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SULFONE REAGENTS IN ORGANIC SYNTHESIS

VI *. SULFONYL- AND SILYL-SUBSTITUTED HYDROCARBONS AS VERSATILE CARBANION PRECURSORS IN ORGANIC SYNTHESIS

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Summary

The basic organometallic chemistry of β-silyl-substituted acetylenic, vinylic and alkyl sulfones has been investigated, with attention being given to metallation, carbometallation and the chemical reduction of carbon–carbon unsaturation. 2-Trimethylsilylvinyl and 2-trimethylsilylalkyl sulfones underwent smooth and stereoselective lithiation with RLi on the carbon α to the sulfonyl group. Carbometallation of vinyl sulfones could be achieved with RMgX or $LiCuR_2$, but acetylenic sulfones carbometallated smoothly only with $LiCuR_2$; with RMgX or RLi, these acetylenes underwent alkyldesulfonylation. The utility in synthesis of these metallo derivatives of sulfonyl-silyl-hydrocarbons is discussed and their value in elaborating carbon skeletons is illustrated for the preparation of alkenes, allenes, carbocycles and stereo-defined vinyl sulfones.

Introduction

The fundamental challenge in organic synthesis requires that the chemist be able to form carbon–carbon and carbon–hydrogen bonds in diverse structural situations, both in highly efficient and in very selective processes. To this end, carbon skeletons are often provided with certain auxiliary functional groups, whose presence activates hydrocarbon groups to selective chemical attack. Two such groups that have proved of great value in synthesis are the sulfonyl (RSO_2) and the silyl (R_3Si) groups. These groups (E) have three electronic effects in common. First, they tend to increase the kinetic and thermodynamic acidity of adjacent C–H bonds (eq. 1), although such an effect is more pronounced with the highly electronegative RSO_2 groups than with

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* For part V see ref. 9.

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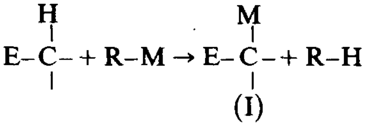
the R_3Si groups [1,2]:



$$\overset{\large H}{\underset{|}{\overset{|}{\text{E–C–}}}} + \text{R–M} \rightarrow \overset{\large M}{\underset{|}{\overset{|}{\text{E–C–}}}} + \text{R–H} \tag{1}$$

(I)

Second, they enhance the tendency of adjacent carbon–carbon unsaturation to undergo carbometallation (eq. 2), apparently because the adduct (II) has negative charge density next to the RSO_2 or R_3Si group (cf. eq. 1). Again, the RSO_2 group is the superior activator for this process [3]:

(II)

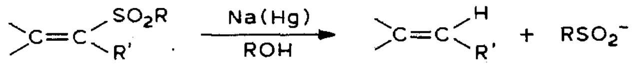
(2)

These general reactions are attractive in synthesis, for intermediates I and II can be alkylated by active alkyl halides to produce new carbon–carbon bonds. In addition, eq. 2 itself involves another carbon–carbon bond formation. Both reactions 1 and 2 are becoming increasingly appreciated in synthesis [3,4].

Third, attachment of RSO_2 or R_3Si directly to acetylenic, vinylic or aryl carbon dramatically increases the tendency of such systems to accept electrons, either from metal reducing agents [5–7] or from organometallics in SET processes [8,9] (eq. 3).

$$\text{E–C}\equiv\text{C–} \xrightarrow{e^-} [\text{E–C}\overset{\bullet}{\equiv}\text{C}]^- \tag{3}$$

In addition to these three common electronic characteristics, what makes sulfonyl and silyl groups particularly useful in synthesis is that they can be readily cleaved from the hydrocarbon skeleton, after they have served their synthetic purpose. The RSO_2 group is often readily cleavable by active metal reduction [10] (eq. 4), and the R_3Si group can be cleaved from *sp* or sp^2 carbon sites by fluoride ion (eq. 5) [11]. Especially noteworthy is the facile synchronous removal of both groups when they are vicinal in alkane derivatives (eq. 6) [12]:



(4)

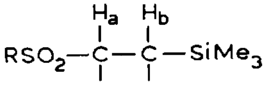
$$\text{–C}\equiv\text{C–SiMe}_3 \xrightarrow[\text{SH}]{F^-} \text{–C}\equiv\text{C–H} + \text{Me}_3\text{SiF} \tag{5}$$

(6)

The foregoing brief survey may be helpful in understanding why the use of organosilanes [13] and sulfones [14] in synthesis has grown so prodigiously. Further accentuating the value of sulfones in preparative chemistry is the wealth of [4 + 2] or

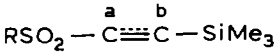
Diels–Alder cycloadditions that vinyl and acetylenic sulfones undergo, leading to six-membered carbocycles [15,16]. When combined with suitable enamines or ynamines, these same vinyl and acetylenic sulfones can also undergo [2 + 2] cycloadditions, thereby producing four-membered carbocycles [17].

For these reasons, the present study sought to examine the basic organometallic chemistry of hydrocarbons having both activating sulfonyl and silyl groups in the same molecule (III and IV). The specific focus of this investigation was the joint effect that vicinal sulfonyl and silyl groups exert on adjacent C–H and C≡C groups



$RSO_2-\overset{H_a}{\underset{|}{\overset{|}{C}}}-\overset{H_b}{\underset{|}{\overset{|}{C}}}-SiMe_3$

(III)



$RSO_2-\overset{a}{C}\equiv\overset{b}{C}-SiMe_3$

(IV)

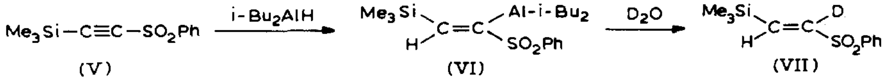
in substrates of types III and IV. The following questions concerning the reactivity of these systems have great pertinence to organic synthesis: (i) What is the net electronic and steric effect of these groups on the ease of metallating III or carbometallating IV? (ii) What is the locoselectivity [18] of proton abstraction in III (viz., H_a or H_b) and what is the regioselectivity for R′M addition to IV (viz., attachment of R′ at C_a or C_b)? (iii) Once a C–M bond is established from metallating III or carbometallating IV, does the resulting C–M bond retain or lose its stereochemical configuration? (iv) In the chemical reduction of IV, either by metal hydride or by active metals, can the stereochemical course be controlled, so as to lead cleanly to either *cis*- or *trans*-reduction?

