7 h) without significant reduction of the aromatic ring. Compound **7b** was not isolated but was converted into **9** (Ac_2O–pyridine, 0 °C, 16 h) which was separated from peracetylated **7b** by column chromatography. Reaction of **9** (dark oil) with triethyl orthoformate in the presence of Me_2SO and a catalytic amount of *p*-toluenesulfonic acid (95–115 °C, 24 h) gave **10** (mp 180–184 °C (from EtOH)),[13] in 5% overall yield. Deacetylation of **10** with concentrated HCl (20 °C, 23 h) provided a 66% yield of 2b (mp 311–313 °C dec).[14] Alternatively, conversion of **7b** (isolated by cation-exchange chromatography; NMR (Me_2SO-d_6) δ 2.14 (s, 3 H), 4.11 (s, 1 H), 6.71 (d, J = 8 Hz, 1 H), 6.75 (s, 1 H), 7.18 (d, J = 8 Hz, 1 H)) into **8b** (mp 253–255 °C dec)[15] and then into **2b** by methods analogous to the synthesis of **2a** was accomplished in overall yield comparable with that via **9** and **10**.

Comparison of **2a** and **2b** with FO, generated from F_{420} by acid hydrolysis,[3] revealed the identity of **2a**, but not to **2b**, with FO. FO and **2a** have identical UV–visible spectra (λ_{max} 420 nm (ϵ 42 000 to 44 000 M^{-1} cm^{-1})), while **2b** shows a 6-nm red shift (λ_{max} 426 nm (ϵ 45 000 M^{-1} cm^{-1})). Stoichiometric complexation of each compound with egg white flavin-binding apoprotein[16,17] produced a bathochromic shift of λ_{max} to 404 nm (ϵ 6000 M^{-1} cm^{-1}) for **2a** and FO, but to 410 nm (ϵ 6000 M^{-1} cm^{-1}) for **2b.** Curiously, **2b** is a substrate for conversion into the FMN and FAD levels by the *B. ammoniagenes* riboflavin kinase-FAD synthetase complex,[6] but **2a** and the FO sample were not. Reduction with borohydride or H_2–Pt bleached the 420- or 426-nm (**2b**) peak and produced the anticipated[3] new transition in the 320–322-nm region (ϵ 10 000), characteristic of the 1,5-dihydro-5-deazaisoalloxazine chromophore.[6] With 175 μg of crude hydrogenase from *Methanobacterium thermoautotrophicum* strain, ΔH, 10 nmol of FO and **2a** were quantitatively reduced in seconds, while **2b** was reduced ca. tenfold more slowly to the 1,5-dihydro species. One-electron reductants of appropriate potential (dithionite, *A. vinlandii* flavodoxin[18]) were ineffective, as in the parent 5-deazaflavin system,[5,6] strongly suggesting that in vivo reduction of F_{420} by methanogen hydrogenase is an obligate two-electron process involving transfer of a hydride equivalent to C-5 of F_{420}.[19] The slow autoxidation of dihydro-F_{420} by O_2 has been suggested[3] and is also a feature of **2a, 2b,** and FO.

The aggregate chemical and biochemical data support the identity of **2a**, but not **2b**, with the riboflavin level acid hydrolysis product (FO) of F_{420} and confirm the proposed[3] structure of the methanogen redox coenzyme as a 7,8-didemethyl-8-hydroxy-5-deazariboflavin derivative.[20] The availability of synthetic material may facilitate studies of the redox role and electron-transfer mechanism of F_{420} in biological methane formation.

Acknowledgment. We gratefully acknowledge from Professor Ralph S. Wolfe and Dr. Bill Ellefson the generous provision of samples of factor 420 and crude methanogen hydrogenase, without which many of the reported experiments could not have been performed. We also thank Dr. Edward F. Rogers for encouragement and support during the course of this work. Research at M.I.T. was supported in part by NIH Grant GM 21643 and the Dreyfus Foundation.

