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The Interaction of π Orbitals with a Carbocation over Three σ Bonds

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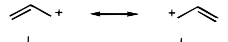
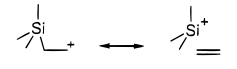
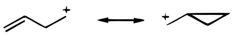
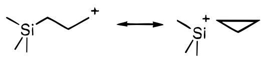
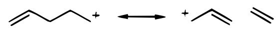
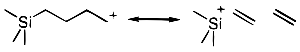
The semi-π analogue of double hyperconjugation ("hyperconjugation/conjugation") has been examined in 4-isopropylidenecyclohexyl mesylate (**4**-OMs) by comparison with the saturated analogue, *trans*-4-isopropylcyclohexyl mesylate (**5**-OMs). The unsaturated substrate reacts in 97% trifluoroethanol only four times faster than the saturated substrate. Raber−Harris plots indicate that both substrates react by k_s mechanisms; i.e., solvolysis occurs with solvent assistance rather than carbocation formation. These results are consistent with the absence of a direct, through-bond interaction of the double bond with the reactive center. The absence is caused at least in part by less than ideal overlap of the γ,δ π orbitals with the α,β σ orbitals. In contrast, an electron-rich tin atom attached to the 4-position provides a large rate enhancement and changes the mechanism to carbocation formation through double hyperconjugation.

Delocalization of positive charge from the empty π-type orbital of carbocations, or its operational reverse, the donation of electrons into the orbital, has intrigued chemists because of the heightened stability conveyed to the reactive intermediate. Such donation may come from filled π, σ, or n orbitals. In its simplest and most fundamental form, π donation is found in the allyl cation, $CH_2{=}CHCH_2^+ \leftrightarrow {}^+CH_2CH{=}CH_2$ (top entry in Table 1). Table 1 refers to this mode in shorthand as $\pi\pi$ since both donor and acceptor orbitals are π-type, and we use the general term "simple conjugation" to indicate that there are no intervening saturated atoms between donor and acceptor. Similar forms of delocalization occur when the donating entity is a lone pair (as on various heteroatoms) or a phenyl ring. These phenomena, respectively, would generate what could be called nπ and $\varphi\pi$ conjugation, along with analogies of the longer range interactions found in Table 1. The present work focuses on π-type delocalization, with n-type and φ-type delocalization considered to be close analogies.

When the donor orbital is a σ bond (second entry in Table 1), the phenomenon is called hyperconjugation or $\sigma\pi$ in shorthand. When the σ bond is C−H or C−C the attendant stabilization is small compared with better σ donors such as Si−C,[2] Ge−C,[3] Sn−C,[3] or Hg−C.[4] Table 1 uses silicon as the exemplar, but more electropositive atoms such as tin are better donors. In this context, the phenomenon has been called the β effect of the element.[2]

The presence of a saturated atom in the bonding pathway between the donor and acceptor orbitals leads to what has been called homoconjugation, or homoallylic in its simplest forms (the third entry in Table 1). As described many years ago by Roberts,[5] the orbital overlap is a mix of σ and π contributions because the π orbitals are not parallel to each other. For want of a better shorthand we will abbreviate homoconjugation as $\pi\sigma$. We derive this notation from the two valence structures that illustrate this mode (Table 1). In $\pi\pi$ conjugation, electrons flow from one π bond to form another. In $\sigma\pi$ conjugation, they flow from a σ bond to form a π bond. In $\pi\sigma$ conjugation, the π bond in one structure becomes a formal σ bond in the other (although the cyclopropyl bond is a hybrid of σ and π).

Table 1. Structural Types of Delocalization

valence structures	shorthand	name
	$\pi\pi$	simple conjugation
	$\sigma\pi$	hyperconjugation
	$\pi\sigma$	homoconjugation
	$\sigma\sigma$	homohyperconjugation
	$\sigma\pi/\pi\pi$	hyperconjugation/conjugation
	$\sigma\pi/\sigma\pi$	double hyperconjugation

Numerous varieties of homoconjugation have been studied,[6] as well as competition between some of them.[7] In the terminology of Hoffmann et al.[8] from their study of interactions between σ orbitals, homoconjugation is primarily direct and through space, because the orbitals of the intervening CH_2 or other saturated center(s) are not involved. The longer range interaction illustrated by **1** is still homoconjugation or $\pi\sigma$, although two CH_2 groups now intervene between the π orbitals.[9] Again, the interaction is direct and through space.