Finally, as a collateral aspect of this study, a search was made for organometallic processes that could achieve the selective removal of either the RSO_2 or the R_3Si group, rather than the simultaneous removal of both groups, as noted for vicinal sulfonyl-silylalkanes (eq. 6). Such controlled demasking methods would enhance the synthetic utility of sulfonyl-silyl-hydrocarbons as synthons.

Results

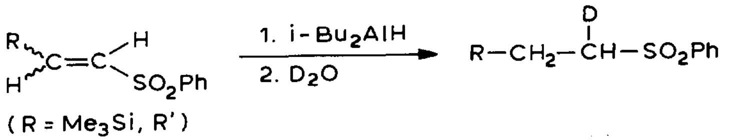
Reduction

The treatment of phenyl trimethylsilylethynyl sulfone (V) with $i\text{-}Bu_2AlH$ led to an exceptionally clean reduction to phenyl (*E*)-2-trimethylsilylvinyl sulfone (VII). Deuterium labeling established that the aluminum precursor was VI (eq. 7):



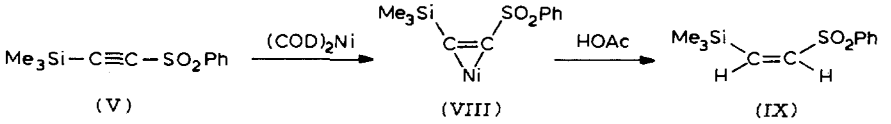
(7)

Such a reduction is quite general for acetylenic and vinylic sulfones, with the $i\text{-}Bu_2Al$ group invariably taking the position α to the sulfonyl group (eq. 8) [19]:



(8)

In a nicely complementary reduction of V, the action of bis(1,5-cyclooctadiene)nickel on V and subsequent treatment with glacial HOAc gave essentially a quantitative yield of phenyl (*Z*)-2-trimethylsilylvinyl sulfone (IX) (eq. 9). From parallel studies in this laboratory [20], such alkynes are known to form firm complexes (VIII), which can be viewed as nickelacyclopropenes and thus undergo protodenickelation to yield the *cis*-alkene *:

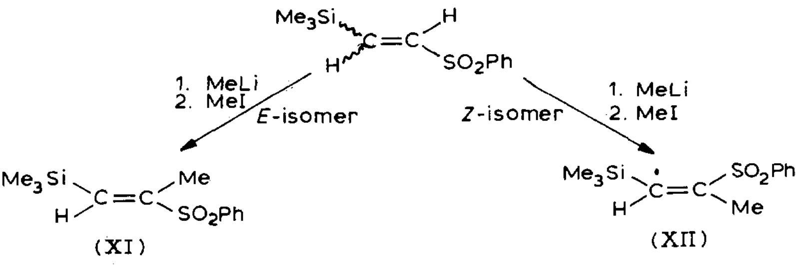


(9)

Such treatment with $(COD)_2Ni$ and then HOAc also achieves the reduction of vinylsulfones VII and IX to form phenyl trimethylsilyethyl sulfone (X), although the stereochemistry is as yet undetermined.

Lithiation

Treatment of either the *E*-sulfone VII or the *Z*-sulfone IX in THF solution with methyllithium at −95°C yielded the corresponding lithio derivative in > 90% yield stereoselectively. That each lithio yielded its own 1-methyl derivative with MeI shows that the lithio compounds retained their configuration (eq. 10).



(10)

The ^1H NMR spectra of XI and XII were distinctly different from each other, and the vinyl and methyl signals of XII showed some broadening, which is indicative of the small coupling characteristic of their *cis* relationship.

Both in the lithiations of VII, IX and that of phenyl 2-trimethylsilylethyl sulfone (X), attack occurred, as far as can be detected, only α to the $PhSO_2$ group **. In fact, both C–H bonds α to the $PhSO_2$ group in X could be lithiated, before any lithiation would occur α to the Me_3Si group. As is illustrated in Scheme 1, such lithiations could be performed simultaneously or in a stepwise manner, thus leading to open-chain (XIII and XIV) or cyclic products (XV) in high yield. Further lithiation of derivatives XIV and XV does occur α to the Me_3Si group, as is evident in the elimination of $PhSO_2Li$ from substrates such as XV.

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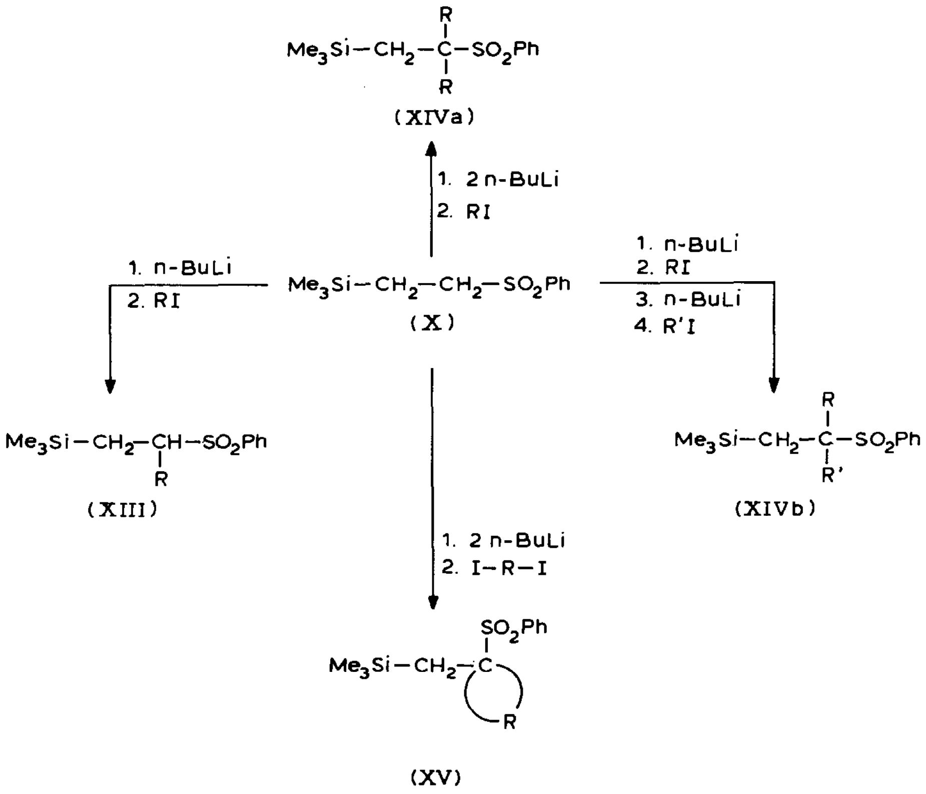
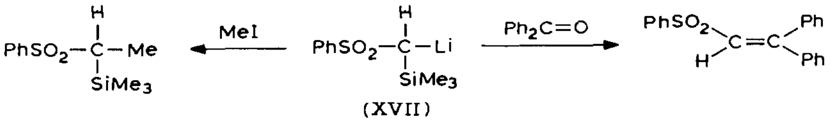
* The catalytic hydrogenation of V to yield either VII or IX has been published; the isolated yields of the pure isomers, after a column chromatographic work-up, are only 48 and 35%, respectively: R.V.C. Carr, R.V. Williams and L.A. Paquette, J. Org. Chem., 48 (1983) 4976.