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(11) NMR (Me_2SO-d_6) δ 3.11, 3.17, 3.27, 3.34 (s, total 6 H), 5.91 (br s, 2 H), 7.0–7.5 (m, 2 H), 7.99 (d, J = 8 Hz, 1 H), 8.88 (s, 1 H), 10.93 (br s, 1 H), 11.27 (br s, 1 H). The complexity of the methoxymethylene signals may result at least in part from the presence of a pair of diastereomers, but the possibility of other positional isomers such as 2',4':3',5'-bis-*O*-methoxymethylene cannot be ruled out.
(12) NMR (Me_2SO-d_6) δ 7.04 (d, J = 9 Hz, 1 H, H-7), 7.40 (br s, 1 H, H-9), 8.01 (d, J = 9 Hz, 1 H, H-6), 8.89 (s, 1 H, H-5), 11.01 (s, 1 H, exchangeable), 11.2 (v br hump, 1 H, exchangeable); NMR (D_2O–7.5% Na_2CO_3) δ 6.3 (s, 1 H, superimposed on adjacent d, H-9), 6.43 (d, J = 9 Hz, 1 H, H-7), 7.04 (d, J = 9 Hz, 1 H, H-6), 7.58 (s, 1 H, H-5) (cf. ref 3); field desorption mass spectrum *m/e* 364 (M^+ + 1); $[\alpha]^{25}_D$ +38° (*c* 0.5, 0.1 N NaOH).
(13) NMR ($CDCl_3$) δ 1.74, 2.07, 2.23, 2.29, 2.36, 2.45 (s, each 3 H), 7.60 (s, 1 H), 7.76 (s, 1 H), 8.79 (s, 1 H), 9.06 (br s, 1 H, exchangeable); mass spectrum *m/e* 587, 588 (M^+, M^+ + 1).
(14) NMR (Me_2SO-d_6) δ 2.30 (s, 3 H, CH_3), 7.57 (s, 1 H, H-9), 8.01 (s, 1 H, H-6), 8.95 (s, 1 H, H-5), 11.11 (s, 1 H, exchangeable); field desorption mass spectrum *m/e* 378 (M^+ + 1).
(15) NMR (Me_2SO-d_6) δ 2.26 (s, 3 H), 3.13 (s, 3 H), 3.28 (s, 3 H), 5.97, 5.99 (overlapping s, total 2 H), 7.24 (s, 1 H), 7.88 (s, 1 H), 8.78 (s, 1 H), 10.91 (s, 1 H), 11.39 (br s, 1 H).
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(19) Reduction of **2a** and FO with D_2–Pt followed by reoxidation with O_2 yielded reoxidized **2a** and FO with >90% deuterium at C-5 by 60 -MHz FT NMR analysis.
(20) Evidence for the D-ribityl side chain in F_{420} was obtained by limited acid hydrolysis to the FMN level and stoichiometric complexation with *A. vinlandii* apoflavodoxin[18] ($K_D \leq 10^{-9}$ M), a protein known to be highly specific for the D-ribityl side chain of FMN derivatives.

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Regiospecific Photosensitized Oxygenation of Vinylsilanes. A Method for Converting Saturated Ketones to 1,2-Transposed Allylic Alcohols. Possible Role of Silicon in Directing the Regioselectivity of Epoxysilane Cleavage Reactions

Sir:

The considerable importance of regiospecificity to organic synthesis makes continued search for such methodology a high priority challenge. Herein we describe the development of a simple procedure capable of shifting the position of a ketone carbonyl by one carbon in an entirely predictable manner with concomitant introduction of a double bond. The new sequence broadens the scope of previously developed carbonyl transposition chemistry[1] and also provides access to α-silylated allylic alcohols, a less well-known class of compounds.[2]

Our approach is based on an awareness that α,β-epoxysilanes experience ring opening with a regioselectivity contrary to that followed by epoxides lacking carbon–metal bonds. Thus, exposure of **1** and its congeners to a variety of reagents, which include Brønsted[3-6] and Lewis acids,[5-8] cuprates,[9] and

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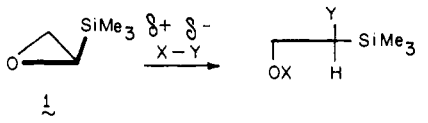
Table I. Reduced Mulliken Overlap Populations[a] Derived from EH Calculations on **1–4**

compd	bond 1-2	bond 2-3	compd	bond 1-2	bond 2-3
1	0.4720	0.5501	**3b**	0.4901	0.5644
2a	0.5086	0.5610	**2c**	0.5257	0.5586
3a	0.4920	0.5571	**3c**	0.4978	0.5496
2b	0.4975	0.5662	**4**	0.5461	0.5620

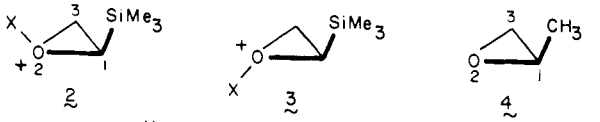
[a] Reference 16.



