Electron-Impact and Pyrolytic Eliminations from 4-*tert*-Butylcyclohexyl Xanthates

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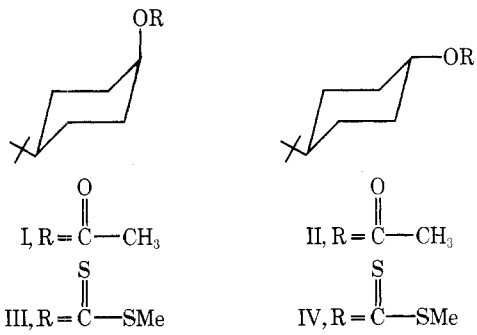
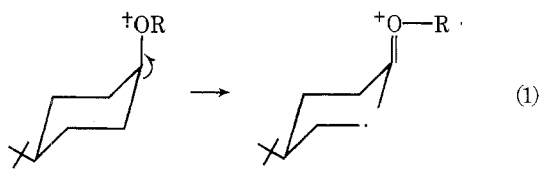
The electron-impact induced[1] and pyrolytic[2a,3] eliminations of xanthic acid from *S*-methyl xanthates are formally analogous to each other, and to the electron-impact induced[4] and pyrolytic[2b-e,3] eliminations of acetic acid from acetates. These reactions proceed largely through six-membered cyclic transition states, and involve predominant elimination of a β hydrogen. A recent investigation of the reactions of *cis*- and *trans*-4-*tert*-butylcyclohexyl acetate confirmed that the pyrolytic elimination of acetic acid occurs with clean cis stereochemistry for these compounds.[5] In contrast, the electron-impact induced elimination from *trans*-4-*tert*-butylcyclohexyl acetate (II) occurs with very predominant elimination



of the trans equatorial hydrogen ($k_{ax}/k_{eq} \approx 0.26$).[5] This dichotomy was considered to be evidence for a nonconcerted mechanism for the electron-impact induced process, although other explanations could not be excluded.[5,6] Further, although the electron-impact induced elimination from the cis axial acetate I was predominantly cis ($k_{ax}/k_{eq} = 0.51$), the reaction was less stereospecific than the fragmentation of the equatorial acetate II. An equatorial acetate group can approach either a cis or trans hydrogen well within the requisite 1.8 Å[7] for hydrogen abstraction; in contrast, if the cyclohexyl ring remains intact and in its stable chair conformer, an axial acetate group can only approach the cis equatorial hydrogen atom. There was little basis to decide whether the considerable trans elimination actually observed was attributable to cyclohexyl ring cleavage (eq 1), to fragmentation through

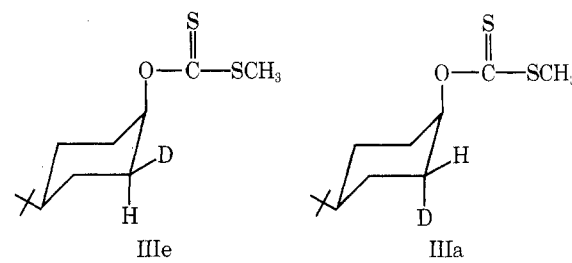


(1)

high-energy boatlike conformers, or to operation of an electronic effect favoring trans abstraction when the product is an ionized alkene.

An investigation into the stereochemistry of the electron-impact induced reactions of the *S*-methyl xanthates III and IV was initiated to shed light on the generality and origins of these effects. The pioneering study of the mass spectral behavior of cyclohexyl-*S*-methyl xanthates permits no firm conclusions about the stereochemistry of reaction of axial and equatorial derivatives.[1] The compounds studied (*cis*- and *trans*-2-methylcyclohexyl-*S*-methyl xanthate) can each exist in two stable chair conformers. Depending on the conformer distribution after ionization and the relative rates of reaction of axial and equatorial derivatives, these xanthates might behave as equatorial or axial esters; information about such factors is, of course, lacking. However, the early study demonstrated that xanthate mass spectra typically exhibit an intense peak corresponding to ionized alkene, that the reaction is largely site specific for β hydrogen abstraction, and that it generates a significant metastable peak. Preliminary studies on unlabeled *cis*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate (III) and the -2,2,6,6-d_4 analogue were consistent with these observations. The ionized alkene was formed with 91–96% elimination of deuterioacetic acid as the ionizing voltage was varied from 70 eV to threshold; similarly, the fragmentation of *trans*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate-2,2,6,6-d_4 is 81–90% site specific. The ionized alkene peak is the base peak in the spectra of III and IV at 70 eV, and its formation generates intense first and second field-free region metastables.

