Table I. Zero-Order Rate Constants for Deacetylation of Acetyl-α-chymotrypsin[a] at pH 7.5 and Equivalent[b] in Mixtures of Protium Oxide and Deuterium Oxide (Atom Fraction Deuterium n) at 25.00 ± 0.05°

n	$10^{11}v_n$,[c] M sec^{-1}
0.000	2649 ± 3
0.175	2425 ± 11
0.261	2239 ± 4
0.398	2126 ± 11
0.485	1878 ± 7
0.497	2064 ± 32
0.583	1791 ± 14
0.745	1479 ± 13
0.765	1459 ± 10
0.995	1102 ± 24

[a] Generated by excess p-nitrophenyl acetate from α-chymotrypsin (Sigma 3× crystallized) at 0.2 mg/ml. [b] All solutions contained 0.7571 g/l. of Trizma Base and 3.7319 g/l. of Trizma-HCl buffer components. Because the pH–rate inflections for α-chymotrypsin respond normally to D_2O ($\Delta pK \sim 0.6$),[1] this will maintain the pH(D) of all solutions at the same relative point on the pH(D)–rate profile. [c] Averages of two–five determinations (spectrophotometric appearance of p-nitrophenol at 400 nm), calculated from an extinction coefficient of 18,000 M^{-1} cm^{-1} for p-nitrophenoxide. Error limits are average deviations from the mean.

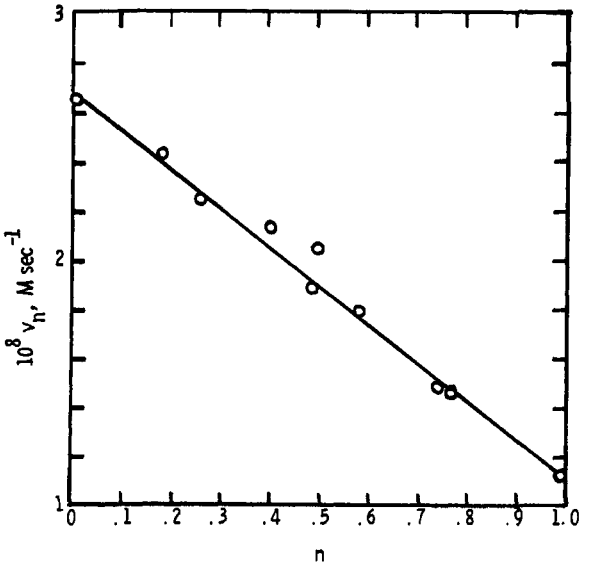

Figure 1. Velocities of deacetylation of acetyl-α-chymotrypsin *vs.* the atom fraction of deuterium in the solvent. The data are from Table I. The dependence is linear, indicating one-proton catalysis.

The linear fall-off in rate with increasing n demonstrates one-proton catalysis because the rate v_n in the mixed isotopic solvent is then just the weighted average of the rates in pure isotopic solvents (v_0 in pure H_2O and v_1 in pure D_2O) as shown in eq 1, where ϕ^* is also known as an isotopic fractionation factor.[2]

$$v_n = nv_1 + (1 - n)v_0 = v_0(1 - n + nv_1/v_0) = v_0(1 - n + n\phi^*) \quad (1)$$

This is true only when each increment of deuterium produces a *proportional* increment in rate, which in turn is true only when a single transition-state hydrogenic site is "titrated" by deuterium. In a more general case, the rate is described[2] by eq 2, where ϕ_i^R and ϕ_i^T are isotopic fractionation factors for the ith exchangeable hydrogenic site in reactant and transition states, respectively. Equation 2 shows that any reasonable circumstance other than one-proton catalysis will necessitate a higher order polynomial fit of $v_n(n)$. For example, two-proton catalysis would yield a linear relation only if there were a highly fortuitous cancellation of n dependences between the second-proton factor and the reactant-state contribution (denominator of eq 2).

$$v_n = v_0\prod_i(1 - n + n\phi_i^T)/(1 - n + n\phi_i^R) \quad (2)$$

This result is consistent with enzymic activated complexes[3] involving motion of a proton between the imidazole function of His-57 and the oxygen of a water molecule or the acyl or ether oxygens of acetylated Ser-195 as long as other protons are not substantially altered in binding state. It is also consistent with a rate-determining conformation change of the acyl enzyme[4] if a single-proton alteration accompanies this process. It is not consistent with the "charge-relay" mechanism[5] in which proton transfer between Asp-102 and His-57 is supposed to cooperate with general catalysis by the latter. This would constitute at least two-proton catalysis.

