phenylacetylene)phenyl DDSQ oligomer– ^{13}C NMR

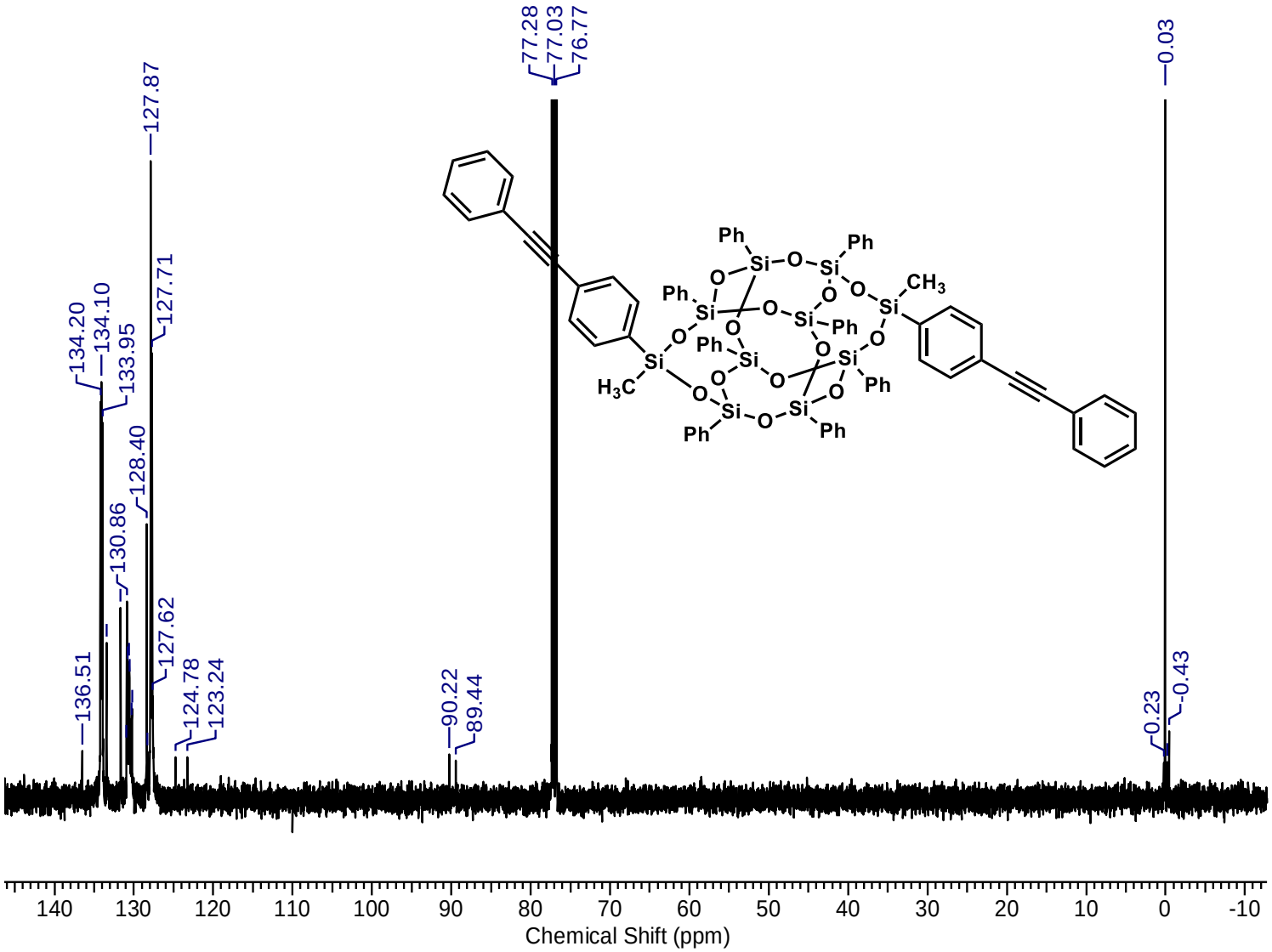


Figure S35 (phenylacetylene)phenyl DDSQ oligomer– ^{29}Si NMR

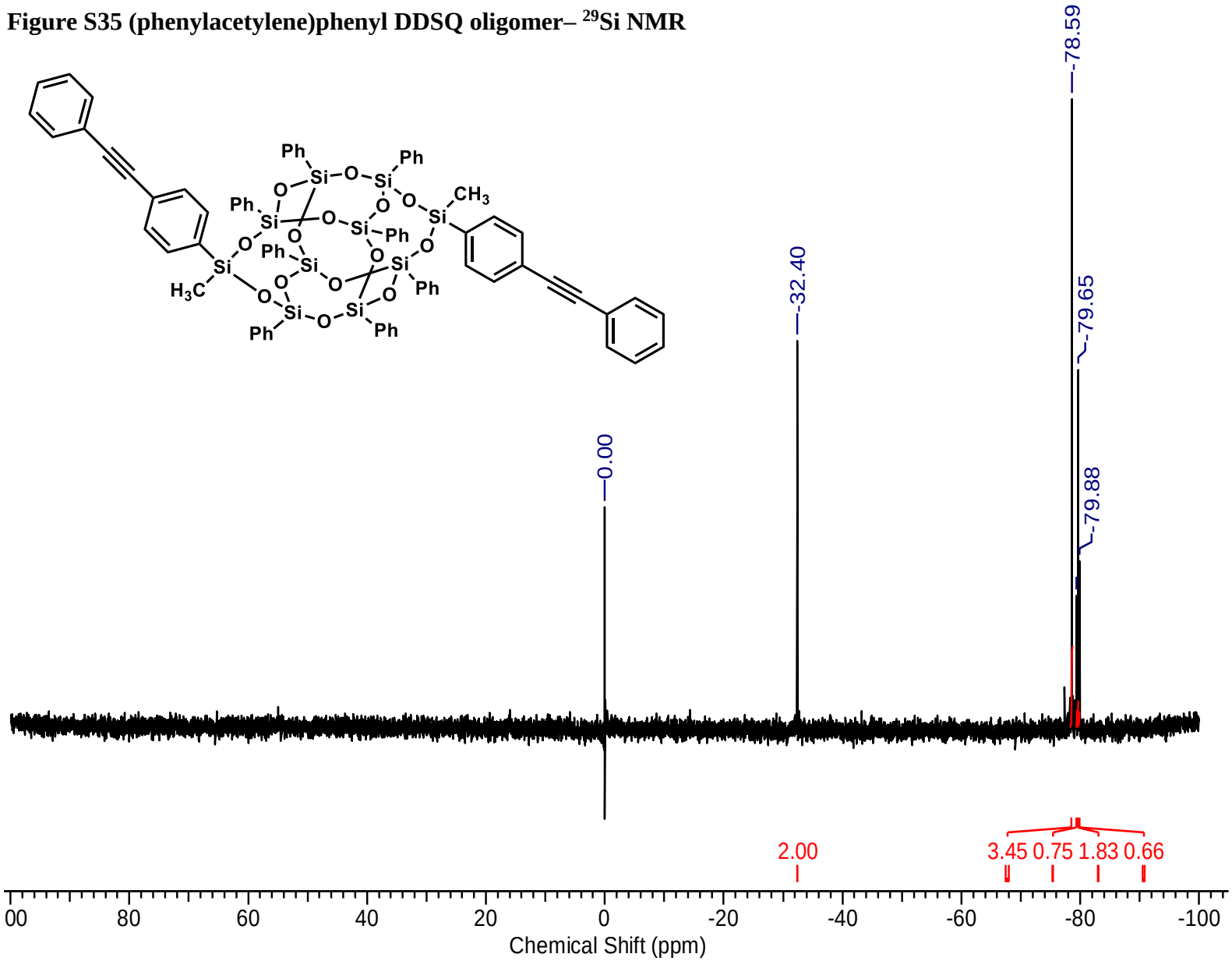


Figure S36 Si-H T7(iBu) –^{1}H NMR

