Secondary Hydrogen Isotopes Effects. VI. Acetolysis Rate of Cyclopentyl-3,3,4,4-d4 Tosylate

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The synthesis of cyclopentyl-3,3,4,4-d_4 p-toluenesulfonate is described. The acetolysis rate constant of this compound at 50.0⁰ was determined. With the help of the IBM 7090 computer a kinetic isotope effect (k_H/k_D) of about 0.95 was found to occur. This small rate increase is interpreted as possibly due to the +I effect of deuterium.

In a previous paper of this series[1] it was shown that an inverse secondary hydrogen isotope effect occurs in the solvolysis of γ-deuterated cyclopropyi-methyl benzenesulfonates. The small rate increase in this case was interpreted in terms of a neighboring group participation with the formation of a non-classical carbonium ion in the rate determining step.

In order to verify the validity of this interpretation it was of interest to investigate the influence of deuterium substitution on the reaction rate in a similarly labeled cyclic system where, however, the neighboring group participation is excluded. Cyclopentyl-3,3,4,4-d_4 tosylate was considered as particularly suitable for this purpose because the solvolysis reaction of the unlabeled[2,3] and different deuterium labeled[4] analogons has been extensively studied by other authors.
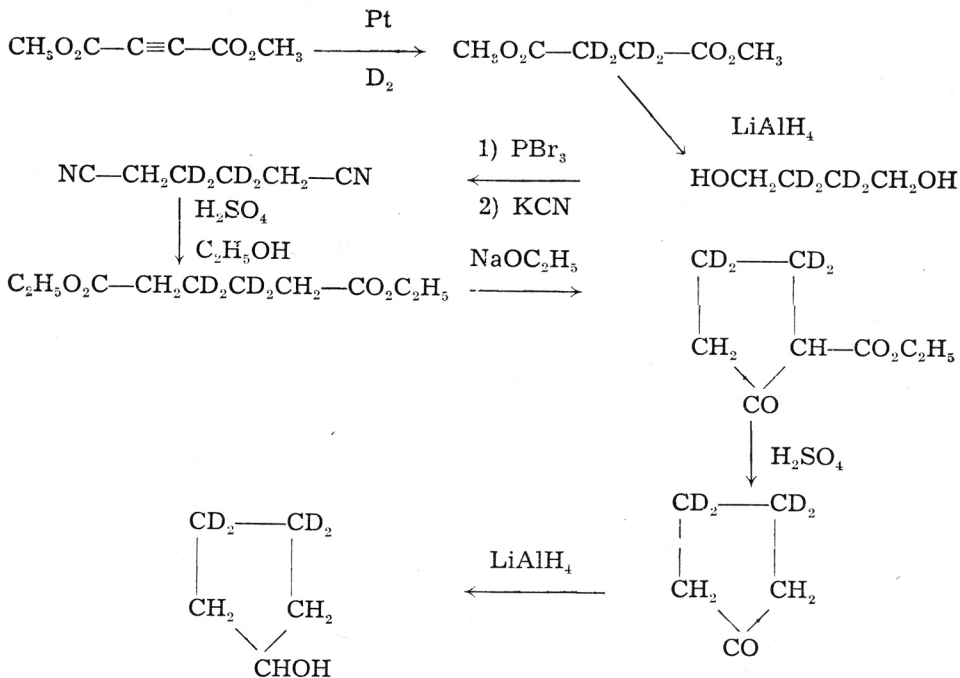
Thus, cyclopentanol-3,3,4,4-d_4 was synthesized according to the scheme on the following page.

The undeuterated and deuterated tosylates were prepared and subjected simultaneously to the reaction with anhydrous acetic acid at 50.0⁰. The reaction rates were measured titrimetrically in the usual manner taking aliquots from both solutions after similar time intervals.

The first order rate constants were calculated from the titers between 15 and 75 per cent reaction with the IBM 7090 computer using a non-linear least squares code[5] and assigning to each point either an equal weight or a weight depending of the size of the titer. The first order rate expression was written for the computer program in the exponential form:

$$\frac{x}{a_0} = 1 - e^{-k(t+b)}$$

where b is the intercept on the t-axis. This method of calculation has advantage over more classical methods[6] in avoiding the errors inherent in the

