“*Syn-Effect*” in the Desilylation Reaction of γ-Silylated Allylic and Vinylic Sulfones

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The desilylation reaction of γ-silylated allylic sulfones was found to proceed through γ-silylated (E)-vinylic sulfones to afford the corresponding allylic sulfones by treatment with DBU and H_2O. The Z/E ratio of the resulting allylic sulfones varied according to the γ-substituents of the γ-silylated sulfones. This stereochemical outcome was rationalized by “*syn-effect*.”

We previously investigated the stereochemistry of the isomerization of α-unsubstituted (E)-vinylic sulfones to the corresponding allylic sulfones and the desulfonylation reaction of α,α-dialkylated allylic sulfones with a base.[1a,b] In both cases, the sterically unfavorable (Z)-allylic sulfones and (Z)-alkadienes were preferentially formed, respectively. These observations were rationalized by “conformational acidity”[1] which essentially implies “*syn-effect*.”[2] We proposed that the “*syn-effect*” is primarily attributed to 6π-electron homoaromaticity and/or $\sigma \rightarrow \pi^*$ interaction.[1b] Very recently we have investigated the “*syn-effect*” in the conversion of α-fluorinated (E)-vinylic sulfones to the corresponding allylic sulfones[1c] and showed that $\sigma \rightarrow \pi^*$ interaction is the most probable explanation for the “*syn-effect*.”

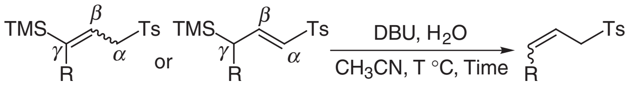
It is well known that the hyperconjugative electron donating ability of C–Si bond is stronger than either C–C or C–H bond.[3] Verlhac and co-workers have reported the desilylation reaction of (E)-α-methoxy allylsilanes bearing various γ-substituents with ^{n}Bu$_4$NF containing H_2O and have shown that the (Z)-enol ethers were obtained as the major products.[4] However, the origin of the formation of (Z)-isomers was not discussed.

In order to observe the “*syn-effect*” under enhanced $\sigma \rightarrow \pi^*$ interaction, we replaced one hydrogen atom at the γ-position of vinylic and allylic sulfones by a trimethylsilyl group and investigated the stereochemistry in the desilylation reaction by treating with DBU in the presence of H_2O. The Z/E ratio of the resulting desilylated allylic sulfones was rationalized by the “*syn-effect*.”

The general procedure for the desilylation reaction was as follows: 0.25 mL of a mixed solution of DBU and H_2O (0.4 M or 0.8 M each; $1\,M = 1\,mol\,dm^{-3}$) in CH_3CN was added to 0.1 mmol of the γ-silylated allylic or vinylic sulfones[5] and stirred at 25 or 0 °C. After completion of the reaction (confirmed by TLC), the reaction mixture was neutralized with an aqueous 1 M HCl solution and worked up as usual. After taking NMR spectrum of the crude product, it was purified by preparative TLC or column chromatography on silica gel. In all cases investigated, the Z/E ratio of the purified products was consistent with that of the crude products. The results are summarized in Table 1.

From the Table, it was found that: i) the Z/E ratio of the products **2** was almost independent of the stereochemistry of the starting materials **1** (Entries 1, 3; 4, 7; 8, 9; 10, 11), which suggested that desilylation did not occur directly from the γ-silylated allylic sulfones **1a**–**g**. It is also noteworthy that **1h** was totally unaffected, suggesting that its isomerization to **1h**′ cannot occur due to a lowering of acidity of α-protons of **1h** by a vinyl ether moiety; ii) the reaction was accelerated by increasing the amount of DBU and H_2O (Entries 4 and 5); iii) the kinetically formed (Z)-**2** was partially isomerized to the thermodynamically favorable (E)-form at higher temperature (Entries 4, 6; 14, 15); iv) (Z)-selectivity of the present reaction was higher than that of the previous rearrangement of γ-unsilylated (E)-vinylic sulfones to the corresponding allylic sulfones as expected above, except the case of ^{i}Pr group probably due to the steric demand.[1a,6] On the other hand, when an equimolar amount of ^{n}Bu$_4$NF (1.0 M THF solution) was used instead of DBU and H_2O under similar conditions, the Z/E ratio was lower even though the reaction proceeded much faster.[4,7,8]

Table 1. Desilylation Reaction of γ-Silylated Allylic and Vinylic Sulfones to the Corresponding Allylic Sulfones[a)]