The stereochemistry of electron impact induced xanthic acid elimination from *cis*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate was assessed from the mass spectra of *cis*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IIIe) and -*trans*-2-*d* (IIIa). The intensity ratio $[M - DOC_2S_2H_3]^{\cdot+}/[M - HOC_2S_2H_3]^{\cdot+}$ in the two spectra is related to the stereochemistry of the eliminations. If the reasonable assumptions are made that the isotope effects for abstraction of an equatorial and an axial deuterium are similar, and that secondary isotope effects can be ignored, a modification of Curtin's analysis[4a,8] can be applied. Thus, for example, for IIIe



$$\frac{[M - DOC_2S_2H_3]^{\cdot+}}{[M - HOC_2S_2H_3]^{\cdot+}} = \frac{k_{eq}I}{k_{eq} + 2k_{ax} + k_i}$$

For IIIa

$$\frac{[M - DOC_2S_2H_3]^{\cdot+}}{[M - HOC_2S_2H_3]^{\cdot+}} = \frac{k_{ax}I}{k_{ax} + 2k_{eq} + k_i}$$

For *cis*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate-2,2,6,6-d_4

$$\frac{[M - DOC_2S_3H_3]^{\cdot+}}{[M - HOC_2S_2H_3]^{\cdot+}} = \frac{[2k_{eq} + 2k_{ax}]I}{k_i}$$

In all three equations k_{eq} and k_{ax} are the rate constants (averaged over all ions energies) for abstraction of a γ-equatorial hydrogen and a γ-axial hydrogen, respectively, k_i is the rate constant for hydrogen elimination from other than the γ position, and I is the isotope effect (k_D/k_H). These equations can be solved for k_{ax}/k_{eq}, the relative rates of axial and equatorial hydrogen abstraction. The results of these calculations appear in Table I.

These experiments demonstrate that cis elimination is the very predominant mode of reaction of the axial xanthate III; at 14 eV, cis elimination is about 30 times as facile as trans elimination. The much more extensive trans elimination observed in the mass spectrum of the acetate I is most plausibly attributed to the greater facility of the α-cleavage process for acetates, since conformational populations and electronic effects should be similar for these closely related reactions. Comparison of the mass spectra of the acetate (V) and xanthate (VI) derived from 4-heptanol demonstrates that α-cleavage is a much more favorable process for the former

Table I. Electron-Impact Induced Elimination of Xanthic Acid from Stereospecifically Labeled 4-*tert*-Butylcyclohexyl-*S*-methyl Xanthates

Registry no.	Compd	Isotopic purity	Ionizing voltage, eV[a]	D loss/H loss[b,c]	k_{ax}/k_{eq}[c]
60239-10-3	*cis*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IIIe)	98% D	70	0.375 ± 0.015	
			12	0.39 ± 0.03	
					0.06 ± 0.03 (70)
					0.03 ± 0.03 (12)
60239-11-4	*cis*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*trans*-2-*d* (IIIa)	98.7% D	70	0.033 ± 0.006	
			12	0.007 ± 0.006	
60239-12-5	*trans*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*trans*-2-*d* (IVe)	97.5% D	*d*	0.11 ± 0.002	
					1.6 ± 0.2
60239-13-6	*trans*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IVa)	98% D	*d*	0.21 ± 0.002	

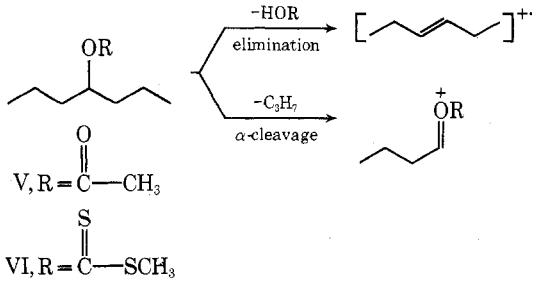
[a] Ionizing voltages are nominal. [b] All data are corrected for isotopic impurities and the occurrence of a small amount of 1,3 and 1,4 elimination. [c] Error limits represent the extreme values observed in at least three separate measurements. [d] Independent of ionizing voltage between 70 and 12 eV.

