Hydrogen Participation vs. Elimination. The Role and Fate of Neighboring Hydrogen in Solvolysis of Neomenthyl Tosylate

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Product composition and α-d_1 and β-d_3 isotope effects in the solvolysis of neomenthyl tosylate (8-OTs) were determined in 70% aqueous trifluoroethanol and 70% aqueous ethanol. Both trifluoroethanolysis and ethanolysis gave 1-2% neomenthol (97% d_3), 12-13% *cis*-4-menthanol (100% d_3), 2-3% *trans*-4-menthanol (100% d_3), 66-70% 3-*p*-menthene (83% d_3 and 17% d_2), and 5-9% 4,8-*p*-menthene (97% d_3), respectively. These results and the high value of the β-d_3 isotope effect (k_H/k_D = 2.45) were interpreted in terms of rate-determining hydride shift followed by elimination which accounts for 75% of all products. In 85% of the elimination products the migrating hydrogen (deuterium) *is not* the one being eliminated.

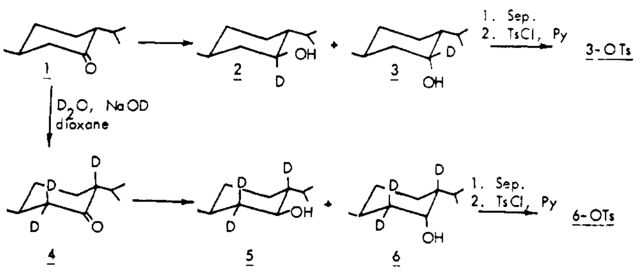
Axial cyclohexyl derivatives such as neomenthyl tosylate (8-OTs) yield, under solvolytic conditions, predominantly elimination products.[1] The antiperiplanar arrangement of the leaving group and the axial tertiary β-hydrogen atom provide the ideal geometry for hyperconjugation and hydrogen participation.[2] It has been shown that both of these interactions can be conveniently studied by means of secondary deuterium isotope effects.[3] Previous studies of the solvolysis of unlabeled derivatives[4-6] could not provide satisfactory answers to questions regarding the participation of neighboring hydrogen in the rate-determining step (possibly via a bridged intermediate) and the fate of this hydrogen in the (subsequent) elimination reaction. Therefore, we considered it of interest to perform a detailed kinetic and product study of the solvolysis of neomenthyl tosylate (8-OTs) and its specifically deuterated analogues 6-OTs and 3-OTs. The synthesis of this material as well as of 3-*p*-menthene (10) and 2-*p*-menthene (11), respectively, and the isomeric *cis*- and *trans*-4-menthanols (12 and 13), which were needed for the purpose of identification and product characterization, is given in Schemes I-III and described in detail in the Experimental Section.

Experimental Section

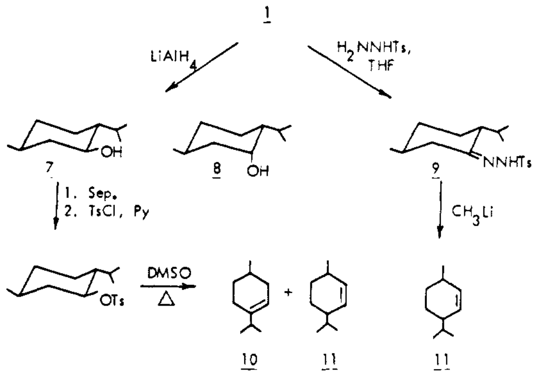
General. Purity of compounds was controlled by GC using a Varian 1800 gas chromatograph. ^{1}H NMR, IR, and mass spectra were recorded on a Varian A-60 spectrometer, a Perkin-Elmer 221 spectrophotometer, and a Varian CH-7 mass spectrometer, respectively. GC separations were carried out on a Varian Aerograph Auto-prep 700 gas chromatograph using $^3/_8$ in. × 10 ft SS columns.

Synthetic Procedures. Menthone-β-d_3-Isomenthone-β-d_3 (4 + 4a).[7] A mixture of commercial menthone (Fluka, menthone-isomenthone, 70:30; 7.72 g, 50 mmol), dry dioxane (45 mL), deuterium oxide (14.5 g, 0.75 mol, 99% deuterium), and NaOD (0.123 g, 1.5 mmol) was refluxed for a week. Subsequently, the ketone was continously extracted overnight with 500 mL of ether. The ether extract was washed with water (3 × 30 mL) and dried over $MgSO_4$. Ether and dioxane were evaporated, and the residue was treated twice more as described above. The crude product was distilled in vacuo [84-86 °C (13 mmHg)] to give 5.85 g (38 mmol, 76%) of menthone-β-d_3-isomenthone-β-d_3 mixture (isotopic purity by mass spectrum, 97.9% d_3, 5.2% d_2).

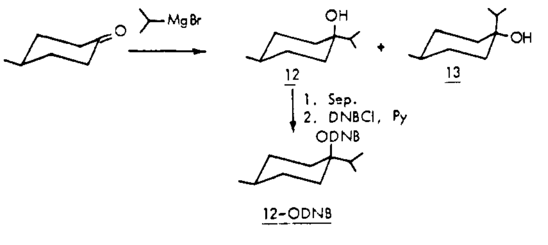
Scheme I



Scheme II



Scheme III



Neomenthol (8) was obtained by $LiAlH_4$ (1 g, 83 mmol) reduction of menthone (3.5 g, 24 mmol) in the presence of anhydrous

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(1) E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw Hill, New York, 1962, p 227.

