of sodium para-toluene sulfonate produced less well-developed multiple peaks.

The strongly multiple voltammetric peaks observed with the first redox process in the present studies appear to be caused by the perchlorate anion used. We notice that perchlorate electrolytes were employed in the electrochemical studies of the LB films of $C_{22}VC_1$ and $C_{22}VC_1$ at ITO surfaces.[4] Perchlorate ions are hydrophobic[7] and may cause positively charged $C_{22}VC_1$ hydrophobic films to become highly compact at the full monolayer coverage, as was the case with the LB films, to produce thermodynamically distinguishable voltammetric peaks. The present procedures to obtain one-electron transfer multiple voltammetric peaks may be significant in that they can be easily applicable for spectroelectrochemical studies to investigate the unusual voltammograms observed at self-assembled viologens on electrode surfaces. Possible origin of multiply peaked voltammograms may be related to the effects of ion pairing or reorientation or both together with strong hydrophobic interations. Spectroelectrochemical sudies to probe the nature of multiple voltammetric peaks associated with the first electrochemical process of self-assembled viologen films are in progress in this labratory.

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Reaction Mechanism of the Ring Enlargement of Cyclic Si Ring Compounds with 1-(Chloromethyl) Substituents

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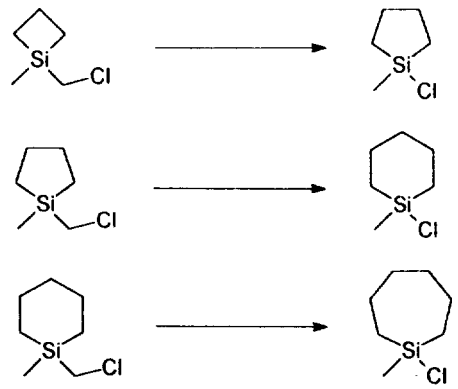
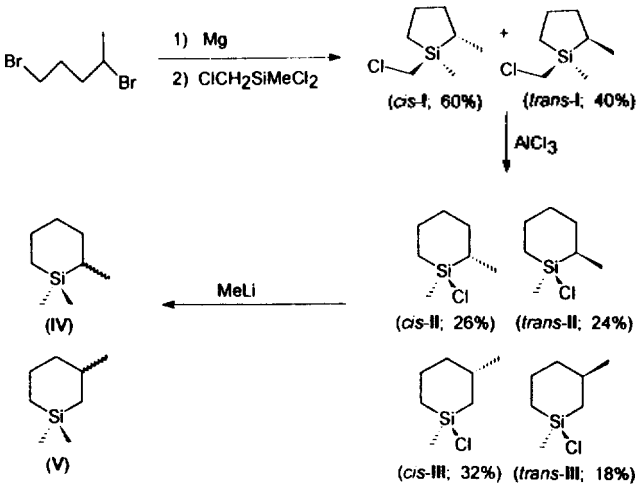
Silicon chemists have had considerable interest in studying the reaction mechanism and synthetic utility of the rearrangement reactions of α-chlorosilanes to chlorosilanes.[1-3] The rearrangement mechanism has been controversial for a long time. Various mechanisms have been proposed from analyses



Scheme 1.



Scheme 2.

of experimental data. Suggested mechanisms are (1) simultaneous double migration of Cl and R,[4] and (2) migration through α-silyl cation,[5] or (3) stepwise migration involving an "inverse-ylide" pentacoordinated Si.[6] The ring enlarging rearrangement reactions are useful methods to provide new cyclic silanes[2,3] (see Scheme 1). 1-(Chloromethyl)-1,2-dimethylsilacyclopentane (**I**) can yield a new silacyclopentane through Me migration or two different chlorosilacyclohexane derivatives (**II** and **III**) by competitive migrations of the two different ring bonds (see Scheme 2). This particular system may allow the study of migratory aptitude of alkyl groups during the ring enlargement reaction.