Table II. First and Second Field-Free Region Metastable Ion Intensities from Stereospecifically Labeled 4-*tert*-Butylcyclohexyl-*S*-methyl Xanthates

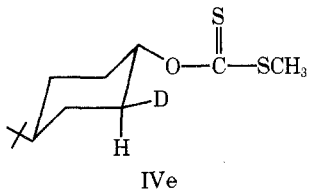
Compd	Transition	(m_1^*)[a]	(m_2^*)[b]
cis-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IIIe)	$\frac{247 \rightarrow 139}{247 \rightarrow 138}$	0.34 ± 0.02	0.30 ± 0.05
cis-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate *trans*-2-*d* (IIIa)	$\frac{247 \rightarrow 139}{247 \rightarrow 138}$	0.025 ± 0.02	0.08 ± 0.05
trans-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*trans*-2-*d* (IVe)	$\frac{247 \rightarrow 139}{247 \rightarrow 138}$	0.11 ± 0.01	0.15 ± 0.05
trans-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate *trans*-2-*d* (IVa)	$\frac{247 \rightarrow 139}{247 \rightarrow 138}$	0.22 ± 0.01	0.25 ± 0.05

[a] Error limits represent the extreme ratios observed in at least four measurements. [b] Data obtained from repeated measurements on chart paper. Error limits are estimated.

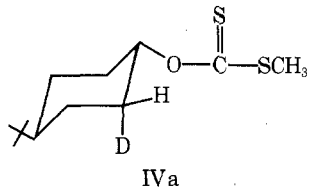
compound. In acyclic compounds, the α-cleavage process is readily detected since it generates a fragment ion; thus, the *intensity ratio* $[M - C_3H_7]^+/[M - HOR]^{\cdot+}$ is a measure of the relative rates of the α-cleavage and elimination reactions. The ratio is ca. 2.0 at all ionizing voltages in the spectrum of acetate V; in contrast, it is less than 0.05 in the mass spectrum of xanthate VI.



The stereochemistry of the electron-impact induced elimination of xanthic acid from *trans*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate was assessed from the spectra of the *trans*-2-*d* (IVe), *cis*-2-*d* (IVa) and 2,2,6,6-d_4 derivatives. As



IVe



IVa

the results in Table I indicate, the equatorial xanthate fragments with little stereospecificity. This result is not surprising. The carbon–sulfur double bond of the xanthate IV should be much longer than the carbon–oxygen double bond of the acetate II.[9] Since sulfur–hydrogen single bonds are typically much longer than oxygen–hydrogen single bonds,[9] hydrogen migration to the thion sulfur may occur over longer distances than migration to the carbonyl oxygen. Both effects will weaken steric interactions between the cyclohexyl ring and the abstracting group in the transition states for hydrogen abstraction. It is notable, however, that the xanthate IV exhibits a slight preference for cis elimination (k_{ax}/k_{eq} = 1.6), in contrast to the preferential trans elimination of the acetate II (k_{ax}/k_{eq} = 0.26). In light of existing uncertainties about the mechanism of xanthate fragmentation, it is pointless to speculate about the origin of the small energy differences that correspond to a rate ratio of 1.6. However, these experiments do demonstrate that trans elimination from equatorial ester derivatives is not a general phenomenon.