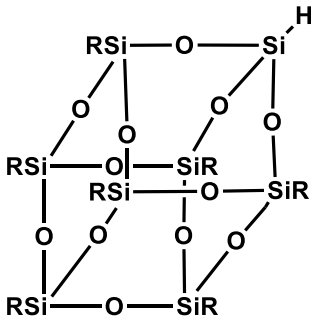


Figure S37 Si- H-T7(iBu) –^{29}Si NMR

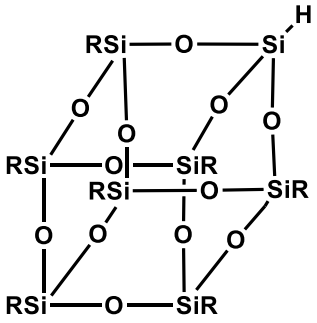


Figure S38 Ph-T7(iBu) –^{1}H NMR

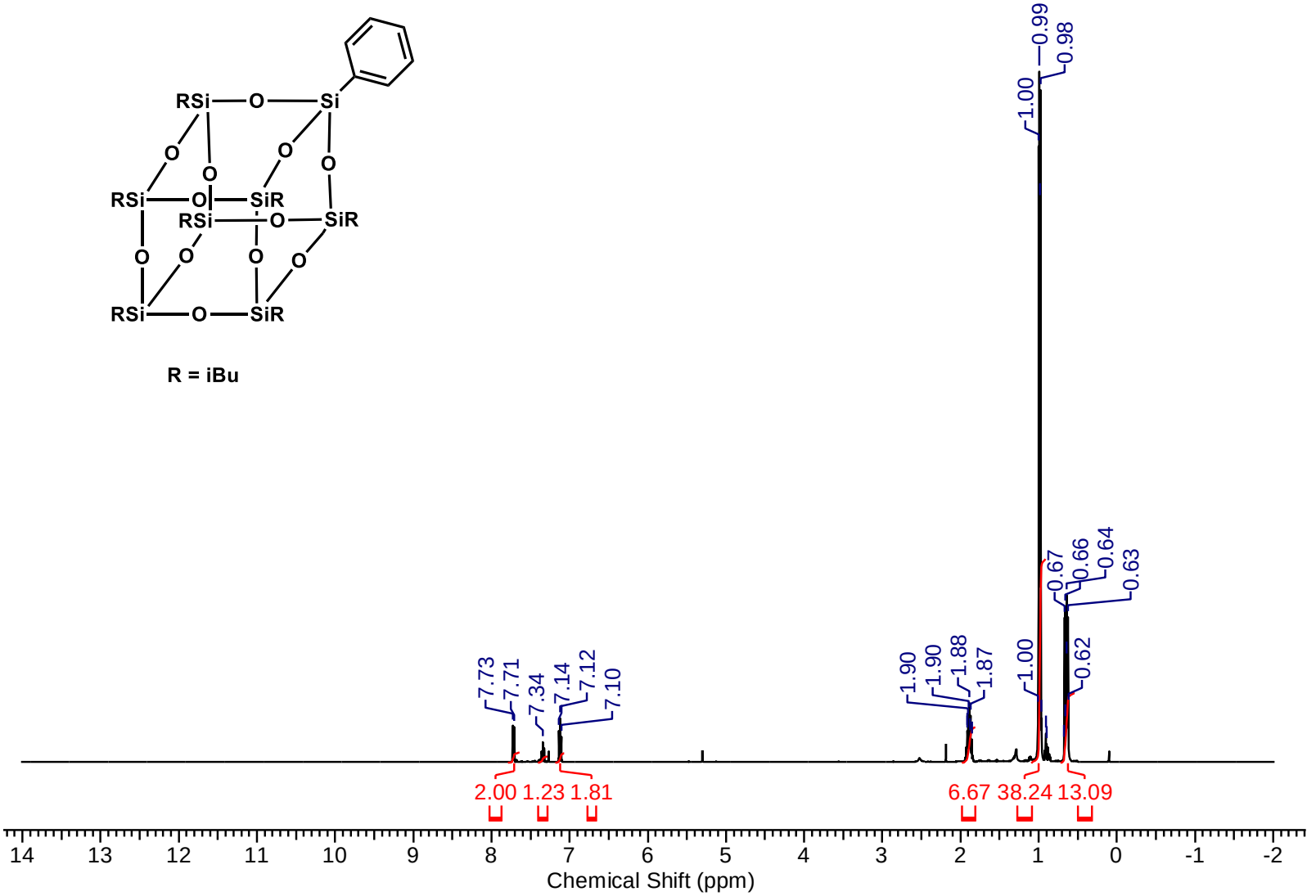
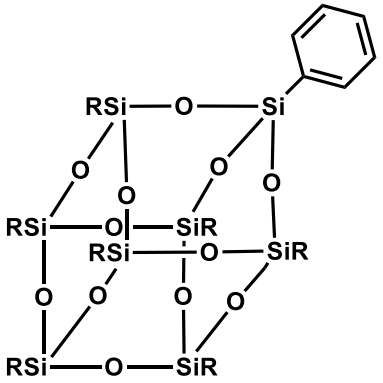