** The stepwise lithiation of X has been adumbrated in a communication, but the experimental data are not available: P.J. Kocienski, Tetrahedron Lett., (1979) 2649.

SCHEME 1



The lithiation of phenyl trimethylsilylmethyl sulfone (XVI), where the $PhSO_2$ and Me_3Si groups activate the same carbon was particularly facile, and the resulting reagent XVII could be alkylated with MeI or made to undergo the Peterson olefination [21] with Ph_2CO (eq. 11) *:



(11)

Carbometallation

Attempted carbolithiation or carbomagnesiation of phenyl trimethylsilylethynyl sulfone (V) with organolithium (RLi, where R = Ph, Me, t-Bu) or Grignard reagents (RMgCl, where R = 5-hexenyl) led, instead, to an alkyldesulfonylation (XVIII) (eq.

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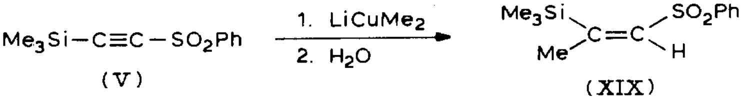
* Contemporaneous with this work, which was published in a thesis (M. Behrooz, Doctoral Dissertation, State University of New York at Binghamton, May, 1983) the reaction of XVII with various carbonyl substrates was published: S.V. Ley and N.S. Simpkins, J. Chem. Soc., Chem. Commun., (1983) 1281.

12):

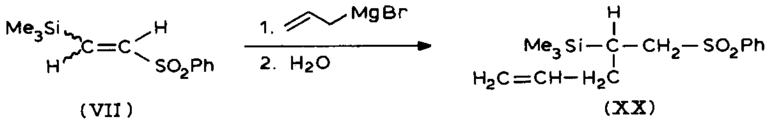
$$\underset{(V)}{Me_3Si{-}C{\equiv}C{-}SO_2Ph} \xrightarrow[-PhSO_2M]{RM} \underset{(XVIII)}{Me_3Si{-}C{\equiv}C{-}R} \qquad (12)$$

In contrast with these failures, it was found that lithium dialkylcuprates ($LiCuR_2$, where R = Me, Ph, allyl) were able to effect a *syn*-carbocupration of V in high yield (eq. 13). Again, the *syn*-stereochemistry of XIX for the case of $LiCuMe_2$ follows from the small, but distinct coupling constant between the vinyl proton and the Me group (the corresponding *trans* H–Me coupling would be virtually zero):



(13)

The phenyl (*E*)-2-trimethylsilylvinyl sulfones could be smoothly carbometallated with Grignard reagents (RMgBr, where R = Ph, allyl) to give adducts XX in high yield (eq. 14):

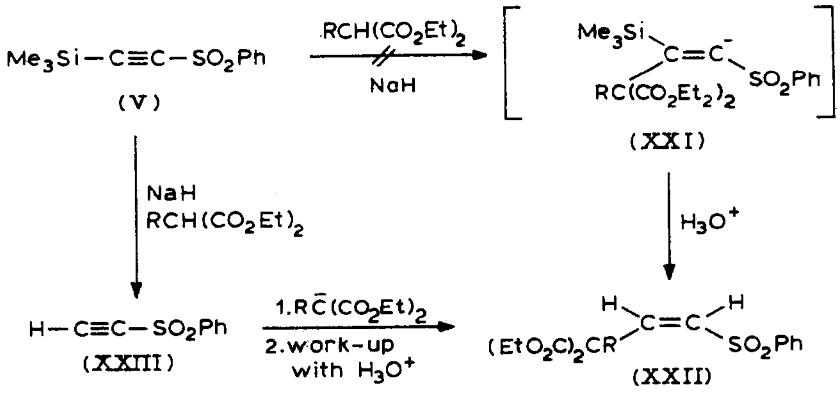


(14)

Of course, organolithium reagents cannot be employed for such a carbometallation, since they preferentially lithiate the α vinylic carbon (cf. eq. 10).

Finally, since organomagnesium and organolithium reagents do not carbometallate X, we were puzzled by a recent report in which various sodium or potassium salts of highly enolic organic compounds were claimed to carbometallate V (Scheme 2) [22]. Also puzzling was the claim that the supposed intermediate XXI had undergone protodesilylation under the mildly acidic conditions used in the work-up. It was further suspicious that such Michael additions could also be brought about by KF. Since we have shown that CsF and oxygen bases rapidly convert X into XXIII, we are forced to reject the claim of the Japanese group that V is the actual reactant.

SCHEME 2



In support of our reinterpretation, we now find that we can start directly with XXIII and obtain excellent yields of XXII in the reaction with NaH and diethyl α-n-butylmalonate. With this finding, our puzzlement over the "unusual Michael reaction" of V and the unusual lability of the Me_3Si group in the putative "intermediate" vanishes: V is in fact not an intermediate in the formation of XXII.

Selective removal of the sulfonyl or the silyl group

As is evident from the reaction depicted in eq. 12, RLi or RMgX reagents can remove the $PhSO_2$ group from V selectively and in high yield. This novel alkyldesulfonylation, as we shall see, is an excellent route to terminal alkynes.

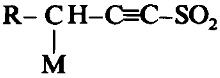
There are several known, selective ways of removing the Me_3Si group from V: mild hydrolysis [23] or the treatment either with silver salts or inorganic fluorides. For the preparation of ethynyl phenyl sulfone (XXIII) from phenylethynyl trimethylsilyl sulfone, either hydrolysis with aqueous K_2CO_3 or attack of CsF under aprotic conditions has proved to be eminently satisfactory.

