Secondary Hydrogen Isotopes Effects. III. Acetolysis of *endo-* and *exo-*Norbornyl-5,6-d_2 *p*-Bromobenzenesulfonates*
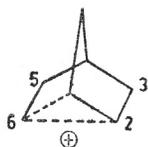
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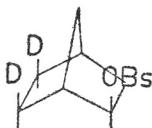*Institute »Ruđer Bošković«, Zagreb, Croatia, Yugoslavia*

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The synthesis of *endo-* and *exo-*norbornyl-5,6-d_2 *p*-bromobenzenesulfonates is described. The rate constants of the acetolysis were measured and an isotope effect was observed in the reaction of the *exo-*isomer. This result is in agreement with the mechanism proposed by Roberts[8] and indicates that the 1,3-hydride shift occurs in the rate determining step.
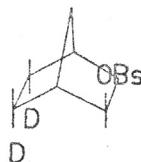
The solvolyses of *exo-*norbornyl derivatives proceed for the chlorides in 80 per cent ethanol about 70 times faster and for the brosylates in acetic acid 350 times faster than with the corresponding *endo* isomers[1,2,3]. Regarding the rate of the *endo* isomers as *normal, i. e.* comparable to the rate of cyclohexyl derivatives, it is apparent that the reactions of the *exo* compounds must be assisted. According to Winstein[4-7], the large relative rates of the *exo* isomer are explicable in terms of neighboring group interaction with the formation of a non-classical *norbornonium* ion I in the rate determining step.
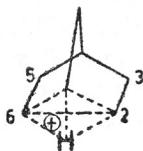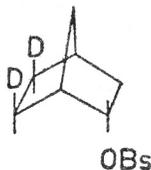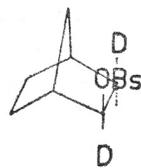
Roberts[8] investigated the skeletal rearrangement implied by structure I. The measurement of radioactivity associated with different carbon atoms in the solvolyses products of *exo*-norbornyl-2,3-C_2^{14} brosylate, demonstrated a more extensive rearrangement than the formation of I would indicate. The results have been accomodated by the assumption that 55 per cent of the acetolysis proceeds *via* I and 45 per cent *via* the *nortricyclonium* ion II.
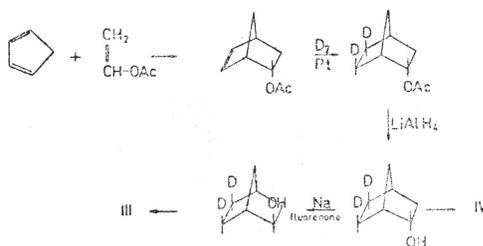
The degree of rearrangement is somewhat solvent dependent leading to the suggestion that the formation of II may be consecutive to the formation of I. A slightly different interpretation was given by Winstein[5] and Bartlett[9] involving also a hydrogen shift subsequent to the formation of I.

In the present work compounds III and IV were synthesized and their acetolysis rates measured. In II the carbon atoms 2 and 6 are equivalent and the latter can be regarded as an α-carbon atom with the migrating hydrogen as the leaving group. Therefore, if II is formed in the rate determining step, an isotope effect can be expected to occur in the acetolysis of the deuterium labeled brosylate III[10,11,12].

On the other hand, the non-assisted acetolysis of the corresponding *endo* isomer IV should not be retarded at all, because the formation of non-classical ions must be consecutive to the rate determining step[4,9]. Thus, the determination of isotope effects in the acetolyses of III and IV might be a feasible method for the investigation of the reaction mechanism.

SYNTHETIC PROCEDURES AND RESULTS

Compounds III and IV were prepared in the following way:

According to the *exo*-addition rule[13], the position of deuterium in III and IV is believed to be *cis-exo*. However, the stereochemistry of deuterium addition is not very important for the purpose of this work (see Discussion). It was assumed that deuterium was not scrambled during the epimerization since no rearrangement was observed in the analogous reaction with the C^{14} labeled carbinol[8].

The results are summarized in Table I and II. A small but significant isotope effect occured in the acetolysis of III, while no such an effect was observed with IV.

TABLE I

Acetolysis rates of exo-norbornyl and exo-norbornyl-5,6-d$_2$ brosylates at 25.0⁰

Run	Compound[a]	Purity[b] per cent	exo[b] per cent	Concentration[b] Moles/l.	$k \cdot 10^5$/sec[c]	k_H/k_D
1	H	89.0	75.1	0.0365	9.40 ± 0.35	1.093 ± 0.049
	D	92.0	77.0	0.0377	8.60 ± 0.22	
2	H	89.0	79.0	0.0365	8.97 ± 0.12	1.078 ± 0.018
	D	92.0	79.4	0.0374	8.32 ± 0.08	
3	H	93.2	77.7	0.0401	9.41 ± 0.19	1.063 ± 0.026
	D	94.8	79.2	0.0401	8.85 ± 0.12	
4	H	93.9	77.9	0.0389	9.28 ± 0.07	1.063 ± 0.018
	D	94.7	78.8	0.0389	8.73 ± 0.13	

TABLE II

Acetolysis rates of endo-norbornyl and endo-norbornyl-5,6-d$_2$ brosylates at 65.0⁰

