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Original Scientific Paper

1,3-Hydrogen Migration in the Solvolysis of 2-(Δ^3 -Cyclopentenyl)ethyl *p*-Toluenesulfonate

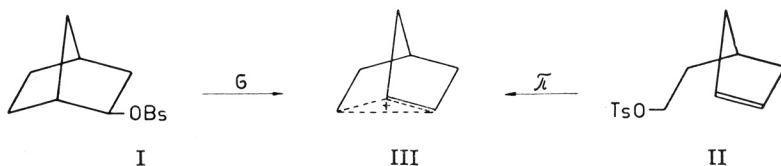
K. Humski, S. Borčić, and D. E. Sunko*

Institute »Ruder Bošković«, Zagreb, Croatia, Yugoslavia

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2-(Δ^3 -Cyclopentenyl)ethyl-1,1- d_2 tosylate was prepared and solvolyzed in 80 per cent aqueous acetic acid. Conversion of the solvolysis products to *exo*-2-norbornanol and integration of the peak areas of its n.m.r. spectrum indicates 10–15 per cent of 1,3-deuterium migration. The hypothesis is advanced that this migration must have taken place *after* the rate determining step of the solvolysis. *exo*-2-Norbornanol- d_2 resulting from this reaction was converted to the corresponding *p*-bromobenzenesulfonate and solvolyzed in acetic acid. Possible explanations for the observed secondary isotope effect (k_H/k_D 1.13) are given.

Significant rate enhancements and extensive skeletal rearrangements observed in solvolytic reactions of *exo*-2-norbornyl derivatives^{1,2}(I) led to the postulation of a reaction mechanism involving neighboring group participation *via* the formation of a »norbornonium« ion in the rate determining step.

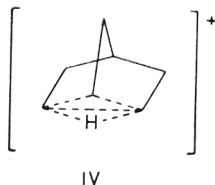


Bartlett³ and Lawton⁴ described a different path leading to the same bicyclo-(2,2,1)-heptyl system. The anchimerically assisted acetolysis of 2-(Δ^3 -cyclopentenyl)ethyl tosylate produces largely *exo*-2-norbornyl acetate. Therefore, it has been proposed that cation III can either be formed by the *sigma* route from I or by the *pi* route from II. Recent investigations of substituent rate effects are consistent with such a mechanism⁵.

The results obtained using C^{14} labeled norbornyl derivatives² indicated that the *sigma* route is accompanied by a 1,3-type hydride shift and that a

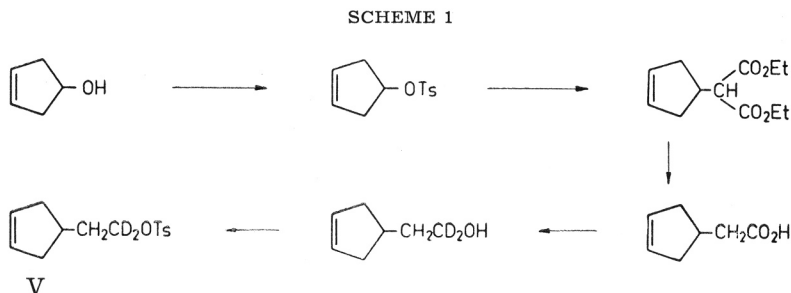
* Professor Vladimir Njegovan ad honorem.

complete description of the reaction mechanism should include a hydrogen bridged structure such as IV either as a transition state or as an intermediate.



The question whether this hydride migration occurs in the rate determining step or subsequent to it was left unanswered.

The purpose of the work described in this paper was to ascertain if the *pi* route is analogous to the *sigma* route in the occurrence of a 1,3-type hydride shift. Since the use of deuterium labeled starting material might provide an answer to this question 2-(Δ^3 -cyclopentenyl)ethyl-1,1- d_2 *p*-toluenesulfonate (V) was prepared by a procedure similar to the one outlined by Lawton⁴ (Scheme I) and subjected to solvolysis in 80 per cent aqueous acetic acid. The product mixture was converted to *exo*-2-norbornanol and the distribution of deuterium determined by n.m.r.



The deuterated *exo*-2-norbornanol thus obtained by the *pi* route was converted to the *p*-bromobenzenesulfonate and its acetolysis rate measured.