1

aluminum hydrides,[1,4,10] generally results in efficient cleavage of the C–O bond proximate to the silicon atom. Since cationic charge β to silicon ($R_3Si-C-C^+<$) enjoys considerable stabilization because of $\sigma-\pi$ hyperconjugation with the C–Si bond,[11,12] while cations in the α position ($R_3Si-C^+<$) are destabilized,[13,14] it is all the more remarkable that epoxysilane chemoselectivity appears not to be governed by similar electronic constraints. Past attempts to rationalize this seemingly anomalous behavior have focused upon the involvement of silicon's vacant d orbitals,[10] the possible intervention of pentacoordinate silicon intermediates,[6,10] as well as an invoking of S_N2 "borderline" behavior.[4]

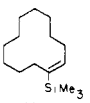
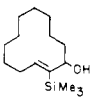
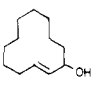
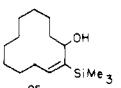
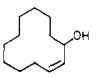
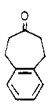
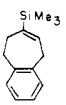
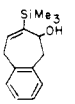
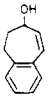
In the present work, Hückel calculations[15] carried out on the model compounds **1–4** prove to be fully consistent with the observed regioselectivity insofar as a smaller value is predicted



2 3 4

a, X = H
b, X = BH_3^-
c, X = O^-

Table II. 1,2-Oxidative Transposition of Vinylsilanes Including the Desilylation Step[a]

ketone	vinylsilane	isold yield, %	α-silylated allylic alcohol[b]	reaction time, h	convn, %	isold yield, %[c]	allylic alcohol	isold yield, %
	 9	91	 10	12	12	25	 11	51
	 5	87	 12	26	100	56	 13	97
	 14	97	 cis/trans=1:3 15	30	50	59	 16	96
	 17	96	 18	4	86	25	 20	98
			 19			16	 21	100
	 22	95	 23	48	59	39	 24	96
			 25			9	 26	96
	 27	89	 28	12	62	76	 30	60[d]
			 29			24		

[a] All compounds were characterized by IR, NMR, and accurate mass spectral measurements. [b] A 5.0-g sample of vinylsilane dissolved in methanol (200 mL) containing rose bengal (200 mg) was irradiated with a Sylvania DYV lamp housed in a water-cooled Pyrex well and also air cooled. Excess sodium borohydride was added to the crude reaction mixture. After 30 min, the solvent was evaporated and the residue partitioned between water and ether. The product was isolated by silica gel chromatography. [c] These yields have been normalized to account for recovered starting material. [d] Partial dehydration occurs upon purification to give 30% benzocycloheptatriene.

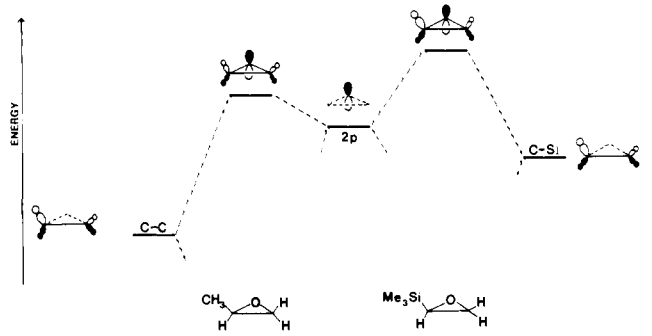


Figure 1. Interaction diagrams for **1** (right) and **4** (left).

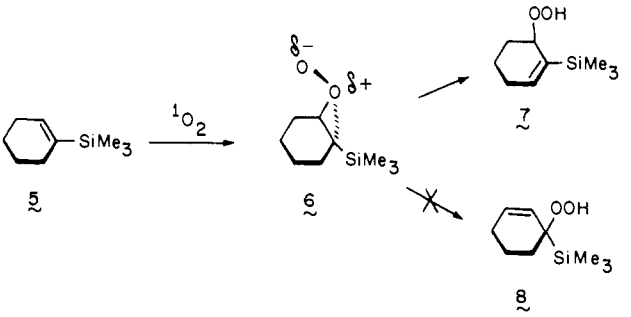
for the reduced overlap population[16] of the C–O bond proximate to the $SiMe_3$ group. Standard bond lengths and parameters were adopted for the oxirane ring and a value of 1.86 Å was selected for the C–Si bond length. The valence-state ionization potentials employed for Si were $H_{ii}(3s)$, −17.3 eV, and $H_{ii}(3p)$, −9.2 eV. The orbital exponents were derived from Burns' rules.[17] The relevant data which are listed in Table I were obtained without consideration of the 3d orbitals on Si; inclusion of these additional orbitals did not alter the relative ordering of the reduced overlap populations.