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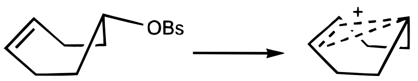
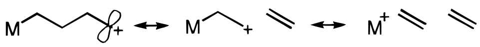


1

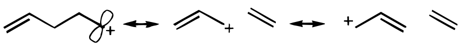
When a saturated center intervenes between a σ donor and the carbocationic acceptor (the fourth entry in Table 1), the phenomenon has been called the γ effect of this element and has been studied for silicon[10] and tin.[11] Some authors have called the interaction percaudal, others homohyperconjugation. Our abbreviation $\sigma\sigma$ indicates that a σ bond in the first structure becomes a σ bond in the second, although again the latter bond actually is a mix of σ and π.[5] The interaction is considered to be primarily direct and through space.

The sixth and last entry in Table 1 illustrates the concept of double hyperconjugation or $\sigma\pi/\sigma\pi$ delocalization, as two stages of hyperconjugation ($\sigma\pi$) are required to bring the effect of the donor element to the empty π orbital (**2**). The phenomenon has been found to be significant for silicon and tin and has been called the δ effect.[12,13] A ζ effect of tin, which would involve triple hyperconjugation ($\sigma\pi/\sigma\pi/\sigma\pi$), has been sought but not found.[14] Both double and triple hyperconjugation involve primarily indirect, through-bond mechanisms.



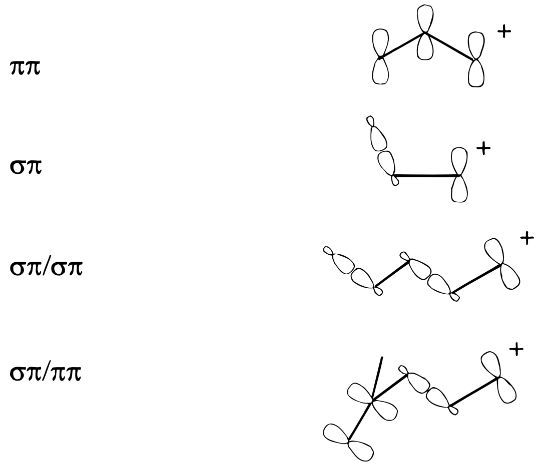
2a **2b**

The sole remaining mode of delocalization to be considered is the fifth entry in Table 1 and is a semi-π analogue of double hyperconjugation. The positive charge moves into the σ system through hyperconjugation ($\sigma\pi$) and then into the π system through simple conjugation ($\pi\pi$), in two stages (**3**). To our knowledge, such an indirect, through bond mechanism has not previously been explored. In shorthand it would be represented by $\sigma\pi/\pi\pi$ to indicate the two stages and would be called hyperconjugation/conjugation. The phenomenon is to be distinguished from the direct, through-space interaction ($\pi\sigma$) in the structurally analogous system **1**. There is a conformational distinction here, as the direct interaction ($\pi\sigma$) should occur when the double bond is spatially close to and backside to the bond between the center of developing charge and the leaving group. The indirect through bond interaction ($\sigma\pi/\pi\pi$) should occur when the segment is in a zigzag conformation that gives favorable anti arrangements. The direct/indirect dichotomy is a theme that runs through this field and must be resolved for any given case.[15] In the context of the β effect, the two modes also have been called vertical (indirect) and nonvertical (direct).

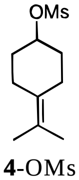


3a **3b**

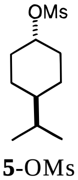
Chart 1



The various orbital interactions are optimized when the appropriate σ or π orbitals are parallel and hence allow maximal overlap. The parallel geometry of the three π orbitals in the allyl cation thus optimizes $\pi\pi$ conjugation (Chart 1), and the parallel geometry of the σ orbital with the π orbital optimizes $\sigma\pi$ conjugation in the β effect.[2] Extension of these concepts to additional orbitals requires the introduction of further parallel relationships. Realization of double hyperconjugation required construction of systems in which two σ bonds were parallel (antiperiplanar) to each other and to the developing π orbital ($\sigma\pi/\sigma\pi$ in Chart 1).[12,13] Realization of the semi-π analogue of double hyperconjugation ($\sigma\pi/\pi\pi$) consequently requires construction of a system in which an intermediate σ bond is parallel to the orbitals of a π bond on one side and the developing π orbital on the other. The two modes of overlap have been realized separately but never together. Overlap of a σ bond with a developing π orbital occurs in the β effect (hyperconjugation), and overlap of a σ bond with a π bond occurs in homoallylic J couplings (**H**C=CC**H**).