I was synthesized as a *cis/trans* mixture[7] (*ca.* 60/40) from ring cyclization using the diGrignard reagent from 1,4-dibromopentane. Since **I** is formed as a mixture enriched in one isomer, we can identify the spectral properties of each signal of the *cis* and *trans*-isomers by using ^{1}H-NMR, ^{13}C-NMR, ^{1}H-^{13}C correlation, and gated proton decoupled spectra.[8]

At first, we attempted the rearrangement reaction under thermal conditions. *cis/trans*-**I** (60/40) was placed in a thick-walled tube, sealed/and immersed in an oil bath at 200℃. After 1 week, no change was observed in proton NMR signals. Hence, a catalytic amount of $AlCl_3$ was added. Within 3 h,[9] the rearrangement is achieved cleanly at room temperature (without solvent). Four new peaks appear in the ^{1}H NMR spectrum at 0.37, 0.39, 0.41, and 0.44 ppm (all singlets)

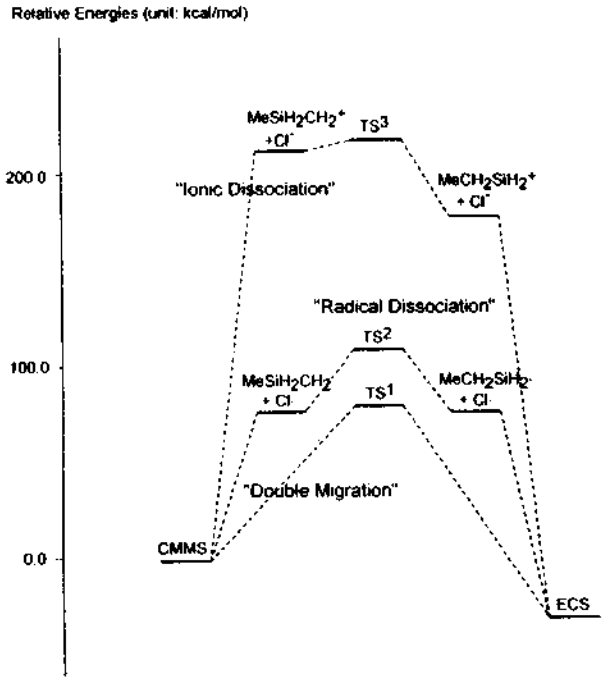


Figure 1. Reaction diagram for the rearrangement of CMMS to ECS calculated by AM1.

which correspond to Me proton attached to Si in *trans*-**II**, *cis*-**III**, *cis*-**II** and *trans*-**III**, respectively.[10] We are confident in assigning these ^{1}H-NMR peaks because we have synthesized these compounds previously by ring cyclization and have identified the ^{1}H-NMR peaks.[11] In addition, hydrolysis and methylation with MeLi revealed that those peaks belong to the chlorosilanes, since they disappeared on methylation and hydrolysis. Methylation with MeLi is useful also (1) for the identification of the Me peaks attached to Si in **II** and **III**, and (2) to identify any exocyclic Me migrated products. From GC and ^{1}H-NMR after treatment with MeLi, we observed only two compounds (**IV** and **V**), not the exocyclic Me migrated products. Although the quantitation using integration of ^{1}H-NMR peaks is relatively crude (*ca.* ± 5% error), the correlation of peaks with rearranged chlorosilanes shows reasonable reproducibility with repeated experiments.

We have surveyed the various possible mechanisms employing the AM1[12] method.[13] (Chloromethyl)methylsilane (CMMS), the basic fragment of this ring enlargement reaction, has been used as the model compound to investigate the transition structure (TS; for a gas phase process without Lewis acid catalysis). AM1 results show that the simultaneous double migration, rather than the stepwise migration (either the radical or ionic dissociation), is the favorable reaction pathway from CMMS to ethylchlorosilane(ECS) (see Figure 1). The ionic mechanism *via* α-silyl cation is unfavorable in the calculation, since it involves highly charged structures. However, the activation energy of ionic dissociation in the solution will be dramatically reduced in the presence of solvents or Lewis-acid catalysts. In addition, our AM1 results show that $MeSiH_2CH_2^+$ ion can migrate to $MeCH_2SiH_2^+$ ion with little energy barrier (0.1 kcal/mol). Thus, the ionic mechanism *via* the α-silyl cation[4,14] should be considered as a possible mechanism for the Lewis-acid catalyzed conditions,