$$CH_3O_2C-C\equiv C-CO_2CH_3 \xrightarrow[D_2]{Pt} CH_3O_2C-CD_2CD_2-CO_2CH_3$$

$$NC-CH_2CD_2CD_2CH_2-CN \xleftarrow[2) KCN]{1) PBr_3} HOCH_2CD_2CD_2CH_2OH$$

with LiAlH₄ arrow from the $CH_3O_2C-CD_2CD_2-CO_2CH_3$ to $HOCH_2CD_2CD_2CH_2OH$

$$\downarrow H_2SO_4 / C_2H_5OH$$

$$C_2H_5O_2C-CH_2CD_2CD_2CH_2-CO_2C_2H_5 \xrightarrow{NaOC_2H_5}$$

Structure:
CD₂——CD₂
| |
CH₂   CH—CO₂C₂H₅
  \ /
   CO

$$\downarrow H_2SO_4$$

Structure:
CD₂——CD₂
| |
CH₂   CH₂
  \ /
   CO

$$\xleftarrow{LiAlH_4}$$

Structure:
CD₂——CD₂
| |
CH₂   CH₂
  \ /
  CHOH

linearisation of the first order rate expression and in the estimation of the *infinity titer*.

The results are given in Table I. The uncertainties of the rate constants correspond to standard errors (66 per cent confidence level) and are defined as follows:

$$\sigma = \sqrt{\frac{\Sigma r^2}{n-2} \, b_{11}}$$

Σr^2 = sum of squares of residuals of fit

n = number of data points

b_{11} = 1,1-element (k-element) of the matrix $(X^TX)^{-1}$, where

X = the matrix of the partial derivatives with respect to the parameters. There are no trends in the residuals of fits showing the absence of systematic errors.

In all three pairs of measurements the isotope effect (k_H/k_D) is smaller than 1 with a mean indicating a significant rate increase for the deuterated compound of about 5%.

For comparison, the isotope effects in solvolyses of other deuterated cyclopentyl tosylates are given in Table II. It can be seen that deuterium in γ-position has the smallest influence on reaction rate.

TABLE I

Acetolysis Rates of Cyclopentyl and Cyclopentyl-3,3,4,4-d₄ Tosylates at 50.0°.

Cyclopentyl tosylate	Purity[a] in per cent	$M/1 \cdot 10^{-2}$	Weight	$k \cdot 10^5 \cdot sec^{-1}$ [b]	k_H/k_D [b]	k_H/k_D [b,c]
H	97	2.58	constant	3.56 ± 0.14		
D	106	2.46	"	3.69 ± 0.06	0.965 ± 0.041	
H	103	3.00	"	3.55 ± 0.04		
D	103	2.87	"	3.84 ± 0.09	0.924 ± 0.024	
H	103	3.04	"	3.65 ± 0.09		
D	104	2.95	"	3.78 ± 0.05	0.966 ± 0.027	0.945 ± 0.017
H	97	2.58	variable	3.46 ± 0.23		
D	106	2.46	"	3.63 ± 0.08	0.953 ± 0.067	
H	103	3.00	"	3.56 ± 0.05		
D	103	2.87	"	3.94 ± 0.13	0.904 ± 0.033	
H	103	3.04	"	3.64 ± 0.13		
D	104	2.95	"	3.76 ± 0.08	0.968 ± 0.040	0.932 ± 0.024

a) As calculated from the infinity titers, b) Uncertainties correspond to 2/3 confidence level, c) Since there is no significant difference between the three series of measurements, they were combined and the mean calculated accordingly.

S. BORČIĆ

This *secondary γ-hydrogen isotope effect** could be caused by the larger $+I$ effect of deuterium as compared to hydrogen. The possibility of such a rate increase due to induction has been discussed several times[7-10].

The conclusion which can be derived from the results of this work is that the isotope effects observed in the solvolyses of both cyclopropylmethyl and cyclopentyl sulfonic esters are of a similar origin, rendering in the former case, the postulation of a non-classical carbonium ion superfluous.

TABLE II

Kinetic Isotope Effects in Acetolyses of Deuterated Cyclopentyl-Tosylates at 50.0⁰

Tosylate	k_H/k_D	$(k_H/k_D - 1) \cdot 100$ per deuterium
Cyclopentyl-1-d^a	1.15	$+ 15$
trans-Cyclopentyl-2-d^a	1.16	$+ 16$
cis-Cyclopentyl-2-d^a	1.22	$+ 22$
Cyclopentyl-2,2,5,5-$d_4{}^a$	2.06	$+ 20$
Cyclopentyl-3,3,4,4-d_4	0.95	$- 1.2$

a) See reference 4. All rates were measured in the presence of added sodium acetate.