RESULTS

N.m.r. Spectrum of exo-2-Norbornanol

The spectrum (Fig. 1) consists, besides the hydroxyl proton resonance peak below 4.0 p.p.m., of a broad doublet centered at 3.60 p.p.m. (1, for numbering convention see Fig. 2), a broad single peak at 2.1 p.p.m. (2 and 3) and a complicated pattern between 1.9 and 0.8 p.p.m. (4—11).

The assignment of resonance peaks is based on analogies^{5a} and relative peak areas as obtained by integration (see Table I).

N.m.r. Spectrum of Deuterated exo-2-Norbornanol

The crude reaction product from the acetolysis of 2-(Δ^3 -cyclopentenyl)ethyl-1,1- d_2 tosylate was treated with lithium aluminum hydride and the resulting deuterated *exo*-2-norbornanol purified by sublimation. The proton

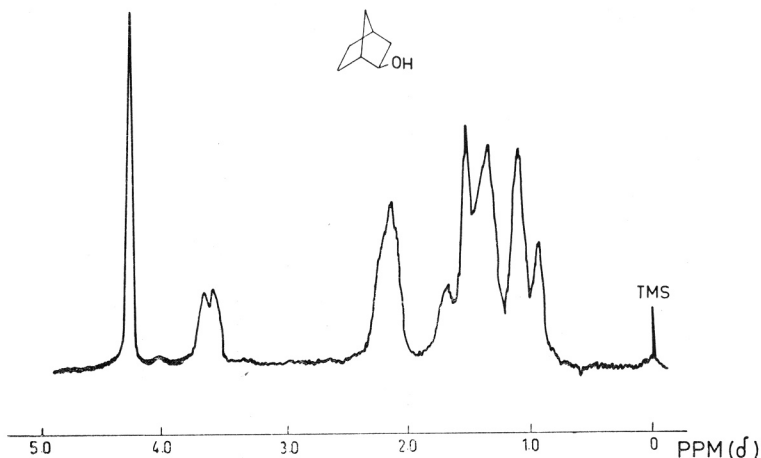


Fig. 1

magnetic resonance spectrum of this compound was recorded and the peak areas integrated.

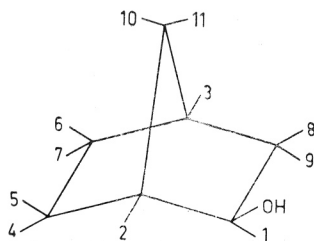


Fig. 2

Using the hydroxyl proton resonance as a reference it was calculated that the product contained 1.78 atoms of deuterium per molecule. An independent deuterium analysis by the falling drop method gave the value of 1.72 atoms D per molecule. From these data and comparing the integral values of the n.m.r. spectrum of pure *exo*-2-norbornanol with that of the

TABLE I

Deuterium Distribution in exo-2-Norbornanol Calculated from N.M.R. Spectra^a

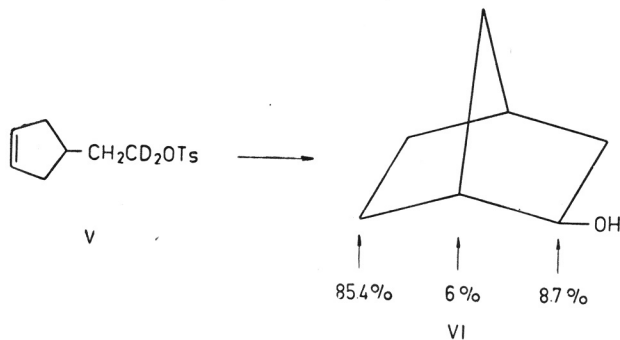
Position ^b	Atoms H in		Atoms D in
	norbornanol	norbornanol-d ₂	norbornanol-d ₂
1	0.974 ± 0.008	0.824 ± 0.008	0.150 ± 0.011
2, 3	2.070 ± 0.008	1.967 ± 0.008	0.103 ± 0.011
4—11	7.951 ± 0.011	6.482 ± 0.009	1.469 ± 0.014

^a uncertainties are standard errors.

^b for numbering convention see Fig. 2.

deuterated compound, the deuterium distribution could be calculated. The results are given in Table I and Scheme 2.

SCHEME 2



The results indicate that about 15 per cent of deuterium migrated to carbon atoms 1 and 2 of the resulting *exo*-2-norbornanol in the course of the solvolysis reaction.