Acknowledgment. This research was supported by the National Science Foundation and the National Institutes of Health.

(2) A. J. Kresge, *Pure Appl. Chem.*, 8, 243 (1964); V. Gold, *Advan. Phys. Org. Chem.*, 7, 259 (1969).
(3) G. P. Hess in "The Enzymes," P. D. Boyer, Ed., Vol. III, 3rd ed, Academic Press, New York, N. Y., 1971, pp 217–234.
(4) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, pp 310–312.
(5) D. M. Blow, J. J. Birktoft, and B. S. Hartley, *Nature (London)*, **221**, 337 (1969).
(6) (a) National Science Foundation Undergraduate Research Participant; Sterling College, Sterling, Kan.; (b) Graduate Honors Fellow; (c) holder of a Research Career Development Award of the National Institute of General Medical Sciences.

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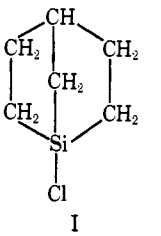
Dramatic Stereochemistry Crossover to Retention of Configuration with Angle-Strained Asymmetric Silicon

Sir:

More than a decade has passed since we reported that the bridgehead chloride, 1-chloro-1-silabicyclo-[2.2.1]heptane (I), in sharp contrast to its carbon analog,



I

hydrolyzes rapidly in moist air, undergoes quantitative rapid titration of its Si–Cl bond with 0.1 N alkali, and also is rapidly reduced by lithium aluminum hydride giving the Si–H compound.[1] The above very rapid reactions of I occur without destruction of the bridge-

(1) L. H. Sommer and O. F. Bennett, *J. Amer. Chem. Soc.*, **79**, 1008 (1957).

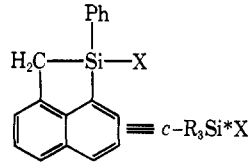
head ring system and therefore must proceed with *retention* of configuration.

Subsequently,[2] we found that a wide variety of acyclic, optically active R_3Si^*Cl compounds undergo both hydrolysis reactions and reduction with lithium aluminum hydride *via* predominant (>95%) *inversion* of configuration.

These two sets of facts could be accommodated by an interesting hypothesis—*angle strain at silicon greatly favors retention of configuration.*

Recent studies by Corriu[3] and Sakurai[4] on silicon contained in 6-rings, and having little or no angle strain, showed that these ring silicon centers behave stereochemically like acyclic R_3Si^*Cl in the great majority of cases studied.[5] These facts tended to support our angle-strain hypothesis (considerable angle strain is present at both of the bridgehead carbons of bicyclo[2.2.1]-heptane, about 17.5° of strain, and this is probably larger in the case of the bridgehead silicon in I because of the larger size of silicon)[6] but real proof required the resolution and stereochemical study of an optically active organosilicon system containing angle-strained asymmetric silicon.

The 1-phenyl-1-silaacenaphthene system (II), *c*-R_3Si^*X,[7]



II

appeared to be ideal for such a study. 1-Silaacenaphthene[8] was monochlorinated and then treated with phenylmagnesium bromide to give a 66% yield of (±)*c*-R_3Si^*H.[9] Chlorination of (±)*c*-R_3SiH followed by addition of (−)-menthol in heptane and removal of the HCl thus formed by bubbling N_2 through the reaction mixture gave a 97% yield of (±)*c*-R_3Si^*(−)OMen.[9] This diastereomeric mixture was separated by fractional crystallization from pentane. The highest melting, mp 74–77°, diastereomer, (+)*c*-R_3Si^*(−)OMen, when treated with diisobutylaluminum hydride (dibal) in *n*-hexane gave (+)*c*-R_3Si^*H, $[\alpha]_D$ +19.2°, in a 91% yield.

