# Racemization of Hindered Biphenyls in H_2O and D_2O

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The solvent isotope effect on the racemization of (+)-2,2′-diiodo-4,4′-dicarboxybiphenyl dianion and (−)-6-nitro-2,2′-dicarboxybiphenyl dianion was found to be about 0 and 8 %, respectively, the heavy solvent giving the slower reaction. The effect is discussed in terms of the difference between the fractionation factors of the carboxylate groups in the reactant molecule and those in the activated complex.

According to the generally accepted theory [1,2] it is possible to interpret the solvent isotope effect in terms of combined contributions from the so-called transfer effect and from what is known as the exchange effect. The former effect may be expressed in terms of a difference in activity coefficients between the isotopic solvents, and the cause of the latter is the fractionation of the isotopic solvent molecules or atoms between solvating and bulk positions. The distinction between these two effects is, however, not really necessary, [3,4] but it has also been claimed that the transfer effect makes a significant contribution to the solvent isotope effect. [5]

I   II
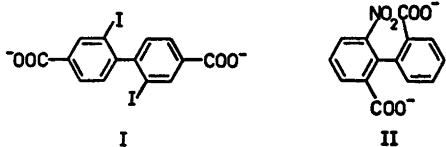
In our search for a model reaction to use in our studies of solvent isotope effects and solvation phenomena in general we have chosen the inversion of optically active biphenyl derivatives which is a simple unimolecular reaction. The rate of the reaction can also be accurately determined by polarimetry.

We now wish to report an investigation of the racemization of (+)-2,2′-diiodo-4,4′-dicarboxybiphenyl dianion (I) and (−)-6-nitro-2,2′-dicarboxybiphenyl dianion (II) in H_2O and D_2O.

As the present reaction involves no catalysing base the only possible fractionation factors are those of the substrate itself in the initial and the transition state. The carboxylate groups present in the two compounds I and II could at least in principle give rise to fractionation although this should be small judging from the results of solvent isotope effect studies on acetate catalysed proton-transfer reactions. [6–8] Anyhow, with one of the substrates, I, possible fractionation factors in the transition state should not deviate measurably from the corresponding ones in the initial state because no charged groups are situated at the centre of reaction. Implicit in this conclusion is the assumption that a possible fractionation due to the $C-I$ bond may be neglected due to the rather weak polarity of this bond. Exchange effects should thus be absent for I. The result (Table 1) shows that there cannot be any significant contribution from a transfer effect either provided that the above conclusion is correct, as $k_{obs}(H_2O)/k_{obs}(D_2O)$ probably equals unity within the limits of the experimental accuracy. The rate enhancement in the last two runs in Table 1 is due to a salt effect. [9]

The other compound used (II) has charged groups at the centre of reaction, but even for this compound the solvent isotope effect is rather weak, $k_{obs}(H_2O)/k_{obs}(D_2O) = 1.08$ (Table 2). The situation is, however, somewhat more complicated in this case due to the possible formation of a chelate between the biphenyl dianion and the cation in the solution. [10] The

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Table 1. Racemization of (+)-2,2'-diiodo-4,4'-dicarboxybiphenyl dianion (I) in H_2O and D_2O at 25.1 ± 0.1 °C.

Solvent	$k_{obs}/10^{-4}$ s^{-1} [a]	$k_{obs}(H_2O)/$ $k_{obs}(D_2O)$
H_2O	0.920 ± 0.006 [b]	
D_2O	0.911 ± 0.009 [b]	1.010 ± 0.017
H_2O	1.024 ± 0.005 [c]	
D_2O	0.997 ± 0.008 [c]	1.027 ± 0.012

[a] Each value is the mean value of two determinations. Errors are maximum deviations from the mean values. [b] Solution was 0.04 M in the sodium salt of compound I. [c] Solution was 0.05 M in the sodium salt of compound I.

dependence of the rate constant on the chelate formation has been investigated [10] and may be expressed by eqn. (1)

$$k_{obs}/2 = k/(1 + K[M^+]) \quad (1)$$

where k_{obs} is the observed rate constant, k is the rate constant for inversion, K is the equilibrium constant for the chelate complex formation and $[M^+]$ is the concentration of Na^+. The underlying assumption is that inversion takes place only with the non-chelated dianion and not with the complex. This leads to an expres-

Table 2. Racemization of (−)-6-nitro-2,2'-dicarboxybiphenyl dianion (II) in H_2O and D_2O at 59.4 ± 0.1 °C.

