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Effect of the "Supersilyl" Group on the Reactivities of Allylsilanes and Silyl Enol Ethers

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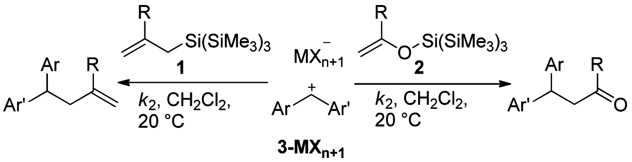
ABSTRACT

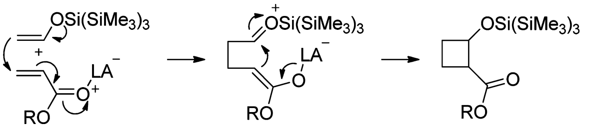


Kinetics of the reactions of allylsilanes (1) and silyl enol ethers (2) with benzhydrylium ions (3) were studied by UV−vis spectroscopy in dichloromethane at 20 °C. The less than three times higher reaction rates of the tris(trimethylsilyl)silyl compounds in comparison to the corresponding trimethylsilyl compounds indicate that the previously reported strong electron-donating effect of the supersilyl group operates only in the α-position and not in the *β*-position.

Allylsilanes and silyl enol ethers represent two important classes of organosilanes. While allylsilanes are widely used as allylating reagents for Lewis acid activated carbonyl compounds (Hosomi−Sakurai reaction),[1] silylated enol ethers are key substrates for the Mukaiyama variant of aldol reactions.[2]

Cyclobutane rings can be formed via Lewis acid catalyzed [2 + 2]-cycloaddition reactions of silyl enol ethers with α,*β*-unsaturated esters.[3] In these reactions, higher yields and *trans*-selectivity were found, when the $SiMe_3$ group was replaced by the bulkier $SiMe_2tBu$ group.[3d] Utilization of the tris(trimethylsilyl)silyl group led to the first [2 + 2] cycloaddition of an acetaldehyde derived silyl enol ether with an acrylic ester (Scheme 1).[4]

Scheme 1. Stepwise [2 + 2] Cycloaddition of a Silyl Enol Ether with an Acrylic Ester



Intrigued by the high yields and selectivities obtained by application of the so-called "supersilyl" group for cycload-

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[‡] University of Chicago.

(1) (a) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673–1675. (b) Chabaud, L.; James, P.; Landais, Y. *Eur. J. Org. Chem.* **2004**, 3173–3199. (c) Sarkar, T. K. In *Science of Synthesis, Houben-Weyl Methods of Molecular Transformations*; Fleming, I., Ed.; Thieme: Stuttgart, 2002; Vol. 4, pp 837−925.

(2) (a) Mukaiyama, T.; Narasaka, K.; Banno, K. *Chem. Lett.* **1973**, 1011–1014. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203–331. (c) Brownbridge, P. *Synthesis* **1983**, 1–28. (d) Bach, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 417–419. (e) Nelson, S. G. *Tetrahedron: Asymmetry* **1998**, *9*, 357–389. (f) Carreira, E. M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfalz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 3, pp 996−1066. (g) Mahrwald, R. *Chem. Rev.* **1999**, *99*, 1095–1120.

(3) (a) Clark, R. D.; Untch, K. G. *J. Org. Chem.* **1979**, *44*, 253–255. (b) Takasu, K.; Ueno, M.; Ihara, M. *Tetrahedron Lett.* **2000**, *41*, 2145–2148. (c) Takasu, K.; Ueno, M.; Ihara, M. *J. Org. Chem.* **2001**, *66*, 4667–4672. (d) Takasu, K.; Ueno, M.; Inanaga, K.; Ihara, M. *J. Org. Chem.* **2004**, *69*, 517–521. (e) Takasu, K.; Nagao, S.; Ueno, M.; Ihara, M. *Tetrahedron* **2004**, *60*, 2071–2078. (f) Inanaga, K.; Takasu, K.; Ihara, M. *J. Am. Chem. Soc.* **2005**, *127*, 3668–3669. (g) Takasu, K.; Ishii, T.; Inanaga, K.; Ihara, M. *Org. Synth.* **2006**, *83*, 193–199. (h) Canales, E.; Corey, E. J. *J. Am. Chem. Soc.* **2007**, *129*, 12686–12687.

(4) Boxer, M. B.; Yamamoto, H. *Org. Lett.* **2005**, *7*, 3127–3129.