Deeper insight into our results can be gained by comparing the two interaction diagrams presented in Figure 1. The left diagram shows that the highest occupied molecular orbital (HOMO) of propylene oxide (**4**) can be regarded as a linear combination of an oxygen 2p orbital and a σ orbital strongly localized on the C–C and C–H bonds. It is important to note that the wave function of the HOMO is C–O antibonding. Replacing one C–C fragment by a C–Si unit leads to a stronger antibonding interaction between the 2p lone pair and the corresponding σ orbital (Figure 1, right). This is due mainly to a reduction of the energy difference between the oxygen 2p orbital and the C–Si σ orbital in comparison with the C–C σ orbital.[18] The enhanced antibonding interaction leads to a weakening of the C–O bond α to silicon. In the case of compounds **2a–c** (**3a–c**),[21] the interaction mentioned above is somewhat mitigated since the 2p lone pair on oxygen is replaced by an sp^n hybrid directed away from the C–Si bond. This is indicated below for **1**, **2a**, and **3a**.

	1	2a	3a
reduced overlap population	0.1730	0.5086	0.4920

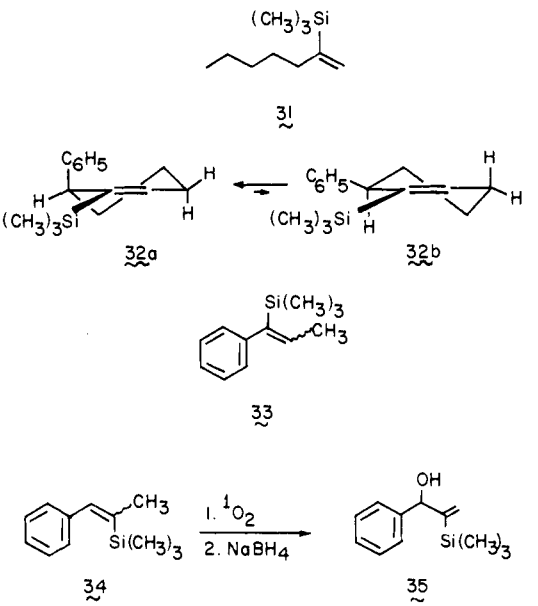
Thus, we see that the C–Si and O_2–C_3 bonds in **1–3** are not favorably aligned for stabilization of a developing positive charge at C_β, and therefore that this geometric constraint cannot account for the facilitation[23] of nucleophilic displacement α to silicon. Rather, the enhanced ground-state electrophilicity of the α carbon is considered to materialize because of the antibonding interactions discussed above. Our calculations also identify the unsymmetrical nature of the perepoxide intermediates **2c** and **3c** which is formalized more explicitly in **6**. The longer C–O bond should reveal itself by a pronounced regioselectivity which delivers an allylic hydroperoxide with a retained (though relocated) vinylsilane moiety (**7**) instead of an α-hydroperoxysilane (**8**). This prediction has been put to rather extensive experimental test and strongly supportive findings uncovered.

As before,[1] the vinylsilanes were prepared from the corresponding ketone benzenesulfonylhydrazones.[24] In such reactions, electronic[25] and steric factors[26] almost always combine



5 6 7 8

to direct the double bond cleanly to the less substituted α position. The vinylsilanes were then exposed to singlet oxygen as generated by the customary dye sensitization technique. It is presently recognized that the relative reactivities of sterically similar π systems toward $^1O_2$ are controlled to a large extent by their ionization potentials.[27] However, photoelectron spectroscopic data reveal that vinylsilanes have π-HOMO energies rather comparable with those of structurally related all-carbon compounds.[28] While dioxetane formation is not expected with such molecules, reactions of the ene type should not on this basis be electronically impeded. We have observed that they are not, except when the double bond is terminal and disubstituted as in **31**.