(2) A. Streitwieser, Jr., "Solvolytic Displacement Reactions", McGraw Hill, New York, 1962, p 142.

(3) (a) V. J. Shiner, Jr., *ACS Monogr.*, No. 164, 90 (1970); (b) S. Winstein and J. Takahashi, *Tetrahedron*, 2, 316 (1958).

(4) E. D. Hughes, C. K. Ingold, and J. B. Rose, *J. Chem. Soc.*, 3839 (1953).

(5) S. Winstein, B. K. Morse, E. Grunwald, H. Jones, D. Trifan, and H. Marshall, *J. Am. Chem. Soc.*, 74, 1127 (1952).

(6) (a) W. Hückel and C. H. Jennewein, *Justus Liebigs Ann. Chem.*, 683, 100 (1965); (b) W. Hückel, H. Feltkamp, and S. Geiger, *ibid.*, 637, 1 (1960).

(7) B. Willhalm and A. F. Thomas, *J. Chem. Soc.*, 6478 (1966).

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$AlBr_3$ (2.7 g, 10 mmol) at -60 °C as described by Hückel.[8] The yield of crude product was 3.3 g (94%). Neomenthol (63%) was separated from menthol (11%) and neoisomenthol (26%) by column chromatography (neutral alumina, activity II/III, eluant pentane–ether, 95:5) followed by GC (OS-138, 150 °C). The yield of neomenthol (98% pure by GC) was 1.38 g (37%) on the basis of the menthone–isomenthone mixture.

Neomenthol-α-d_1 (3) and neomenthol-β-d_3 (6) were obtained by $LiAlD_4$ ($LiAlH_4$) reduction of menthone (1) and menthone-β-d_3 (4), respectively, using the same procedure as described above.

Neomenthyl tosylates (8-OTs, 3-OTs, 6-OTs) were prepared in 62–66% yield from **8**, **3**, and **6** by the usual method.[6] Neomenthol could not be detected by IR and NMR spectroscopy.

2-*p*-Menthene (11).[9] A mixture of menthone (1.54 g, 10 mmol), *p*-toluenesulfonylhydrazine (1.86 g, 10 mmol), tetrahydrofuran (15 mL), and a drop of concentrated HCl was refluxed with stirring for 6 h. The water formed in the reaction was removed by azeotropic distillation with benzene. After the solution cooled to 0 °C, 10 mL (20 mmol) of 0.2 M methyllithium solution in ether was added dropwise with stirring during a period of 0.5 h. Water (15 mL) was then added carefully and the resulting mixture was extracted with pentane (3 × 30 mL). The combined extracts were washed with water and dried. The solvent was distilled off and the residue was purified by GC (10% Carbowax 20M, 130 °C) to give 0.49 g (37%) of pure 2-*p*-menthene. IR and mass spectra were identical with the spectra reported in the literature.[10,11]

3-*p*-Menthene (10) was obtained in a mixture with 2-*p*-menthene (74% 3-*p*-, 23% 2-*p*-menthene) from menthyl tosylate.[12] A solution of the tosylate (0.84 g, 40 mmol) in Me_2SO (10 mL) was refluxed for 6 h. Upon cooling the product mixture was extracted with pentane (3 × 30 mL). The extracts were washed with water and saturated brine and dried over $MgSO_4$. The solvent was removed by distillation and 3-*p*-menthene was isolated by GC as described for 2-*p*-menthene. The IR spectrum showed the absorption band at 815 cm^{-1}, characteristic for 3-*p*-menthene.[10]

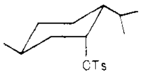
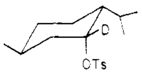
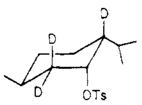
***cis*- and *trans*-4-Menthanols (4-methyl-1-isopropylcyclohexanol)(12 and 13)**[13] were obtained from 4-methylcyclohexanone and isopropylmagnesium bromide by following the procedure of Hückel.[14] The crude mixture (cis/trans, 2:1) was separated by GC on a 15% Carbowax 20M (125 °C) column. *cis*-4-Menthanol was 92% pure by GC.

***cis*-4-Menthanyl-3,5-dinitrobenzoate (12-ODNB).** A mixture of *cis*-4-menthanol (0.53 g, 3.4 mmol), dry pyridine (12 mL), and 3,5-dinitrobenzoyl chloride (0.87 g, 3.8 mmol) was stirred for 4 days at 25 °C. The reaction mixture was poured onto ice–water and extracted with 3 × 30 mL of ether. The combined extracts were washed with cold 10% HCl, saturated $NaHCO_3$, and water and dried over $CaSO_4$. The solvent was evaporated and the residue crystallized from *n*-hexane. The crude product was purified by chromatography on silica gel using benzene as eluant to give 0.5 g (42%) of **12**-ODNB.