EXPERIMENTAL

All melting points are corrected, boiling points uncorrected. The deuterium analysis was performed by the falling drop method.

Dimethyl succinate-2,2,3,3-d_4[11]

Dimethyl acetylenedicarboxylate (23.4 g.) was hydrogenated with deuterium gas over Adams catalyst in anhydrous ether. After filtration, removal of the solvent and distillation, 22.5 g. of the deuterated succinate, b. p. $80 — 82^0/19$ mm., $n_D^{22.5}$ 1.4171, were obtained.

Butane-2,2,3,3-d_4-1,4-diol

Deuterated dimethyl succinate (21.5 g.) was reduced with lithium aluminum hydride in the usual manner. Thus, 7.5 g. of the product, b. p. $140—145^0/40$ mm., n_D^{19} 1.4435, were obtained.

1,4-Dibromobutane-2,2,3,3-d_4

Deuterated butanediol (4.6 g.) was added at 0^0 under stirring and exclusion of moisture to 15 g. of phosphorous tribromide. The mixture was stirred at room temperature for 1 hr. and at 80^0 over night. Water was then added and the product extracted with ether. The extracts were washed with sodium hydrogencarbonate solution and dried with sodium sulfate. The solvent was then removed and the residue fractionated yielding 8.2 g. of the product, b.p. $99—102^0/35$ mm., n_D^{22} 1.5117.

Hexane-3,3,4,4-d_4-1,6-dinitrile

A solution of potassium cyanide (6.8 g.) and deuterated dibromobutane (8.2 g.) in 80 per cent aqueous ethanol was refluxed for 2 hrs. The solvent was then evaporated and the residue extracted with ethyl acetate. The extracts were dried

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* K. T. L e f f e k, J. A. L l e w e l l y n, and R. E. R o b e r t s o n, *J. Am. Chem. Soc.* **82** (1960) 6315, have observed a small inverse isotope effect in S_N2 solvolyses of γ-deuterated *n*-propyl derivatives. This effect has been atributed to steric causes.

with calcium sulfate, the solvent removed and the residue distilled yielding 3.8 g. of the product, b.p. 90—92⁰/0.15 mm., n_D^{21} 1.4370.

Diethyl adipate-3,3,4,4-d₄

Deuterated dinitrile (3.8 g.), anhydrous ethanol (25 ml.) and concentrated sulfuric acid (25 g.) were mixed and refluxed for 6 hrs. Water was then added to the reaction mixture and the product extracted with ether. The extracts were dried with calcium sulfate, the solvent removed and the residue distilled yielding 4.2 g. of the product, b.p. 125—128⁰/15 mm., n_D^{22} 1.4252.

2-Carbethoxy-cyclopentanone-3,3,4,4-d₄

Dieckman condensation[12] of the deuterated diethyl adipate (4.2 g.) gave 2.1 g. of the product, b.p. 104—105⁰/13 mm., n_D^{21} 1.4496.

Cyclopentanol-3,3,4,4-d₄

2-Carbethoxy-cyclopentanone-3,3,4,4-d_4 (2.1 g.) was refluxed with $2N$ sulfuric acid (10 ml.) for 4 hrs. The reaction product was steam distilled, extracted with ether, the extracts dried with sodium sulfate and the main amount of the solvent removed over a column. Lithium aluminum hydride reduction of the ketone, carried out in the usual manner, gave 0.85 g. of the carbinol, b.p. 135⁰/740 mm., n_D^{19} 1.4500. The 3,5-dinitrobenzoate, m.p. 114—115⁰, contained 3.70 atoms of deuterium per molecule.

p-Toluenesulfonates

were prepared in the usual manner. They were used for kinetic measurements without purification. The purities, as calculated from the *infinity titers,* are given in Table I.

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IZVOD

Sekundarni hidrogenski izotopski efekti. VI. Brzina acetolize ciklopentil-3,3,4,4-d_4 p-toluensulfonata

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Opisana je sinteza ciklopentil-3,3,4,4-d_4 p-toluensulfonata. Mjerena je brzina acetolize ovoga spoja kod 50.0⁰. Kinetski podaci analizirani su s pomoću IBM 7090 elektronske računske mašine. Pronađeno je da kod reakcije dolazi do kinetskog izotopskog efekta od ca. 0.95 (k_H/k_D). Kao mogući razlog ovom ubrzanju reakcije naveden je +I efekt deuterija.

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