Discussion

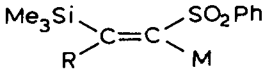
From the foregoing results, it is evident that various carbanionic sites can be generated from acetylenic, vinylic and alkyl sulfones by a combination of metallation and/or carbometallation processes. The carbanionic reagents thereby formed can be outlined thus:

(1) Acetylenic sulfones yield:

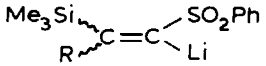
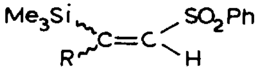
(a) $M{-}C{\equiv}C{-}SO_2Ph$ from $Me_3Si{-}C{\equiv}C{-}SO_2Ph$ and MF, MH;

(b) 

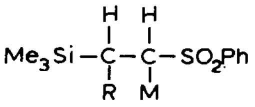
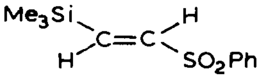
$R{-}\underset{M}{\underset{|}{C}}H{-}C{\equiv}C{-}SO_2Ph$ from $RCH_2{-}C{\equiv}C{-}SO_2Ph$ and R'Li;

(c)  from V and $LiCuR_2$;

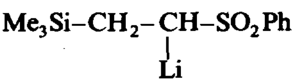
(2) Vinylic sulfones yield:

(a)  from  and R'Li;

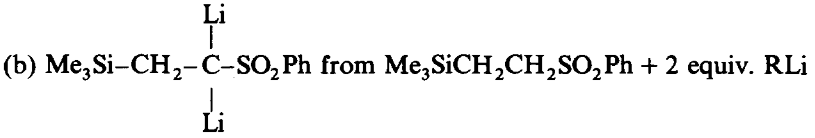
(R = H, R")

(b)  from  and RMgX ;

(3) Alkyl sulfones yield:

(a) 

$Me_3Si{-}CH_2{-}\underset{Li}{\underset{|}{C}}H{-}SO_2Ph$ from $Me_3SiCH_2CH_2SO_2Ph$ + 1 equiv. RLi



$$\text{(b) } Me_3Si{-}CH_2{-}\overset{\displaystyle Li}{\underset{\displaystyle Li}{C}}{-}SO_2Ph \text{ from } Me_3SiCH_2CH_2SO_2Ph + 2 \text{ equiv. RLi}$$

Particularly noteworthy are the great locoselectivity for metallating α to the sulfonyl group, the regioselectivity in carbometallation for alkylating β to the sulfonyl group and the stereochemical stability of the C–M bonds formed in 1(c) and 2(a).

Most of the C–M bonds formed from such sulfones can be stereoselectively alkylated in high yield to yield new carbon–carbon bonds (eq. 15):

$$R{-}M + R'{-}X \rightarrow R{-}R' + MX \qquad (15)$$

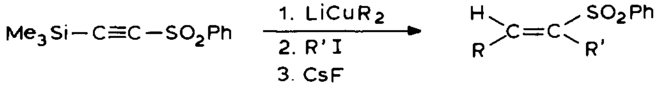
Experience teaches that, for the highest yields of pure alkylation products, the X in R'X should be iodo and that R' should be methyl, ethyl, n-alkyl, allyl or benzyl. Where possible, moderately donor solvents, such as ethers, tertiary amides and polar halides, provide the most satisfactory reaction media. Finally, such alkylations should be conducted at as low a temperature as is practical, in order to minimize dehydrohalogenative side reactions.

By combining the foregoing chemistry with the subsequent removal of either both the $PhSO_2$ and Me_3Si groups, or of just one group, these reactions offer favorable synthetic routes to a number of compound types. The following examples are illustrative of the scope of these reagents:

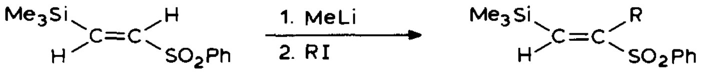
(1) Terminal alkynes:

$$Me_3Si{-}C{\equiv}C{-}SO_2Ph \xrightarrow[\text{2. CsF}]{\text{1. RM (M = Li, MgX)}} H{-}C{\equiv}C{-}R \qquad (16)$$

(2) (*E*)-Vinylsulfones:

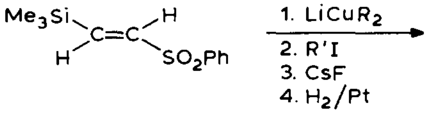


(17)



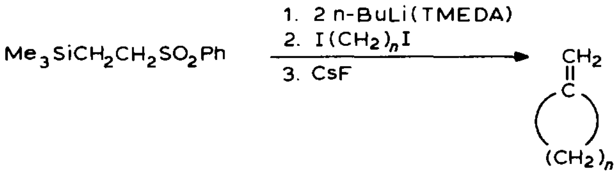
(18)

(3) n-Alkanes



$$R{-}CH_2{-}CH_2{-}R' \qquad (19)$$

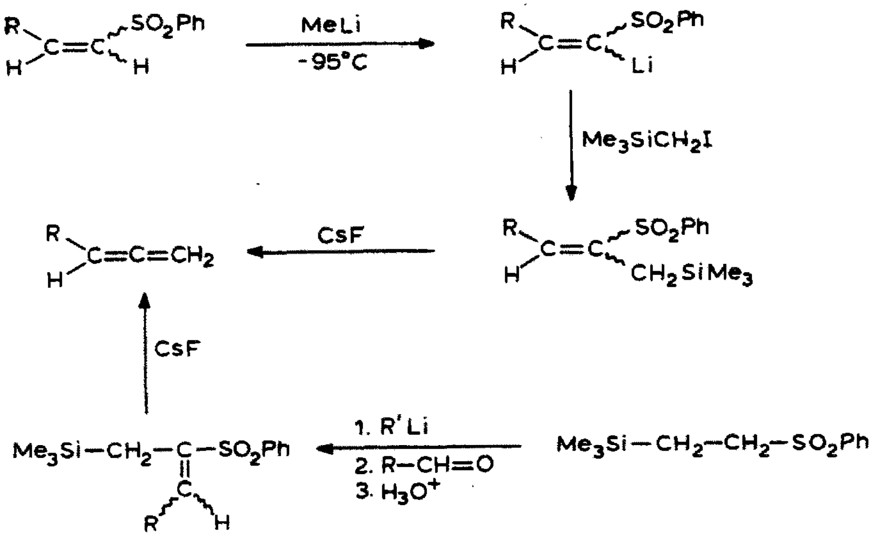
(4) Methylenecycloalkanes:



(20)

(5) Allenes (Scheme 3) [24]:

SCHEME 3



Another dimension to the synthetic utility of these methods is that several yield vinylic sulfones of defined stereochemistry, such as those produced in eqs. 17 and 18. These sulfones thus can function as useful dienophiles or cycloaddends in [4 + 2] or [2 + 2] cycloaddition processes and thus yield substituted cycloalkanes [15–17].