An unusual[10] aspect of the electron-impact induced behavior of the xanthates III and IV is that their spectra exhibit intense first[11] and second field free region metastable peaks for loss of xanthic acid. Thus, the stereochemistry of the reaction can be studied as a function of ion lifetime. The results of these studies appear in Table II. Within experimental error, there is no difference between the stereospecificity of xanthic acid elimination at 70 eV and in the metastable regions. This result is unexpected, since metastable ions should be less energetic, and are expected to fragment with greater stereospecificity than ions decomposing in the source.[12] Further

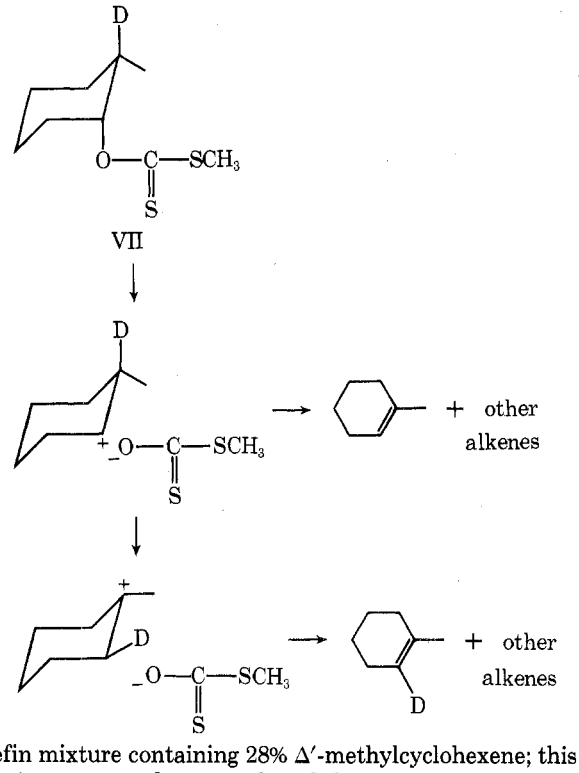
Table III. Pyrolytic Elimination of Xanthic Acid from Stereospecifically Labeled 4-*tert*-Butylcyclohexyl-*S*-methyl Xanthates

Compd	D loss/H loss[a,b]	k_{ax}/k_{eq}	I
cis-4-*tert*-Butycyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IIIe)	0.025 ± 0.015	0.08 ± 0.05	1.65 ± 0.2
cis-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*trans*-2-*d* (IIIa)	0.53 ± 0.02		
trans-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*trans*-2-*d* (IVe)	0.47 ± 0.01	0.04 ± 0.04	2.0 ± 0.2
trans-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate-*cis*-2-*d* (IVa)	0.01 ± 0.01		

[a] Numbers appearing in this table were obtained by injecting 5-μl sample onto a stainless steel column at 300 °C. Injection onto a Pyrex glass column gave values which agreed within experimental error. [b] Error limits represent extreme values observed in at least three pyrolyses.

experiments will be required to establish the generality of this result. It may simply reflect the existence of a competing hydrogen–deuterium randomization process whose rate is fortuitously close to that of the elimination process among the metastable ions.

The pyrolytic elimination of xanthic acid has been much more thoroughly investigated than the electron-impact induced reaction. There is considerable evidence to indicate that the concerted cyclic E_i mechanism is not the exclusive elimination pathway.[2] Perhaps the most thoroughly studied reaction is the pyrolysis of *cis*- and *trans*-2-methylcyclohexyl-*S*-methyl xanthates.[3] The trans isomer pyrolyzes with a normal isotope effect ($k_H/k_D \approx 1.6$) and gives the expected products. In contrast, pyrolysis of the cis isomer VII generates



an olefin mixture containing 28% Δ′-methylcyclohexene; this alkene is 44% monodeuterated, and the isotope effect for its formation is 1. These effects were rationalized by postulating a carbonium ion intermediate which either loses a proton or deuteron directly, or isomerizes to the more stable carbonium ion. Other cases of net trans elimination have been reported.[2] It is notable that in every case where such anomalous behavior has been reported in the cyclohexyl ring system, an α carbon was substituted such that cis elimination to form the more stable alkene product was impossible. It appeared worthwhile to measure the facility of the trans elimination process in a cyclohexyl system devoid of alkene stabilizing groups on the α carbon. The results of pyrolyzing the labeled *S*-methyl xanthates IIIe, IIIa, IIIe, and IVa appear in Table III. Interestingly, these experiments demonstrate that the pyrolysis of cyclohexyl-*S*-methyl xanthates unsubstituted at the α carbon occurs with predominant cis elimination and normal isotope effects regardless of the stereochemistry of the starting xanthate. Thus, the unusual effects observed in earlier studies must be strongly facilitated by α substituents. Trans elimination is only a minor pathway to alkene formation in the pyrolysis of cyclohexyl-*S*-methyl xanthates unsubstituted at the α carbons. Further, these experiments demonstrate that the pyrolytic and electron-impact induced eliminations of xanthic acid from *cis*- and *trans*-4-*tert*-butylcyclohexyl-*S*-methyl xanthate occur with similar stereochemistry.