1a-g **1a'-h'** **2a-h**

Entry	1,	R	E/Z of **1**	T/°C	t/h	**1/2**	Yield /%[b)]	Z/E of **2**[c)]
1	**a**,	CH_3	100/0	25	2.75	0/100	91	93/7
2	**a**,	CH_3	100/0	0	30.5	0/100	quant.	94/6
3	**a**,	CH_3	0/100	25	4.5	8/92	86	92/8
4	**b**,	CH_3CH_2	100/0	25	4.5	0/100	89	78/22
5[d)]	**b**,	CH_3CH_2	100/0	25	2.25	0/100	98	78/22
6	**b**,	CH_3CH_2	100/0	0	47.0	0/100	90	84/16
7	**b**,	CH_3CH_2	0/100	25	5.25	0/100	quant.	73/27
8	**c**,	$PhCH_2$	100/0	25	3.0	0/100	quant.	55/45
9	**c**,	$PhCH_2$	0/100	25	4.5	0/100	98	51/49
10	**d**,	$(CH_3)_2CH$	100/0	25	8.0	0/100	93	34/66
11	**d**,	$(CH_3)_2CH$	0/100	25	9.0	0/100	93	32/68
12	**e**,	$(CH_3)_3C$	0/100	25	18.0	37/63[e)]	63	0/100
13	**f**,	Ph	84/16	25	1.25	0/100	quant.	5/95
14	**g**,	PhS	8/92	25	0.25	0/100	92	42/58
15	**g**,	PhS	8/92	0	0.42	0/100	86	74/26
16[f)]	**h**′,	CH_3O	100/0	25	1.0	0/100	80	98/2

a) 0.25 mL of a mixed solution of DBU and H_2O (0.4 M each) in CH_3CN was used for 0.1 mmol of **1**. b) Isolated total yield of (Z)- and (E)-**2**. c) The ratios were determined by 400 MHz ^{1}H NMR spectra. d) 0.25 mL of a mixed solution of DBU and H_2O (0.8 M each) in CH_3CN was used for 0.1 mmol of **1**. e) 37% of the γ-silylated (E)-vinylic sulfone **1e**′ was isolated (see text). f) The allylic sulfone **1h** was not affected under the similar conditions.

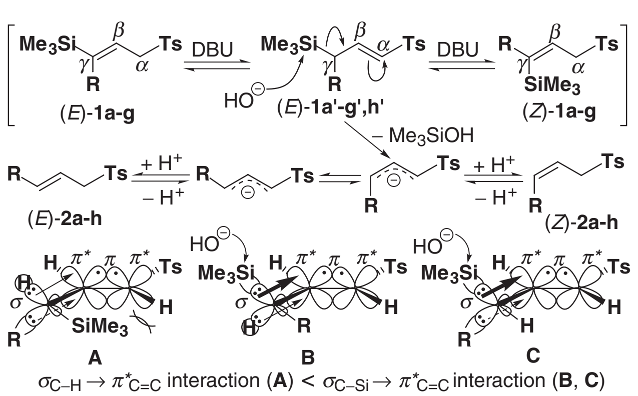
In the case of γ-alkyl substituents, the ratio of (Z)-isomer of products **2** decreased in the order: CH_3– > CH_3CH_2– > $PhCH_2$– > $(CH_3)_2CH$– > $(CH_3)_3C$–, as intuitively predicted from the difference of their bulkiness (Entries 1, 4, 8, 10, 12). In the case of γ-phenyl substituent, high (E)-selectivity was observed (Entry 13). γ-Methoxy group showed the highest (Z)-selectivity (Entry 16), while γ-phenylthio substituent afforded almost 1/1 mixture of (Z)- and (E)-desilylated product **2** (Entry 14). The relative degree of Z/E ratio in desilylation reaction of **1** depending on the γ-substituents was found to follow the order:

$$CH_3O– > CH_3– > CH_3CH_2– > PhCH_2– > PhS– >$$
$$(CH_3)_2CH– > Ph– > (CH_3)_3C–$$

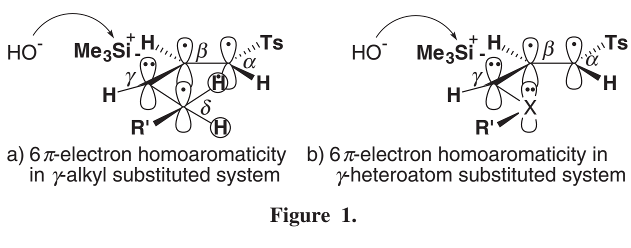
In the presence of DBU, the γ-silylated (E)- or (Z)-allylic sulfones **1a**–**g** can be converted to the corresponding vinylic sulfones **1a**′–**g**′,[1a] namely (*E*)-α-substituted allylsilanes, and then the hydroxide anion (generated from the reaction of DBU and H_2O) attacks the silyl group to produce the desilyalted allylic sulfones **2** (Scheme 1).[9] An evidence to support this mechanism was found in Entry 12 where the γ-silylated (*E*)-vinylic sulfone **1e**′ produced by isomerization of **1e** was isolated in 37% yield.