Although many research groups have already contributed various useful methods based upon sulfone and silane chemistry, activity in this field shows little sign of abating.

Experimental

General techniques

Most manipulations involved in the preparation, storage and transfer of organometallic substrates and their reaction products were conducted under an atmosphere of dry oxygen-free nitrogen; those operations involving organonickel compounds were carried out under argon. Techniques followed in the preparation, handling and analysis of organoaluminum alkyls and hydrides have already been described [25].

All solvents were purified by standard procedures before distillation for use. Hexanes, heptanes and toluene were first extracted thoroughly with concentrated sulfuric acid to remove olefins and thiophenes. Then the solvents were successively washed with water, potassium or sodium hydroxides and brine before drying over anhydrous magnesium sulfate. Under an inert atmosphere, the solvents were refluxed over freshly ground calcium hydride overnight. Finally, they were distilled into the distillation apparatus and heated at reflux over sodium for several hours.

Tetrahydrofuran (THF) and other ethers were purified first by filtration through an activated alumina column (under an inert atmosphere) to remove peroxides. Small aliquots of the solvents were then tested for peroxides prior to refluxing over and distilling from $LiAlH_4$ or sodium-potassium alloy.

Melting points were determined in capillary tubes placed in the oil bath of a Thomas-Hoover apparatus and are uncorrected. The ^1H NMR spectra were measured with a Varian spectrometer, model EM360, and the values of signals are reported on the δ-scale, downfield from TMS, while the coupling constants are given in hertz units. Infrared spectra were recorded with Perkin-Elmer spectrometers, models 238B and 457. Mass spectra were obtained either with a Dupont spectrometer, model 21-491B, or an MS 902/CIS 2 instrument that was provided with a VG Datasystem computerized recorder, model 2040. Gas chromatographic analyses were performed on an F&M dual-column instrument having temperature-programming, thermal conductivity detection and 12-ft columns packed with Chromosorb W which were coated with UC-W98. Elemental analyses were carried out by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y. and by Atlantic Microlab, Inc., Atlanta, Georgia.

Preparation of starting materials

Organometallics. Commercially available n-butyllithium and t-butyllithium in hydrocarbon solution and methyllithium in ethereal solution were employed, after samples were analyzed by standard techniques. Diisobutylaluminum hydride (Texas Alkyls) was purified, distilled and analyzed by standard, published procedures. Bis(1,5-cyclooctadiene)nickel was synthesized by a published modification of a known procedure [26].

Phenyllithium, allylmagnesium bromide and 5-hexenylmagnesium chloride were prepared in the usual manner from the purified halides in anhydrous diethyl ether. Aliquots were hydrolyzed and titrated with standard acid, in order to determine the concentration of the organometallic [25].

Organosilicon reagents

(a) Phenyl trimethylsilylethynyl sulfones (V). In a modification of a known procedure [23], freshly distilled benzenesulfonyl chloride (19.3 g, 0.11 mol) was added to freshly sublimed and powdered aluminum chloride (14.7 g, 0.11 mol) in 100 ml of dichloromethane. (N.B.: The $AlCl_3$ must be of a good quality, with little sign of having absorbed any moisture.) The mixture was maintained at room temperature for 14 min, then filtered quickly through glass wool under N_2 and added during 30 min to an ice-cold solution of bis(trimethylsilyl)acetylene (17.0 g, 0.1 mol) in 100 ml of dichloromethane. The reaction mixture was stirred under a nitrogen atmosphere at room temperature for 12 h and then added to an aqueous slurry of 0.1 *N* HCl and crushed ice. The organic layer was separated, washed twice with water, dried ($MgSO_4$) and then distilled. The unreacted benzenesulfonyl chloride was removed below 130°C at 0.6 mmHg. The dark distillation residue was washed with n-pentane and crystallized to give pure phenyl trimethylsilylethynyl sulfone (17.9 g, 75%), m.p. 65–66°C. The NMR spectrum agreed with published data [23].

(b) Phenyl (E)-2-trimethylsilylvinyl sulfone (VII). In a modification of a known procedure [27] a glass pressure bottle, which was maintained under a nitrogen atmosphere and equipped both with a magnetic stirrer and a pressure controller, was charged with 50 mg cupric chloride, 15.0 ml of dichloromethane, 2.0 g of acetonitrile, 5.0 g (50 mmol) of trimethyl(vinyl)silane and 8.82 g (50 mmol) of freshly distilled benzenesulfonyl chloride. The sealed reaction mixture was allowed to react over a

10-h period at 130°C. After cooling, the reaction product was then washed twice with both aqueous 2 *N* HCl and an aqueous solution of disodium ethylenediaminetetraacetate and finally dried ($MgSO_4$). Evaporation of the solvent gave a crude material which was subsequently distilled to yield pure 1-benzenesulfonyl-2-chloro-2-trimethylsilylethane (9.67 g, 70%), b.p. 150°C at 0.7 mmHg. The ^1H NMR spectrum agreed with that reported previously [27].

For dehydrochlorination of this intermediate, 8.29 g (30 mmol) were dissolved in 200 ml of benzene and 10 ml of triethylamine. After 48 h at 25°C the reaction mixture was washed with aqueous HCl, neutralized, dried and freed of benzene to give a crude liquid. Upon distillation at reduced pressure the unreacted material was removed and the residue was crystallized from n-pentane to give 4.35 g (60%) of phenyl (*E*)-2-trimethylsilylvinyl sulfone, m.p. 60–62°C. The ^1H NMR spectrum agreed with that of a known sample [27].