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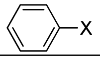
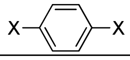
dition reactions, the corresponding tris(trimethylsilyl)silyl enol ethers were used for Mukaiyama aldol reactions.[5] High diastereoselectivities and yields were even obtained with acetaldehyde-derived substrates. Moreover, sequential reactions with diverse reagents opened the pathway to the facile synthesis of molecules with substructures known for their biological activity.[5c−f]

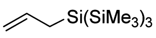
The observed reactivities have been explained by the steric demand and the electronic properties of the tris(trimethylsilyl)silyl group. Bock and co-workers reported that the first vertical ionization energies (IE_1^{v}) for supersilyl-substituted benzenes are much smaller than those of the corresponding trimethylsilyl derivatives (Table 1); the supersilyl group has, therefore, been considered as a very strong electron donor.[6] As demonstrated by the last entry of Table 1, the hyperconjugative effect of the trimethylsilylmethyl substituent causes a slightly weaker decrease of the ionization energy. In contrast, hydride abstractions from trialkylsilanes and tris(trimethylsilyl)silane have been reported to proceed with comparable rates.[7]

Table 1. First Vertical Ionization Energies for Silyl-Substituted Benzenes Reported by Bock and Coworkers[6]

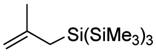
	IE_1^{v} (eV)	
X		
$SiMe_3$	9.05	8.70
$Si(SiMe_3)_3$	8.04	7.37
CH_2SiMe_3	8.35	7.86

Kinetic investigations of the nucleophilicities of allylsilanes and silyl enol ethers with $Si(SiMe_3)_3$ substitution have so far not been performed.

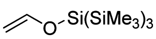
We now report on the application of the benzhydrylium method[8] for characterizing the nucleophilic reactivities of the tris(trimethylsilyl)silyl-substituted allyl compounds **1** and enol ethers **2** and the comparison with the corresponding allyltrimethylsilanes[8a,9] and trimethylsilyl enol ethers.[8a,10]



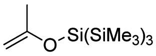
1a



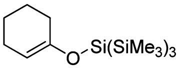
1b



2a



2b



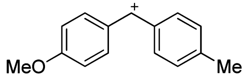
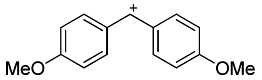
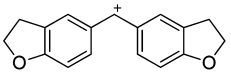
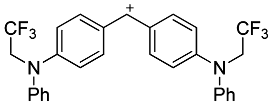
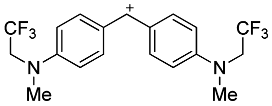
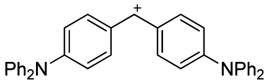
2c

Benzhydrylium ions with variable *p*- and *m*-substituents, which cover a broad range of reactivity while the steric shielding of the reaction center is kept constant, have been used as reference electrophiles for the construction of a comprehensive nucleophilicity scale based on eq 1, in which electrophiles are characterized by one parameter (E) and nucleophiles are characterized by the solvent-dependent parameters s (sensitivity) and N (nucleophilicity).[8a]

$$\log k(20\ ^\circ\mathrm{C}) = s(N + E) \qquad (1)$$

In this investigation, benzhydrylium ions **3a−f** (Table 2) with electrophilicity parameters E ranging from −5 to +1.5 were used because they reacted with the organosilanes **1** and **2** with conveniently measurable rates.

Table 2. Reference Electrophiles Utilized for Quantifying the Nucleophilicities of **1** and **2**

	reference electrophile	E^a
3a		1.48
3b		0.00
3c		−1.36
3d		−3.14
3e		−3.85
3f		−4.72

^{a} Empirical electrophilicities E of reference electrophiles from ref 8a.

Compounds **1b** and **2b** reacted with the colored benzhydrylium salt **3f-BF$_4$** in CH_2Cl_2 to give the desilylated products **5** (Scheme 2), as previously reported for the corresponding trimethylsilyl compounds.[8a,9,10]

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(5) (a) Boxer, M. B.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 48–49. (b) Boxer, M. B.; Yamamoto, H. *Nat. Protoc.* **2006**, *1*, 2434–2438. (c) Boxer, M. B.; Yamamoto, H. *J. Am. Chem. Soc.* **2007**, *129*, 2762–2763. (d) Boxer, M. B.; Yamamoto, H. *Org. Lett.* **2008**, *10*, 453–455. (e) Boxer, M. B.; Akakura, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2008**, *130*, 1580–1582. (f) Boxer, M. B.; Albert, B. J.; Yamamoto, H. *Aldrichimica Acta* **2009**, *42*, 3–15. (g) Yamaoka, Y.; Yamamoto, H. *J. Am. Chem. Soc.* **2010**, *132*, 5354–5356. (h) Albert, B. J.; Yamamoto, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 2747–2749.