In the transition state of desilylation, the conformation **B** or **C** is more favored rather than conformation **A**, as the hyperconjugating ability of C–Si bond is stronger than C–C or C–H bond.[3] The steric hindrance of the TMS group must be also considerable in favoring the conformation **B** or **C** (Scheme 1). It should be noted that hyperconjugation of developing anion generated by the interaction of hydroxide anion with trimethylsilyl group becomes more effective in the conformations **B** and **C**, in both of which the developing anion is aligned with the $\pi^*_{C=C}$ orbital and other conformations can be neglected (Scheme 1). Our recent proposal that $\sigma \rightarrow \pi^*$ interaction is the most probable explanation for the "*syn-effect*" is well consistent with this consideration.[1c] At the desilylation step, the CC-eclipsed form **B** might be preferred rather than CH-eclipsed form **C** because hyperconjugative electron donation by C–H bond is larger than that by C–C bond,[3c,10] especially under basic conditions by induction of the negative charge aligned with the $\pi^*_{C=C}$ orbital.[11] In the case of γ-methoxy substituted sulfone, CH-eclipsed form **C** is much less favored due to low donor ability of C–O bond[12] compared with C–C bond, thus the highest (*Z*)-selectivity was observed for **1h**′.

In the present investigation except ^{i}Pr, ^{t}Bu, and Ph substituents, it is also possible to stabilize the *syn*-conformation at the transition state by 6π-electron homoaromaticity (another origin of "*syn-effect*") involving the developing charge at the γ-position and a pseudo *p*-orbital of the δ-CH_2 ($R = R'CH_2$), or a lone pair of electrons in a *p*-orbital of the hetero atom (Figures 1a and 1b).[1,13] In the case of ^{i}Pr substituent, 6π-electron homoaromaticity is difficult to be considered, but still remarkable amount (34%) of the sterically unfavorable (*Z*)-isomer was obtained (Entry 10). Accordingly, it is clear that the "*syn-effect*" is primarily arisen from the $\sigma \rightarrow \pi^*$ interaction. In the case of ^{t}Bu and Ph substituted sulfones, (*E*)-isomer was obtained as the major product, probably due to the bulkiness of the ^{t}Bu and Ph groups that precludes *syn*-conformation in the transition state.



Scheme 1.



a) 6π-electron homoaromaticity in γ-alkyl substituted system b) 6π-electron homoaromaticity in γ-heteroatom substituted system

Figure 1.

In the case of γ-phenylthio substituted sulfone, the contribution of the empty *d*-orbital of S-atom, such as $\sigma_{C-H} \rightarrow d$, is still unclear, but $\sigma_{C-S} \rightarrow \pi^*$ interaction,[11,14] as shown in the CH-eclipsed form **C** (R = PhS) in Scheme 1, may be responsible to decrease (*Z*)-selectivity (Entries 14 and 15) compared with the cases of γ-methoxy (Entry 16) and γ-alkyl substituted sulfones (Entries 1–9). Eventually, the relative degree of "*syn-effect*" for the γ-substituents remained almost the same as that previously found in the conversion of α-unsubstituted vinylic sulfones to the corresponding allylic sulfones.[1a]

In conclusion, the stereochemical outcome of the desilylation reaction of γ-silylated allylic and vinylic sulfones was well rationalized by "*syn-effect*" which was accounted for by the $\sigma \rightarrow \pi^*$ interaction and/or 6π-electron homoaromaticity. In the reaction using γ-methoxy substituted vinylic sulfone, the highest (*Z*)-selectivity was observed.

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7 (*Z*)-Selectivity of **2** obtained from (*E*)-**1a**,**b**, **1g** and **1h**′ were 83 (25 °C, 10 min, **1**/**2** = 10/90, 86% yield), 60 (25 °C, 40 min, **1**/**2** = 6/94, 89% yield), 50 (0 °C, 7 min, **1**/**2** = 0/100, 86% yield) and 91% (25 °C, 7 min, **1**/**2** = 0/100, 80% yield), respectively; which were 7–24% lower compared with DBU and H_2O system. Those results suggest that more basic conditions are favored to discriminate the conformation **B** from **C** (Scheme 1).

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