Experimental Section

Xanthate mass spectra were obtained on an AEI MS902 mass spectrometer using a direct insertion technique. The source temperature was maintained below 40 °C during all measurements. Pyrolyses were accomplished by injection of neat 5-μl samples of the *S*-methyl xanthates onto a 10-ft glass or stainless steel column (0.25 in. o.d.) mounted in a Hewlett-Packard 5450 gas chromatograph maintained at 300 °C. Helium flow rate was adjusted to allow a reaction time of ca. 5 min. Under these conditions, reaction was essentially complete. The 4-*tert*-butylcyclohexene was isolated by preparative gas chromatography performed on a Hewlett-Packard 5750 gas chromatograph containing a 6 ft × 0.125 in. column packed with 10% UCW 98 on 80–100 Chromosorb S and maintained at 130 °C. The isotopic composition of the alkene was determined by repeated mass spectral measurements.

NMR spectra were obtained using deuteriochloroform solvents on a Varian Model A-60 spectrometer. The chemical shift values are expressed in δ values (parts per million) relative to a tetramethylsilane internal standard.

trans-4-*tert*-Butylcyclohexanol-*cis*-2-*d* and -*trans*-2-*d* and *cis*-4-*tert*-butylcyclohexanol-*cis*-2-*d* and -*trans*-2-*d* were prepared as already described.[5] Conversion to the corresponding *S*-methyl xanthates were accomplished by analogy to the procedure of Briggs and Djerassi.[1,3]

***trans*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate (IV)** was purified by preparative TLC (silica gel, hexane, repeated elution) or preparative gas chromatography (on a 10 ft × 0.125 in. Teflon-lined column packed with 3% OV-210 on 80/100 Chromosorb W-HP at 130 °C). The resulting white solid exhibited mp 45–46 °C; NMR δ 0.87 [9 H, s, $(CH_3)_3C$–], 2.53 (3 H, s, CH_3S), 5.44 (1 H, m, broad, HCOCS–), 0.88–2.5 (9 H, aliphatic H); mass spectrum, M^+ at 246.1103 ($C_{12}H_{22}S_2O$ requires 246.1112).

***cis*-4-*tert*-Butylcyclohexyl-*S*-methyl xanthate (III)** was purified similarly. A sample exhibited mp 56–57 °C; NMR δ 0.87 [9 H, s, $(CH_3)_3C$–], 2.53 (3 H, s, CH_3S), 5.83 (1 H, m, HCOCS–), 0.88–2.5 (9 H, aliphatic H); mass spectrum, M^+ at 246.116 ($C_{12}H_{22}S_2O$ requires 246.1112).

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Registry No.—III, 60239-14-7; IV, 60239-15-8.

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A Special-Salt Effect upon the Hydride Shift during the Acetolysis of Cyclohexyl Tosylate

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Lambert and Putz[1b] have recently suggested from stereochemical studies that the substitution product formed during the acetolysis of cyclohexyl tosylate arises from nucleophilic attack on an intimate ion pair (IIP). This interpretation is based upon the observation that cyclohexyl acetate was selectively formed with inversion of configuration. To our knowledge, this is the only study of the intermediate(s) leading to substitution on an unsubstituted cyclohexyl system, although Winstein and Holness[2] had previously suggested similar behavior in the solvolysis of *trans*-4-*tert*-butylcyclohexyl tosylate. On the other hand, Elakovich and Traynham[3] concluded from a study of the special salt effect that the cyclohexyl acetate was formed from a solvent separated ion pair (SSIP) during a chlorinolysis in acetic acid. With the exception of the work discussed above, most reports on the cyclohexyl system have been oriented toward the study of the possible conformation of the transition state.[4]

In this paper we report studies involving the special-salt effect and hydride shifts which are directed toward the elucidation of the product determining intermediates in the acetolysis of cyclohexyl tosylate. The results of the acetolysis of 2,2,6,6-tetradeuteriocyclohexyl tosylate at 50 °C are summarized in Table I.