Figure S39 Ph-T7(iBu) –^{29}Si NMR



R = iBu

Figure S40 H-T7(Ph) –^{29}Si NMR

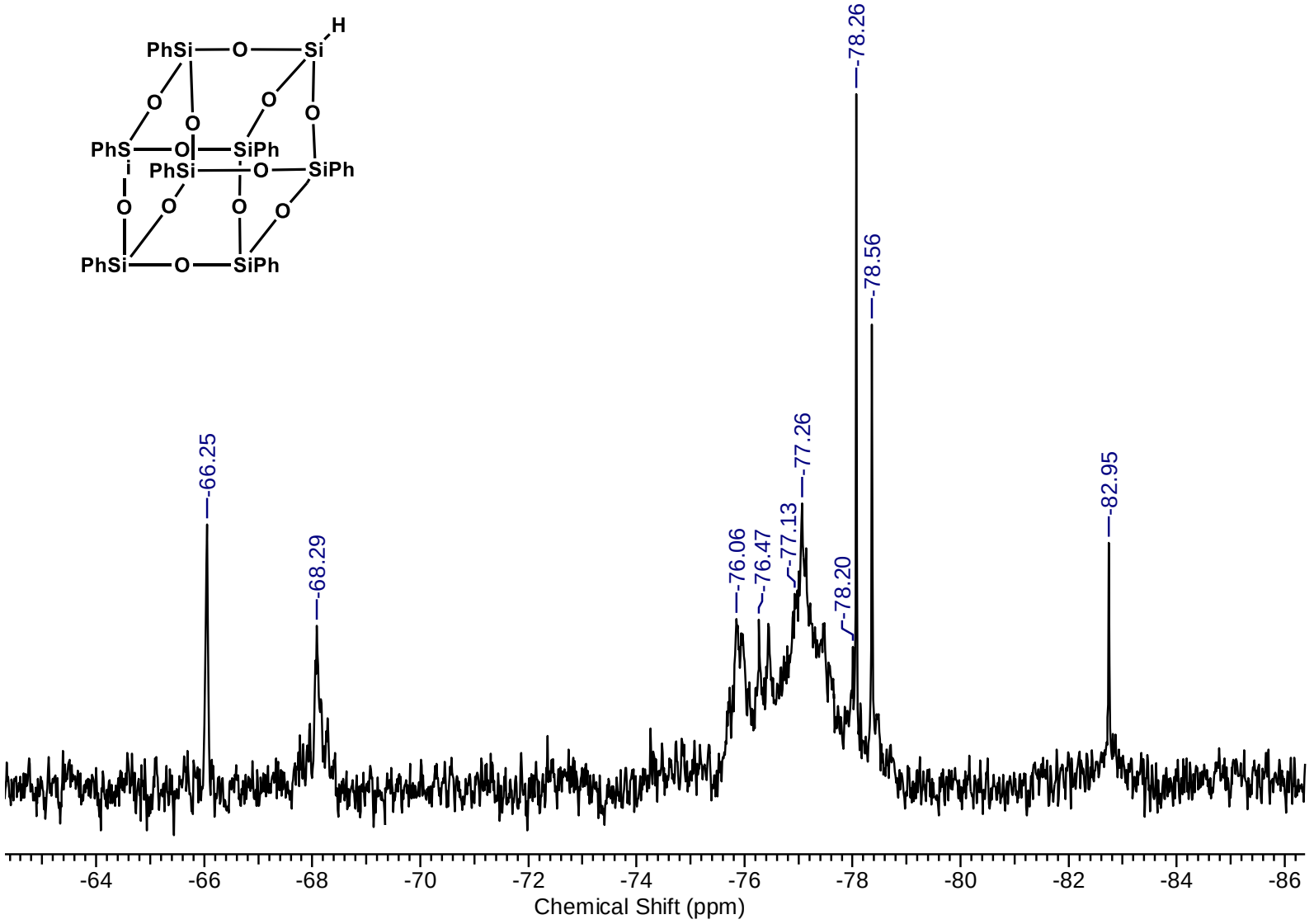


Figure S41 H-T7(Ph) –^{1}H NMR

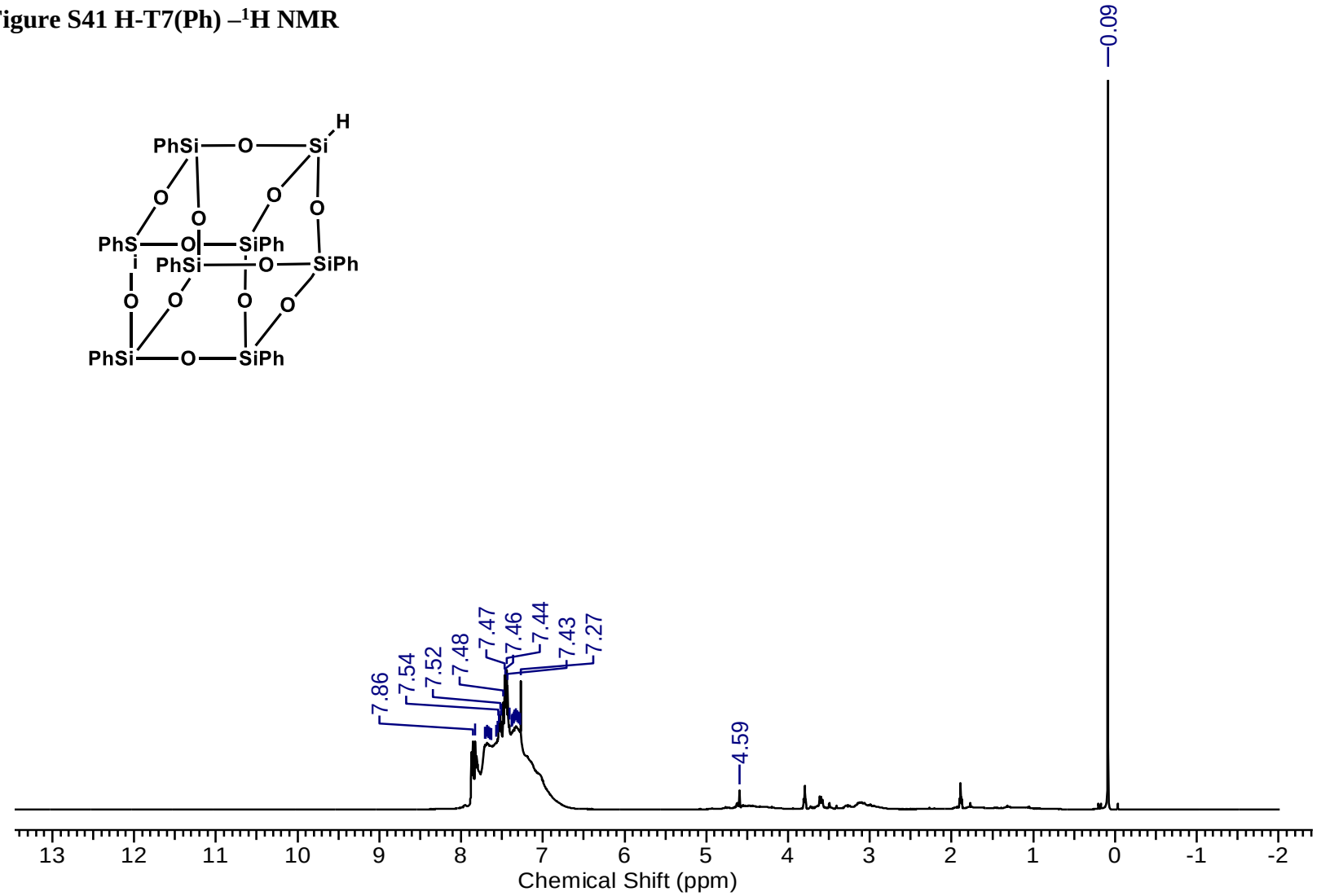