4-OMs



5-OMs

The present study was designed to examine $\sigma\pi/\pi\pi$ delocalization in a structure that is conformationally constrained to prohibit or minimize the direct, through-space alternative and to maximize overlap of the necessary orbitals. We have compared the kinetic properties of **4**-OMs with those of its saturated analogue **5**-OMs, in which the $\sigma\pi/\pi\pi$ mode is absent. The double bond in **4** is constrained by the ring from achieving a backside geometry with respect to the leaving group that could lead to the direct mechanism (homoconjugation or $\pi\sigma$), as in **1**. For the chair conformation of the carbocation **6**, the valence bond structure (**7**) represents the direct interaction and involves both angle strain and a long bond. The structures of the $\sigma\pi$ (**8**) and $\pi\pi$ (**9**) stages of hyperconjugation/conjugation ($\sigma\pi/\pi\pi$) are conformation-

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[10] Shiner, V. J., Jr.; Ensinger, M. W.; Rutkowske, R. D. *J. Am. Chem. Soc.* **1987**, *109*, 804−809. Grob, C. A.; Gründel, M.; Sawlewicz, P. *Helv. Chim. Acta* **1988**, *71*, 1502−1507. Bentley, T. W.; Kirmse, W.; Llewellyn, G.; Söllenböhmer, F. *J. Org. Chem.* **1990**, *55*, 1536−1540.

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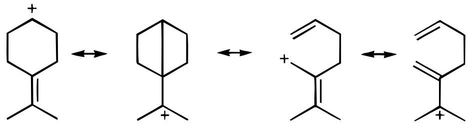
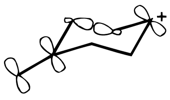
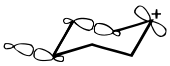


6 **7** **8** **9**

ally viable. Structure **10** illustrates the orbitals involved in $\sigma\pi/\pi\pi$ delocalization, and structure **11** provides the analogous representation for $\sigma\pi/\sigma\pi$ delocalization, which we studied previously and which proved to be a viable mechanism.[12]



10 (σπ/ππ)



11 (σπ/σπ)

It is evident from the drawing **10** that the system does not provide perfect overlap along the orbital ribbon. Use of an equatorial leaving group optimizes overlap between the σ bond and the developing π overlap. Although the system is not locked conformationally, the equatorial form is preferred and should be readily available for reaction. A more serious problem is overlap between the *exo*-methylene π orbitals and the σ bond. Examination of models suggests that the orbitals are about 40−50° off parallel (0 or 180° would be parallel, 90° orthogonal). A deviation of 60° reduces the interaction to about a quarter ($\cos^2 60° = 0.25$, as overlap depends on the cosine squared of the dihedral angle). This deviation dilutes the effect, although in the β effect of silicon or tin, larger angular deviations still permit substantial overlap and give rise to significant rate accelerations.

We report herein the synthesis and kinetic study of the mesylates **4** and **5** in order to test whether a π bond is as effective as an electron-rich σ bond at a δ position in providing stabilization of positive charge through two stages of conjugation. We use the isopropylidene group rather than a simple *exo*-methylene (vinylidene) group in order to have heightened properties of electron donation. The system **5** provides a saturated analogue for comparison. It should be noted that the heteroatom analogue of hyperconjugation/conjugation ($\sigma\pi/n\pi$) would involve a heterocycle with a donor atom such as oxygen or nitrogen at the 4-position to the leaving group.

Results

The synthesis of 4-isopropylidenecyclohexanol (**4**-OH) was accomplished by the procedure of Scheme 1. The acetal-protected 1,4-cyclohexanedione was converted to the dibromomethylene derivative by treatment with carbon tetrabromide and thence to the protected isopropylidene system with dimethylcopperlithium.[16] After hydrolytic deprotection,[17] the resulting ketone was reduced with sodium borohydride or sodium borodeuteride to produce the desired alcohol, **4**-OH, or its α-deuterated derivative. Synthesis of the comparison substrate **5**-OH was accomplished by a literature procedure that involved hydrogenation of 4-isopropylphenol.[18]

Scheme 1

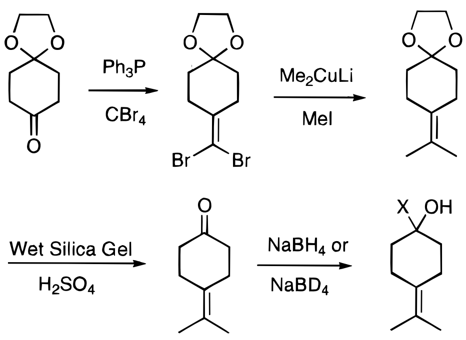


Table 2. Solvolysis Rates of 4-Isopropylidenecyclohexyl Mesylate (4-OMs) and 4-Isopropylcyclohexyl Mesylate (5-OMs)