Kinetic Procedure. The rate measurements were performed by the potentiostatic technique, using a pH-stat (Radiometer, Copenhagen, SBR-2/TTT 11) at a constant pH of 6.7 for ethanolysis and 6.0 for trifluoroethanolysis. The liberated acid was titrated with 0.002 M sodium alkoxide. The infinity titers were in accordance with the theoretical values.

The concentration of tosylate was ~0.002 M in all experiments. The double-jacketed titrimetric cell with solvent was allowed to stabilize at the corresponding temperature prior to addition of the substrate. At least six measurements were conducted for each compound, alternating the solvolysis of the labeled and unlabeled tosylate. The rate data were evaluated by a nonlinear least-squares-fitting program. No trend was observed in the rate constants between 20 and 80% of reaction completion.

Table I. First-Order Rate Constants and Isotope Effects in the Solvolysis of Neomenthyl Tosylates at 25 °C

compd[a]	solvent	$k \times 10^4$ s^{-1} [b]	k_H/k_D
 **8-OTs**	97 TFE[c]	1.31 (1)	
	70 TFE	1.70 (1)	
 **3-OTs**	97 TFE	1.19 (1)	1.17 (1)
	70 TFE	1.46 (2)	1.15 (1)
 **6-OTs**	97 TFE	0.565 (3)	2.45 (1)
	70 TFE	0.711 (4)	2.39 (1)

[a] Initial concentrations 0.06–0.03 mol/L. [b] Uncertainties are given as standard errors. [c] 97 TFE = 97 w/w % aqueous 2,2,2-trifluoroethanol.

Product Studies. The following typical experiment describes the general procedure used in all required product analyses.

Neomenthyl tosylate (0.325 g, 1.5 mmol) was solvolyzed for 10 half-lives in 22 mL of 70% aqueous TFE or 40 mL of 70% aqueous ethanol, respectively, in the presence of 2,6-lutidine (0.180 g, 1.7 mmol). After cooling to room temperature the reaction mixture was extracted with pentane (3 × 30 mL) and the combined extracts were washed with water (2 × 20 mL) and dried over $MgSO_4$. The water washings were checked by GC to verify the absence of solvolysis products. The solvent was distilled off through a Vigreux column, and the residue was analyzed by GC (FFAP column at a temperature programmed from 60 to 100 °C). The mixture of olefins was separated from the alcohols by GC (20% Carbowax 20M, 80 °C) and then analyzed on a 30% $AgNO_3$/ethylene glycol column at 50 °C.[15]

The relative amounts of the products were computed from the peak area obtained by a digital integrator. The products were identified by GC comparison with authentic samples used as internal standards and/or by the mass spectra obtained on a GC–mass spectrometer.

The deuterium content in the solvolysis products of **6**-OTs was determined by GC–mass spectrometry, using a 10% FFAP column for the alcohols and a 30% $AgNO_3$/ethylene glycol column for the olefins.

Results and Discussion

The solvolysis rates of neomenthyl tosylates (**3**-OTs, **6**-OTs, and **8**-OTs) in trifluoroethanol–water mixtures are given in Table I. The solvolysis products data are presented in Table II.

The solvolysis of neomenthyl tosylate in aqueous TFE is about 30 times faster than the solvolysis rate of menthyl tosylate. This ratio seems to be strongly solvent and leaving group dependent, which can be ascribed to different degrees of solvent participation in the solvolysis of menthyl tosylate **7**-OTs (see Table III). The latter substrate is considered to solvolyze by a limiting mechanism in TFE.[16a] This is believed to be the consequence of the retained chair conformation of the cyclohexane ring in the transition state which renders a backside attack by solvent less feasible for steric reasons.[16b] The greater reactivity of **8**-OTs relative to **7**-OTs cannot be due to any significant

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[8] W. Hückel, M. Maier, E. Jordan, and W. Seeger, *Justus Liebigs Ann. Chem.*, **616**, 46 (1958).

[9] W. G. Dauben, M. E. Lorber, N. D. Vietmeyer, R. H. Shapiro, J. H. Duncan, and K. Tomer, *J. Am. Chem. Soc.*, **90**, 4762 (1962).

[10] B. M. Mitzner, E. T. Theimer, and S. K. Freeman, *Appl. Spectrosc.*, **19**, 169 (1965).

[11] A. F. Thomas and B. Willhalm, *Helv. Chim. Acta*, **47**, 475 (1964).

[12] H. P. Nace, *J. Am. Chem. Soc.*, **81**, 5428 (1959).

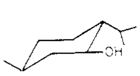
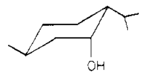
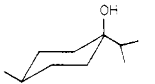
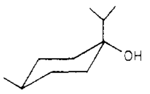
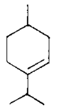
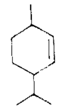
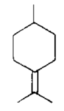
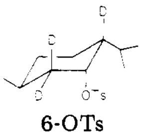
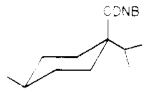
[13] Stereochemistry specified with respect to the hydroxy group at the tertiary center.

[14] W. Hückel, D. Mancher, O. Fechtig, J. Kurz, M. Heinrel, and A. Hubele, *Justus Liebigs Ann. Chem.*, **645**, 115 (1961).

[15] J. Herling, J. Shaktai, and E. Gil-Ar, *J. Chromatogr.*, **8**, 349 (1962).