Figure S42 Decomposed DDSQ cage –^{29}Si NMR

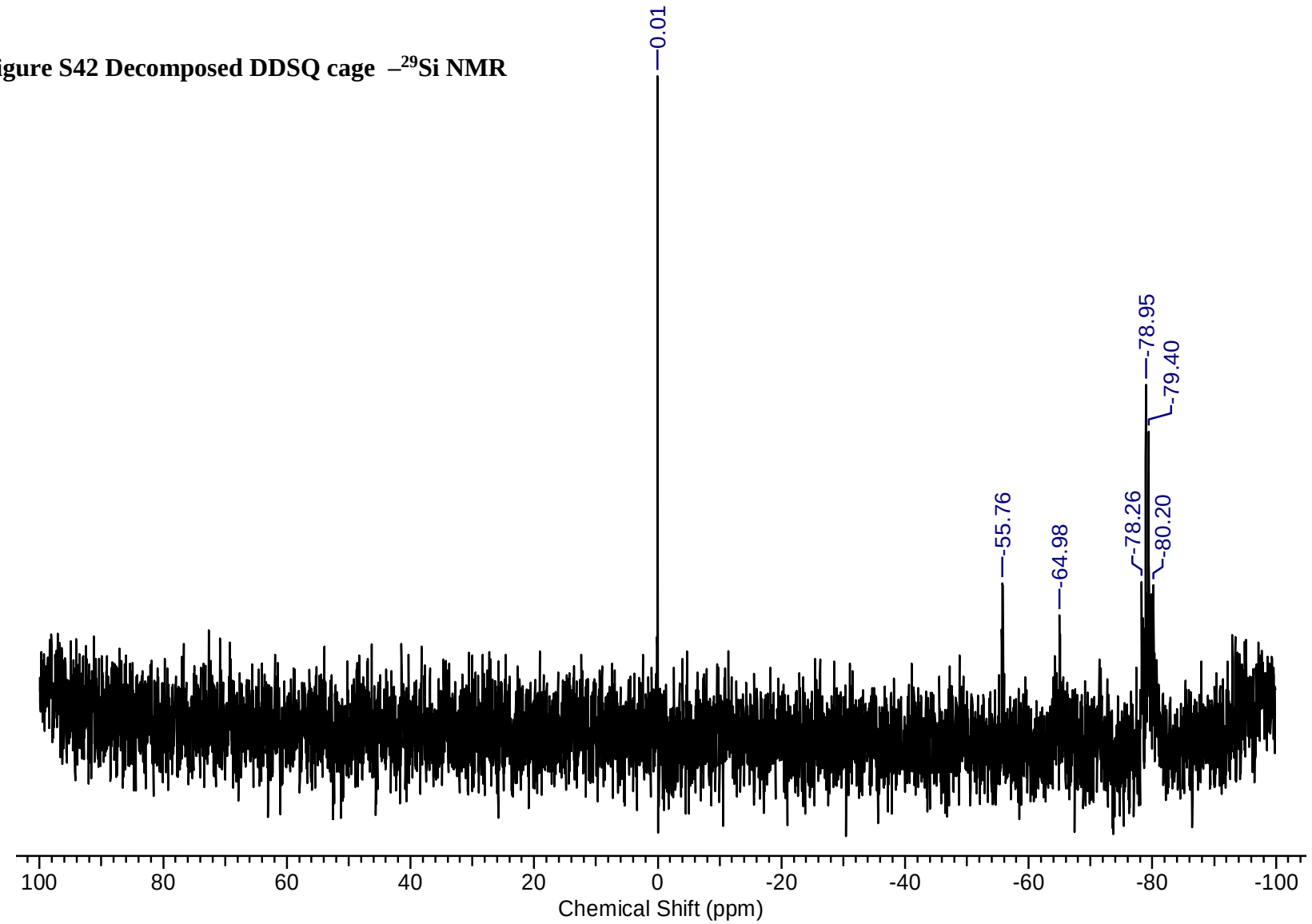


Figure S43 Iodo benzene –^{1}H NMR

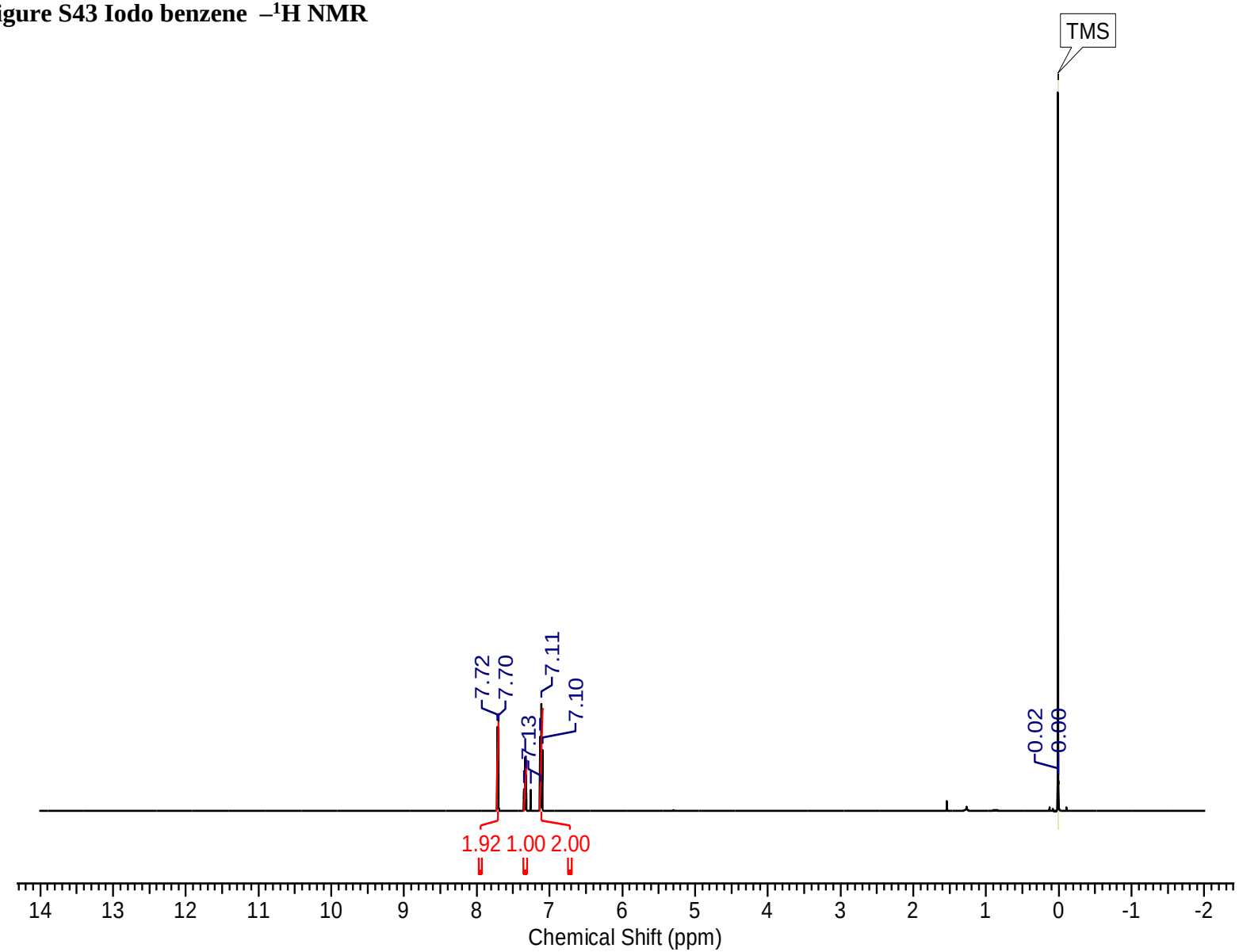


Figure S44 Red-Sil –SS ^{29}Si NMR