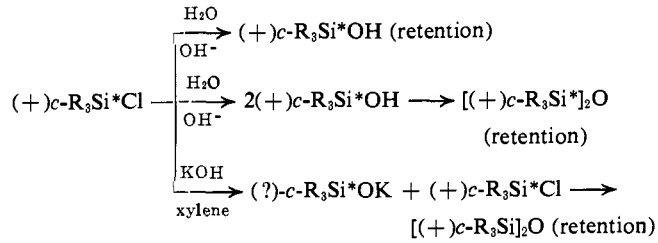
Chlorination of (+)*c*-R_3Si^*H with Cl_2 in CCl_4 gave (+)*c*-R_3Si^*Cl. In order to correlate the configurations of (+)*c*-R_3Si^*H and (+)*c*-R_3Si^*Cl, the free radical chlorination using CCl_4 and benzoyl peroxide was carried out on (+)*c*-R_3Si^*H to give (+)*c*-R_3Si^*Cl. Since this reaction has been shown to go through a silyl radical intermediate,[10] the formed chloride must either be racemic or be formed with *retention* of configuration. Therefore (+)*c*-R_3Si^*H and (+)*c*-R_3Si^*Cl have the same configuration. Reduction of (+)*c*-R_3Si^*Cl with either dibal in hexane or lithium aluminum hydride in diethyl ether went with predominant *retention*, 98.8 and 87.5%, respectively, to give (+)*c*-R_3Si^*H.[11] The dramatic effects of angle strain in *c*-R_3Si^*X on stereochemistry (see below for the strain in the C–Si–C ring angle) are perhaps best illustrated by the two Walden cycles (eq 1 and 2) in which all four reactions have a high stereospecificity.

$$(+)R_3Si^*H \;(+34°) + Cl_2 \xrightarrow{\text{retention}} (-)R_3Si^*Cl + LiAlH_4 \xrightarrow{\text{inversion}} (-)R_3Si^*H\ (-34°) \quad (1)$$

$$(+)c\text{-}R_3Si^*H \;(+19°) + Cl_2 \xrightarrow{\text{retention}} (+)c\text{-}R_3Si^*Cl + LiAlH_4 \xrightarrow{\text{retention}} (+)c\text{-}R_3Si^*H\ (+15°) \quad (2)$$

When (+)*c*-R_3Si^*Cl is added to a heterogeneous mixture of water, triethylamine and pentane, it reacts to form a mixture of (+)*c*-R_3Si^*OH and [(+)*c*-$R_3Si^*]_2O$. Allowing (+)*c*-R_3Si^*Cl to react with potassium hydroxide in *p*-xylene gave [(+)*c*-$R_3Si^*]_2O$. When [(+)*c*-$R_3Si^*]_2O$ was reduced with dibal in hexane, (+)*c*-R_3Si^*H was produced with 85.4% predominant retention. Dibal in *n*-hexane, an electrophilic reducing agent, reduces *all* silicon functional groups so far studied with *retention* of configuration.[11] These groups include –F, –Cl, and –OR leaving groups among others. It is therefore reasonable to assume that [(+)*c*-$R_3Si^*]_2O$ was reduced with *retention* of configuration. Although we have been unable to reduce (+)*c*-R_3Si^*OH stereoselectively,[12] it must represent an intermediate in the formation of [(+)*c*-$R_3Si^*]_2O$. Thus (+)*c*-R_3Si^*Cl, (+)*c*-R_3Si^*OH, [(+)*c*-$R_3Si^*]_2O$, and (+)*c*-R_3Si^*H must all have the same configuration. Therefore, we arrive at the stereochemical reactions given in Scheme I. In dramatic contrast to the above stereochemical results of *retention* for reactions of *c*-R_3Si^*Cl, the corresponding reactions of R_3Si^*Cl *all* proceed with predominant *inversion of configuration*.

Scheme I



The 1-Np–Si–CH_2 angle in *c*-R_3SiPh has been shown by X-ray crystallography to be 93.4°,[13] indicating that the system does contain considerable angle strain at the silicon as is the case for the bridgehead I. The fact that the chloride in *c*-R_3Si^*Cl is displaced with *retention*

(2) (a) L. H. Sommer, "Stereochemistry, Mechanism and Silicon," McGraw-Hill, New York, N. Y., 1965; (b) L. H. Sommer, *Intra-Sci. Chem. Rep.*, in press.

(3) R. Corriu and J. Masse, *Bull. Soc. Chim. Fr.*, 3491 (1969).

(4) H. Sakurai and Murakami, *J. Amer. Chem. Soc.*, **94**, 5081 (1972).

(5) Deviation from the stereochemical behavior of acyclic R_3Si^*X is claimed by Corriu and coworker for certain reactions of unstrained ring silicon centers with organolithium and organomagnesium reagents. *Cf.* R. Corriu and J. Masse, *Chem. Commun.*, 1373 (1968); *Tetrahedron Lett.*, 5197 (1968).