Solvent	$k_{obs}/10^{-4}$ s^{-1}	$k_{obs}(H_2O)/$ $k_{obs}(D_2O)$
H_2O	0.663 ± 0.007 [a]	
D_2O	0.615 ± 0.014 [a]	1.078 ± 0.037
H_2O	0.649 ± 0.003 [b]	
D_2O	0.604 ± 0.001 [b]	1.075 ± 0.009

[a] Mean value of four determinations. Error is the maximum deviation from the mean value. Solution was 0.04 M in the sodium salt of compound II. [b] Mean value of two determinations. Error is the maximum deviation from the mean value. Solution was 0.04 M in the sodium salt of compound II and 0.08 M in sodium chloride.

sion for the observed isotope effect on the racemization [eqn. (2)].

$$k_{obs}(H_2O)/k_{obs}(D_2O) = k(H_2O)/k(D_2O)$$
$$\{(1 + K(D_2O)[M^+])/(1 + K(H_2O)[M^+])\} \quad (2)$$

that includes two factors, both of which may contribute to the observed effect provided that the equilibrium constant for complex formation is dependent on the isotopic composition of the solvent. If this is the case, the observed isotope effect should vary with $[M^+]$, and the observed values of $k_{obs}(H_2O)/k_{obs}(D_2O)$ at $[M^+] = 0.08$ M and $[M^+] = 0.16$ M would differ significantly. As can be seen in Table 2, however, they are the same within the experimental accuracy. It is therefore improbable that $K(D_2O)$ and $K(H_2O)$ should differ appreciably and thus we attribute the observed effect of 8 % to the rate of inversion.

The fractionation factor theory [1] adapted to the present case, neglecting any free-energy transfer terms, leads to eqn. (3).

$$k_{obs}(H_2O)/k_{obs}(D_2O) = \prod_{i=1}^{m} \phi_{Ri} / \prod_{j=1}^{p} \phi_{Tj} \quad (3)$$

for the limiting rate constant ratio. The symbols ϕ_{Ri} and ϕ_{Tj} are fractionation factors for the initial state and the transition state, respectively, and m and p are the number of solvating hydrogen atoms in the initial state and the transition state, respectively.

Unfortunately it is not possible to assign definite values to the fractionation factors for either the reactant or the transition state, but it can be of some interest to speculate on the magnitude of them. By assuming for simplicity that all ϕ_{Ri} are equal and equal to ϕ_R and all ϕ_{Tj} are equal and equal to ϕ_T eqn. (4) is obtained:

$$k_{obs}(H_2O)/k_{obs}(D_2O) = \phi_R{}^m/\phi_T{}^p \quad (4)$$

In terms of the magnitude of the observed rate ratio that gives eqn. (5).

$$\phi_R{}^m/\phi_T{}^p = 1.08 \quad (5)$$

and hence eqn. (6).

$$\phi_T = \phi_R \left(\frac{\phi_R{}^{m-p}}{1.08} \right)^{1/p} \quad (6)$$

Provided that $m - p \geqslant 0$ and $\phi_R < 1$ this gives eqn. (7).

$$\phi_T/\phi_R < 1 \tag{7}$$

It can also be seen that for large values of p, $\phi_T/\phi_R \rightarrow 1$. Qualitatively this can be explained in the following way. It is likely that in the reactant molecule the nitro group and also the carboxylate groups will be coplanar with the rings to which they are attached. This allows charge delocalization from the carboxylate groups into the phenyl rings. In the transition state this is no longer possible due to steric interactions and the result would be less delocalized charges at the carboxylate groups compared to the reactant molecule. The net effect would be a stronger interaction with the solvent in the transition state and hence the fractionation factors in the transition state should be lower than those in the reactant molecule. How much lower depends, as has been shown above, upon the actual values of m and p and the following will clarify the point too.