(c) Phenyl 2-trimethylsilylethyl sulfone (X). To 50 ml of THF containing 30 mmol of TMEDA and cooled to −78°C were added, first, 4.68 g (30 mmol) of methyl phenyl sulfone and after 15 min, 15 ml of 2.1 molar n-butyllithium in hexane. After the addition of n-butyllithium was complete and the reaction mixture allowed to come to −40°C, 3.92 g (32 mmol) of chloromethyl(trimethyl)silane was added. The mixture was hydrolyzed with aqueous 2 *N* HCl and the organic layer extracted into ether. The dried ethereal extract was evaporated to give 95% of essentially pure product. Recrystallization from an ether/pentane pair gave an 82% yield, m.p. 50–51°C. Spectral data: ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.7–1.1 (m, 2H), 2.8–3.2 (m, 2H), 7.3–7.9 (m, 5H); IR (neat) 3030, 2960, 1450, 1200, 1020, 850, 750 and 680 cm^{-1}. Anal. Found: C, 54.73; H, 7.53. $C_{11}H_{18}O_2SSi$ calcd.: C, 54.54; H, 7.53% [28].

(d) Methyl phenyl sulfone. In a 500-ml, 2-necked round-bottomed flask equipped with a magnetic stirrer, a pressure-equalizing dropping funnel and a reflux condenser cooled with ice water were added at 0°C a solution of 6.20 g (50 mmol) of thioanisole and 25 ml of glacial acetic acid. Then 35 ml of 30% hydrogen peroxide were added dropwise over a period of 30 min. After the addition was complete, stirring was continued while the suspension was heated at reflux for 2 h. The reaction mixture was cooled and extracted with ether. The ethereal extracts were washed with aqueous sodium bicarbonate solution and then the organic part was tested for the presence of peroxides. After the complete removal of peroxides by washing with portions of aqueous ferrous sulfate solution and water, the organic solution was dried and concentrated to give the crude product. Crystallization of the product from n-pentane provided the pure product in 85% yield, m.p. 83-85°C, identified as methyl phenyl sulfone. Spectral data: ^1H NMR ($CDCl_3$) δ 3.1 (s, 3H), 7.4–8.0 (m, 5H); IR (neat) 3020, 2930, 1450, 1280, 1150, 750, and 680 cm^{-1}.

(e) Phenyl trimethylsilylmethyl sulfone (XVI). To a stirred solution of 5.09 g (32 mmol) of methyl phenyl sulfone dissolved in 50 ml of THF containing 30 mmol of TMEDA and maintained at −78°C was added over 5 min a solution of 15.2 ml of 2.1 molar n-butyllithium in hexane. After the addition was complete, the reaction mixture was allowed to come to −40°C over 2 h. Chloro(trimethyl)silane (3.4 g, 32 mmol) was added and after 15 min the cooling bath was removed and the reaction allowed to continue for 24 h. After hydrolysis and work-up as in section c, a semi-solid crude product was obtained which was recrystallized from an ether/pentane pair. As a result, 6.5 g (90%) of phenyl trimethylsilylmethyl sulfone, m.p. 77–79°C, was obtained. Spectral data: ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 2.6 (s, 2H),

7.2–8.0 (m, 5H); IR (neat) 3040, 2960, 1450, 1300, 1085, 1000, 850, 690 and 600 cm^{-1}. Anal. Found: C, 52.97; H, 7.44. $C_{10}H_{16}O_2SSi$ calcd.: C, 52.63; H, 7.0%.

Stereochemical reductions of phenyl trimethylsilylethynyl sulfone (V)

(a) Phenyl (E)-2-trimethylsilylvinyl sulfone (VII). A solution of 600 mg (2.5 mmol) of V dissolved in 30 ml of toluene and cooled to −20°C was treated dropwise with a solution of 600 mg (2.5 mmol) of i-Bu_2AlH in 25 ml of toluene. After a 2-h stirring period the reaction mixture was cautiously treated with 2 ml of methanol. Thereupon water and ethyl ether were added, and the organic layer was separated by filtration and dried with anhydrous $MgSO_4$. Solvent removal gave a residue of pure VII (NMR) in 95% yield. Crystallization from pentane gave 78% of VII, m.p. 61–62°C [27].

When an identical i-Bu_2AlH reduction was conducted and the reaction mixture quenched with D_2O, the vinyl signal of the proton α to the $PhSO_2$ group was absent from the ^1H NMR spectrum.

(b) Phenyl (Z)-2-trimethylsilylvinyl sulfone (IX). A solution of 2.79 g (11.7 mmol) of V and 3.22 g (12 mmol) of bis(1,5-cyclooctadiene)nickel in 50 ml of THF was allowed to stand for 6 h at 25°C. Then 10 ml of glacial acetic acid were added and the mixture stirred for a further 15 h. Work-up with water and ether, separation of the organic layer and washing it with aqueous $NaHCO_3$ and the drying of the extract over $MgSO_4$ gave, upon solvent evaporation, a crude, colorless residue. Column chromatography on silica gel and elution with a 1/1 CH_2Cl_2/pentane pair gave 2.45 g (88%) of IX as an oil. The characteristic vinyl AB pattern in the ^1H NMR spectrum with J 13 Hz identified it as the *cis*-isomer [29].

Lithiations of the isomeric phenyl 2-trimethylsilylvinyl sulfones with stereochemical retention

(a) E-isomer (VII). A stirred solution of 1.70 g (7 mmol) of VII in 40 ml of THF was cooled to −95°C with an acetone-liquid nitrogen bath and then over 3 min treated with 5 ml of 1.4 M methyllithium solution in ether. The mixture was allowed to warm up to −60°C over 30 min, during which time methane was evolved. Thereupon, 610 mg (10 mmol) of methyl iodide in 5 ml of THF were added and cooling was discontinued after 5 min. After the mixture attained 25°C, water and ether were added. Separation, drying ($MgSO_4$) and evaporation of the organic layer gave a crude product that was chromatographed on silica gel with an ether/hexane pair as eluant. The first product was 1.5 g (90%) of a colorless oil, (E)-1-benzenesulfonyl-1-methyl-2-trimethylsilylethene (XI). Spectral data: ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 1.7 (s, 3H), 6.7 (s, H), and 7.2–7.7 (m, 5H). Anal. Found: C, 56.58; H, 7.31; S, 12.64. $C_{12}H_{18}O_2SSi$ calcd.: C, 56.65; H, 7.13; S, 12.60%.