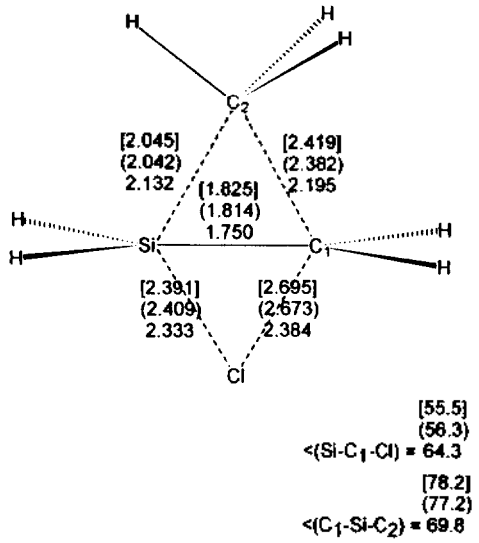


Figure 2. Transition structure for the simultaneous double migration. Geometric parameters are from AM1 (HF/3-21G*) [HF/6-31G*]. Values are lengths in Å, and angles in deg.

Table 1. Calculated Activation Energies (kcal/mol) for the Rearrangement of CMMS to ECS

Calculational level	Activation energy
AM1	67.9
MNDO	75.6
HF/3-21G*//HF/3-21G*[a]	67.3 (64.9)[b]
MP2/3-21G*//HF/3-21G*	68.5 (66.1)
MP3/3-21G*//HF/3-21G*	69.2 (66.8)
MP4(SDTQ)/3-21G*//HF/3-21G*	66.3 (63.9)
MP/6-31G*//HF/6-31G*	70.0 (67.6)
MP2/6-31G*//HF/6-31G*	74.7 (72.3)
MP3/6-31G*//HF/6-31G*	74.7 (72.3)
MP4(SDTQ)/6-31G*//HF/6-31G*	71.5 (69.1)

[a] Pople's notation, [b] The values in pharentheses are corrected for zero-point vibration energy.

although it is unlikely in the thermal reaction. Our AM1 results are consistent with recent thermal gas-phase studies.[4c] Early kinetic experiments by Eaborn and coworkers[4a] were also consistent with a doubly bridged TS for the $AlCl_3$-catalyzed rearrangement. Various alkyl substituents, except H, have little effect on the activation energy barriers. Hence, the migratory aptitude of alkyl groups is probably governed by steric effects in the TSs.

In order to assess the performance of AM1, the doubly bridged TS was computed by *ab initio* methods.[15] The geometric parameters of the TS are shown in Figure 2. The shape of TSs is almost identical, although the AM1 calculated TS is a little tighter than the *ab initio* calculated ones. The activation energies are summarized in Table 1. The results of semi-empirical methods are in excellent agreement with the ones of high-level *ab initio* theories. Our best estimate, MP4(SDTQ)/6-31G*//HF/6-31G* (with the zero-point vibration energy correction), is 69.1 kcal/mol, while AM1 gives

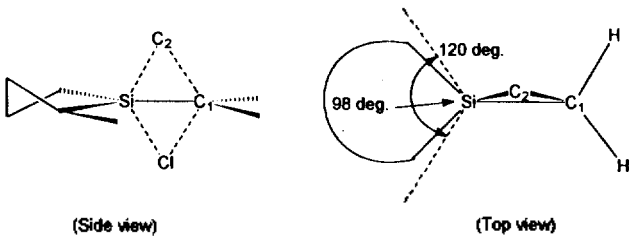


Figure 3. Transition structure for exocyclic me migration of **1**.