(6) Bock, H.; Meuret, J.; Baur, R.; Ruppert, K. *J. Organomet. Chem.* **1993**, *446*, 113–122.

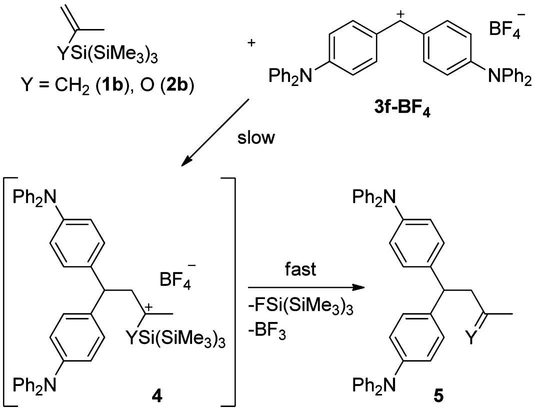
(7) Mayr, H.; Basso, N.; Hagen, G. *J. Am. Chem. Soc.* **1992**, *114*, 3060–3066.

(8) (a) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; Schimmel, H. *J. Am. Chem. Soc.* **2001**, *123*, 9500–9512. (b) Lucius, R.; Loos, R.; Mayr, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 91–95. (c) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66–77. (d) Mayr, H.; Ofial, A. R. In *Carbocation Chemistry*; Olah, G. A., Prakash, G. K. S., Eds.; Wiley: Hoboken, NJ, 2004; Chap. 13, pp 331−358. (e) Mayr, H.; Ofial, A. R. *Pure Appl. Chem.* **2005**, *77*, 1807–1821. (f) Mayr, H.; Ofial, A. R. *J. Phys. Org. Chem.* **2008**, *21*, 584–595. (g) Richter, D.; Hampel, N.; Singer, T.; Ofial, A. R.; Mayr, H. *Eur. J. Org. Chem.* **2009**, 3203–3211.

(9) Nucleophilicities of allylsilanes were determined by using the benzhydrylium method: Hagen, G.; Mayr, H. *J. Am. Chem. Soc.* **1991**, *113*, 4954–4961.

(10) Nucleophilicity parameters for silyl enol ethers determined by using the benzhydrylium method: Burfeindt, J.; Patz, M.; Müller, M.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 3629–3634.

Scheme 2. Reactions of **1b** and **2b** with the Benzhydrylium Salt **3f-BF$_4$**



As the intermediates **4** and the products **5** are colorless, the nucleophilic attack at the electrophilic center was followed spectrophotometrically. Addition of at least 7 equiv of the supersilanes **1** and **2** to solutions of the benzhydrylium tetrahaloborates, tetrachlorogallates, or pentachlorostannates **3-MX$_{n+1}$** in CH_2Cl_2 led to monoexponential decays of the electrophiles' absorbances (Figure 1).

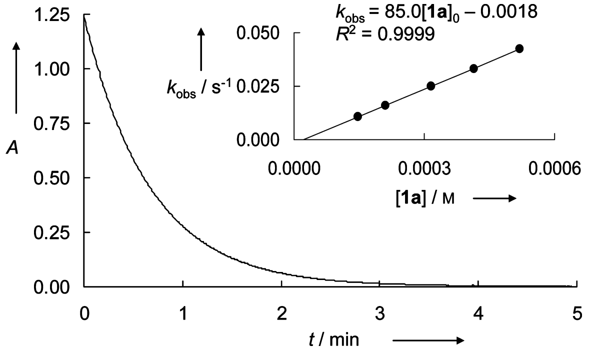


Figure 1. Exponential decay of the absorbance at 513 nm during the reaction of **1a** (c = 3.16 × 10^{-4} M) with **3b-SnCl$_5$** (c = 2.09 × 10^{-5} M) at 20 °C in CH_2Cl_2. Inset: Determination of the second-order rate constant $k_2 = 85.0$ M^{-1} s^{-1} as the slope of the correlation between the first-order rate constant k_{obs} and the concentration of **1a**.

The resulting first-order rate constants k_{obs} correlated linearly (with R^2 values ranging from 0.935 to 0.9999) with the concentrations of the nucleophiles **1** and **2** as depicted in Figure 1. The second-order rate constants k_2 given in Tables 3 and 5 were derived from the slopes of such correlations.

