

Isotope Effects in Proton-transfer Reactions

III.* Determination of the Equilibrium Constant for the Protium-deuterium Exchange between 2-Methyl-3-phenylpropionitrile and Methanol

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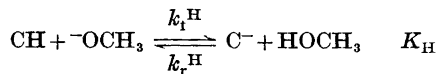
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A very weak kinetic isotope effect was observed in the methoxide-ion catalyzed racemization of 2-methyl-3-phenylpropionitrile in methanol and mixtures of methanol and dimethyl sulfoxide. This very weak isotope effect was interpreted in terms of a highly unsymmetric transition state, the proton being almost completely transferred to the methoxide ion.¹

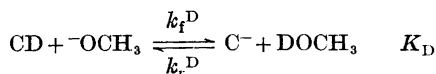
In a reaction where the transition state is very product-like the isotope effect can be very weak and the limiting value will be dependent on the equilibrium isotope effect.² For the reverse reaction the transition state will be very reactant-like and the isotopic rate ratio will hence differ only little from unity.² The isotope effect for the reverse reaction, in this case a very rapid abstraction of a proton from a methanol molecule by a carbanion, can be calculated if the equilibrium isotope effect and the isotope effect for the forward reaction are known.

An attempt has now been made to determine the equilibrium isotope effect for a comparison with the observed kinetic one and for the calculation of the kinetic isotope effect in the reverse reaction. The equilibrium isotope effect offers also a valuable opportunity of checking theoretical predictions from force-constant data against an experimental result.³

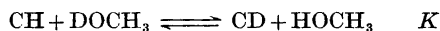
The reactions involved are:



* For Part II of this series, see Ref. 2.



where $K_{\text{H}} = k_f^{\text{H}}/k_r^{\text{H}}$ and $K_{\text{D}} = k_f^{\text{D}}/k_r^{\text{D}}$. Thus $K_{\text{H}}/K_{\text{D}} = (k_f^{\text{H}}/k_r^{\text{D}})/(k_r^{\text{H}}/k_f^{\text{D}})$ and $k_r^{\text{H}}/k_f^{\text{D}} = (k_f^{\text{H}}/k_r^{\text{D}})/(K_{\text{H}}/K_{\text{D}})$. It is obvious that $K_{\text{H}}/K_{\text{D}} = K$ where K is the equilibrium constant for the exchange equilibrium:



It should thus be possible to determine the ratio $K_{\text{H}}/K_{\text{D}}$ by equilibrating 2-methyl-3-phenylpropionitrile with a mixture of ordinary and heavy methanol using sodium methoxide as a catalyst.

The results obtained from the equilibrium measurements are gathered in Fig. 1.

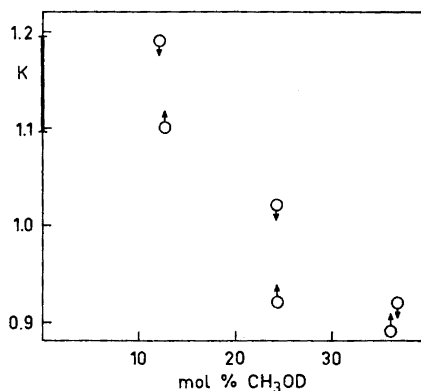


Fig. 1. Equilibrium constant for the protium-deuterium exchange between 2-methyl-3-phenylpropionitrile and methanol in different mixtures of MeOH and MeOD. Temperature 60°C. For further explanations, see the text.

In three runs the starting material was light nitrile and in three runs heavy nitrile. The equilibrium will then be approached from two sides as indicated by the arrows in the figure. Runs were made in different mixtures of methanol-*O-d* and methanol. It is obvious that there is an increase in the K with decreasing content of methanol-*O-d* in the medium, and a reasonable value for $K = K_{\text{H}}/K_{\text{D}}$ in ordinary methanol would lie around 1.2.

The specific-rate ratio for the forward reaction has been determined to be $k_H/k_D = 1.16 \pm 0.05$ (corrected for incomplete deuteration in the heavy nitrile sample)¹ and if a correction factor equal to the square root of the inverse ratio between the two isotopic reduced masses of the product molecules is used² the heavy line on the K axis represents the region in which the K_H/K_D ratio will lie if an "infinitely unsymmetric" transition state is assumed. This is in fairly good agreement with the estimated region in which the extrapolated K can lie.

The result from this investigation can also be compared with the K_H/K_D value determined from a theoretical calculation on the system.³ In an attempt to simulate the effect of hydrogen bonding a value of $K_H/K_D = 1.11$ was obtained for the equilibrium constant ratio at 60°C with a force field that was also able to reproduce the O-H stretching frequency in liquid methanol.³

Experimental. The preparation of the substrates used is described elsewhere.^{1,4}

Commercial methanol with a water content less than 0.05 % was dried by passage through a column packed with Linde type 4 A molecular sieves into a flask and distilled into a receiver equipped with a syringe needle which made it possible to transfer the methanol into a glass bottle closed with a rubber plug and a metal closure. All the procedure was performed under an atmosphere of nitrogen and in dried glassware. The glass bottles with purified methanol were stored in a desiccator.