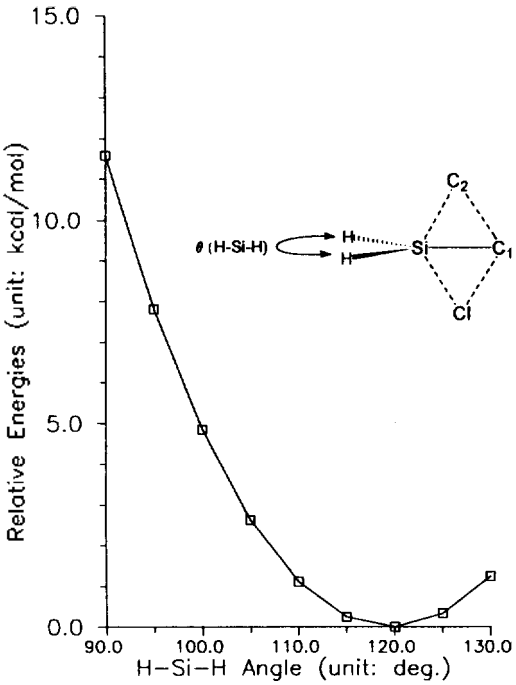


Figure 4. Relative energies (kcal/mol) due to the H-Si-H angle bending. Values are from *ab Initio* HF/6-31G* single point calculations by restricting Si, C_1, and two hydrogens in a plane (values are relative to the lowest energy conformation with the H-Si-H angle=119.78°, where total energy is −828.1034636 hartree).

67.9 kcal/mol. We are confident that AM1 methods gives the excellent estimates in geometries and energetics in this particular system.

Our molecular mechanics (MM2)[16] calculations predict that both **1** and chlorosilacyclopentane derivatives are stable in half-chair forms.[17] Although either the AM1-calculated TS from **1** or force field modeling of TS from CMMS will describe more accurately about the favorable reaction mechanism, plugging the TS of CMMS into the silacyclopentanes can provide qualitative conformational nature of the TS. If the intrinsic migratory aptitude among alkyl groups are not greatly different, the new silacyclopentanes as well as silacyclohexanes should be obtained from the rearrangement reaction from **1**. However, we have not seen any evidence of the presence of new silacyclopentanes. This result comes from either (1) the inferior migratory aptitude of Me group, or (2) the other steric nature of TS. The fact that two ring bonds (Et and *iso*-Pr moieties) migrate competitively prompts us to investigate the additional steric effect in the TS when an exocyclic ring bond migrates. Figure 3 depicts the TS for the exocyclic Me migration. In the exocyclic Me migration, there is an extra energy barrier due to the ring strain. We attempted to estimate the ring strain from the deviation of H-Si-H angle in the *ab initio* calculations while other geometric parameters are constrained to the ones at the fully optimized TS (see Figure 4). Since the endocyclic angles centered to the Si atom for 4-, 5-, and 6-membered cyclic silanes are about 90°, 100°, and 105° respectively, the additional energy barriers contributed from ring strain are estimated as 11.6, 4.9, and 2.7 kcal/mol[18] from HF/6-31G* level theory. Hence, the migration of exocyclic Me is difficult probably due to the ring strain present in the TS.

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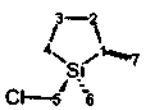
7. The notation of *cis* and *trans* is based on the relation between the two Me substituents.
8. The NMR peak assignments are as follow:

Atom	*cis*-**1**		*trans*-**1**	
	^{1}H	^{13}C	^{1}H	^{13}C
1	0.90-1.15(m)	17.81	0.80-1.15(m)	20.29
2	1.00-1.25(m)	36.86	1.10-1.25(m)	37.00
	1.80-1.95(m)		1.80-1.90(m)	
3	1.35-1.50(m)	24.78	1.40-1.50(m)	24.58
	1.70-1.90(m)		1.75-1.90(m)	
4	0.40-0.95(m)	11.08	0.65-0.85(m)	10.65
5	2.83(s)	29.43	2.86(s)	27.88
6	0.16(s)	−7.78	0.21(s)	−5.39
7	1.04-1.09(d)	15.00	1.06-1.10(d)	14.18



9. The rearrangement time (2h to several days) and regioselectivity (55/45 to 70/30) has shown some variations according to the amount of added $AlCl_3$. In general, lower

reactivity and greater selectivity can be obtained by adding a reduced amount of $AlCl_3$.
10. The chemical shifts of these 4 ^{1}H-NMR peaks, which have been assigned to 4 different compounds, are consistent with the our previous publication (for a detail, see Table 3 in ref. 11).
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15. Calculations have been performed with GAUSSIAN-92. Optimized structures have been determined at the HF/3-21G* and HF/6-31G* level. The TS was located by the eigenvector following routine (OPT=(TS, EF)), and confirmed by the frequency calculation (TS have only one imaginary frequency; $-619.8i$ cm^{-1} at HF/3-21G* and $-593.4i$ cm^{-1} at HF/6-31G*). Single-point energy calculations have been performed at the MP2, MP3, and MP4 levels to incorporate the electron correlation effect. Corrections also have been made for zero-point vibrational energies. Calculations have been run on a CRAY Y-MP2 E/232.
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18. Since these values are from the bending of H-Si-H angle, the estimated ring strains may have errors which come from the comparison between the H-Si-H and C-Si-C angle changes. However, the approximate force constant (0.38 mdyn.A°/rad^2) for the H-Si-H angle bending is smaller than the one (0.48 mdyn.A°/rad^2) for the C-Si-C angle bending. Therefore, the actual ring strains will be greater than our values.