Table 3 shows that the rates of the reactions of allyltris(trimethylsilyl)silane (**1a**) with the benzhydryl cation **3b** are only slightly affected by the counterion, indicating the rate-determining formation of intermediate **4** (Scheme 2) as previously observed for the corresponding trimethylsilyl compounds.[9,10]

Table 3. Second-Order Rate Constants for the Reactions of **1a** (1.4 × 10^{-4} to 5.2 × 10^{-4} M) with Different Benzhydrylium Salts **3b-MX$_{n+1}$** (1.6 × 10^{-5} to 2.3 × 10^{-5} M)

MX_{n+1}^-	k_2/M^{-1} s^{-1}
BCl_4^-	84.9
BF_4^-	74.8
$GaCl_4^-$	77.5
$SnCl_5^-$	85.0

The rate-determining formation of the C−C bond is furthermore supported by the independence of the rate constants of the concentration of $Bu_4N^+BCl_4^-$ (Table 4).

Table 4. First-Order Rate Constants for the Reactions of **1a** with **3b-BCl$_4$** (1.9 × 10^{-5} M) in the Presence of Various Amounts of $Bu_4N^+BCl_4^-$

[**1a**]$_0$/M	[$Bu_4N^+BCl_4^-$]$_0$/[**1a**]$_0$	k_{obs}/s^{-1}
1.87 × 10^{-4}	0	1.76 × 10^{-2}
1.85 × 10^{-4}	1	1.73 × 10^{-2}
1.84 × 10^{-4}	5	1.77 × 10^{-2}
1.84 × 10^{-4}	100	1.77 × 10^{-2}

Table 5 compares the second-order rate constants for the attack of the nucleophiles **1** and **2** at the reference electrophiles with the previously reported values for the corresponding trimethylsilanes **6** and **7**.[9,10]

Plots of log k_2 for the reactions of the supersilylated nucleophiles **1** and **2** with the reference electrophiles **3** versus the empirical electrophilicity parameters E are linear (Figure 2), indicating that eq 1 is applicable, thus providing the N and s parameters for the supersilyl derivatives **1** and **2** (Scheme 3).

Table 5 and Scheme 3 show that the allylsilanes **1** which carry supersilyl groups are less than 2-times more nucleophilic than the structurally analogous allyltrimethylsilanes **6**. Exchange of $SiMe_3$ by $Si(SiMe_3)_3$ has also a marginal effect on the reactivities of enol ethers. While the acetone-

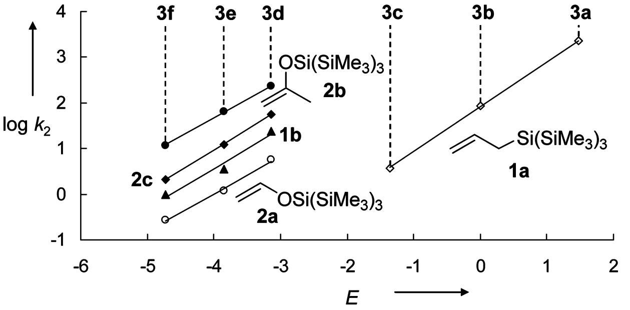
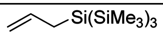
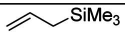
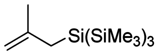
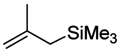
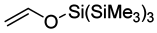
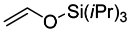
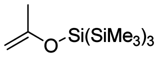
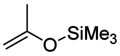
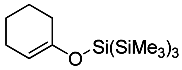
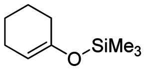


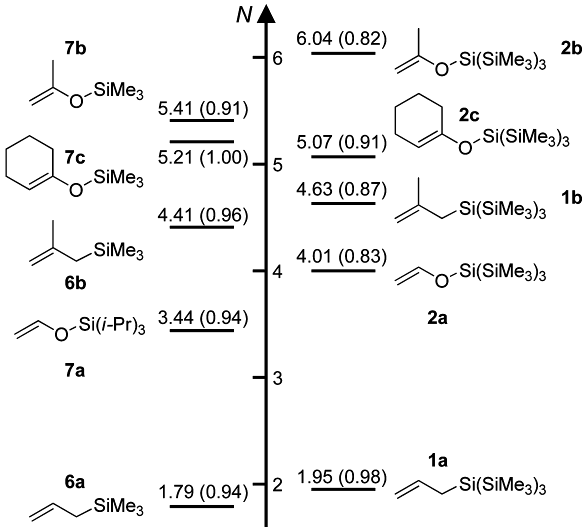
Figure 2. Plots of log k_2 for the reactions of **1** and **2** with benzhydrylium ions **3** in CH_2Cl_2 at 20 °C versus the corresponding electrophilicity parameters E.