[16] (a) For a discussion of menthyl tosylate solvolysis see D. J. Raber, W. C. Neal, Jr., M. D. Dukes, J. M. Harris, and D. L. Mount, *J. Am. Chem. Soc.*, **100**, 8137 (1978). The suggestion that this substrate might react by a k_Δ process involving the neighboring carbon-carbon σ-bond is not supported by product analysis.[16b] (b) S. Hiršl-Starčević, Z. Majerski, and D. E. Sunko, *J. Am. Chem. Soc.*, **96**, 3659 (1974).

Table II. Solvolysis Products of Neomenthyl Tosylates and *cis*-4-Menthanyl-3,5-dinitrobenzoates

		products, mol %[a,b]						
compd[c]	conditions[d]	 **7**	 **8**	 **12**	 **13**	 **10**	 **11**	 **14**[e]
 8-OTs	A		2	13	3	66		9
	B		1	12	2	70		5
 6-OTs	A		3 (97% d_3)[f]	10 (100% d_3)[f]	2 (100% d_3)[f]	69 (83% d_3 + 17% d_2)[f]		8 (97% d_3)[f]
 12-ODNB	C					71[g]		25[g]

[a] The products were identified by comparison with authentic samples. The stereochemistry of the 4-menthanols[13] (**12** and **13**) was established by comparing their IR spectra with the published spectra of authentic compounds and confirmed by means of ^{1}H NMR spectra using the shift reagents and by ^{13}C NMR spectra of **12** and **13**. [b] Rounded up average values for two independent experiments and 5–6 GC analyses of each product mixture. All products were shown to be stable under the reaction conditions used. The differences to 100% are mixtures of ethers which were not analyzed. [c] Initial concentrations 0.06–0.08 mol/L buffered with 1 equiv of 2,6-lutidine. [d] A, 70% TFE, 20 °C; B, 70% EtOH, 60 °C; C, 80% TFE, 20 °C. [e] Identified by comparison of mass spectral data with those published previously for 4,8-*p*-menthene.[11] [f] Determined by mass spectral analysis. [g] Unidentified product (4%) was also detected.

Table III. Solvolysis Rates and Rate Ratios of Neomenthyl (**8**) and Menthyl (**7**) Derivatives in Different Solvents

system	solvent[a]	temp, °C	k, s^{-1}	rate ratio	ref
8-Cl	80 EtOH	124.9	1.63×10^{-4}	40	4
7-Cl	80 EtOH	124.9	4.02×10^{-6}		
8-OTs	AcOH	25.0	4.09×10^{-6}	170	5
7-OTs	AcOH	25.0	2.39×10^{-8}		
8-OTs	EtOH	49.9	7.11×10^{-5}	127	5, 6
7-OTs	EtOH	50.0	5.64×10^{-7}		
8-OTs	AcOH	49.9	9.90×10^{-5}	77	5
7-OTs	AcOH	49.9	1.28×10^{-6}		
8-OTs	97 TFE	25.0	1.31×10^{-4}	30	16
7-OTs	97 TFE	25.0	4.40×10^{-6} (4.22×10^{-6})	(31)[b]	
8-OTs	70 TFE	25.0	1.70×10^{-4}	36	16
7-OTs	70 TFE	25.0	4.76×10^{-6} (5.01×10^{-6})	(34)[b]	

[a] 80 EtOH = 80 vol % aqueous ethanol, 97 TFE = 97 wt % aqueous trifluoroethanol. [b] Values in parentheses, this work.

backside solvent assistance since no product of inverted configuration could be detected (Table II). On the other hand, the axial tosylate leaving group can account for a rate enhancement of only 3 to 5.[17] Thus, a factor of 5 to 10 should be ascribed to the 1,2-hydride shift from a tertiary to a secondary carbon. This is a more acceptable value than the higher one suggested by Winstein[5] on the basis of the 8-OTs/7-OTs rate ratio of 170.[1] Both a favorable steric situation and the formation of the tertiary cation make it rather difficult to assess the contribution of the migrating hydrogen to the overall solvolysis rate. However, the assumption that the solvolysis of 8-OTs is a k_Δ process is corroborated by the small sensitivity of the solvolysis rates of 8-OTs to changes in the water content of the TFE solvent. The product composition also did not change significantly when the solvent was changed from 70% aqueous TFE to 70% aqueous ethanol. Considering in this case hydrogen participation as the dominant mechanism, the remaining question concerns the structure of the intermediate carbocation and of the transition state leading to it. The α-effect is smaller ($k_H/k_D = 1.17$) than the maximum value for a sulfonyl leaving group (1.23)[18,19,21] and little sensitive to changes of the water content of TFE. This is probably more a consequence of a partially hydrogen-bridged transition state than of any significant solvent participation or ion-pair return to the original position.[18,19] Solvolyses in TFE usually favor the formation of the solvent-separated ion pair (k_2 rate determining)[19] which, in the present case, undergoes additional stabilization from the participating hydrogen.