system	solvent[a]	temp, °C	$R^{2\,b}$	rate, s^{-1}
4-OMs	97% TFE	65	0.9999	3.55×10^{-4}
		55	0.9998	1.22×10^{-4}
		50	0.9999	7.27×10^{-5} [c]
		45	0.9999	4.07×10^{-5}
	80% TFE	50	0.9998	1.30×10^{-4}
	60% TFE	50	0.9999	2.53×10^{-4}
	80% EtOH	50	0.9999	3.05×10^{-5}
	70% EtOH	50	0.9998	7.73×10^{-5}
	60% EtOH	50	0.9999	1.21×10^{-4}
	97% TFE	55	0.9999	1.03×10^{-4} [d,e]
5-OMs	97% TFE	65	0.9999	9.37×10^{-5}
		55	0.9999	3.23×10^{-5}
		50	0.9998	1.73×10^{-5}
		45	0.9995	9.83×10^{-6}
	80% TFE	50	0.9999	3.03×10^{-5}
	60% TFE	50	0.9999	5.80×10^{-5}
	80% EtOH	50	0.9997	7.38×10^{-6}
	70% EtOH	50	0.9999	1.58×10^{-5}
	60% EtOH	50	0.9999	3.05×10^{-5}

[a] TFE stands for 2,2,2-trifluoroethanol (w/w %); ethanol (EtOH) values are v/v %. [b] Correlation coefficient squared. [c] Average of two runs. [d] Average of three runs. [e] Rate for **4**-OMs with deuterium at the 1 position.

The alcohols were converted to their mesylates for the kinetic studies. Rates were measured by conductance in aqueous trifluoroethanol (TFE) as a function of water concentration and temperature and in aqueous ethanol (EtOH) only as a function of water concentration (Table 2). The activation parameters were measured from Arrhenius plots in 97% TFE: (for 4-isopropylidenecyclohexyl mesylate, **4**-OMs) $\Delta H^{\ddagger} = 23.4$ kcal mol^{-1}, $\Delta S^{\ddagger} = -5.1$ cal deg^{-1} mol^{-1}, $\Delta G^{\ddagger} = 24.9$ kcal mol^{-1}; (for 4-isopropylcyclohexyl mesylate, **5**-OMs) $\Delta H^{\ddagger} = 24.5$ kcal mol^{-1}, $\Delta S^{\ddagger} = -4.5$ cal deg^{-1} mol^{-1}, $\Delta G^{\ddagger} = 25.9$ kcal mol^{-1}. Raber−Harris plots were constructed from the data in Table 2 and are presented in Figures 1 and 2.[19]

Product studies were carried out in 97% TFE and 80% EtOH at 55 °C in a sealed tube for at least 10 half-lives, and the mixtures were analyzed by gas chromatography and mass spectrometry. In 80% EtOH, the unsaturated substrate **4**-OMs afforded an elimination product (**12**, 60%) and two substitution products (**13**, 37%, and **14**, 3%). In TFE, there were five isomeric elimination products (37% total), six substitution products (47%, including 4% of **14**), and 16% of high molecular weight material. The saturated substrate **5**-OMs in 80% EtOH also afforded elimination (**15**, 86%) and substitution (**16**,

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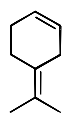

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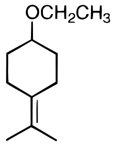

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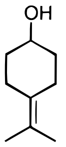
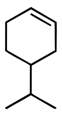


14

8%, and **17**, 6%). In TFE there was 90% elimination and 10% substitution.



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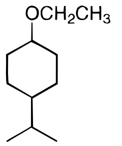

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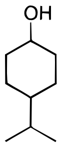

17

Solvolysis of the unsaturated substrate (**4**-OMs) is not accompanied by a rate acceleration of significance compared to the rate of the saturated substrate (**5**-OMs). At 50 °C, the unsaturated/saturated rate ratio is 4.2 in 97% TFE and 4.1 in 80% EtOH. The value is essentially the same at the other temperatures and concentrations and is too small to imply anchimeric assistance. The ratio is within the normal range of steric effects in six-membered rings. In contrast, introduction of a trimethylstannyl group at the 4-position of cyclohexyl brings about a 42-fold acceleration in 97% TFE at 25 °C (compared with cyclohexyl).[12] We conclude that there is little or no rate acceleration attendant upon the introduction of the double bond at the 4-position.

The free energies of activation reflect the small differences in rate between **4**-OMs and **5**-OMs. Moreover, the breakdown into enthalpic and entropic components is almost identical for the two substrates, with entropies of activation (−5.1 and −4.5) that suggest no difference in mechanism.