A later fraction (160 mg, 8%) m.p. 185–186°C, seemed to be a dimeric impurity: ^1H NMR ($CDCl_3$) δ 0.1. (s, 9H), 0.7 (s, 9H), 1.80 (d, 3H), 4.1 (m, H), 7.0–8.5 (m, 11H). Anal. Found: C, 55.42; H, 6.65. $C_{23}H_{34}O_4S_2Si_2$ calcd.: C, 55.87; H, 6.88%.

(b) Z-isomer (IX). A solution of 2.2 mmol of IX methyllithium in 10 ml of THF was cooled to −120°C and then treated with a pre-cooled solution of 500 mg (2.06 mmol) of IX in 15 ml of THF. Over 20 min the solution was allowed to warm up to −100°C as methane was evolved. Then 1.1 molar equivalents of methyl iodide in 5 ml of THF was added and the temperature allowed to come to 25°C. Usual work-up and column chromatography of the crude product on silica gel with an elution by

95/5 CH_2Cl_2/pentane gave 450 mg (90%) of (*Z*)-1-benzenesulfonyl-1-methyl-2-trimethylsilylethene (XII). Spectral data: ^1H NMR ($CDCl_3$ 0.0 (s, 9H), 1.41 (br. s, 3H), 5.9 (br. s, H) and 6.9–7.6 (m, 5H). Anal. Found: C, 56.45; H, 7.44; S, 12.40. $C_{12}H_{18}O_2SSi$ calcd.: C, 56.65; H, 7.13; S, 12.60%.

Carbometallations of phenyl trimethylsilylethynyl sulfone (V)

(a) Phenyllithium. A solution of 300 mg (1.25 mmol) of V in 40 ml of THF was cooled to −78°C and then treated with 1.0 ml of 1.9 *M* solution of phenyllithium in ether. After 2 h the reaction mixture was brought to −30°C and thereafter allowed to warm slowly to 25°C. Quenching with water and addition of ether gave a suspension, from which the solid was filtered off. This solid proved to be benzenesulfenic acid, m.p. 83–85°C (78%), as verified by IR spectral comparison. Evaporation of the organic layer and column chromatography of the organic layer on silica gel by elution with hexane gave an 85% yield of phenylethynyl(trimethyl)silane.

Analogous reactions of V with methyllithium and with t-butyllithium were also carried out. In each case > 70% of benzenesulfenic acid was formed and the volatile $Me_3Si{-}C{\equiv}C{-}R$ (R = Me, t-Bu) was detected by gas chromatography.

(b) Lithium dimethylcuprate. In a 50-ml flask, equipped with a magnetic stirrer bar under N_2 gas was placed 0.73 g (3.82 mmol, 2% in excess of the alkyllithium reagent to be used) of cuprous iodide. After oven-drying, the flask was cooled while flushing with N_2 and 15 ml of dry THF was injected. To the resulting suspension at 0°C was added 2.1 ml (3.74 mmol) of 1.78 *M* solution of methyllithium in diethyl ether over a 2 min period. The resulting suspension of methylcopper(I) (25% excess) was cooled to −78°C for 15 min and a solution of 0.72 g (2.99 mmol) of phenyl trimethylsilylethynyl sulfone in 15.0 ml of dry THF, pre-cooled to −78°C, was injected rapidly. After stirring for 1.5 h at −78°C the reaction mixture was quenched by injecting 5 ml of methanol pre-cooled to −78°C and then pouring into 25 ml of saturated aqueous ammonium chloride solution. Extraction with dichloromethane (3 × 25 ml), drying over $MgSO_4$, and evaporation under reduced pressure gave a viscous liquid which was identified as phenyl (*Z*)-2-trimethylsilyl-1-propenyl sulfone, XIX (95% yield). Column chromatography on silica gel gave 70% of an analytically pure sample. Spectral data: ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 1.9 (d, 3H, J 1.5 Hz), 6.25 (d, H, J 1.5 Hz) and 7.1–7.8 (m, 5H); IR (neat) 3060, 2960, 1450, 1340, 1150, 1080, 720, and 700 cm^{-1}. Anal. Found: C, 56.87; H, 7.35. $C_{12}H_{18}O_2SSi$ calcd.: C, 56.65; H, 7.13%.

(c) Cesium fluoride. A mixture of 1.0 g (4.15 mmol) of V, 700 mg of anhydrous cesium fluoride and 660 mg of methyl iodide in 30 ml of THF was maintained for 30 min at −78°C and then warmed to 20°C for 30 min. Usual work-up with water and ether gave a 95% yield of ethynyl phenyl sulfone (XXIII).

When another run was conducted and the solution heated for 16 h at reflux before hydrolysis, a mixture of XXIII and phenyl 1-propynyl sulfone was formed.

Reaction of ethynylphenyl sulfone (XXIII) with diethyl α-n-butylmalonate

A mixture of 650 mg (3.0 mmol) of this ester in 40 ml of THF was treated with 0.60 equivalent of sodium hydride at 25°C for 1 h. Then this mixture was cooled to −78°C and treated with 500 mg of XXIII in 10 ml of THF, which had been pre-cooled to −78°C. After 2 h at −78°C and 12 h at 20°C, hydrolytic work-up and usual separation gave an 85% yield of 3,3-bis(ethoxycarbonyl)-1-benzenesulfonyl-2-trimethylsilyl-1-heptane (XXII). From the ^{1}H NMR spectrum, which displayed a vinylic *AB* pattern with a *J* of 13 Hz, this product was the *Z*-isomer.

Carbometallation of phenyl (E)-2-trimethylsilylvinyl sulfone

A 2.40 g sample of VII (0.01 mol) dissolved in 100 ml of diethyl ether was added over a period of 4 h to a stirred solution of allylmagnesium bromide in diethyl ether (prepared from magnesium (3.0 g, 0.123 mol) and allyl bromide (16.7 g, 0.138 mol) in 60 ml of ether). The reaction mixture was allowed to stir for 48 h at room temperature. Hydrolysis of the reaction mixture with aqueous ammonium chloride was followed by an extractive work-up with ether to yield a crude product (2.8 g, 98%) of a viscous liquid, which was identified as 5-benzenesulfonyl-3-trimethylsilyl-1-pentene (XX). Column chromatography on silica gel with a hexane eluant provided 80% of an analytically pure product. Spectral data: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9H), 1.0–1.4 (m, 1H), 2.1–2.5 (m, 2H), 2.8–3.15 (t, 2H), 4.65–5.9 (m, 3H), 7.3–7.9 (m, 5H); IR (neat) 3080, 2960, 1450, 1310, 1250, 1150, and 840 cm^{-1}. Anal. Found: C, 59.43; H, 7.92. $C_{14}H_{22}O_2SSi$ calcd.: C, 59.57; H, 7.80%.

