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THE SOLVOLYSIS OF 2,2,4,4-TETRAMETHYLCYCLOBUTANE DERIVATIVES

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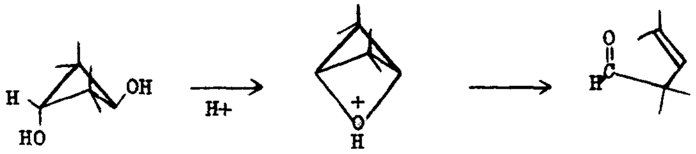
The observation that trans-2,2,4,4-tetramethylcyclobutane-1,3-diol is cleaved in acid much more rapidly than the cis-isomer has been interpreted to indicate internal participation by hydroxyl in the trans isomer (1).



Our interest in four-membered cyclic oxonium ions led us to study this problem in greater detail. Wilcox and Nealy have found that the study of the rate of cleavage of the diols with acid is inconvenient but it is likely that the solvolysis of the corresponding hydroxy tosylates is quite similar to the acid-catalyzed decomposition of the diols (2). In accord with the results of Wilcox and Nealy (2) our kinetic studies show that the trans-hydroxy tosylate solvolyzes much more rapidly than the cis-isomer. Extrapolating our data for the cis-isomer, the trans/cis rate ratio at 45° in 80% ethanol-water is about 1000. We find that the trans-hydroxy tosylate yields the unsaturated aldehyde, 2,2,4-trimethyl-3-pentenal, in 85% yield and the *cis*-hydroxy tosylate yields the unsaturated aldehyde and its hydration product, 3,3,5,5-tetramethyltetrahydro-2-furanol (2), each in 45% yield. Our kinetic results are summarized in Table I.

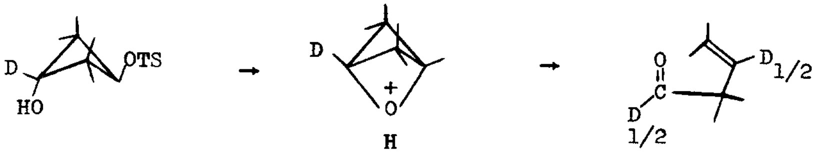
TABLE I

Rate Constants for the Solvolysis of *cis* and *trans*-2,2,4,4-Tetramethylcyclobutane Derivatives in 80% Ethanol-Water

Compound	Temp. °C.	$10^5 k_1$ sec^{-1}	ΔH* kcal.	ΔS* e.u.
cis-3-Hydroxy-2,2,4,4-tetramethylcyclobutyl Tosylate	99.90	7.78±0.26	26.9±0.3	-5.4±0.5
	114.60	32.1±1.4		
cis-3-Hydroxy-2,2,4,4-tetramethylcyclobutyl Tosylate-3-*d*	99.90	7.00±0.24		
trans-3-Hydroxy-2,2,4,4-tetramethylcyclobutyl Tosylate	44.51	17.8±1.2		

Wilcox and Nealy have presented further kinetic evidence that there is no internal participation by hydroxyl in the transition state for the solvolysis of the *trans*-hydroxy tosylate (2). However, no evidence has been presented which rigorously excludes an intermediate bicyclic oxonium ion.

If the symmetrical bicyclic oxonium ion intervenes in the solvolysis of either hydroxy tosylate, the carbons initially bearing the hydroxyl and tosylate groups become equivalent. The substitution of deuterium for hydrogen at the hydroxyl bearing carbon would thus result in olefinic aldehyde equally labeled at the vinyl position and the aldehyde carbon.



With this in mind we examined the preparation of cis and trans-3-hydroxy-2,2,4,4-tetramethylcyclobutyl tosylates-3-d. The labeled tosylates can be prepared by the reduction of the corresponding keto tosylate. The keto tosylate was obtained in 95% yields from the chromic acid oxidation (3) of the mixture of monotosylates prepared by treating the commercially available diol mixture with one equivalent of p-toluenesulfonyl chloride in pyridine. The keto tosylate, m.p. 121.5 - 123°, showed the expected elemental composition and spectroscopic properties. Reduction of the keto tosylate with sodium borohydride or lithium aluminum hydride afforded pure cis-hydroxy tosylate in 70% yields.* The remainder of the material was not accounted for and may well represent trans-isomer which was not stable under the basic reaction conditions. Reduction of the keto tosylate with diborane yielded a mixture of hydroxy tosylates containing about 35% of the trans-isomer as analyzed by infrared spectroscopy and rate measurements. The mixture of cis and trans-hydroxy tosylates could not be separated by fractional crystallization or

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* Pure cis and trans-hydroxy tosylates were prepared from the pure alcohols essentially as described by Wilcox and Nealy (2). In our hands, reaction times of 2 hours give higher yields than those previously reported.

chromatography partly because of the high reactivity of the trans-isomer. Similar reduction of the keto tosylate with lithium aluminum deuteride and diborane-$\underline{d}_6$ yielded the required labeled hydroxy tosylates.

Pure cis-3-hydroxy-2,2,4,4-tetramethylcyclobutyl tosylate-3-d was solvolyzed in 80% ethanol-water and the product 2,2,4-trimethyl-3-pentenal was isolated and purified by vapor phase chromatography. The proton magnetic resonance spectrum of the product aldehyde showed no aldehyde proton absorption near 0.64 τ and the ratio of the vinyl proton absorption to methyl proton absorption was unchanged from that of unlabeled material. The labeled aldehyde was converted to the corresponding 2,4-dinitrophenylhydrazone and its proton magnetic resonance spectrum lacked the aldimine proton peak at 2.43 τ which was present in unlabeled material. A mixture of the labeled derivative containing 5% of the normal 2,4-dinitrophenylhydrazone exhibited a readily observable peak at 2.43 τ.

The study of the labeled trans-hydroxy tosylate was complicated by the inaccessibility of pure trans-material. However, solvolysis of the tosylate mixture in 80% ethanol-water for 7 minutes at 100° results in complete reaction of the trans-isomer whereas only 3% of the cis-isomer is destroyed. Labeled cis-hydroxy tosylate was recovered from the reaction mixture in 62% yield. The 2,2,4-trimethyl-3-pentenal obtained from the solvolysis of the labeled trans-hydroxy tosylate was again found to contain deuterium only at the aldehyde carbon. These results clearly rule out a symmetrical bicyclic oxonium ion intermediate in the solvolysis of both the cis and trans-3-hydroxy-2,2,4,4-tetramethylcyclobutyl tosylates.

Although it appears that internal participation by oxygen is not involved in the solvolysis of the trans-hydroxy tosylate, the origin of the large trans/cis rate ratio is not clear. In an effort to gain some additional information, we have measured the kinetic isotope effect caused by the introduction of deuterium at C-3 in the cis-hydroxy tosylate. The isotope effect was determined from several sets of rate measurements carried out simultaneously on labeled and unlabeled material. We find $k_H/k_D = 1.1 \pm 0.05$ which is larger than expected for an ordinary secondary isotope effect caused by an isotopic substitution so remote from the reacting center (4). While this result cannot be interpreted with confidence, the magnitude of the effect is about that observed for the solvolysis of exo-2-norbornyl brosylate-exo-5,6-d_2 (4,5). Thus it appears that there is participation by carbon 3 in the transition state. The carbonium ion shown below may be an important contributor.

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