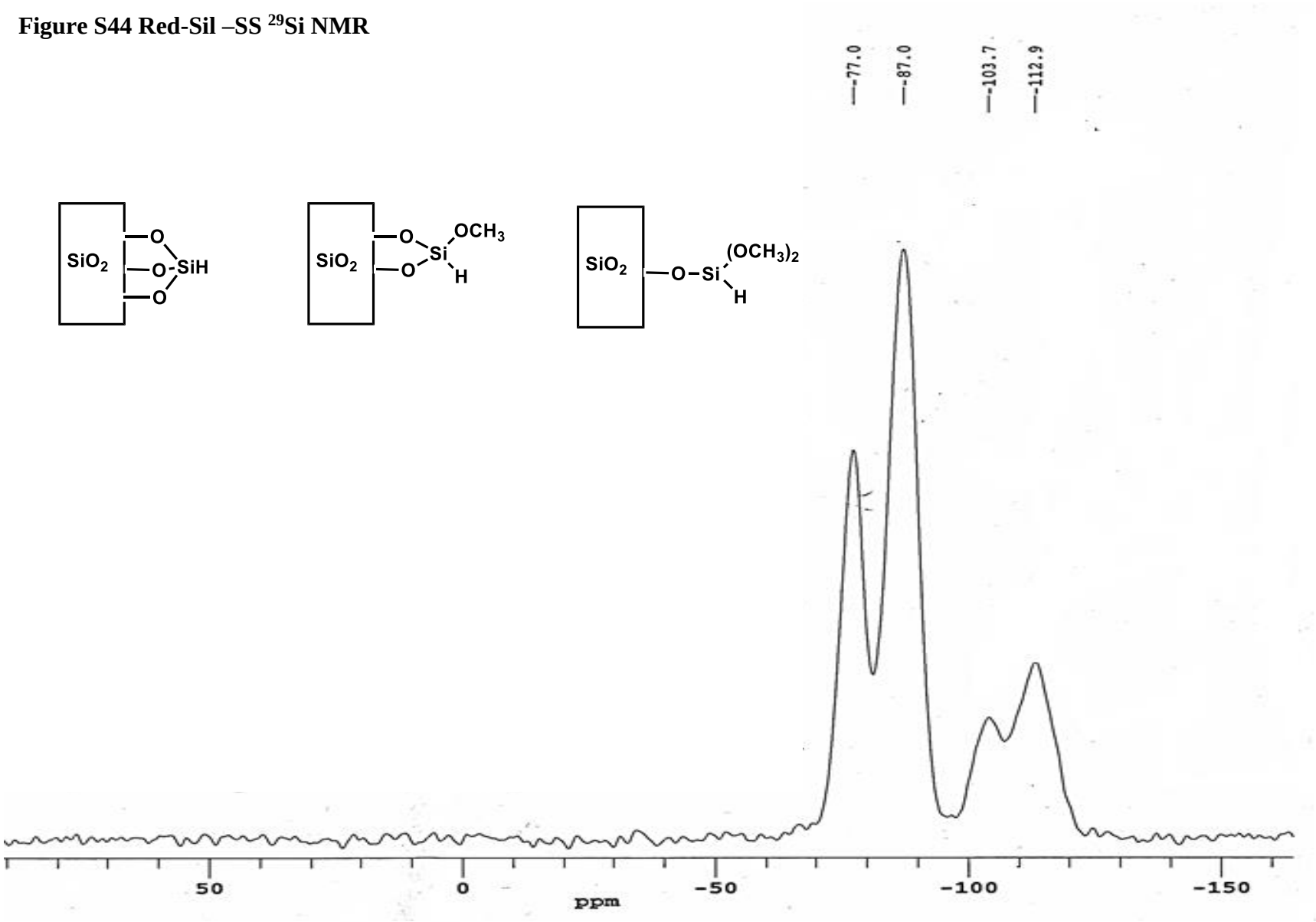


Figure S45 Red-Sil –SS ^{13}C NMR

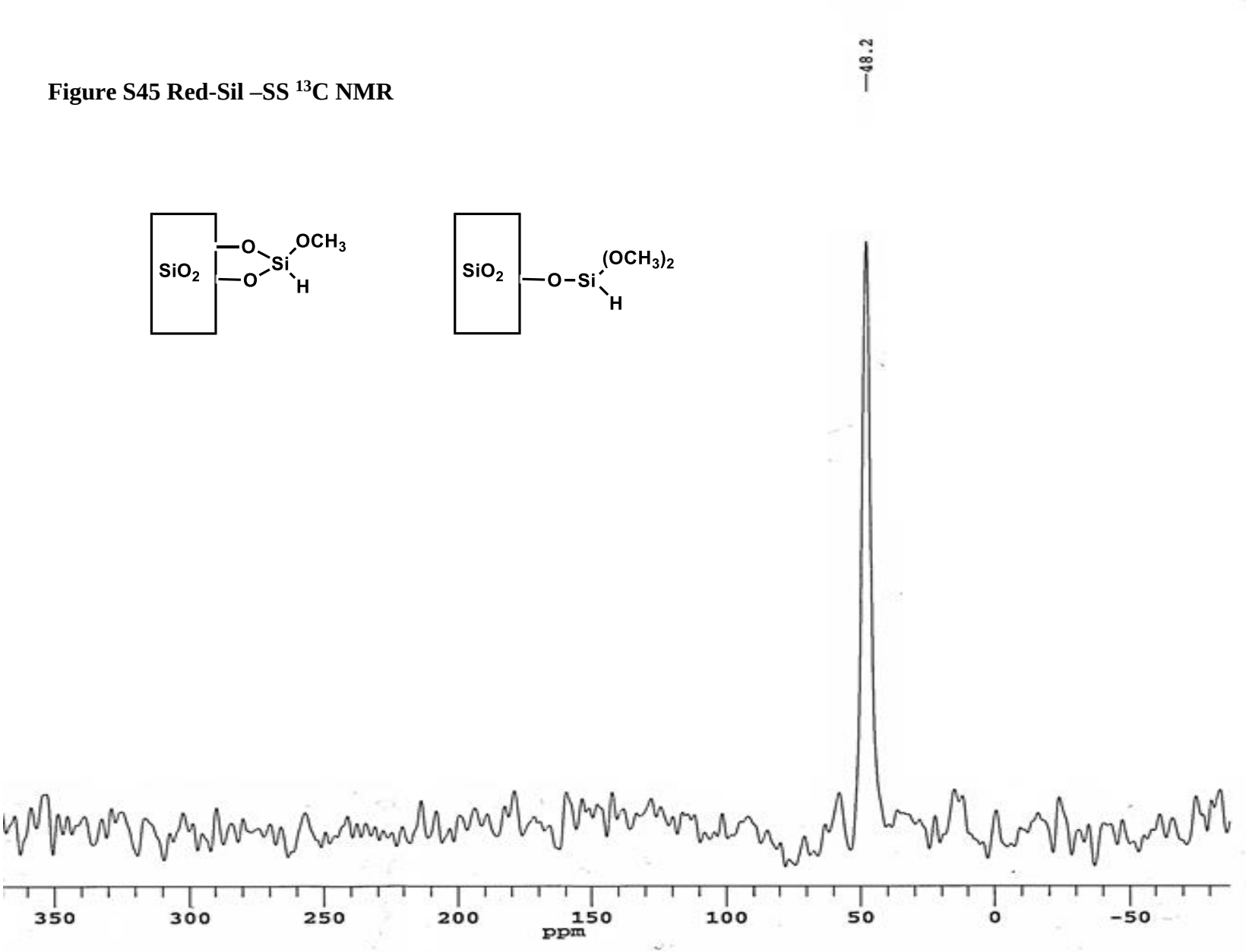


Figure S46 DDSO attached Red-Sil – Method A –SS ^{29}Si NMR

