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KINETIC SOLVENT ISOTOPE EFFECT
IN AROMATIC NUCLEOPHILIC SUBSTITUTION

I.R.Bellobono , P.Beltrame , M.G.Cattania and M.Simonetta

Istituto di Chimica Fisica , Università di Milano
20133 Milano , Italy

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Being interested in the analogies of nucleophilic substitutions at aromatic and ethylenic centers , we thought it worthwhile to compare kinetic solvent isotope effect (KSIE) for hydroxylic solvents in such reactions. As we could not find literature data on KSIE of any simple aromatic nucleophilic substitution , experimental determinations were made.

Ethanol and ethanol-O-d were chosen as solvents , ethoxide ion and pyridine as nucleophiles , to avoid complications arising from reactants isotopically different in the two solvents , like $OH^-(OD^-)$ in $H_2O(D_2O)$. 2,4-Dinitrochlorobenzene (2,4-DNCB) was the substrate. For the ethoxide ion reaction , kinetic runs were carried at 25.0° ; analyses were spectrophotometric , in most cases at 300 mm. The pyridine reaction was studied by kinetic measurements at 90.0° ; chloride ion was determined by potentiometric titrations with silver nitrate. Reaction products were controlled in both solvents.

Several independent runs were performed in each case. Average results are shown in the Table , rate constants being indicated with their standard deviation. The KSIE , as given by $\underline{k}_{EtOD}/\underline{k}_{EtOH}$, amounts to 1.84 for ethoxide ion reactions at 25° , and to 1.30 for pyridine reactions at 90°.

TABLE

Rate constants for reactions of 2,4-DNCB (C_o= $4-9\times10^{-5}$ M) with ethoxide ion ($10^{-3}-10^{-2}$ M), and of 2,4-DNCB (C_o= $4-5\times10^{-2}$ M) with pyridine (C_o= $9-21\times10^{-2}$ M).

Solvent, isotopic purity	Temperature	N° of runs	Nucleophile	k ($l.mole^{-1}sec^{-1}$)
EtOH ,	25°	13	EtO^-	$(8.42 \pm 0.32)\times10^{-2}$
EtOD , 95%	25°	7	EtO^-	$(15.10 \pm 0.43)\times10^{-2}$ [a]
EtOH ,	90°	10	Pyridine	$(1.178 \pm 0.038)\times10^{-4}$
EtOD , 91%	90°	6	Pyridine	$(1.499 \pm 0.064)\times10^{-4}$ [b]

[a] By applying a linear correction, the value calculated for 100% EtOD is: $k_{EtOD}=15.45\times10^{-2}$

[b] Calculated value for 100% EtOD: $k_{EtOD}=1.530\times10^{-4}$

The solvent isotope effect on reaction equilibrium constants has been associated with changes in zero-point energy due to changes in hydrogen bonding from initial to final states; the Bigeleisen equation,[1] in a simplified form,[2] has been applied to estimate the isotope effects, including solvent isotope effect, on acid-base equilibrium constants.[3] The same treatment has been applied to KSIE[4] by using approximate models of transition states, and the formula (I):

$$\Sigma\nu_H - \Sigma\nu_H' = 12.53\ T \log(k_{SH}/k_{SD}) \qquad (I)$$

where $\Sigma\nu_H$ and $\Sigma\nu_H'$ are the sum of hydrogen stretching frequencies (cm^{-1}) in the initial and transition states, respectively, and T is the temperature (°K); k_{SH} and k_{SD} are the rate constants in the H-solvent and the D-solvent, respectively. Librational and bending frequencies were neglected. Simple rules were given to determine how many hydrogen bonds should be considered, in particular for the case of water.[4]

This treatment has been applied to the evaluation of KSIE in the cases of the Table. It was assumed that each ethanol molecule in the pure solvent accepts one hydrogen and donates one hydrogen,[5] while pyridine and ethoxide ion in solution accept one and three hydrogens , respectively , from the solvent. The following approximate values of the stretching frequencies were used : O...H for liquid ethanol , 3350 cm^{-1} ;[6] EtO^{-}...H for hydrogens of ethanol donated to ethoxide ion , 3000 cm^{-1} (taking the value given for hydroxide ion in water[3]) ; N...H for hydrogens of ethanol donated to pyridine , 3175 cm^{-1} (as for p-aminophenol ;[7] similar values were found also in oximes[7]). Two extreme models were chosen for each transition state , one having the nucleophile electron pair still on the reactant , and a purely electrostatic partial bond , the other with a fully covalent partial bond and a complete transfer of charge from the nucleophile to the substrate.[4] Leaving group was assumed covalently bonded in both models of transition state. Because of delocalization of charge , nitro-groups were considered to be hydrogen-bond acceptors approximately as good in the initial as in the transition states , and were therefore neglected.

For the ethoxide ion reaction , with the "electrostatic" model of transition state , it is : $\Sigma\nu_H - \Sigma\nu'_H = 3 \times 3000 - 2 \times 3000 - 3350 = -350$ cm^{-1} , where the 3350 figure is subtracted because the ethoxide ion accepts one hydrogen less in the transition state than in the initial state , and that hydrogen must be accepted by a solvent molecule.[3] For the "covalent" model of transition state one obtains : $\Sigma\nu_H - \Sigma\nu'_H = 3 \times 3000 - 3 \times 3350 = -1050$ cm^{-1}, where the same frequency value was used for O...H bonds between ethanol molecules and from ethanol to neutral oxygen in transition state.

Both models of transition state give the same result in the case of the pyridine reaction : $\Sigma\nu_H - \Sigma\nu'_H = 3175 - 3350 = -175$ cm^{-1}.

Using eq.(I) , the following KSIEs were calculated :

Nucleophile	Temperature	k_{EtOD}/k_{EtOH}
EtO^{-}	25°	1.24 ("electrostatic") 1.91 ("covalent")
Pyridine	90°	1.09

In the case of ethoxide ion , the observed solvent isotope effect is intermediate between the two calculated values , and close to the larger one. For the pyridine reaction , both calculation and experiment indicate a smaller effect than in the ethoxide case , although in the same direction. The agreement is as good as can be expected from such an oversimplified model.

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