Lithiations of phenyl trimethylsilylmethyl sulfone (XVI) and derivatization [30]

(a) Methylation. To a stirred solution of 1.31 g (6 mmol) of phenyl trimethylsilylmethyl sulfone in 40 ml of THF, which contained an equimolar amount of freshly distilled TMEDA, was added over 5 min 3 ml of a solution of 2 *M* n-butyllithium. The bath was allowed to warm to −60°C over a period of 1 h. Methyl iodide (0.4 ml, 6 mmol) was added and after 5 min the cooling bath was removed. After 14 h at room temperature a water/ether work-up gave the crude product as a solid. Recrystallization from ether/hexane gave 1.9 g (80%) of 1-benzenesulfonyl-1-trimethylsilylethane, m.p. 50–51°C. Spectral data: ^{1}H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.7–1.0 (d, 3H), 2.2–2.5 (q, 1H), 7.0–7.7 (m, 5H). Anal. Found: C, 55.15; H, 7.42. $C_{11}H_{18}O_2SSi$ calcd.: C, 55.54; H, 7.53%.

(b) Chloro(trimethyl)silane. A similar reaction was carried out as explained in section a, except that the lithiated intermediate was trapped by an equimolar amount of chloro(trimethyl)silane. The crude product, which was formed in 80% overall yield, was crystallized from ether/pentane, m.p. 102–104°C, and identified as benzenesulfonyl[bis(trimethylsilyl)]methane. Spectral data: ^{1}H NMR ($CDCl_3$) δ 0.2 (s, 18H), 2.6 (s, 1H), 7.3–7.9 (m, 5H). Anal. Found: C, 52.97; H, 7.44. $C_{10}H_{18}O_2SSi$ calcd.: C, 52.64; H, 7.0%.

(c) Benzophenone. The same procedure as described in section a was followed, except that when the lithiation was completed, the reaction mixture was allowed to react with a solution of 1.10 g (6 mmol) of benzophenone in 10 ml THF. After treatment of the reaction mixture with an acidic solution (0.1 *N* HCl) and following the same work-up method, a solid was obtained in 95% yield. Recrystallization of the crude product from ether/pentane gave 2,2-diphenylethenyl phenyl sulfone, m.p. 110–111°C. Spectral data: ^{1}H NMR ($CDCl_3$) δ 6.8–6.9 (s, 1H), 7.0–7.6 (m, 15H). Anal. Found: C, 74.68; H, 5.16. $C_{20}H_{16}O_2S$ calcd.: C, 75.00; H, 5.0%.

Lithiations of phenyl 2-trimethylsilylethyl sulfone (X) and derivatizations

(a) General. This sulfone was monolithiated or dilithiated according to the general procedure described in the foregoing section. To obtain principally the dilithio intermediate, slightly over two equivalents of n-butyllithium-TMEDA com-

plex were employed for each equivalent of X. The derivatizing agent was added, the reaction mixture was hydrolyzed with aqueous 2 *N* HCl and the separated organic layer was dried and freed of solvent. Column chromatography on silica gel and/or recrystallization provided the pure organic derivative in 75–90% yield.

By conducting a monolithiation of X and adding a derivatizing agent, a 1-substituted derivative of X could be formed. Resubjecting this derivative to monolithiation, followed by adding a different derivatizing agent, produced a 1,1-hetero-disubstituted derivative of X. For example, 1-methyl-1-allyl derivative of X could be prepared by the sequence: (1) n-BuLi-TMEDA; (2) MeI; (3) n-BuLi-TMEDA; (4) $CH_2{=}CHCH_2I$.

In the following sections, some illustrative derivatives made in this manner are described.

(b) 1-Trimethylsilyl X. Monolithiation, followed by Me_3SiCl; m.p. 81–82°C; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.6 (s, 9H), 1.2–1.3 (d, 2H), 2.8–3.1 (t, H) and 7.7–8.3 (m, 5H). Anal. Found: C, 53.83; H, 8.14. $C_{14}H_{26}O_2SSi$ calcd.: C, 53.50; H, 8.21%.

(c) 1-Methyl-1-trimethylsilyl X. Stepwise lithiation, m.p. 80–81°C; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.4 (s, 9H), 1.4 (s, 2H), 1.6 (s, 3H) and 7.6–8.2 (m, 5H). Anal. Found: C, 55.13; H, 8.51. $C_{15}H_{28}O_2SSi$ calcd.: C, 55.0; H, 8.50.

(d) 1-Allyl X. Colorless oil; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.9–1.5 (m, 2H), 2.3–3.4 (m, 3H), 4.7–5.9 (m, 3H) and 7.3–8.0 (m, 5H). Anal. Found: C, 59.65; H, 7.87. $C_{14}H_{22}O_2SSi$ calcd.: C, 59.60; H, 7.80%.

(e) 1-(4-Pentenyl) X. Colorless oil; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.6–1.1 (m, 2H), 1.4–2.1 (m, 6H), 2.7–3.2 (m, H), 4.70–5.80 (m, 3H) and 7.4–7.9 (m, 5H). Anal. Found: C, 26.04; H, 8.60. $C_{16}H_{26}O_2SSi$ calcd.: C, 6.20; H, 8.40%.

(f) 1-(5-Hexenyl) X. Colorless solid, m.p. 103–105°C; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 0.7–1.1 (m, 2H), 1.1–3.4 (m, 9H), 4.80–5.7 (m, 3H) and 7.4–8.0 (m, 5H).

(g) 1,1-Dimethyl X. Colorless oil; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 1.2 (s, 2H), 1.3 (s, 6H) and 7.4–8.0 (m, 5H).

(h) 1,1-Diallyl X. Colorless oil; ^1H NMR ($CDCl_3$) δ 0.2 (s, 9H), 1.2 (s, 2H), 2.5 (d, 4H), 4.8–6.2 (m, 6H) and 7.4–7.9 (m, 5H).

(i) 1-Benzenesulfonyl-1-trimethylsilylmethylcyclopentane. Dilithiation of X, followed by addition of 1,4-diiodobutane; colorless oil; ^1H NMR ($CDCl_3$) δ 0.0 (s, 9H), 1.0 (s, 2H), 1.3–1.9 (m, 8H) and 7.4–8.1 (m, 5H).

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