Kinetic Studies

The deuterated *exo*-2-norbornanol was converted to the corresponding brosylate and its acetolysis rate measured. The results presented in Table II show a 13 per cent rate retardation of the solvolysis of the deuterated compound. The reaction was cleanly first order without any significant drift of the rate constant.

TABLE II
Acetolysis Rates and Isotope Effects at 44.6°

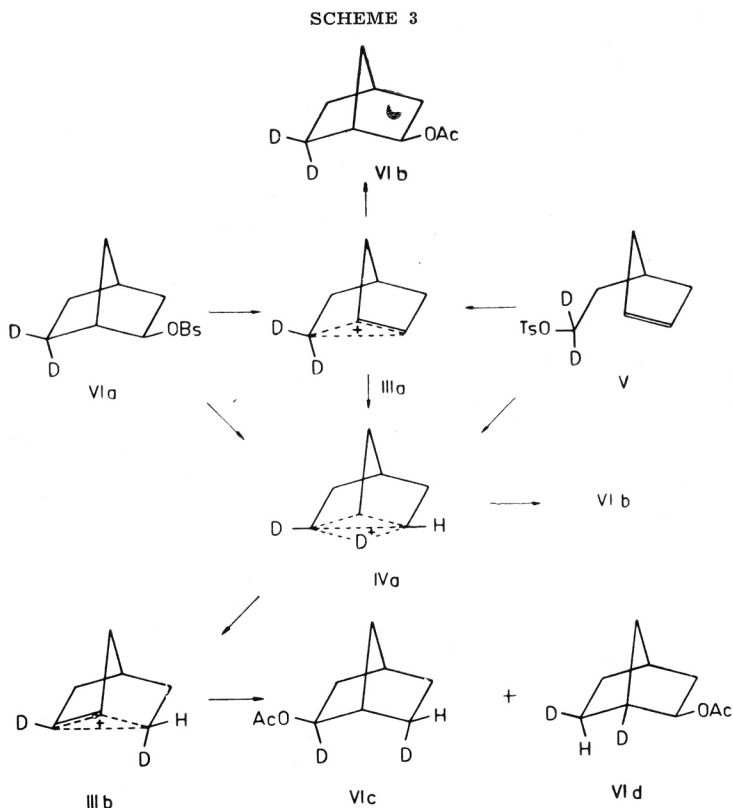
Compound	$k \cdot 10^4 \cdot \text{sec}^{-1}$	k_H/k_D
<i>exo</i> -2-norbornyl brosylate	9.55 ± 0.016	1.126 ± 0.004
<i>exo</i> -2-norbornyl- d_2 brosylate	8.46 ± 0.01	

DISCUSSION

The experimental results presented in this paper indicate that, similarly to *exo*-2-norbornyl derivatives, the solvolysis of 2-(Δ^3 -cyclopentenyl)ethyl *p*-toluenesulfonate leads to *exo*-2-norbornyl products with the same 1,3-type hydride shift. The possible mechanistic sequences, as derived from the work of Winstein¹, Roberts² and Bartlett^{3,5} are given in Scheme 3. Two different mechanisms can be proposed:

Mechanism 1

The solvolysis of either *exo*-2-norbornyl-6,6- d_2 brosylate (VIa, *sigma* route) or of 2-(Δ^3 -cyclopentenyl)ethyl-1,1- d_2 tosylate (V, *pi* route) give the same nor-



boronium ion IIIa in the rate determining step. Subsequently, IIIa either reacts with the solvent to give a product with the same structure (VIb) or rearranges to the bridged intermediate IVa. The reaction of IVa with solvent then yields products VIb, VIc and VI d. Ion IVa can also be considered as a transition state in the rearrangement of IIIa to IIIb with the same overall results.

Mechanism 2

The ionization of V and/or VIa leads directly to *both* intermediates IIIa and IVa from which all products are formed.

The main difference between these two mechanisms is that the first postulates only carbon-carbon participation in the rate determining step, while the second postulates carbon-carbon *and* carbon-hydrogen (deuterium) participation. The direct formation of cation IVa (mechanism 2) would, however, require that the leaving group and the hydrogen (deuterium) atom with both electrons depart the same carbon atom simultaneously. It is difficult to visualize the driving force for such a process so that the first mechanism seems to be more probable.

Therefore, it seems that the 1,3-hydride shift leading to cation IVa occurs in the solvolysis of V and/or VIa *after* the rate determining step.