The value of ϕ_R can be estimated in the following way. Using the derived value of the degenerate activity coefficient for transfer of the acetate ion from H₂O to D₂O, $\gamma_{OAc} = 1.15$,[11] and assuming that each acetate group is solvated by four water molecules an approximate value of the fractionation factor for the water molecules solvating the acetate ion is given by [3,4] eqn. (8).

$$\phi_{OAc} = (1/1.15)^{1/4} = 0.97 \tag{8}$$

Provided that $\phi_R = \phi_{OAc} = 0.97$ and that each carboxylate group is solvated by four water molecules we have eight sites, in the reactant molecule, each with a fractionation factor of 0.97. For the transition state we assume that the carboxylate group which has to pass the nitro group can be solvated only by two water molecules. In the transition state we thus have six sites each with a fractionation factor of ϕ_T. Using the above formula for ϕ_T we obtain eqn. (9), i.e. a very moderate decrease in the

$$\phi_T = 0.97 \left(\frac{0.97^2}{1.08}\right)^{1/6} = 0.95 \tag{9}$$

fractionation factors of the transition state would account for the observed effect of 8 % on the reaction rate.

EXPERIMENTAL

The substances I and II were kindly given to us by Dr. Peder Berntsson. The fact that the substances had been stored for about five years gave rise to the question of whether the materials were free of contamination or not. The excellent first-order kinetic behaviour of II did, in spite of a very small quantity of insoluble material on some occasions, suggest that this substance was satisfactory. The substance I, however, was not optically pure since a minor optical activity remained after the completion of reaction. Treatment of the data with the computer program PROGAEXP, assuming a rate equation: $y = Ae^{kt} + A_0$, gave rate constants with high accuracy indicating that the unidentified impurity showed constant optical rotation throughout the reaction and so did not interfere with the kinetics.

The sodium hydroxide solutions were prepared as follows. All but one of the light-water base solutions were prepared by diluting aqueous NaOH from commercially available ampoules to 0.1 M and 0.08 M in volumetric flasks. The additional base solution was prepared from solid sodium hydroxide dissolved in distilled water in a volumetric flask. The heavy-water base solutions were prepared in two ways, either from solid sodium hydroxide or through dilution with D₂O of very concentrated, 4.92 M, light-water bases produced from ampoules, giving H₂O/D₂O mixtures of atom fraction D greater than 0.98. The deuterium oxide used had an atom fraction of D not less than 0.997. For control, some of the base solutions were titrated with a Radiometer TTT 1C automatic titration assembly.

The reaction solutions were prepared by dissolving the proper quantity of solid biphenyl as dicarboxylic acid in 2 ml of a solution containing two equivalents of base. In some runs (Table 2) NaCl was added to change the concentration of Na⁺. The solutions were filtered into the polarimeter cell.

All kinetic runs were performed on a Zeiss Old 5 digital polarimeter using the wavelengths 436 and 546 nm for II and I, respectively, the accuracy in each reading was ± 0.001°. The racemization took place in a 10 cm thermostated polarimeter cell, the temperature of which was controlled by a Hetotherm Ultrathermostat 02 Pt 623 UO together with a Hetofrig cooling bath, type CB6. A Compucorp 425 G Scientist calculator, interfaced on line with the polarimeter, collected polarimeter data and times, and with II it was used to calculate rate constants using a least-squares program.

REFERENCES

1. Kresge, A. J. *Pure Appl. Chem.* 8 (1964) 243.
2. Gold, V. *Adv. Phys. Org. Chem.* 7 (1969) 259.
3. Gold, V. *Trans. Faraday Soc.* 64 (1968) 2143.
4. Albery, J. In Caldin, E. F. and Gold, V. Eds., *Proton-Transfer Reactions*, Chapman and Hall, London 1975, Chapter 9.
5. Halevi, E. A. *Israel J. Chem.* 9 (1971) 385, and references given there.
6. Reitz, O. and Kopp, J. *Z. Phys. Chem. (Leipzig) A 184* (1939) 429.
7. Long, F. A. and Watson, D. *J. Chem. Soc.* (1958) 2019.
8. Hibbert, F. and Long, F. A. *J. Am. Chem. Soc. 93* (1971) 2836.
9. Berntsson, P., Wanger, M. and Carter, R. E. *Acta Chem. Scand. 21* (1967) 879.
10. Berntsson, P. and Carter, R. E. *Acta Chem. Scand. 22* (1968) 2141.
11. Dahlberg, D. B. and Long, F. A. *J. Am. Chem. Soc. 95* (1973) 3825.