is estimated from the straight line[14] from *p*H 7.6 to 12 as $1.00 \pm 0.04 \times 10^6\ M^{-1}\ \text{sec.}^{-1}$ at $\mu = 0.10$ and *p*H 10.0. It decreases with increasing ionic strength as predicted by the Brönsted–Christiansen–Scatchard equation ($z_A z_B = -1$). The value of k_{H_2O} is estimated as $2 \pm 1 \times 10^{-9}\ M^{-1}\ \text{sec.}^{-1}$. The fact that the rate does not become completely independent of *p*H is ascribed to a small negative salt effect on the borohydride–water reaction. At a constant *p*H with 0.09 and 1.09 *M* sodium hydroxide solutions, where the water reaction predominates, the addition of sodium and potassium salts steadily decreases the rate. Lithium chloride gives a small acceleration. Variation of the buffer strengths at constant ionic strength permits assignment of $k_{H_2PO_4^-}$ as $1 \pm 4 \times 10^{-2}\ M^{-1}\ \text{sec.}^{-1}$, $k_{H_3BO_3}$ as $1 \pm 5 \times 10^{-4} M^{-1}\text{sec.}^{-1}$ and $k_{HCO_3^-}$ as $9 \pm 4 \times 10^{-5} M^{-1}\ \text{sec.}^{-1}$. Thus the Brönsted α is about 0.8. The fact that α is near unity and $k_{H_3O^+}$ is so large means that general acid catalysis is difficult to observe.[15]

The hydrolysis in heavy water gives HD Thus no exchange occurs between the hydride and the solvent, and an electronically unlikely BH_5 intermediate of high symmetry is excluded. A mechanism consistent with the data is

$$BA_4^- + HA_i \rightleftarrows \begin{bmatrix} H^+BH_4^- \\ A_i^- \end{bmatrix}^* \longrightarrow H_2 + (BH_3)_{aq.} + A_i^-$$

$$(BH_3)_{aq.} \xrightarrow{\text{fast}} \text{products}$$

Diborane can be prepared from borohydrides in concentrated sulfuric acid.[16] The borane also can be trapped as the trimethylamine adduct when lithium borohydride is treated with trimethylamine hydrochloride in anhydrous ether.[17]

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[14] The best line through the points gives an order of 0.92 ± 0.03 in hydronium ion.

[15] Thus at *p*H 9.24 in a borate buffer solution (0.05 *M* borax), 99% of the reaction is with H_3O^+ and about 1% with the H_3BO_3 present.

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AN INVERSE HYDROGEN ISOTOPE EFFECT IN THE HYDROLYSIS OF SODIUM BOROHYDRIDE[1,2]

Sir:

Kinetic study of the hydrolysis of sodium borohydride in aqueous buffers[2] suggested that cleavage of a B–H bond is the first step and the rate-determining step. In a further study, $NaBD_4$ of 99% purity was prepared from B_2D_6 and $NaB(OCH_3)_4$ on a vacuum line with recrystallization from diglyme.[3] Its rate of decomposition was measured as before[2] in borate buffers under nitrogen. The results are reported in Table I.

TABLE I

HYDROLYSIS IN AQUEOUS BORATE BUFFERS AT 25.00 ± 0.01°

*p*H ±0.02	μ, *M*	$NaBH_4$ 10^4k_1, sec.$^{-1a}$	$NaBD_4$ 10^4k_1, sec.$^{-1}$	k_H/k_D
9.70	0.10	1.74 ± 0.02	2.62 ± 0.02	0.67 ± 0.02
9.96	.05	1.02 ± .02	1.33 ± .03	.77 ± .03
10.20	.10	0.587 ± .008	0.835 ± .007	.70 ± .03
10.20[b]	.10	0.59 ± .01	0.84 ± .01	.70 ± .03

[a] Rate = $k_1[BH_4^-]$ where $k_1 = k_2[H_3O^+]$. Limits given are standard deviations. Rate constants during a given run were constant to 85–90% reaction. [b] Experiments where infinite solutions were used again and isotopes crossed.

The purity of each material was tested kinetically for trace metal contamination.[4] The remaining solution after a borodeuteride run was used as the initial solution for a borohydride run. The other combination was also tried. The *p*H remained constant and the inverse isotope effect was identical; thus the borodeuteride is free from catalytic impurities.

The tritium isotope effects for alcoholyses of lithium borohydride and lithium aluminum hydride were reported by Kaplan and Wilzbach as $k_H/k_T = 0.8\text{–}1.2$.[5] Apparently experimental problems prevented their estimating the direction of the effect.

We ascribe the inverse isotope effect to a secondary isotope effect of the *other* hydrogen or deuterium atoms not undergoing the protonolysis reaction in the rate-determining step. There is a greater reluctance of HB^- bonds to change to HB (uncharged) in aquated borane than that of DB^- bonds to change to DB. The effect is analogous to the greater basicity and nucleophilicity of DO^- compared to HO^-.[6] Thus borodeuteride should be a stronger base than borohydride. The non-reacting hydrogen or deuterium atoms have more zero-point vibrational energy in the transition state than in the ground state.

