THE DELTA EFFECT OF TIN: SECOND SPHERE HYPERCONJUGATION IN CYCLOHEXANES

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Abstract: The carbon-tin bond participates significantly in the development of positive charge at the delta position through the anti-gaucheanti pathway in the unbiased cyclohexyl framework, possibly through second sphere hyperconjugation.

The accelerating effect of silicon in the departure of nucleofugic groups that are on beta or gamma carbons has been attributed largely to hyperconjugation and homohyperconjugation, respectively.¹ When silicon is placed at the delta position with respect to the nucleofuge (SiCCCCX), there is little or no accelerating effect for secondary nucleofuges² and only a small effect even for primary nucleofuges, for which electron demand would be large.³

We recently reported that the beta effect of tin is considerably larger than that of silicon or germanium.⁴ Consequently, we felt that it was worthwhile to examine the magnitude of the delta effect of tin. We have chosen to investigate the simple 1,4-disubstituted cyclohexyl systems, 1 and 2, as they



give a very stringent test of the delta effect. Davis and Black³ previously demonstrated the existence of a delta effect in primary systems, and Adcock et al.⁵ found a large delta effect in the rigid adamantyl framework. Our cyclohexyl systems are secondary, with much lower electron demand than those of Davis and Black. Moreover, the systems are conformationally flexible. We report herein that the delta effect of tin is manifested in the anti-gaucheanti arrangement between electrofuge and nucleofuge in the trans isomer 1 but not in the gauche-gauche-anti arrangement in the cis isomer 2. The delta effect is demonstrated by a rate enhancement, by solvent sensitivity to ionizing power rather than nucleophilicity, by the products, and by the alpha secondary deuterium isotope effect.

The synthesis of 1 and 2 began with 7-oxanorbornane, which on treatment with trimethylsilyl chloride in the presence of sodium iodide produced trans-1-iodo-4-(trimethylsiloxy)cyclohexane. Reaction of the iodide with trimethylstannyllithium gave a 1/2 cis/trans mixture of 1-(trimethylsiloxy)-4-(trimethylstannyl)cyclohexane. The ether mixture was allowed to react with tetrabutylammonium fluoride to produce the alcohols, which were separated into the component isomers by fractional distillation, flash column chromatogra-The separate alcohol isomers were converted to the phy, and sublimation. respective tosylates 1 and 2. Both alcohols gave satisfactory analyses. The cis or trans identity was proved by the location and linewidth of the CHO To obtain the alpha-deuterated material, the alcohol was oxiresonance. dized to the ketone, which was reduced with lithium aluminum deuteride back to a mixture of separable alcohols.

The overall mechanism was assessed by the effect of solvent on the rate constant, according to the method of Raber and Harris.⁶ Rates for both 1 and 2 were measured conductometrically in 60, 80, and 97% aqueous trifluoroethanol and in 60, 70, and 80% aqueous ethanol. The cis isomer gave the typical two-line logarithmic plot for the rate vs. that of 1-adamantyl bromide, indicative of high sensitivity to nucleophilicity and low sensitivity to ionizing power, as expected for a $k_{\rm S}$ (S_N2) mechanism. In contrast, the trans isomer gave the typical one-line plot that is indicative of low sensitivity to nucleophilicity and high sensitivity to ionizing power, as expected for the $k_{\rm C}$ (E1 or S_N1) mechanism. Thus the two molecules follow entirely different mechanisms, and the trans form passes through a carbocation-like intermediate.

We have made previous rate comparisons in 97% trifluoroethanol,⁴ because of its high ionizing power and low nucleophilicity. In this medium at 25°C, we found that the trans isomer $(k(25^{\circ}C) = 5.72 \times 10^{-5} \text{ s}^{-1})$ reacted 42 times more rapidly than cyclohexyl tosylate (1.37×10^{-6}) , and the cis isomer reacted only 6 times more rapidly (8.08×10⁻⁶) than cyclohexyl. Thus the trans isomer experiences a clear rate acceleration.

The only product observed for the trans isomer was 1,5-hexadiene. The

cis isomer produced several products, of which 1,5-hexadiene was a minor constitutent. The high yield of the fragmentation product from the trans isomer is consistent with a strong interaction between the tin atom and the developing positive charge.

The α -deuterated trans substrate $(k_{\rm D}(50^{\circ}{\rm C}) = 6.84\times10^{-4})$ reacted more slowly than the fully protonated material $(k_{\rm H}(50^{\circ}{\rm C}) = 8.17\times10^{-4})$ $(k_{\rm H}/k_{\rm D} = 1.19\pm0.01)$.

The solvent effects eliminate two important alternative mechanisms for the trans substrate (1). The low sensitivity to nucleophilicity indicates that solvent or other nucleophiles are not attacking the substrate in the rate-determining step. The mechanisms removed from consideration by this observation include $S_N 2$ attack at the tosylate carbon (simple substitution), E2 attack on tin (which would lead to 1,2 elimination), and concerted fragmentation (which would require attack by the nucleophile on the electrofugal tin at the same time that the bond breaks to the nucleofugal X group). The sensitivity to ionizing power supports a carbocation intermediate, 3.



The observation of 1,5-hexadiene as the sole product of the reaction of 1 is consistent either with concerted fragmentation (a mechanism eliminated by the above solvent effects) or with the carbocation intermediate 3 stabilized by second sphere⁷ (or double) hyperconjugation 4. 1,5-Hexadiene is an unlikely product to be derived from a boat intermediate 5, formed by internal bridging, because orbitals are inappropriately aligned. The observation of a mixture of products with the cis form 2 is consistent with a nonparticipative mechanism for that substrate.

The rate acceleration by tin in 1 is consistent with a stabilizing role as provided either by second sphere hyperconjugation (4) or by direct attack by tin to form the boat intermediate (5). Formation of the carbocation 3 should be associated with a positive alpha deuterium isotope effect, whereas formation of the bridged intermediate 5 via an S_N^2 -like transition state should be associated with a small negative ($k_H/k_D < 1.0$) isotope effect. The observed value of 1.19 therefore is strong evidence for the open carbocation and hence for stabilization by second sphere hyperconjugation.

The magnitude of the rate acceleration in 1 is much lower than that ob-

served in the rigid adamantyl system.⁵ The lower value implies either that dihedral angle arrangements are not optimal in the transition state leading to 3 or that alternative and unfavorable conformations are populated in the ground state. Nonchair forms are a good possibility,⁸ but the gamma effect of silicon increases from 450 in the simple, unbiased cyclohexyl system (cis-1,3)⁹ to 33,000 in the rigid norbornyl framework.¹⁰ Even the beta effect of silicon increases by a factor of 400 between the unbiased cyclohexyl system (trans-1,2) and the tert-butyl-locked system.¹¹ The flexibility of unbiased cyclohexyl clearly has a diminishing effect on this family of electronic effects.

In summary, the delta effect of tin is manifested in the unbiased trans-1,4-cyclohexyl system (1), as evidenced by solvent effects, the rate acceleration, the alpha isotope effect, and product structures, but the acceleration is reduced with respect to rigid analogues.

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