31 32a 32b 33 34 35

The rates of reaction of trisubstituted vinylsilanes with singlet oxygen do vary qualitatively from system to system, presumably a reflection of the differing degrees of steric congestion about the π bond. Remarkably, however, sodium borohydride reduction of the hydroperoxidic product gives rise only to β-silylated allylic alcohols, there being no evidence for formation of α-silylated derivatives except in the special case of **25** (Table II).

The degree to which these oxygenation reactions are regiospecific is perhaps best dramatized by (a) the conversion of **27** into **28** and **29** in a ratio of 3:1, despite the customary high reactivity of benzylic hydrogens toward singlet oxygen;[29] (b) the unreactivity of 1-trimethylsilyl-6-phenylcyclohexene which exists for steric reasons[30] chiefly in the conformation depicted by **32a** and therefore realistically has only "regioreversed" allylic hydrogens available for abstraction; and (c) the stability of **33** to conditions which transform **34** into **35** (40% conversion).

Further, it has been found that photooxygenation of more flexible vinylsilanes affords mixtures of cis- and trans-α-silylated allylic alcohols (Table II) which can efficiently be sep-

arated by VPC and/or column chromatographic methods.[31,32]

To convert the α-silylated allylic alcohol products into their desilylated counterparts, advantage was taken not only of the affinity of fluoride ion for silicon, but also for the accelerative effect of the β-hydroxyl group.[33] The most effective conditions uncovered involved heating with tetra-*n*-butylammonium fluoride (10 equiv) in dry acetonitrile. Requisite reaction times varied from 1 to 36 h, with the more flexible, open systems reacting faster. Of particular note here is the preservation of geometry about the π linkage during Si–C bond fission.[34]

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A Novel Pyrimidine to Pyridine Ring Transformation Reaction. A Facile Synthesis of 2,6-Dihydroxypyridines[1,2]

Sir:

The synthesis of a new heterocyclic ring by transformation of another ring system via a nucleophilic reaction has been an important subject of chemistry.[3] It has been known[4] that uracil can be converted into pyrazolone and isoxazolone by reaction with hydrazine and hydroxylamine, respectively. These reactions have been exploited extensively in the chemical modification of nucleic acids.[5] Several examples of the ring conversion of the pyrimidine system into the pyridine system have been reported in the literature;[6-8] however, none of them involves the direct replacement of the N_1–C_2–N_3 portion of the pyrimidine by a C–C–N fragment.

In this report we describe the first transformation of the pyrimidine ring into the pyridine system via direct displacement of the N_1–C_2–N_3 portion by a C–C–N fragment. In this investigation 1,3-dimethyluracil derivatives (**1**) were used as the pyrimidine while various α-substituted acetamides (**2**) served as the ambident C–C–N donors. Thus, treatment of 1,3-dimethyluracil (**1a**) with malonamide (**2a**) in ethanolic sodium ethoxide[9] at reflux for 30 min, followed by neutralization of the reaction mixture with concentrated HCl, afforded the known[10] 2,6-dihydroxynicotinamide (**3a**) and 1,3-dimethylurea. The structure of **3a** was confirmed further by its conversion into 2,6-dihydroxypyridine[11] by hydrolytic decarboxylation.

On the basis of the isolation of 1,3-dimethylurea from the reaction mixture and the fact that the reaction product is a 2,6-dihydroxypyridine derivative (a 2,4-dihydroxypyridine analogue was not detected in this reaction), the plausible mechanism shown in Scheme I is suggested. Nucleophilic attack of the carbanion of **2a** on C_6 of **1a** would occur first to give rise to Michael adduct A.[12,13] Abstraction of the proton from the exocyclic α position of A in basic medium accompanied by scission of the N_1–C_6 bond to give the open-chain intermediate B would then be followed by intramolecular cyclization on C_4 to afford **3a** and 1,3-dimethylurea. The near-quantitative recovery of starting materials from the attempted reaction of **1a** with methylmalonamide (which lacks the abstractable α proton as in A) lends further support to this proposed mechanism.

When acetamide derivatives bearing electron-withdrawing R′ substituents (**2b–d**) were employed instead of malonamide (**2a**) in the above reaction, the corresponding 5-substituted 2,6-dihydroxypyridines (**3b–d**) were obtained.[14] Acetamide

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