Run	Compound[a]	Purity[b] per cent	Concentration[b] Moles/l.	$k \cdot 10^5$/sec[c]	k_H/k_D
1	H	93.6	0.0402	5.94 ± 0.07	1.026 ± 0.015
	D	93.6	0.0411	5.79 ± 0.05	
2	H	93.8	0.0391	5.62 ± 0.10	0.991 ± 0.027
	D	94.0	0.0387	5.67 ± 0.12	
3	H	93.2	0.0398	5.92 ± 0.11	1.017 ± 0.026
	D	94.4	0.0403	5.83 ± 0.10	

a H=unlabeled brosylate, D=deuterium labeled brosylate
b Purity was calculated from the *infinity* titers at 100⁰. The ratio of *infinity* titers at 25.0⁰ and 100⁰ gave the fraction of *exo* brosylate present in the starting material. Concentration is given for pure brosylates; in Table I for *exo* and in Table II for both *exo* and *endo*.
c Arithmetic mean (from 8—10 measurements) ± standard error.

DISCUSSION

A complicating factor in the acetolysis of III is the so called *internal return* reaction[5]. This phenomenon, also observed in other systems[14,15], is illustrated in Fig. 1.

$$\text{R-X} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{R}^+\text{X}^- \overset{k_2}{\longrightarrow} \text{R}^+ + \text{X}^- \qquad k_{-1} > k_2$$
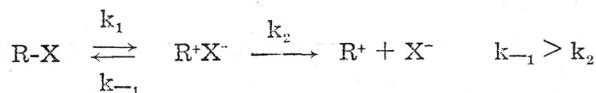
Fig. 1

By this process some rearrangement at the ion-pair stage causing deuterium scrambling in the starting material must be considered. A shift from C_6 bonding with C_1 to bonding C_2, possibly *via* I, would yield V, while a hydrogen migration from C_6 to C_2, possibly *via* II, would produce VI.

The presence of V in the starting material would affect the acetolysis rate in a manner similar to III. An isotope effect will occur in the acetolysis of V if the C—D bond is broken in the rate determining step, *i. e.* if a nortricyclonium ion is formed. However, this effect would only be a fraction of a primary isotope effect, because the energy surplus required for the fission of the C—D bond will be partially compensated by the formation of the new bond.

On the other hand, the appearance of VI might, in principle, obscure the issue of the present work as it would cause an isotope effect even if the 6,2-hydrogen migration does not occur in the rate determining step. Fortunately, from the available data[8] one can assume that the amount of rearranged brosylate must be very small* so that the rate retardation caused by VI would become negligeable.

Consequently, the isotope effect observed in the acetolysis of III indicates that the 1,3-hydrogen shift occurs in the rate determining step of the reaction, possibly *via* the nortricyclonium ion II.

<div align="center">EXPERIMENTAL</div>

All melting points are corrected. The deuterium content was determined by the falling drop method.

endo-Norborneol-5,6-d$_2$

Norbornylene acetate (9 g.), obtained by Diels-Alder condensation of cyclopentadiene and vinyl acetate[16], was deuteriated in anhydrous tetrahydrofurane (10 ml.) over Adams' platinum catalyst (0.1 g.) at room temperature and atmospheric pressure. The product was distilled at 78°/11 mm. (7.5 g., 82%), and hydrolized with lithium aluminum hydride in ether (70 ml. of a 0.8 M solution)[4]. The crude alcohol was purified by sublimation *in vacuo*. Yield, 4.9 g. (92%), m. p. 134°. This procedure should give a product which contains about 20 per cent of the *exo* isomer[4].

p - B r o m o b e n z e n e s u l f o n a t e was prepared in the usual manner[8,17] and recrystalized from ether — petroleum ether, m. p. 53—55°.

exo-Norborneol-5,6-d$_2$

The above *endo* carbinol (7.5 g.) was epimerized with sodium (50 mg.) and fluorenone (150 mg.) in boiling toluene (18 ml.) for 48 hours[8], yielding after sublimation 5.7 g. of the isomerization product, m. p. 110°, which was found to contain 1.72 atoms of deuterium per molecule.

p - B r o m o b e n z e n e s u l f o n a t e, m. p. 48—51°, was found to contain 21—25 per cent of the *endo* isomer by analysis of its acetolysis rate curve.

Kinetic measurements

The measurements of the rate constants were accomplished by the usual techniques[18]. A better precision in the determination of the isotope effects was obtained by maintaining the experimental conditions for both compounds as similar as possible (simultaneous acetolysis, same concentrations, titrations after same time intervals *etc.*).

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* The amount of rearranged brosylates V and VI can be estimated from the difference in the extent of rearrangement between *exo-* and *endo*-norbornylbrosylates (61%, resp. 56%). It is probable that only a part of this difference is due, if at all, to the rearrangement of the *exo* isomer at the ion-pair stage (see Ref. 8, page 4503—4). Only the two species, V and VI, can be formed by the internal return rearrangement.

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IZVOD

Sekundarni hidrogenski izotopski efekti. III. Acetoliza *endo* i *ekso*-norbornil-5,6-d_2 p-brombenzensulfonata

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Opisana je sinteza *endo* i *ekso*-norbornil-5,6-d_2 p-brombenzensulfonata. Mjerene su konstante brzine acetolize i nađen je izotopski efekt kod reakcije *ekso* izomera. Ovaj se rezultat slaže s mehanizmom predloženim po Robertsu i ukazuje da do hidridnoga pomaka dolazi u procesu, koji određuje brzinu reakcije.

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