Table 5. Second-Order Rate Constants k_2 for the Reactions of the Silanes **1**, **2**, **6**, and **7** with the Benzhydrylium Ions **3**

	Nucleophiles	3	k_2 / $M^{-1}s^{-1}$		Nucleophiles	3	$k_2{}^{a}$ / $M^{-1}s^{-1}$	$k_2(Si(SiMe_3)_3)$ / $k_2(Si(alkyl)_3)$
1a		**3a**	$2.30 \times 10^{3,b}$	**6a**		**3a**	1.41×10^{3}	1.63
		3b	8.49×10^{1}			**3b**	4.69×10^{1}	1.81
		3c	3.75			**3c**	2.14	1.75
1b		**3d**	2.40×10^{1}	**6b**		**3d**	1.35×10^{1}	1.78
		3e	3.54			**3e**	2.97	1.19
		3f	9.65×10^{-1}			**3f**	6.13×10^{-1}	1.57
2a		**3d**	5.59	**7a**		**3d**	1.91^{c}	2.93
		3e	1.19			**3e**	$4.12 \times 10^{-1,c}$	2.89
		3f	2.72×10^{-1}			**3f**	$6.26 \times 10^{-2,c}$	4.35
2b		**3d**	2.32×10^{2}	**7b**		**3d**	$1.16 \times 10^{2,c}$	2.00
		3e	6.58×10^{1}			**3e**	$2.63 \times 10^{1,c}$	2.50
		3f	1.18×10^{1}			**3f**	4.25^{c}	2.78
2c		**3d**	5.70×10^{1}	**7c**		**3d**	$1.17 \times 10^{2,c}$	0.487
		3e	1.23×10^{1}			**3e**	2.17×10^{1}	0.567
		3f	2.10			**3f**	2.05	1.02

[a] Data from ref 8a if not stated otherwise. [b] Calculated by using the Eyring equation with k_2 values for temperatures varying from −71 to −22 °C (for details see Supporting Information). [c] Calculated by using eq 1 from N and s in ref 8a and E from Table 2.

Scheme 3. Nucleophilicities of **1** and **2** Compared to the Corresponding Allyltrimethylsilanes **6** and Trialkylsilyl Enol Ethers **7**[a]



[a] s values given in parentheses.

derived enol ether **2b** is 2−3 times more reactive than **7b**, the cyclohexanone-derived enol ether **2c** is even slightly less reactive than **7c**. The somewhat reduced reactivity of **2c** might be explained by the shielding of the reaction center by the tris(trimethylsilyl)silyl group in the preferred conformation of the cyclohexenyl ether. The slightly higher ratios for the acetaldehyde-derived enol ethers **2a**/**7a** may be due to the fact that **7a** bears the Si(i-Pr)$_3$ group instead of the SiMe$_3$ group.

Scheme 3 shows that with the exception of **1a**/**6a** the supersilyl derivatives **1b** and **2a**−**c** generally have smaller s values than the corresponding trimethylsilyl derivatives **6b** and **7a**−**c**. As a consequence, the Si(SiMe$_3$)$_3$/SiMe$_3$ ratio can be expected to decrease slightly, when the electrophilicity of the reaction partner is increased.

The kinetic data in Table 5 and Scheme 3 show that the exchange of SiMe$_3$ by Si(SiMe$_3$)$_3$ in allylsilanes and silylated enol ethers has little effect on the rates of reactions of these electron-rich π-nucleophiles. The significantly lower first vertical ionization energies of tris(trimethylsilyl)silyl-substituted benzenes compared to the trimethylsilyl analogues, which indicates a stronger α-effect of the Si(SiMe$_3$)$_3$ group compared with SiMe$_3$, obviously does not have a consequence for the reactivities of allylsilanes and silylated enol ethers bearing the supersilyl group.

One can, therefore, conclude that the high selectivities observed for [2 + 2] cycloadditions and aldol reactions with supersilyl-substituted enol ethers cannot be attributed to electronic effects but are due to the steric bulk and the umbrella like structure created by the Si(SiMe$_3$)$_3$ group.

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Supporting Information Available: Details of product characterization and the kinetic experiments. This material is available free of charge via the Internet at http://pubs.acs.org.

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