The magnitude of the β-effect is typical for systems where 1,2-hydride migration occurs in the rate-determining step.[3b,20,21] Some examples are given in Table IV. If, as implied in this mechanism, a significant charge delocalization due to neighboring-hydrogen participation (and migration) takes place in the rate-determining transition state, the nonmigrating deuterium atoms in the β-position on the secondary carbon atom should give rise to a significantly smaller isotope effect.[22] We estimate this effect to be on the average $k_H/k_{\beta\text{-}d_2} = 1.2$, with the axial deuterium being the main hyperconjugatively contributing atom.[23] Thus, the observed effect of $k_H/k_{\beta\text{-}d_3} = 2.4$ could be regarded as being composed of the effect associated with the migrating deuterium ($k_H/k_D \sim 2.0$) and the effect of the two nonmigrating deuterium atoms. Moreover, the

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(17) See ref 1, p 229.

(18) V. J. Shiner, Jr., *ACS Symp. Ser.*, No. 11, 163 (1975).

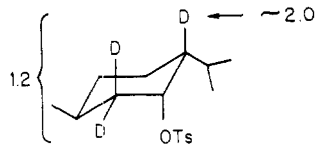
(19) V. J. Shiner, Jr., J. A. Nollen, and K. Humski, *J. Org. Chem.*, **44**, 2108 (1979).

(20) (a) M. Pankova, J. Sicher, M. Tichý, and M. C. Whiting, *J. Chem. Soc. B*, 366 (1968); (b) J. Hapala and M. Tichý, *Collect. Czech. Chem. Commun.*, **41**, 2928 (1976).

(21) V. J. Shiner, Jr., and R. C. Seib, *Tetrahedron Lett.*, 123 (1979).

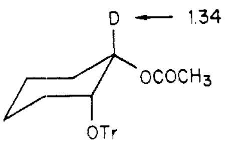
(22) V. J. Shiner, Jr., and J. G. Jewett, *J. Am. Chem. Soc.*, **87**, 1385 (1965).

(23) D. E. Sunko, I. Szele, and W. J. Hehre, *J. Am. Chem. Soc.*, **99**, 5000 (1977).



large effect of the migrating hydrogen arises from the superposition of primary (participating) and secondary (hyperconjugative) effects.

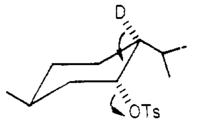
The problem of distinguishing between these two interactions by means of kinetic deuterium isotope effects is subject to limitations on theoretical grounds because there is no dichotomy between hyperconjugation and participation.[24] The only example we know of where hyperconjugation is favored, but hydrogen migration (participation) does not occur, is the solvolysis of *cis*-2-acetoxycyclohexyl-2-*d* tresylate[25] (17-OTr). Here, the



17-OTr

isotope effect observed for the nonmigrating (tertiary) β-hydrogen was 1.34 (95 °C; 97% TFE). The difference of ~1.4[26] between this value and the one estimated for the analogously situated deuterium atom in 8-OTs (k_H/k_D ~2.0) is likely to be due to the additional lowering of stretching and bending frequencies of the participating C–D bond[27] as a consequence of partial bridging in the transition state.[18]

The involvement of neighboring hydrogen in the rate-determining transition state as deduced from isotope effects unfortunately does not answer the question regarding the structure of the intermediate carbocation. In the neomenthyl system hydrogen migration occurs from a tertiary carbon, and a transition state similar to 18 could collapse directly to tertiary ion 20, bypassing the structure 19 as an intermediate of any appreciable lifetime.



18

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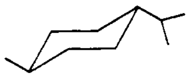


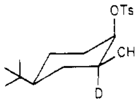
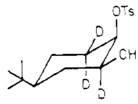
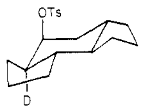
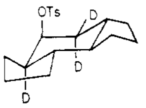
20

As one referee pointed out "the magnitude of the α-effect is just what one might have calculated for conversion of the reactant CHOTs to CH_2. Neglecting any hyperconjugation to a neighboring center of electrons binding *this* CH, one might want to consider possible rate-limiting transition states with fully migrated hydrogen". However, studies with optically active 8-OTs by Hückel et al.[6] showed that in methanolysis the resulting 3-*p*-menthene was only 22% racemized, thus ruling out 20 as the main symmetrical intermediate. This is apparently not the case for the reaction in formic acid where only racemic 3-*p*-menthene (10) was isolated.[2] It is the product studies performed with racemic material (see Table II), both protium and deuterium labeled, which provide important additional information regarding the structure of the principal intermediate. The inspection of these data revealed the following.

(1) No substitution product (alcohol) of inverted configuration (menthol 7) was formed. This definitely rules out a k_s process.