Characterization of Conformational Changes in [d(ACGTATACGT)]$_2$-echinomycin and [d(ACGTTAACGT)]$_2$-echinomycin complexes by proton NMR studies

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Echinomycin derived from streptomyces is cyclic depsipeptide containing two planar quinoxaline rings that bisintercalate into DNA[1,2]. Echinomycin has antitumor activities and is now being used in phase II clinical trials for the treatment of human tumors[3]. Recently, a series of crystal and solution structure determinations of the complexes between echinomycin and DNA oligonucleotide fragments have been carried out in order to visualize how a drug can be accommodated by the DNA double helix[4-6]. According to the crystal structure of echinomycin complex with DNA hexamer [d(CGTACG)]$_2$, two echinomycins bind to each DNA duplex with the quinoxaline rings bracketing the CpG steps[4]. A remarkable feature of this structure is that the central A·T base pairs are Hoogsteen base paired. Using specifically deuterated DNA hexamer we also proved that the Hoogsteen base pair formation detected in X-ray crystallographic analysis was definitely retained in solution[7,8].

At this situation, it is of interest to ask how many Hoogsteen base pairs are formed near the binding sites when echinomycins bind to a DNA oligonucleotide in which the CpG binding sites are separated by more than two A·T base pairs. For example, in a complex between a DNA decamer [d(ACGTATACGT)]$_2$ and echinomycin, is it possible to form the Hoogsteen base pairs in the four central A·T base pairs? In order to address this question, we have examined two DNA decamers, [d(ACGTATACGT)]$_2$ and [d(ACGTTAACGT)]$_2$ in which echinomycin binding sites are separated by four base pairs.

The decamers, [d(ACGTATACGT)]$_2$ and [d(ACGTTAACGT)]$_2$ were synthesized on an Applied Biosystems DNA synthesizer using β-cyanoethyl phosphoramidite chemistry on a 2 μmole scale. The oligonucleotides were purified by Sephadex G-25 gel filtration column chromatography. Echinomycin was a gift from National Cancer Institute, USA. A saturated echinomycin-DNA complex of two drugs per DNA decamer was formed by adding 2 equivalents of echinomycin in methanol to the DNA sample in the NMR tube as reported previously[8]. All NMR experiments were done on a Bruker AMX-500 spectrometer.

A comparison of the imino and aromatic spectra of the two decamers, [d(ACGTATACGT)]$_2$ and [d(ACGTTAACGT)]$_2$ and their echinomycin complexes are shown in parts A and B of Figure 1, respectively. The imino protons have been assigned from a combination of NOE and temperature dependence measurements. The G3 and G9 imino resonances of both decamers shift upfield approximately 1 ppm when echinomycins bind. The T10 imino resonances also shift upfiled approximately 1 ppm at 1℃ (data not shown). These large upfield shifts are due to intercalative drug binding. The central T imino resonances of both decamers, however, shift only 0.2 ppm upfield or do not show any changes in chemical shift values. Previous NMR results showed that the central T imino resonance of the DNA hexamer [d(CGTACG)]$_2$-echinomycin complex were upfield-shifted by 1 ppm and A·T Hoogsteen base pairs were formed[8]. Therefore the central A·T base pairs of the present two decamers probably would not be Hoogsteen base pairs. As shown in Figure 1, the central T imino resonances of the [d(ACGTATACGT)]$_2$-echinomycin complex are much broader than those of the free DNA or [d(ACGTTAACGT)]$_2$-echinomycin complex, indicating that echinomycin binding destabilizes the base pairs in 'TATA' sequence. It is interesting that the imino resona-