The Raber−Harris plots (Figures 1 and 2) also are nearly identical and hence indicate similar dependencies of the two substrates on solvent nucleophilicity and ionizing power. Moreover, the form of the plots is a pair of nonparallel lines that is characteristic of primary involvement of solvent in a nucleophilic or basic role (k_s).[19] Raber, Harris, and their co-workers found that when the primary involvement of solvent is to promote unimolecular ionization (k_c) a single line is present in the plot (because the x axis also reflects a substrate with a k_c mechanism).[19] Both saturated and unsaturated substrates solvolyze by the k_s mechanism that involves participation of solvent in the transition state. Thus, the cation-stabilizing abilities of the *exo*-methylene π bond and the intermediate ring σ bonds are insufficient to alter the mechanism from the normal k_c of cyclohexyl itself. In contrast, the presence of a trimethylstannyl group attached to the 4-position of cyclohexyl results in the single line characteristic of a k_c mechanism (carbocation formation).[12] For both the unsaturated (**4**-OMs) and the saturated (**5**-OMs) substrates, the slopes of the TFE lines are about 1.0 and those of the EtOH lines are about 0.5. As only nucleophilicity changes with addition of water to TFE but only ionizing power changes with addition of water to EtOH, the rates are clearly more sensitive to solvent nucleophilicity. The mixture of elimination and substitution products is typical for the solvolysis of cyclohexyl substrates. We failed to find triene products derived from the valence form **9** from **4**-OMs that would have been suggestive of charge delocalization into the isopropylidene double bond.

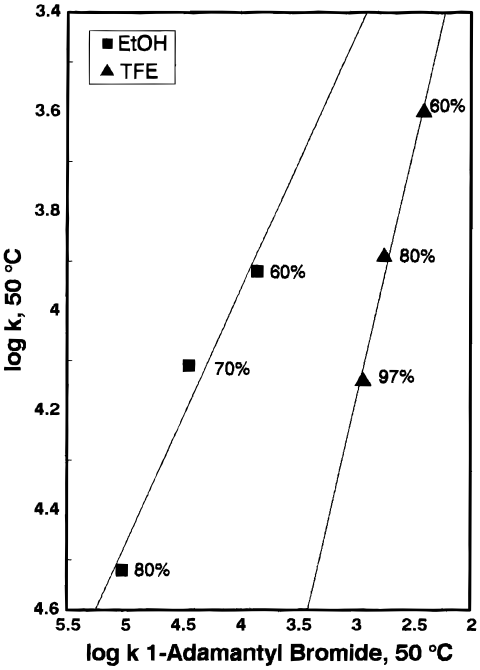

Figure 1. Raber−Harris plot for 4-isopropylidenecyclohexyl mesylate (**4**-OMs) at 50 °C.

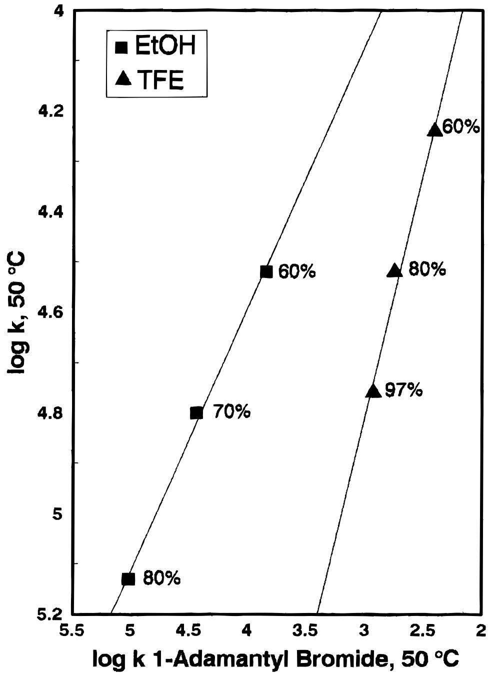

Figure 2. Raber−Harris plot for *trans*-4-isopropylcyclohexyl mesylate (**5**-OMs) at 50 °C.

The isotope effect (k_H/k_D) for **4**-OMs (deuterium at the 1-position) is 1.18 in 97% TFE. Raber and Harris took 1.15 in cyclopentyl tosylate as evidence for a k_s mechanism, because of its reduced value from 1.22−1.25 range expected for carbocation mechanisms. The value of 1.22 for cyclohexyl tosylate, a known k_s substrate, then is seemingly contradictory. Solvolysis of six-membered rings, however, is predominantly an elimination rather than a substitution reaction. It is the substitution component that should have a greatly reduced secondary deuterium isotope effect (1.00−1.05). The magnitude of the isotope effect indicates changes of hybridization between ground and transition states. If the transition state for elimination is not too early, then hybridization at the 1 position is moving toward sp^2, similar to the k_c transition state that leads to a carbocation. We suspect that the relatively large isotope effects observed here for **4**-OMs, but also for cyclopentyl and for cyclohexyl, are reflective of hybridization changes in the large elimination component of the reaction. Because solvent is present as a base in the transition state for elimination, such a reaction can give both a relatively high isotope effect and solvent dependence characteristic of a k_s process in the two-line Raber–Harris plot.