Commercial MeOD with a deuterium content >99 % was used without further purification. The ampoules were broken in a dry-box under an atmosphere of purified nitrogen immediately before use.

The desired sodium methoxide solution was made by dissolving a proper amount of clean sodium metal in purified methanol under an atmosphere of purified nitrogen in a dry-box. The bottle with the sodium methoxide solution was closed with a rubber plug and a metal closure and removed from the dry-box. The concentration of the sodium methoxide solution was determined by titration against a known amount of potassium hydrogen phthalate dissolved in water. The sodium methoxide solution was transferred from the bottle to the burette by inserting a syringe needle which was connected to the burette and applying a slight pressure in the bottle. The titrations were made on a Radiometer Titri-graph.

All mixtures of methanol, methanol-*O-d*, sodium methoxide and the substrates were made in a dry-box under an atmosphere of purified nitrogen. The different components were carefully weighed out in order to ascertain a known isotopic composition of the reaction mixtures. A typical run contained: 2.5 ml of methanol, 10 ml of 0.33 M sodium methoxide solution, 7.5 ml of methanol-*O-d* and 125 mg of nitrile. Glass bottles of the same type as described before were used. After they were closed they were removed from the dry-box and placed in a Colora thermostat filled with polyethylene glycol at $60.0 \pm 0.2^\circ\text{C}$.

After 4–6 half-lives of the reaction¹ the bottles were removed from the thermostat one at a time and cooled in an ice-water mixture. The bottle was opened and the reaction was quenched in a mixture of 4 ml of 1 M HCl+5 ml of water+5 g of ice. The nitrile was extracted with three portions of 5 ml of ether+5 ml of pentane each. The combined extracts were washed twice with water and dried over MgSO_4 . The ether and the pentane were removed *in vacuo*. The residue was analysed by gas chromatography (GLC). A minor by-product (~10 %) was detected. The formation of that product was probably due to impurities extracted from the rubber plug by the hot methanol (as indicated by GLC on a sample from a run with only methanol in the bottle) and was assumed to have no decisive effect on the equilibrium. The mixture was chromatographed on alumina with benzene as eluent and the product was isolated free from the above by-product as shown by GLC. The benzene was removed *in vacuo* and the nitrile analysed for the deuterium content by mass spectrometry on an AEI MS 902 mass spectrometer.*

The fact that the P peak is not the base peak in the spectrum may be troublesome in a mass spectrometric determination of deuterium in a compound of this type.⁵ In the spectrum of 2-methyl-3-phenylpropionitrile the base peak is at $m/e = 91$ corresponding to the benzyl cation. The peak at $m/e = 145$ is still of such size that it is measurable. Another factor which can give rise to irreproducibility with compounds of this kind is that the $(P+1)/P$ ratio can vary with the ionisation potential.⁵ In order to investigate this the $(P+1)/P$ ratio was determined at 70 eV, 30 eV, 20 eV, and 16 eV. No obvious trend could be detected. The spectra were then run at 16 eV to avoid any contribution to the parent peak of fragment peaks from the heavy isotopic species.

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The light compound was analysed first and the $(P+1)/P$ ratio was determined. Two samples of known composition and the heavy compound were then run. The light reference compound was finally analysed again to verify a constant $(P+1)/P$ ratio. The samples to be determined were then run and the determination was ended by running the two samples of known composition. The composition of the known samples determined by mass spectrometry agreed within 1% with the calculated values. The reproducibility was better than 0.5%.

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Preparation and Crystal Structures of Various Forms of SbOF

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The heating of mixtures of SbF_3 and Sb_2O_3 in the mole ratio 1:1 in sealed gold or platinum capsules at temperatures between 150 and 450°C results in the formation of four different forms of SbOF. Rapid quenching in ice-cold water from temperatures 350–400°C gives a colourless glass. When this material, or a mixture of SbF_3 and Sb_2O_3 , is heated for a few hours at 350°C, a crystalline substance is obtained. Its X-ray powder pattern can be indexed in the cubic system, and we define this form as H-SbOF.

H-SbOF transforms at temperatures around 275°C into an orthorhombic form which we name M-SbOF. This form can also be prepared by the direct reaction of SbF_3 and Sb_2O_3 . During the hydrolysis of SbF_3 at 150°C, beautiful, rodshaped crystals were formed with a composition analyzed to be SbOF. Heat treatment of the glass, or of a mixture of Sb_2O_3 and SbF_3 , at temperatures around 150°C, resulted in the same phase, named L-SbOF.

The crystallographic constants for H-, L-, and M-SbOF are given in Table 1. Single crystal data have been collected for the L- and M-forms, and the crystal structure of the L-form has been refined to an *R*-factor of 6.5%.¹ The structure of M-SbOF has also been solved, and refinement is in progress.²

The configuration around antimony in L-SbOF is typical for an element having a stereochemically active lone pair, and is

Table 1. Crystallographic constants for the various forms of SbOF.

Space group	L-SbOF	M-SbOF	H-SbOF
	<i>Pnma</i> (No. 62)	<i>Pbca</i> (No. 61)	
<i>a</i> Å	8.873	11.618	11.72
<i>b</i> Å	4.099	5.616	
<i>c</i> Å	5.483	12.281	
<i>d</i> _{calc}	5.22	5.20	5.17