Moreover, carbon-hydrogen participation should in this case result in a comparatively large kinetic isotope effect. Lee and Wong⁶ found in the

acetolysis of 2-(Δ^3 -cyclopentenyl)ethyl-1,1- d_2 *p*-nitrobenzenesulfonate an isotope effect (k_H/k_D) of 1.15 which is smaller than usually observed with α -deuterated compounds.*

The isotope effect observed in the solvolysis of the deuterated norbornyl brosylate is small if the bridged cation IVa is formed in the rate determining step. From the n.m.r. data it was calculated that about 75 per cent of the norbornanol molecules have deuterium atoms in the *endo*-6-position which is favorable to participation. Winstein and Takahashi⁸ observed a kinetic isotope effect larger than 2 in the solvolysis of 3-methyl-2-butyl-3- d *p*-toluenesulfonate which was explained by carbon-hydrogen participation.

If one compares the isotope effect reported in this paper (13%) with the one measured in the acetolysis of *exo*-2-norbornyl-*exo*-5,6- d_2 *p*-bromobenzenesulfonate⁹ (6 — 8%) it seems as if the replacement of a hydrogen atom by deuterium at the 6 position in the *exo*-brosylate has about the same retarding effect on acetolysis regardless whether the deuterium is *exo* (unfavorable to participation) or *endo* (favorable to participation).

However, here are several factors (e.g. internal rearrangement) which complicate a clear cut rationalization of this result. Work is in progress to answer this question in a less ambiguous way.

EXPERIMENTAL

All melting and boiling points are uncorrected. The purity of volatile compounds was checked by vapor phase chromatography. The infrared spectra were taken on a Perkin-Elmer Model 221 spectrophotometer and the 60 Mcps n.m.r. spectra on a Varian A-60 spectrometer. Carbon tetrachloride solutions were used and the chemical shifts are given as p.p.m. relative tetramethylsilane.

Δ^3 -Cyclopentenyl *p*-toluenesulfonate

To a stirred solution of Δ^3 -cyclopentenol (10.0 g., 0.12 mole) in 100 ml. of dry pyridine cooled to -15° *p*-toluenesulfonyl chloride (27 g., 0.14 moles) was added during 3 hours. The stirring was continued for one hour and the solution left to stand at 0° overnight. The solution was then poured into a mixture of ice (400 g.) and concentrated hydrochloric acid (300 ml.) and the product extracted with three 400 ml. portions of ether. The extract was washed with water and sodium hydrogencarbonate solution and dried with calcium sulfate. After removing the solvent *in vacuo* the oily residue was recrystallized from a mixture of petroleum ether and benzene. Yield, 15.7 g. (56%), m.p. $53 - 54^\circ$ (recorded¹⁰ m.p. $53.4 - 54.2^\circ$).

Δ^3 -Cyclopentenylmalonic Acid

The above tosylate (30.0 g., 0.126 moles), dissolved in toluene, was added to a stirred solution of diethyl sodiomalonate (from 20.3 g. of diethyl malonate and 2.9 g. of sodium) in dry toluene (350 ml.). The mixture was gently warmed and stirred overnight. After cooling to room temperature water (20 ml.) was added to the resulting slurry, and the organic layer separated. Toluene was removed under reduced pressure and the crude ester (34.0 g.) hydrolyzed by refluxing it for 7 hours with 100 ml. of a 20% aqueous potassium hydroxide solution. After careful neutralization with concentrated hydrochloric acid, the solution was extracted with three 50 ml. portions of ether. The removal of solvent from the dried solution left 14.0 g. of

* The authors suggest that the observed reduced isotope effect is due to the neighboring group participation which results in the formation of the norbornonium ion. We should like to point out that in our opinion, although this interpretation may be the correct one it is by no means unambiguous. Thus, the solvolysis of cyclopropylcarbinyl-1,1- d_2 benzenesulfonate⁷, a reaction for which the evidence for the formation of a nonclassical ion intermediate is compelling, displays a kinetic isotope effect rather larger than usual (1.30 for acetolysis and 1.40 for ethanolysis).

a yellow product. Recrystallization from a mixture of ether and petroleum ether afforded 9.7 g. (44%) of Δ^3 -cyclopentenylmalonic acid as slightly yellow crystals, m.p. 147.5—149.5° (dec.). Recorded⁴ m.p. 149—150°.