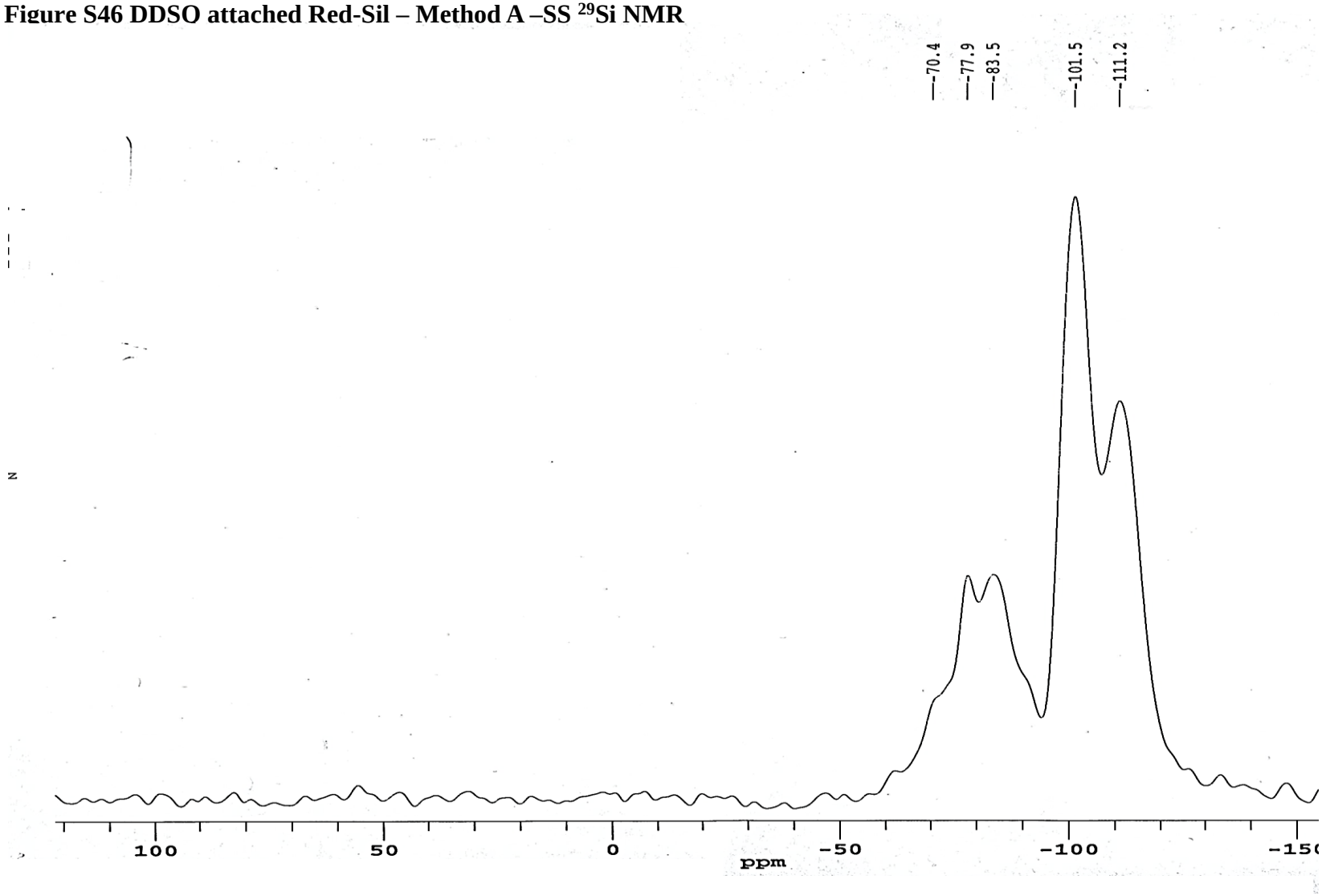


Figure S47 DDSO attached Red-Sil – Method B –SS ^{29}Si NMR

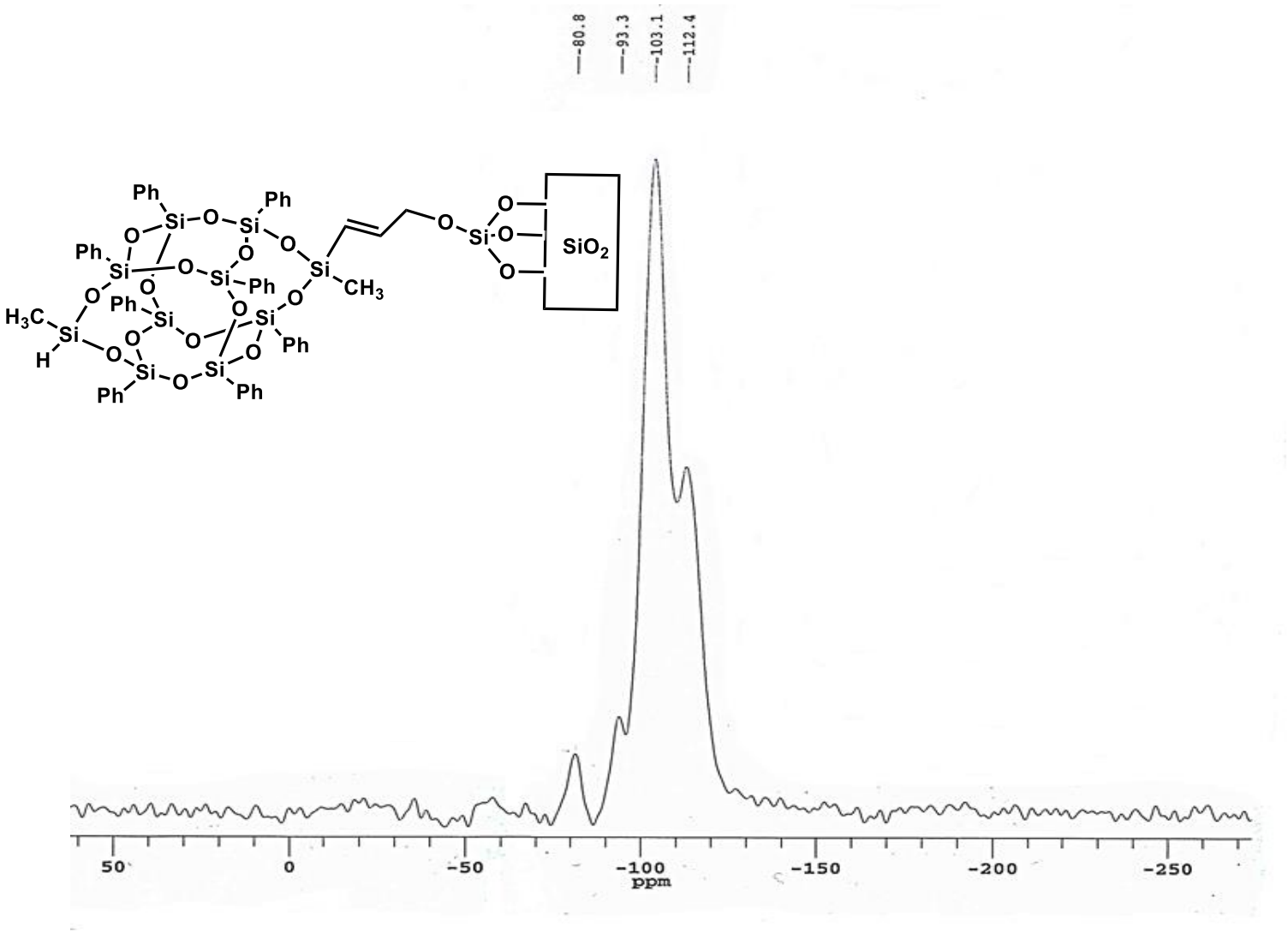


Figure S48 DDSQ attached Red-Sil – Method C –SS ^{29}Si NMR

