

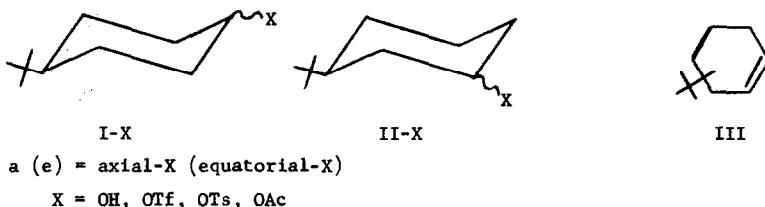
ACETOLYSIS OF CIS- AND TRANS-4-TERT-BUTYL-1-CYCLOHEXYL TRIFLATES

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Studies of organic reaction mechanisms are inextricably tied to solvolyses of alkyl sulfonates. During the past few years, the range of reactivities accessible to study has been extended by a factor of about 10^5 by the use of trifluoromethanesulfonates (triflates).²⁻⁵ Fast solvolyses occur with primary alkyl triflates,^{2,3} and some bicyclic⁴ and vinyl⁵ systems, which are almost inert when the substituent group is chloride or arenesulfonate, react at reasonable rates when the leaving group is triflate. Although ethyl triflate apparently reacts through "a transition state with comparatively little positive charge,"³ reactions of cyclic vinyl triflates are accompanied by carbocation-like ring contractions and methyl migrations.^{5a} Authors of two recent publications, reporting that acyclic vinyl triflates undergo solvolyses to give substitution products with predominant but not exclusive inversion of configuration, concluded that rather tight ion pairs are intermediates in these systems.^{5b,c} No stereochemical studies appear to have been reported for saturated alkyl triflates. In this communication, we report what we believe to be the first product study of acetolyses of alkyl triflates involving sec-alkyl systems (4-tert-butyl-1-cyclohexyl) whose arenesulfonates already react at conveniently rapid rates. Even though these triflates (I-OTf) still react about 10^5 times as rapidly⁴ as do the corresponding p-toluenesulfonates (tosylates; I-OTS), the product analyses reveal that little separation between the leaving triflate and the cyclohexyl moiety occurs before substitution product formation.



We have earlier summarized the stereochemistry of product formation from a variety of 4-tert-butyl-1-cyclohexyl systems which are presumed to react by carbocation mechanisms.⁶ In most cases, the configuration of the reactant determines the predominant configuration of the

product(s). Closely-associated ion pairs, rather than carbocations free from the stereochemical influence of the counterion, appear to be the immediate precursors of the products.⁷ Two recent studies demonstrated that acetolyses of deuterium-labeled^{8a} and 4,4-dimethyl-labeled^{8b} cyclohexyl tosylates occur almost entirely by an inversion mechanism; there was no evidence for formation of a free carbocation at position 1.⁸ It was of interest, then, to learn whether cyclohexyl triflates, which were expected to be extraordinarily reactive compared to the corresponding cyclohexyl tosylates, would generate carbocations free from the stereochemical influence of the leaving group.

Pentane solutions (approx. 67 mM) of Ia-OTf and Ie-OTf were prepared separately from the corresponding alcohol; the esters were not isolated as pure compounds. To an ice-chilled stirred solution prepared by mixing at room temperature 1 mmolar quantities of the alcohol (Ia-OH or Ie-OH)⁶ and butyllithium (Merck 20% solution in hexane) in 10 ml of pentane was added 1 mmol of trifluoromethanesulfonic anhydride⁹ in 5 ml of pentane. Naphthalene was included as an internal standard for gas chromatographic (gc) analysis. The chilled mixture was stirred for 2 hr, washed quickly with ice water to remove acid, anhydride, and salt, and dried over MgSO₄ in a refrigerator. The infrared spectrum of the mixture included sharp absorptions characteristic of the trifluoromethanesulfonyloxy group¹⁰ (1424, 1251, 1217, 1203, and 1153 cm⁻¹ for Ie-OTf and 1422, 1249, 1217, 1203, and 1152 cm⁻¹ for Ia-OTf), but little absorption for O-H. The pentane solution was added to 5 ml of dry acetic acid containing 1 mmol of anhydrous sodium acetate, the mixture was stirred at room temperature for 3-4 hr, and it was diluted with water. The pentane layer was washed with saturated sodium bicarbonate solution, dried with MgSO₄, and analyzed by gc and spectroscopic techniques.¹¹

Each mixture consisted of some original alcohol (15-17%) but no isomeric alcohol, four isomeric acetates⁶ (9-18%), and olefin III (76-65%).¹² The product distributions are summarized in the following table.

<u>Reactant</u>	<u>Products, mol %</u>				
	<u>Ie-OAc</u>	<u>Ia-OAc</u>	<u>IIe-OAc</u>	<u>IIa-OAc</u>	<u>III</u>
Ie-OTf	1.2	18	2.2	0.5	78
Ia-OTf	4.9	1.6	1.5	3.2	89

As is true for I-OTs,¹³ the two triflates, Ie-OTf and Ia-OTf, undergo acetolysis to give extensive elimination, a small amount of rearranged acetate (II-OAc, formed stereoselectively by 1,2-hydride shift), and unarranged acetate (I-OAc) formed with predominant (but not exclusive) inversion of configuration. For products I-OAc, the extent of inversion is 94% from

Ie-OTf and 75% from Ia-OTf.

Therefore, even with such reactive systems as sec-alkyl, the triflate mechanism appears to be substantially identical to the tosylate mechanism.¹⁴ The activation energy for ion pair formation is much lower for triflate than for tosylate as leaving group, but in neither case is the carbocation free from a stereochemically-determinative influence by the anion.

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11. When the same procedure was used, with the exception that the trifluoromethanesulfonic anhydride was omitted, the original alcohol was recovered with only a detectable amount of acetate.

12. With the focus of our attention on the stereochemistry of the substitution process, we chose gc conditions which favored acetate analysis but not olefin isomer resolution. Gc retention time for the olefin product matched that of an authentic sample of 4-tert-butyl-1-cyclohexene, but we cannot exclude or confirm the presence of small amounts of other tert-butylcyclohexenes^{13b} from our data.

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14. The same conclusion has been reached for primary alkyl systems on the basis of kinetic solvent and isotope effects,³ and is implied by the constancy of the triflate:tosylate rate ratio for a variety of systems.⁴