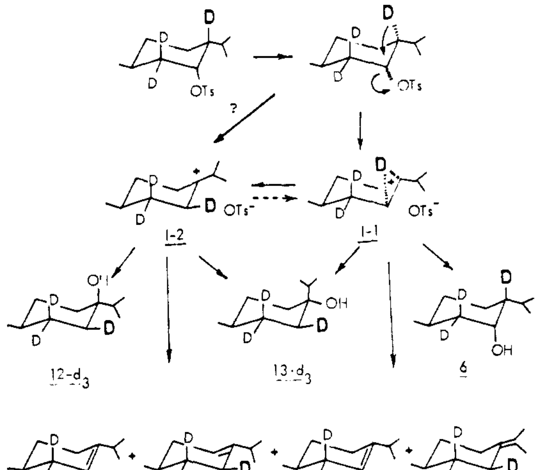
(2) The main product is 3-*p*-menthene (10), the amount of which does not significantly change when deuterium labeled 6-OTs was used or TFE was replaced with EtOH. The deuterium analysis revealed that 83% of 10 still contains three deuterium atoms per molecule, demonstrating that only a small portion (17%) of the participating deuterium is eliminated. This percentage roughly corresponds with the degree of racemization observed by

Table IV. β-Deuterium Isotope Effects in the Solvolysis of Some Axial Cyclohexyl Derivatives in 70% EtOH[a]

system	k_H/k_D	$\frac{k_H/k_{\beta\text{-}d_1}}{k_H/k_{\beta\text{-}d_3}}$ [b]
 15-d_1	2.07	1.17
 15-d_3	2.43	
 16-d_1	2.07	1.11
 16-d_3	2.30	

[a] Reference 20. [b] 2-Methyl-4-*tert*-butylcyclohexyl tosylate (15) solvolyses in AcOH with 100% rearrangement to 1-methyl-3-(*tert*-butylacetoxy)cyclohexane (26% of all products). The ratio of isotope effects for β-d_1 and β-d_3 compounds (2.07 vs. 2.43) gives the fraction of the total effect caused by two secondary nonparticipating deuterium atoms.

Scheme IV



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[24] R. Hoffmann, C. Radom, J. A. Pople, P. v. R. Schleyer, W. J. Hehre, and L. Salem, *J. Am. Chem. Soc.*, **99**, 6221 (1977).

[25] S. Richter, I. Bregovec, and D. E. Sunko, *J. Org. Chem.*, **41**, 785 (1976).

[26] Extrapolation of the effect observed at 95 °C to 25 °C according to $\log (k_H/k_D)_{T_1} = T_2/T_1) \log (k_H/k_D)_{T_2}$ increases the β-effect in 17-OTr to 1.47. It is, however, doubtful whether β-effects follow the same temperature dependence as α-effects (ref 3a, p 148).

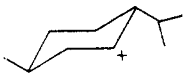
[27] C. F. Wilcox, Jr., I. Szele, and D. E. Sunko, *Tetrahedron Lett.*, 4457 (1975).

Hückel[6] and might be accounted for by the formation of cation **20**, which does not discriminate between the two β-positions. The possible role of the leaving group in this reaction will be discussed later.

(3) All other products are formed without practically any loss of deuterium, which speaks in favor of the formation of a bridged though not necessarily symmetrical cation **I-1** in the form of a solvent-separated ion pair. The presence of the counterion can explain the preferable formation of *cis*-4-menthanol (**12**) relative to the trans isomer **13** by successive ion-pair return and backside attack by solvent on the intermediate second ion pair **I-2** (see Scheme IV).

(4) Separate product studies in the solvolysis of *cis*-4-menthanyl-3,5-dinitrobenzoate (**12-ODNB**),[28] which presumably leads to the classical tertiary cation **20**, resulted in the formation of elimination products **10** and **14** only. Therefore, in the solvolysis of **8-OTs**, cation **20** cannot account either for the formation of ca. 10% of *cis*-4-menthanol (**12**) or for the formation of the two minor substitution products **8** and **13**.[29]

(5) Neomenthol (**8**) could arise either from the unrearranged secondary cation **21**, which is highly improbable,



21

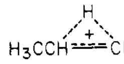
or from the hydrogen-bridged ion **19**. The absence of **7** and **11** among the products also rules out cation **21** as an intermediate.

Summing up, the results of the work described herein can be rationalized in terms of the mechanism shown in Scheme IV (the participating deuterium atom is shown in boldface).

In the ionizing step of the solvolysis reaction in TFE, the departure of the leaving group is facilitated by the neighboring tertiary axial hydrogen. Some backside bonding of this hydrogen with the cationic carbon decreases the α-isotope effect to some extent while increasing simultaneously the β-effect due to partial C–D bond breakage.[30]

The available experimental evidence does not allow the assessment of the relative importance of the two intermediates **I-1** and **I-2** which are represented as solvent-separated ion pairs. **I-1** can be made responsible for the formation of *all* products with the exception of *cis*-4-menthanol (**12**). This main substitution product requires **I-2** as the second intermediate which by backside solvent attack at the tertiary carbon affords **12**. For reasons mentioned before (vide infra) a free tertiary ion corresponding to **I-2** can be excluded from this mechanistic scheme. On the other hand, the tertiary cation **I-2** in the form of an ion pair could also account for all products as well as for the observed α- and β-isotope effects, with one important exception, namely, the formation of neomenthol (**8**). It is difficult to conceive that **8** could be formed by frontside displacement in the secondary ion pair *prior* to hydride migration or from the tertiary fully rearranged cation **I-2** by a reversible hydrogen migration. Therefore we must consider an unsymmetrically hydrogen-bridged cation similar to **I-1** as a more acceptable alternative structure for the initially formed intermediate.