Conclusions

The introduction of a double bond at the 4 position to a center of potential production of a carbocation in the cyclohexane skeleton engenders no through-bond stabilization of positive charge. The mechanism remains k_s, as also found in analogous saturated cyclohexyl systems. We find no evidence for the $\sigma\pi/\pi\pi$ (hyperconjugation/conjugation) mode of positive charge stabilization, in contrast to the $\sigma\pi/\sigma\pi$ (double hyperconjugation) mode in structurally analogous systems. It is possible that this result is caused by the less than optimal overlap of the *exo*-methylene double bond π orbitals with the ring σ bonds. Comparison of structure **10** with the ideal depicted in Chart 1 suggests deviation from parallelism of 40–50° between the π and σ orbitals. Although this geometry should not extinguish the effect, it may reduce it by up to a factor of about four. A more nearly ideal geometry should be sought to explore the existence of hyperconjugation/conjugation.

Experimental Section

4-(Dibromomethylene)cyclohexanone Ethylene Ketal.[16] A mixture of commercially available 1,4-cyclohexanedione monoethylene ketal (2.5 g, 0.016 mol), triphenylphosphine (20.98 g, 0.08 mol), and CBr$_4$ (13.26 g, 0.04 mol) in 200 mL of dry benzene was stirred at reflux under N$_2$ overnight. The mixture was cooled to room temperature, the solid material was removed by filtration, and the filtrate was concentrated under vacuum. The crude oil was placed in the refrigerator, and after most of the excess Ph$_3$P had crystallized, the product was triturated and extracted with hexane. After removal of the solvent, the crude product was sublimed twice to give 7 g (70%) of a white solid: ^{1}H NMR (C$_6$D$_6$) δ 1.48 (t, 4H), 2.4 (t, 4H), 3.8 (s, 4H); ^{13}C NMR (C$_6$D$_6$) δ 31.6, 34.5, 64.3, 83.5, 107, 143; MS *m/z* 310 (M$^+$, 15), 231 (M$^+$ − Br, 100), 152 (10), 99 (17), 83 (6), 55 (5).

4-Isopropylidenecyclohexanone Ethylene Ketal.[16] An ethereal solution of dimethylcopperlithium was prepared at 0 °C under N$_2$ from cuprous iodide (29 g, 0.15 mol) and 1.4 M CH$_3$Li (198 mL, 0.27 mol) in 100 mL of ether. To this solution was added 4-(dibromomethylene)cyclohexanone ethylene ketal (4.9 g, 0.015 mol), and the reaction was stirred for 4 days at room temperature. The reaction was cooled to 0 °C, and CH$_3$I (5 mL) was added very slowly. The reaction was allowed to warm to room temperature and was stirred for 4 h. The mixture was poured into 300 mL of saturated aqueous NH$_4$Cl. The solid was removed by filtration, and the aqueous layer was extracted with ether. The combined ether layers were washed with brine, dried (MgSO$_4$), and filtered, and the solvent was removed by rotary evaporation. The product was distilled at 70 °C under vacuum to give 2.8 g (95%) of a clear oil: ^{1}H NMR (C$_6$D$_6$) δ 3.5 (s, 4H), 2.4 (t, 4H), 1.7 (t, 4H), 1.0 (s, 4H); ^{13}C NMR (C$_6$D$_6$) δ 138, 116, 109, 64, 36, 34, 27; MS *m/z* 182 (M$^+$, 72), 167 (44), 153 (35), 123 (31), 99 (20), 86 (100), 67 (19), 41 (21).

4-Isopropylidenecyclohexanone.[17] In a 500 mL, round-bottomed flask, 34 g of silica gel was suspended in 100 mL of CH$_2$Cl$_2$. To this suspension was added 2 mL of 15% H$_2$SO$_4$. The solution was stirred for a few minutes, and the above ketal (2.8 g, 15 mmol) was added dropwise. The reaction was stirred for 5 h, and the silica gel was filtered and washed with ether. The solvent was removed by rotary evaporation, and 1.9 g (89%) of product was obtained: ^{1}H NMR (C$_6$D$_6$) δ 2.0 (s, 8H), 1.4 (s, 6H); ^{13}C NMR (C$_6$D$_6$) δ 210, 126, 124, 40, 27, 20; IR 1715; MS *m/z* 138 (M$^+$, 100), 123 (20), 109 (10), 96 (50), 81 (100), 67 (51), 53 (23), 41 (33).