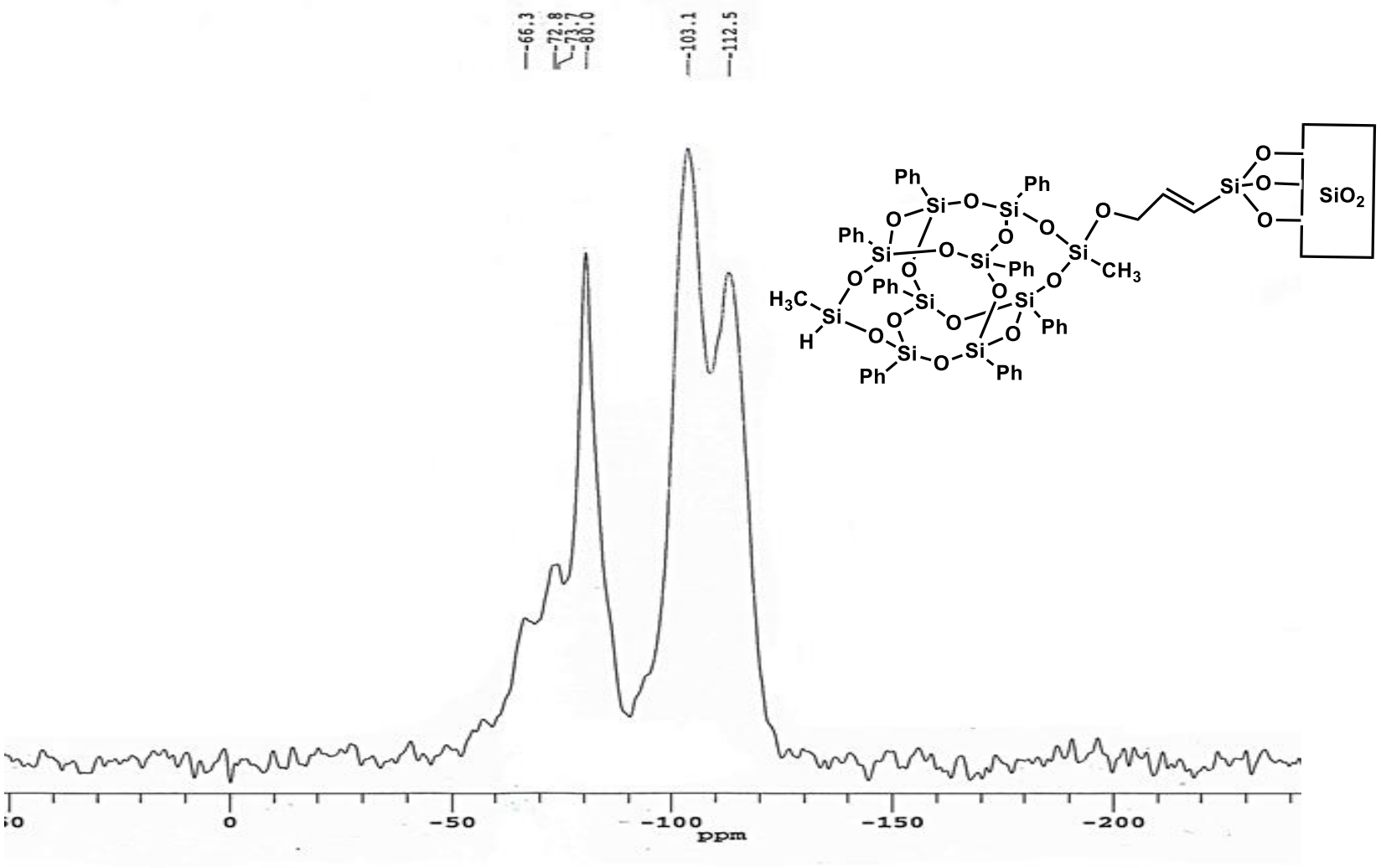


Figure S49 Propargylic alcohol attached

Red-Sil – Method C –SS ^{29}Si NMR

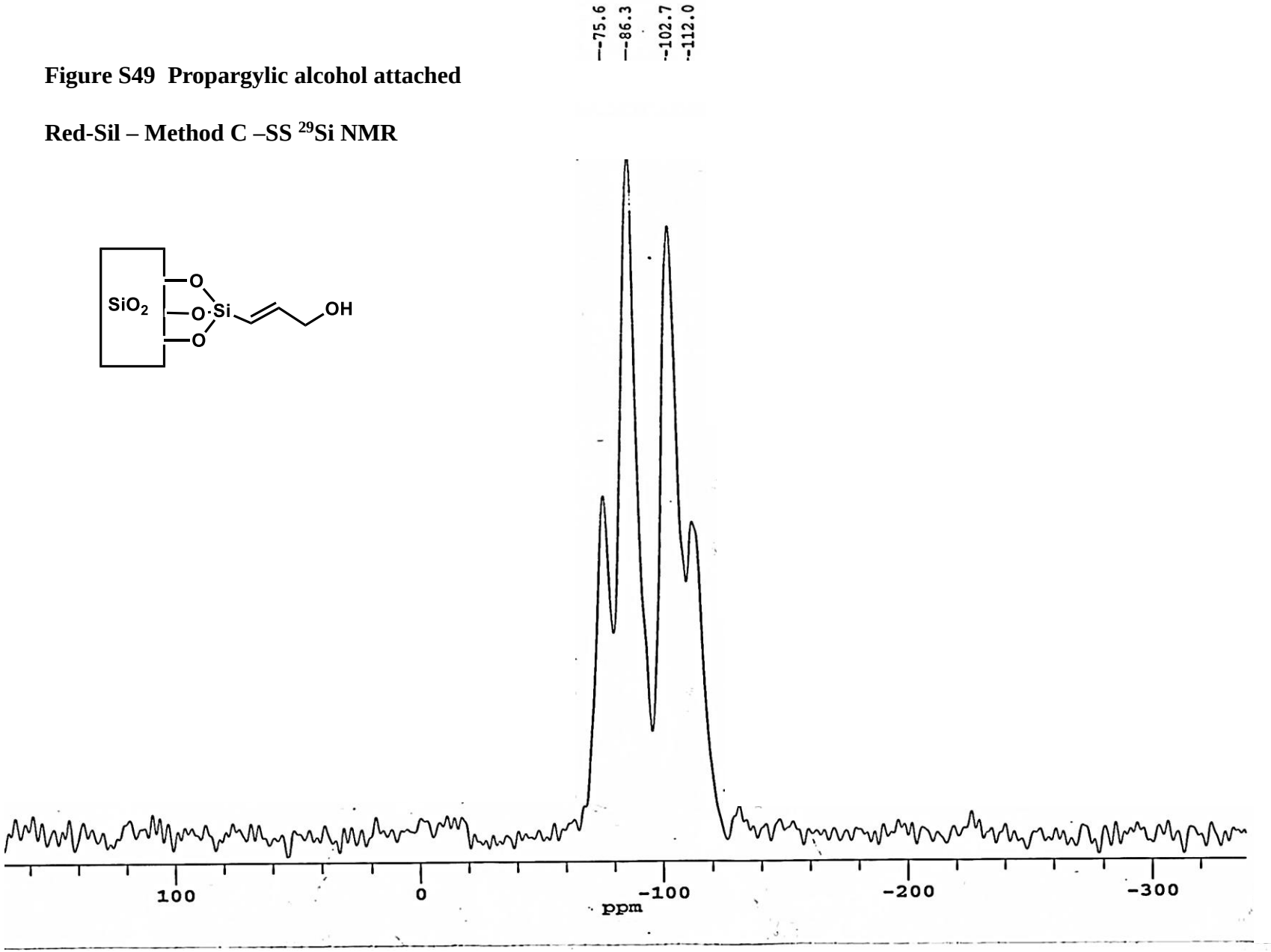


Figure S50 Propargylic alcohol attached Red-Sil – Method C – ^{13}C NMR