Δ^3 -Cyclopentenylacetic Acid

The decarboxylation was affected by heating Δ^3 -cyclopentenylmalonic acid in a round bottomed flask connected to a ice-cooled receiver by means of an oil bath to 160—170° in a vacuum of 100 mm. After foaming ceased, the pressure was decreased to 14 mm. and the product distilled into the receiver. From 9.0 g. of the malonic acid 6.2 g. (93%) of pure Δ^3 -cyclopentenylacetic acid was obtained. B.p. 135—136°/16 mm.

Ethyl Δ^3 -Cyclopentenylacetate

The ester was prepared by azeotropic esterification of the acid (6.0 g.) with a mixture of absolute ethanol (25 g.) and benzene (50 g.) in the presence of a catalytic amount of *p*-toluenesulfonic acid. Yield 6.0 g. (82%), b.p. 102—104°/35 mm.

2-(Δ^3 -Cyclopentenyl)ethanol-1,1- d_2

A solution of ethyl Δ^3 -cyclopentenyl acetate (6.0 g.) in ether was slowly added to a stirred slurry (1.1 g.) of lithium aluminum deuteride (Metal Hydrides, Inc.) in ether. The mixture was refluxed for 6 hours and then decomposed by carefully adding a slight excess of water. The ether solution was decanted and the precipitate washed with three 50 ml. portions of ether. The combined extracts were dried over magnesium sulfate and the solvent removed by distillation. The product was distilled *in vacuo*. Yield 3.97 g. (90%), b.p. 95—95.5°/24 mm.

2-(Δ^3 -Cyclopentenyl)ethyl-1,1- d_2 *p*-toluenesulfonate

The compound was prepared according to the method outlined by Tipson¹¹ and used without further purification in the next experiment.

exo-Norbornanol- d_2

The crude oily tosylate (from 3.8 g. of the alcohol) was added to a mixture of glacial acetic acid (150 g.) and water (40 ml.) and acetylated during 40 hours at 70°. To the cooled solution about 100 ml. of water was added and the acetic acid carefully neutralized with potassium hydroxide. The neutral solution was continuously extracted with ether for 24 hours, the extract dried with Drierite and the solvent removed by distillation over a Vigreux column. The residue was dissolved in ether (10 ml.) and reduced in the usual manner with lithium aluminum hydride (1.0 g. in 25 ml. of ether). The crude product was purified by sublimation at 70° and 14 mm. pressure. Thus, 2.4 g. (63%) of pure deuterated *exo*-norbornanol was obtained. M.p. 124—126°. Deuterium analysis (falling drop method) showed the presence of 1.72 atoms of deuterium per molecule. The *p*-bromobenzenesulfonate prepared in the usual manner was recrystallized from ether-petroleum ether. M.p. 52.5—53°. The purity, as determined from the neutralization equivalent of a hydrolyzed sample was 92.3%.

Measurements of Rate Constants

The rates of solvolysis of *exo*-norbornanol and *exo*-2-norbornanol- d_2 in 100 per cent acetic acid at 44.6° were followed by continuous titration of the liberated acid using an automatic recording pH-stat (Radiometer, Copenhagen, Type TTT-1). A 0.05 *N* solution of sodium acetate in acetic acid was used for the titrations and the rates were determined from the usual plot of $\log((a-x)/a)$ versus time. Experimental »infinity titres« as obtained after 10 half-lives were used and the reactions were usually followed from 20 to 80 per cent completion.

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1,3-Hidridni pomak kod solvolize 2-(Δ^3 -ciklopentenil)etil *p*-toluensulfonata

K. Humski, S. Borčić i D. E. Sunko

Pripremljen je 2-(Δ^3 -ciklopentenil)etil-1,1- d_2 tozilat te je solvoliziran u 80%_v-tnoj vodenoj octenoj kiselini. Produkti reakcije prevedeni su u 2-norbornanol te je pomoću n.m.r. spektara pokazano da kod solvolize dolazi do 10–15% 1,3-vodi-kovog pregrađivanja. Predložena je hipoteza da do ovakvog pomaka dolazi poslije sporoga stupnja reakcije.

Dobiveni norbornanol- d_2 preveden je u brozilat te je mjerena njegova brzina reakcije sa octenom kiselinom. Diskutiraju se mogući uzroci izmjenjenoga sekundarnog izotopskog efekta ($k_H/k_D = 1.13$).

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ZAGREB

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