4-Isopropylidenecyclohexanol (4-OH). In an oven-dried, three-necked flask was suspended NaBH$_4$ (0.41 g, 10.8 mmol) in 20 mL of THF. A solution of the ketone (1.5 g, 10.8 mmol) in 10 mL of THF was added slowly under N$_2$. The reaction was refluxed for 4 h and cooled, and 10 mL of H$_2$O was added slowly. The aqueous layer was extracted three times with ether. The ether layers were combined and dried (MgSO$_4$), and the solvent was removed by rotary evaporation. Chromatography with silica gel with a 3/1 hexane/ether solvent mixture produced a white solid: 1.05 g (69%); mp 85 °C; ^{1}H NMR (C$_6$D$_6$) δ 3.5 (m, 1H), 2.4 (t, 2H), 1.7 (t, 4H), 1.6 (s, 6H), 1.3 (t, 2H), 1.1 (s, 1H); ^{13}C NMR (C$_6$D$_6$) δ 130, 121, 69, 36, 27, 20; MS *m/z* 140 (M$^+$, 31), 122 (44), 107 (100), 93 (15), 79 (66), 67 (13), 55 (12), 41 (17). Anal. Calcd for C$_9$H$_{16}$O: C, 77.05; H, 11.53. Found: C, 76.46; H, 11.37.

4-Isopropylidenecyclohexanol-*1-d*. The deuterated alcohol was made analogously by reducing the corresponding ketone (1.3 g, 9.4 mmol) with NaBD$_4$ (0.4 g, 9.4 mmol) to give 0.82 g (61%): mp 82 °C; ^{1}H NMR (C$_6$D$_6$) δ 2.5 (m, 2H), 1.7 (m, 2H), 1.59 (s, 6H), 1.3 (t, 2H), 0.75 (s, 1H), 0.45 (s, 1H); ^{13}C NMR (C$_6$D$_6$) δ 130, 121, 69, 36, 26.9, 20; MS *m/z* 141 (M$^+$, 30), 123 (47), 108 (100), 94 (14), 80 (62), 67 (16), 55 (12), 41 (20).

***trans*-4-Isopropylcyclohexanol (5-OH).**[18] Commercially available *p*-isopropylphenol (6 g, 0.043 mol) was dissolved in 20 mL of 95% EtOH, and rhodium catalyst on an aluminum support (1 g, 5% Rh) was added. Hydrogenation was carried out at 60 psi overnight. The reaction was filtered, 10 mL of H$_2$O was added, and the product was extracted with ether. The organic layer was washed with 10 mL portions of 5% KOH and brine and dried over MgSO$_4$. A 50/50 mixture of *cis*- and *trans*-4-isopropylcyclohexanol (5.7 g, 90%) was obtained: MS *m/z* 142 (M$^+$, 30), 124 (33), 109 (24), 81 (100), 67 (20), 55 (33), 43 (35).

A small amount of this alcohol mixture was oxidized to the ketone. Sodium dichromate (0.76 g, 2.5 mmol) was dissolved in 0.6 mL of concentrated H$_2$SO$_4$ and diluted to 10 mL. This solution was added slowly to a cooled solution of *cis*/*trans*-4-isopropylcyclohexanol (1 g, 7 mmol) in 20 mL of ether. After 2 h, the product was extracted with ether. Removal of the solvent yielded 0.4 g (42%) of 4-isopropylcyclohexanone: MS *m/z* 140 (M$^+$, 80), 122 (25), 107 (28), 97 (40), 84 (65), 69 (80), 55 (60), 43 (100).

For isomer equilibration, in a three-necked flask under N$_2$, AlCl$_3$ (3.76 g, 0.028 mol) was suspended in 15 mL of dry ether. The flask was cooled in an ice bath, and LiAlH$_4$ (0.29, 0.008 mol) in 15 mL of ether was added. To this suspension, the cis/trans mixture of alcohols (4 g, 0.028 mol) and the previously made ketone (0.23 g, 1.7 mmol) in 15 mL of ether were added. The reaction was stirred at gentle reflux overnight and quenched with H$_2$O, and the product was extracted with ether. The organic layer was washed with brine and dried (MgSO$_4$), and the solvent was removed by rotary evaporation. The product was distilled under vacuum at 45 °C to give 3.0 g (75%) of a colorless oil. The product was identified by GC as being 91% rich in the trans isomer.

An ester derivative was prepared for recrystallization by dissolving 3,5-dinitrobenzoic acid (4.48 g, 0.02 mol) in 80 mL of dry pyridine. To this solution was added *p*-toluenesulfonyl chloride (8.06 g, 0.04 mol). The flask was cooled in an ice bath, and the trans-rich 4-isopropylcyclohexanol (3.0 g, 0.02 mol) was added. The reaction was kept cool and was stirred for 2 h. The reaction mixture then was poured into 100 mL of ice–water. The solid was suction filtered and recrystallized from hot CH$_3$OH. It was then dried under vacuum to remove traces of pyridine and recrystallized one more time from hot CH$_3$OH to give an off-white solid: 4.9 g (70%); mp 120 °C; ^{1}H NMR (C$_6$D$_6$) δ 0.77 (d, 6H), 0.81 (m, 3H), 1.23 (m, 3H), 1.45 (d, 2H), 1.98 (d, 2H), 4.9 (m, 1H), 8.43 (t, 1H), 8.7 (d, 1H); ^{13}C NMR (C_6D_6) δ 19.9, 27.6, 31.7, 32.4, 42.8, 76.3, 121.75, 123.8, 128.6, 148.2, 161.8.