(6) For example, the ring C–Si–C angle in II is 93.4° whereas the corresponding C–C–C angle in acenaphthene is 105.2°; see H. W. W. Ehrlich, *Acta Crystallogr.*, **10**, 699 (1957).

(7) R_3Si^*X has become a common abbreviation for the α-NpPhMeSiX system. Since II has basically the same types of groups attached to the silicon, it seemed natural to abbreviate it as *c*-R_3Si^*X.

(8) Prepared by the method of E. A. Chernyshev and N. G. Tolstikova, *J. Gen. Chem. USSR, Engl. Trans*, **40**, 1039 (1970).

(9) All new compounds mentioned in this communication have given suitable nmr, ir, and elemental analysis.

(10) (a) L. H. Sommer and L. A. Ulland, *J. Org. Chem.*, **37**, 3878 (1972); (b) H. Sakurai, M. Murakami, and M. Kumada, *J. Amer. Chem. Soc.*, **91**, 519 (1969).

(11) L. H. Sommer, J. McLick, and C. M. Golino, *ibid.*, **94**, 669 (1972).

(12) Reduction of *c*-R_3Si^*OH with either dibal or lithium aluminum hydride is also exceedingly slow.

(13) H. Hope and N. Kim, private communication.

even by strong nucleophiles, such as lithium aluminum hydride and potassium hydroxide, dramatically illustrates the effect of angle strain on displacements at silicon.[14] It now seems clear, as was postulated in our original communication,[1] that the effects at strained bridgehead or strained monocyclic silicon can be accommodated by having an intermediate or transition state in which an apical-equatorial geometry obtains for two nonreacting groups forming a strained angle with the silicon. This leads to *retention* of configuration as the favored stereochemistry *even in the present case in which* (contrasting sharply with the bridgehead case) *inversion of configuration is also possible*, but, nevertheless, does not occur.[15]

Acknowledgment. Support of this work by a grant from National Science Foundation is gratefully acknowledged. We also thank L. Arlie Ulland for originally calling our attention to the reported synthesis of the ring system of compound II.

(14) For a recent review of dramatic rate effects at phosphorus produced by angle strain, see M. J. Gallagher and I. D. Jenkins, *Top. Stereochem.*, 3, 70 (1968). See also, F. H. Westheimer, *Accounts Chem. Res.*, 1, 70 (1968).

(15) Presented in part as a plenary lecture at the Third International Symposium on Organosilicon Chemistry, Aug 23, 1972.

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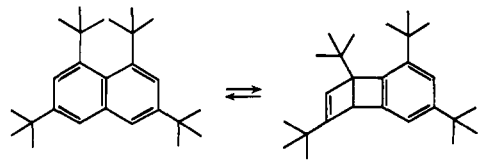
Photoisomerization of *peri*-Di-*tert*-butylnaphthalenes

Sir:

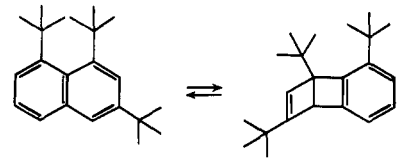
The initial preparation of a benzene valence isomer was accomplished by a photoisomerization reaction in 1962.[1] Since that original impetus, there have been published many photochemical and synthetic studies on benzene valence isomers.[2] In the naphthalene series, there have been two cycloaddition type syntheses of a Dewar isomer[3] and one construction of a benzvalene isomer *via* carbenoid insertion.[4] We here report the first photoisomerizations of intact naphthalenes to their Dewar isomers.[5]

The tetra-*tert*-butylnaphthalene (**1**) upon irradiation with a Hanovia, 450-W high-pressure lamp with a Pyrex filter, in cyclohexane or hexane, affords a photostationary state in which isomer **2** is present in 94% yield. The photoproduct was isolated from the yellow solution by first removing the solvent at room temperature, then by rapid chromatography through neutral alumina (activity 2). The solid product was recrystallized from warm methanol, affording material in the melting range 54–78°, *m/e* 352, whose uv showed no naphthalenic absorption. *Anal.* Found: C, 88.4; H, 11.4. The product was further characterized by its nmr [(CCl_4) δ 1.00 (9 H, s), 1.13 (9 H, s), 1.30 (9 H, s), 1.38 (9 H, s),