At this point a brief commentary of some theoretical studies is in order. The simplest cutoff model for the ion derived from **8-OTs** is the 1-propyl cation. Its rearrangement of the 2-propyl cation by a 1,2-hydride shift must proceed via the bridged ion **22**. The relative energy



$$H_3CCH \overset{\overset{H}{+}}{=\!=\!=} CH_2$$

22

of this ion, using the 4-31G basis set, was found to be 0.8 kcal/mol above the energy of the 1-propyl cation. Inclusion of a polarization function is likely to lower the energy and allow for a direct rearrangement to 2-propyl cation.[32]

The two elimination products still retaining the participating hydrogen (deuterium) could arise from both intermediary ion pairs **I-1** and **I-2**, respectively, by leaving-group-assisted proton abstraction. However *only* **I-2** can also eliminate the participating hydrogen (deuterium). In this intermediate the tosylate anion must not necessarily discriminate between the two adjacent hydrogens on the same carbon and could also to a lesser degree eliminate the other axial β-hydrogen. This could explain the 20% of racemization observed by Hückel.[6] In our opinion, concerted elimination of the migrating hydrogen by solvent is not probable because any increase in nucleophilicity of the TFE–water mixture by increasing the water content (from 97% TFE to 70% TFE) should increase the degree of elimination and consequently the (primary) isotope effect, which is obviously not the case.

Thus, we can confidently conclude that in 1,2-hydride migration from a tertiary to a secondary carbon atom in the solvolysis of **8-OTs** the *migrating hydrogen* in the hydrogen bridged intermediate *is not the one involved in the elimination reaction*, which is the major product-forming path. In solvents of low nucleophilicity and high ionizing power as with TFE (and probably even more with HFIP), elimination occurs most probably by attack of the leaving group on the β-hydrogen of the rearranged cation **20**. The bridged ion **I-1** is probably of comparable stability as **I-2**, from which it is separated by a low-energy barrier, but being formed first it could also account for most of the elimination products. There is no a priori reason why this counterion-assisted elimination could not occur from a bridged intermediate. Theoretical studies of the symmetrical bridged $C_2H_5^+$ ion have shown only small differences in charge distribution between the bridging and the peripheral hydrogen atoms. The latter (four) hydrogens account for 80% of the positive charge on all hydrogens.[33]

We are not aware of similar studies for the bridged propyl cation. Further studies are needed to rationalize the racemization process (if it occurs at all in TFE–water solvents) and to find out the generality of the observation that the neighboring (participating) hydrogen atom is not eliminated in E1 reactions.

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[28] This substrate solvolyzed in 80% TFE at 60 °C with $k = 1.6 \times 10^5\ s^{-1}$.

[29] It is interesting to compare the product composition given in Table II with the corresponding data for the solvolysis of 8-OTs in methanol. Hückel[6a] isolated 84% 3-*p*-menthene, 3% 4,8-*p*-menthene, and 11% of the tertiary menthyl ether.

[30] Neighboring groups acting as internal nucleophiles decreases the α-effect in the order $\sigma < \pi < n$. Neighboring hydrogen appears to induce the smallest decrease.[31]

[31] D. E. Sunko and S. Borčić, *ACS Monogr.*, No. 164, Chapter III (1970). See also E. Polla, S. Borčić, and D. E. Sunko, *J. Org. Chem.*, **44**, 4096 (1979).

[32] L. Radom, J. A. Pople, V. Buss, and P. V. R. Schleyer, *J. Am. Chem. Soc.*, **94**, 311 (1972).

[33] D. A. Dixon and W. N. Lipscomb, *J. Am. Chem. Soc.*, **95**, 2853 (1973).

formed the chemical shift and ^{13}C NMR analyses.

Registry No. 1, 89-80-5; **3**-OH, 73908-31-3; **3**-OTs, 73908-32-4; **4**, 4789-24-6; **4a**, 73908-33-5; **6**-OH, 73908-34-6; **6**-OTs, 73908-35-7; **7**-Cl, 29707-60-6; **7**-OTs, 7212-65-9; **8**-Cl, 26348-39-0; **8**-OH, 491-01-0; **8**-OTs, 14539-76-5; **10**, 500-00-5; **10**-d_3, 73908-36-8; **11**, 5256-65-5; **12**-OH, 3239-03-0; **12**-OH-d_3, 73908-37-9; **12** ODNB, 73908-38-0; **13**-OH, 3239-02-9; **13**-OH-d_3, 73908-39-1; **14**, 1124-27-2; **14**-d_3, 73908-40-4; **15**, 19140-67-1; **15**-*d*, 62222-93-9; **15**-d_3, 62222-94-0; **16**-*d*, 62239-64-9; **16**-d_3, 62239-65-0; **17**-OTs, 57573-68-9; menthol, 1490-04-6; neoisomenthol, 491-02-1; 1-methyl-3-(*tert*-butylacetoxy)cyclohexane, 73908-41-5.