For saponification, the recrystallized ester (4.0 g, 0.012 mol) was dissolved in 50 mL of CH_3OH, and KOH (2.86 g, 0.05 mol) in 10 mL of H_2O was added. The mixture was refluxed for 3 h. After the mixture had cooled, 50 mL of H_2O was added to dissolve all the salts, and the product was extracted with ether. The organic layer was washed with brine and dried ($MgSO_4$), and the solvent was removed by rotary evaporation. The crude product was distilled under vacuum at 45 °C to give 0.97 g (57%) of a clear colorless oil: ^{1}H NMR (C_6D_6) δ 3.4 (m, 1H), 2.62 (s, 1H), 0.78 (d, 6H), 1.97 (d, 2H), 1.24 (m, 3H), 0.85 (m, 3H); ^{13}C NMR (C_6D_6) δ 20, 28, 33, 36, 43, 71.

4-Isopropylidenecyclohexyl Mesylate (4-OMs).[20] In a dry Erlenmeyer flask was dissolved 4-isopropylidenecyclohexanol (1.4 g, 0.01 mol) in 30 mL of dry pyridine. The solution was cooled in an ice bath, and methanesulfonyl chloride (3.4 g, 0.03 mol) was added slowly under N_2. The solution became yellow, and it was left in the refrigerator overnight. The next day the solution was darker, and precipitate was present. This solution was poured into a mixture of water and ice. The aqueous layer was extracted three times with ether. The combined organic layers were washed with saturated $CuSO_4$, $NaHCO_3$, and brine and dried over $MgSO_4$. The solvent was removed by rotary evaporation. The solid was dried under vacuum for several hours to remove traces of pyridine. An off-white solid (1.78 g, 81.6%) was obtained: mp 72 °C; ^{1}H NMR (C_6D_6) δ 0.45 (s, 1H), 1.48 (s, 6H), 1.55 (m, 1H), 2.2 (s, 3H), 2.25 (m, 2H), 4.68 (m, 1H); ^{13}C NMR (C_6D_6) δ 19.9, 26.2, 33.3, 38.1, 79.8, 122.3, 128.5. Anal. Calcd for $C_{10}H_{18}O_3S$; C, 54.99; H, 8.33; S, 14.69. Found: C, 54.81; H, 8.28; S, 14.86.

4-Isopropylidenecyclohexyl-1−*d* Mesylate. The previously described procedure was carried out with the deuterated alcohol, and 1.09 g (87%) of a yellow solid was obtained: mp 71 °C; ^{1}H NMR (C_6D_6) δ 0.46 (s, 1H), 1.48 (s, 6H), 1.56 (m, 1H), 1.7 (m, 4H), 2.2 (s, 3H), 2.26 (m, 2H); ^{13}C NMR (C_6D_6) δ 128, 122, 79, 38, 33, 26, 20.

4-Isopropylcyclohexyl Mesylate (5-OMs). The previously described procedure was carried out with 4-isopropylcyclohexanol, and 1.1 g (74%) of a yellow solid was obtained: mp 62 °C; ^{1}H NMR (C_6D_6) δ 0.24 (s, 1H), 0.6 (m, 2H), 0.68 (d, 3H), 1.1 (m, 1H), 1.2−1.4 (m, 4H), 1.99 (d, 2H), 2.23 (s, 3H), 4.41 (m, 1H); ^{13}C NMR (C_6D_6) δ 80.9, 42, 38, 33, 32, 27.5, 20. Anal. Calcd for $C_{10}H_{20}O_3S$: C, 54.48; H, 9.17; S, 14.56. Found: C, 54.47; H, 9.18; S, 14.82.

Kinetic Rates. Solvents were prepared according to published procedures.[3] Rates of solvolysis were determined by conductance measurements on 30 mL of approximately 10^{-3} M solutions in a conductance cell with Pt electrodes and a capacity of 35 mL. The cell was heated with a Precision H8 bath. The change in conductance was followed with a YSI model 32 conductance meter. The rate constant, k, was calculated by Lotus 1−2−3 linear regression analysis, according to eq 1,

$$\ln(\Lambda_{\mathrm{inf}} - \Lambda_t) = kt + b \qquad (1)$$

in which Λ_{inf} is the infinity conductance and Λ_t is the conductance at time t.

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