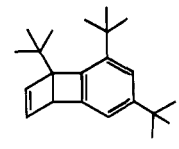
1 2

3.91 (1 H, d, J = 1.5 Hz), 6.10 (1 H, d, J = 1.5 Hz), 6.89 (1 H, d, J = 1.5 Hz), 7.08 (1 H, d, J = 1.5 Hz)], its uv [max (hexane) 273 nm (log ϵ 2.83), 282 (2.82)], and its thermal reversion to **1** (thus ruling out any more deep-seated photoisomerization). Rate constants for this reversion were determined to be 1.07 ± 0.06 × 10^{-5} sec^{-1} at 50° ($t_{1/2}$ 18.3 hr), 5.8 ± 0.20 × 10^{-5} sec^{-1} at 65° ($t_{1/2}$ 3.35 hr), and 2.6 ± 0.1 × 10^{-4} sec^{-1} at 80° ($t_{1/2}$ 0.75 hr). These values may be compared to half-lives of 4.0 hr at 38° for the parent Dewar naphthalene,[3a] 1.5 hr at 70° for the tetramethyl case,[3b] and 2.9 hr at 150° for hexamethyl(Dewar benzene).[6] From our data, Arrhenius activation parameters of E_a = 24.0 ± 1.0 kcal/mol and log A = 11.3 ± 0.8 can be derived. We note the small log A (negative entropy of activation) compared to most literature values for Dewar benzene ring openings.[7] An explanation based on the restricted rotation of *tert*-butyl groups observed in the product,[8] requiring constraints on the rotational freedom of the Dewar isomer in order that it might proceed along the reaction coordinate to the transition state, will be presented in our full paper. The tri-*tert*-butylnaphthalene (**3**) was photolyzed to afford Dewar isomer **4**



3 4

(colorless oil, *m/e* 296; isolation, *vide supra*) which was characterized by its nonnaphthalenic uv and by nmr (CCl_4): δ 1.00 (9 H s), 1.13 (9 H,s), 1.38 (9 H s), 3.97 (1 H, d, J = 1.5 Hz), 6.14 (1 H, d, J = 1.5 Hz), 6.67–7.17 (3 H, m). Thermal reversion of **4** to **3** occurred at 50° with a half-life of 14.7 hr. By our nmr analytical method, the isomer **5** could not be detected. One inter-



5

pretation of this result is that it is evidence for buttressing effects between the *m*-*tert*-butyl groups.[9,10] It is clear from an examination of models that if small re-

(1) E. E. van Tamelen and S. P. Pappas, *J. Amer. Chem. Soc.*, 84, 3789 (1962).

(2) E. E. van Tamelen, *Accounts Chem. Res.*, 5, 186 (1972).

(3) (a) R. N. McDonald, D. G. Frickey, and G. M. Muschik, *J. Org. Chem.*, 37, 1304 (1972); (b) D. T. Carty, *Tetrahedron Lett.*, 4753 (1969).

(4) T. J. Katz, E. J. Wang, and N. Acton, *J. Amer. Chem. Soc.*, 93, 3782 (1971).

(5) Irradiations of simple naphthalenes result in dimer formation: *cf.*, P. J. Collin, D. B. Roberts, G. Sugowdz, D. Wells, and W. H. F. Sasse, *Tetrahedron Lett.*, 321 (1972).

(6) J. F. M. Oth, *Recl. Trav. Chim. Pays-Bas*, 87, 1185 (1968).

(7) (a) P. Cadman, E. Ratajczak, and A. F. Trotman-Dickinson, *J. Chem. Soc. A*, 2109 (1970); (b) H. C. Volgen and H. Hogeveen, *Recl. Trav. Chim. Pays-Bas*, 86, 830 (1967); these investigators report activation parameters differing significantly from those given by Oth in ref 6; (c) R. Breslow, J. Napierski, and A. H. Schmidt, *J. Amer. Chem. Soc.*, 94, 5906 (1972).

(8) J. E. Anderson, R. W. Franck, and W. L. Mandella, *ibid.*, 94, 4608 (1972).

(9) E. M. Arnett, J. C. Sanda, J. M. Bollinger, and M. Barber, *ibid.*, 89, 5389 (1967). The discrepancy in $\Delta\Delta H$ isomerism between *m*- and *p*-di-*tert*-butylbenzene (1 kcal mol) with respect to *o*-di-*tert*-butylbenzene may be due to this buttressing.

(10) H. C. Brown and B. Kanmer, *ibid.*, 75, 3865 (1953).