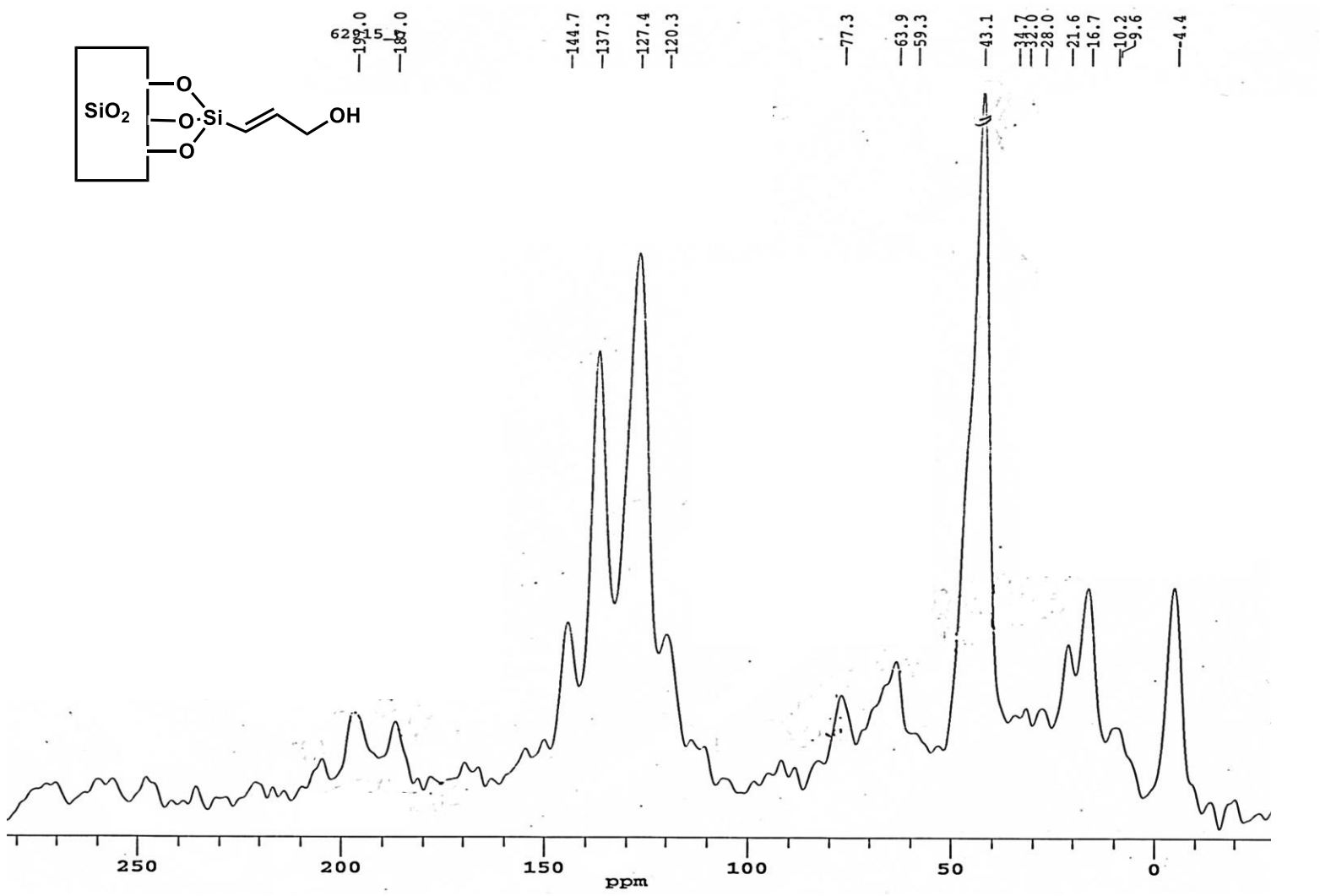
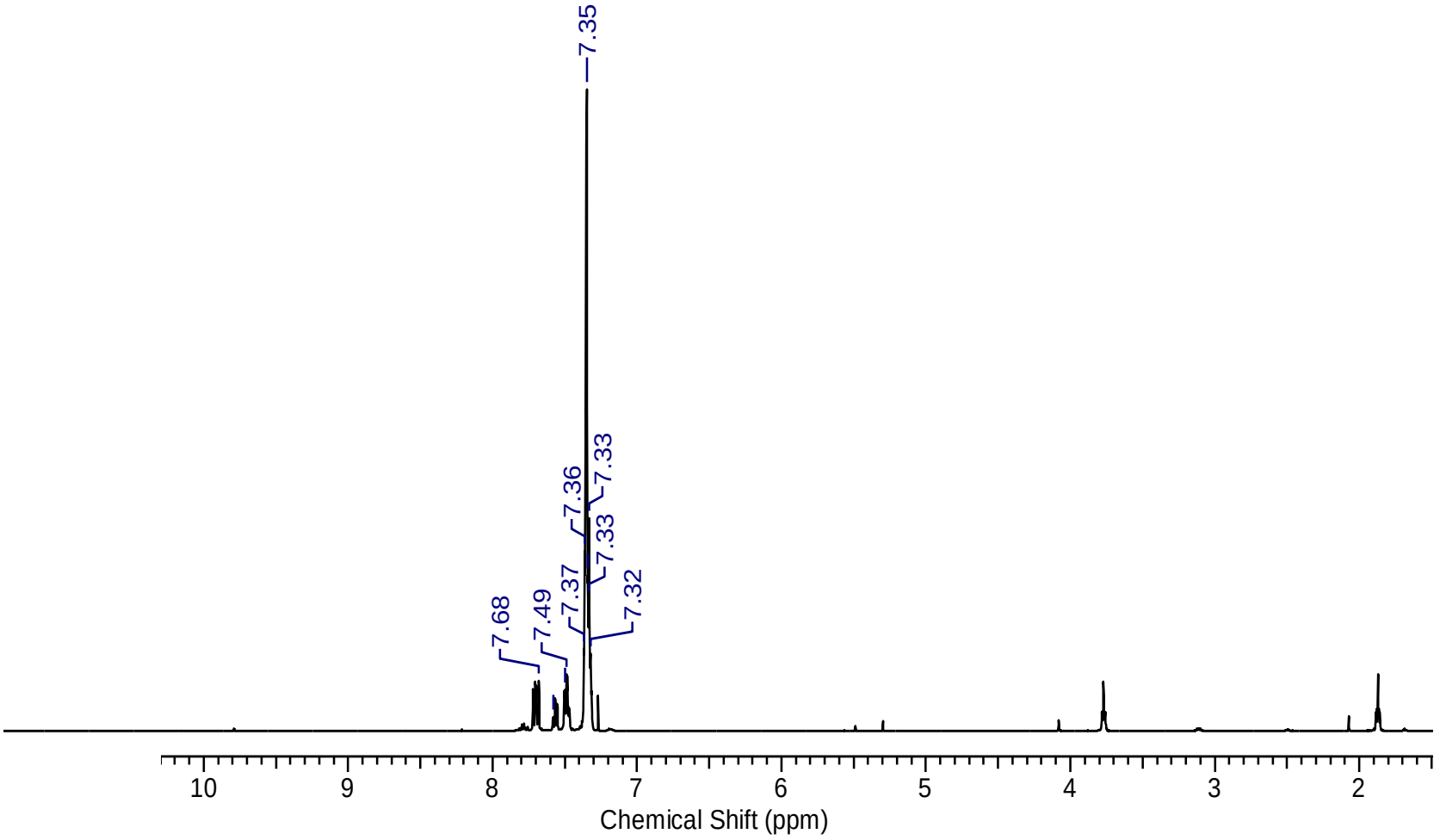


Figure S51 After ozonolysis – ^{1}H NMR



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