Tri-*n*-butyltin Hydride: A Selective Reducing Agent for 1,3-Dithiolanes

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Received October 2, 1979

Tri-*n*-butyltin hydride has been found to be an effective and selective agent for complete or partial desulfurization of 1,3-dithiolanes 1. The reaction of 1 with 4 equiv of tri-*n*-butyltin hydride in the presence of 2,2′-azobis(isobutyronitrile) results in complete desulfurization, giving hydrocarbons 2 in good yield, ethane, and bis(tri-*n*-butyltin) sulfide. Two equivalents of hydride specifically cleave the two geminal C–S bonds in 1 to give hydrocarbons 2 and bis(tri-*n*-butylstannyl) ethanedithiolate. One equivalent of tri-*n*-butyltin hydride reduces 1 quantitatively to the β-[alkyl(or aryl)thio]ethyl tri-*n*-butyltin sulfides 11.

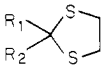
The hydrogenolysis of dithioacetals and dithioketals has been extensively utilized as an alternative to the Wolff–Kishner or Clemmensen reduction of the parent aldehyde or ketone. These desulfurizations have most commonly been achieved by the use of Raney nickel[1] or alkali metals in ammonia (or alkylamine) solution.[2] Reagents such as hydrazine,[3] cupric chloride–zinc chloride–lithium aluminum hydride,[4] and nickel boride[5] have also been used. While these procedures are excellent where complete desulfurization is desired, they do not generally allow for the selective reduction of one carbon–sulfur bond, leaving others in the same molecule intact.[6] We wish to report the use of tri-*n*-butyltin hydride as an effective and selective agent in the reduction of dithioketals and dithioacetals.

Although there have appeared a limited number of studies wherein organotin hydrides have reduced an organosulfur functionality,[7] there was, at the start of this study, no clear indication which of the four carbon–sulfur bonds in dithiolanes 1, if any, would be cleaved by tri-*n*-butyltin hydride. Initially we attempted complete desulfurization of 1 to hydrocarbon 2 by using 4 equiv of the organotin hydride with the anticipation that the reaction represented by eq 1 would proceed.

Table I. Reduction of 1,3-Dithiolanes 1 by 4 Equiv of Tri-*n*-butyltin Hydride[a]

ethylene thioketal or -acetal of	no.	hydrocarbon product 2	% isolated yield
cyclohexanone[b]	3	cyclohexane	76[e]
benzaldehyde[b]	4	toluene	73[e]
6-methoxy-α-tetralone[c]	5	6-methoxytetralin	95[e]
heptanal[b]	6	heptane	80[e]
10-methyl-$\Delta^{1,9}$-2-octalone[c,d]	7	10-methyl-$\Delta^{1,9}$-octalin[d] (8) and 10-methyl-$\Delta^{1,2}$-octalin (9)[g]	74[f]

[a] 2,2′-Azobis(isobutyronitrile) (1%) used as catalyst. [b] Reference 6. [c] Benzene used as reaction solvent. [d] Reference 13. [e] By short-path distillation into a cooled flask. [f] By column chromatography on silica gel. [g] In a 4.2:1 ratio, respectively.



1

$$+ \; 4Bu_3SnH \rightarrow \underset{\mathbf{2}}{R_1R_2CH_2} + CH_3CH_3 + 2(Bu_3Sn)_2S \quad (1)$$

Treatment of the ethylene dithioketal of cyclohexanone with 4 equiv of the organotin hydride did indeed produce some cyclohexane and bis(tri-*n*-butyltin) sulfide. Ethane was presumably also formed, but no attempts were made to trap it. The reaction was less than half complete after 39 h (as monitored by the disappearance of the SCH_2CH_2S ^{1}H NMR signal of starting material). However, the reaction was completed in less than 2 h upon addition of 1% azobis(isobutyronitrile) (AIBN) in a subsequent experiment. On the other hand, the presence of hydroquinone or galvinoxyl inhibited the reduction. The above experiments suggest free-radical intermediates, the involvement of which is well documented in many organotin hydride reactions.[8]

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[1] For reviews, see: G. R. Pettit and E. E. van Tamelan, *Org. React.*, **12**, 356 (1962); H. Hauptman and W. F. Walter, *Chem. Rev.*, **62**, 347 (1962).

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[3] E. J. Corey, M. Ohno, R. B. Mitra, and P. A. Vatakenchery, *J. Am. Chem. Soc.*, **86**, 478 (1964).

[4] T. Mukaiyama, *Int. J. Sulfur Chem.*, **7**, 173 (1972).

[5] R. B. Boar, D. W. Hawkins, J. F. McGhie, and D. H. R. Barton, *J. Chem. Soc., Perkin Trans. 1*, 654 (1973).

[6] Selective desulfurization of 1,3-dithiolanes has been achieved by calcium in ammonia: B. C. Newman and E. L. Eliel, *J. Org. Chem.*, **35**, 3641 (1970).

[7] J. G. Noltes and G. J. M. Van der Kerk, *Tin Res. Inst., Publ.*, **73**, 115 (1958); M. Pang and E. I. Becker, *J. Org. Chem.*, **29**, 1948 (1964); J. G. Noltes and M. J. Janssen, *J. Organomet. Chem.*, **1**, 346 (1964); D. H. Lorenz and E. I. Becker, *J. Org. Chem.*, **28**, 1707 (1963); D. H. R. Barton and R. Subramanian, *J. Chem. Soc., Chem. Commun.*, 867 (1976); T. H. Haskell, P. W. K. Woo, and D. R. Watson, *J. Org. Chem.*, **42**, 1302 (1977).

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