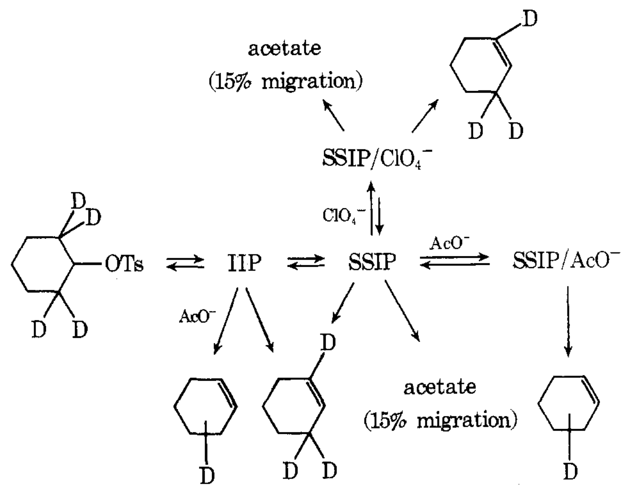
Substitution. The observation that the 0.13 D at position 1 of unreacted tosylate in the absence of $LiClO_4$ is suppressed by the presence of this salt clearly suggests the intermediacy of an external ion pair. Although Winstein[5] did not observe a special salt effect upon the rate of similar reactions, a contradiction does not necessarily exist. The special salt effect upon each of various reaction steps can sometimes be hidden in measurement of the overall rate since not all of the individual rate constants play a rate-determining role. Winstein, himself, recognized this as he admitted the possibility of external return, especially in the light of a very large normal salt effect (b = 37.2 at 50 °C). In terms of Winstein's[6] classic scheme

$$\mathrm{RX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\mathrm{IIP}}{\mathrm{R^+X^-}} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{\mathrm{SSIP}}{\mathrm{R^+//X^-}} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \mathrm{R^+} + \mathrm{X^-} \quad (1)$$

this result indicates that the equilibrium goes at least as far as the SSIP, suggesting the possibility of a reaction involving such a species, even in the absence of $LiClO_4$.

The intermediacy of a SSIP in the substitution reactions seems logical upon consideration of the following results. There is no change in the extent of deuterium scrambling in the acetate buffered reaction upon the inclusion of $LiClO_4$ in the reaction mixture. Observation of two identical patterns of deuterium scrambling for products arising from two different kinds of ion pairs is unlikely.[7] Since addition of $LiClO_4$ presumably increases the SSIP/IIP rates, the observed increase in the substitution/elimination (S/E) ratio upon addition of this salt suggests that the SSIP is more prone to substitution than the IIP.

Scheme I



The present suggestion that the SSIP might be an intermediate in the substitution may, at first, seem in contradiction with the stereoselective inversion reported by Putz and Lambert.[1b] Nevertheless, there exists no definitive proof that a SSIP intermediate cannot react with such stereoselectivity, especially if the nucleophile is not the particular solvent molecule thought to separate the ions. In fact, reaction of a SSIP to form an inverted alcohol has been recently proposed by Shiner et al.[8] Such a possibility has also been recently suggested in two recent reformulations of the original Winstein equilibrium.[9,10]

We suggest two possible mechanisms that are consistent with substitution of a SSIP with inversion of configuration:

(a) The nucleophile could be an acetic acid that attacks the SSIP from the rear. This idea is in accord with a recent suggestion by Schleyer et al.[9]

(b) Another possibility is the simple collapse of the so-called anion–cation-stabilized intermediate (ACSI) which has recently been proposed by one of us as an alternative model for the SSIP[10] (reaction 3).

(2)