As the tetrahedral borohydride forms a transition state which resembles one-half of the diborane molecule,[2] the normal B–H stretching vibrations ($A_1(\nu_1)$) at 2264 cm.$^{-1}$ become more like the B–H stretching frequencies of diborane which occur at 2524 cm.$^{-1}$ ($A_g(\nu_1)$).[7,8,9] Thus in loose terminology, the non-reacting B–H bonds stiffen in the transition state.

Some data on the isotope effect of boranes would seem to support this conclusion. The isotope effect of the hydrolysis of trimethylamine borane in 1.40 *M* hydrochloric acid at 25° is $k_H/k_D = 1.05 \pm 0.02$. Several reactions with diborane have isotope effects very close to unity. Apparently, it is the placing of the fourth deuterium atom on the boron which leads to an inverse isotope effect. The order of magnitude (0.7) is very comparable to the effect found in the hydroxide ions (0.6–0.7).

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[1] Supported in part by a research grant and a fellowship to C. K. from the Research Corporation. Mr. W. J. Wallace aided this study by material assistance in the synthesis of the deuterium compound.

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The inverse isotope cannot be explained entirely in terms of the difference of steric factors (*i.e.*, the fact that an X–D bond is about 0.01 Å. shorter than the X–H bond due to the anharmonicity of the Morse curve potential). Nor does the effect find its explanation in any possible electronic differences of hydrogen or deuterium.[2,10]

Robertson has reported inverse secondary isotope effectsi n the solvolyses of propyl and propyl-γ-d_3 compounds (k_H/k_D of 0.92–0.95)[11] and of methyl and methyl-d_3 compounds (bromide 9.90, iodide 0.87, tosylate 0.96).[12] Elliot and Mason found 0.86 for the pyridine-catalyzed reactions of aniline and aniline-N,N-d_2 with benzoyl chloride in benzene solutions at 25°.[13]

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KINETIC STUDIES OF ADP REACTIONS WITH THE TEMPERATURE JUMP METHOD

Sir:

A previous communication[1] described kinetic studies of the reactions of adenosine 5′-triphosphate (ATP) with Ca^{++}, Mg^{++} and a proton donor-acceptor system (phenol red). The purpose of this note is to present the results of a similar study with adenosine 5′-diphosphate (ADP). The temperature jump method[2,3] was used to obtain the relaxation spectrum of three systems: ADP and proton donor-acceptors (chlor phenol red = CPR, and phenol red = PR); ADP, Mg^{++} and a proton donor-acceptor (CPR); and ADP, Ca^{++} and a proton donor-acceptor (CPR). The method of analysis of the spectrum of relaxation times obtained is similar to that described previously[1] so that only the results and significant differences will be presented here.

As with ATP, a short relaxation time (10–70 μsec.) was found identically for all three systems (under equivalent conditions), while in the case of the system containing Mg^{++} (with CPR) a longer relaxation time (100–250 μsec.) was also present. The short relaxation time could be identified with the mechanism

$$\begin{tikzcd}
\underset{\mathrm{III}}{\mathrm{HIn} + \mathrm{ADP}^{-3}} \arrow[rr, shift left, "k_{34}"] \arrow[dr, shift left, "k_{35}"] & & \underset{\mathrm{IV}}{\mathrm{In}^{-2} + \mathrm{ADPH}^{-2}} \arrow[ll, shift left, "k_{43}"] \arrow[dl, shift left, "k_{45}"] \\
& \underset{\mathrm{V}}{\mathrm{In}^{-2} + \mathrm{H}^{+} + \mathrm{ADP}^{-3}} \arrow[ul, shift left, "k_{53}"] \arrow[ur, shift left, "k_{54}"] &
\end{tikzcd}$$

where In represents the pH indicator used as the proton donor-acceptor (either CPR or PR) and all other symbols have their obvious meaning. By studying the concentration dependence of the relaxation time, all rate constants except k_{45} and k_{54} could be obtained. The results obtained for both ADP and ATP are summarized in Table I.

TABLE I

The temperature was 13° (±2°) for experimental reasons,[1] and the ionic strength 0.1 (KNO$_3$). The experimental error is about ±30%, from the evaluation of the relatively complicated form of the relaxation times (which are measured with a precision of about ±10%). For both ATP and ADP k_{54} can be estimated to the order of magnitude of 10^{11} M^{-1} sec.$^{-1}$. The equilibration of this step always was complete within the time of measurement. The longer relaxation time found in the presence of Mg^{++} can be explained by the mechanism

$$\begin{tikzcd}
\mathrm{I}\quad \mathrm{MeADP}^{-} + \mathrm{HIn}^{-} \arrow[r, shift left, "k_{12}"] \arrow[d, shift right, "k_{13}"'] & \mathrm{MeADPH} + \mathrm{In}^{-1}\quad \mathrm{II} \arrow[l, shift left, "k_{21}"] \arrow[d, shift right, "k_{24}"'] \\
\underset{\mathrm{III}}{\mathrm{Me}^{+2} + \mathrm{ADP}^{-3} + \mathrm{HIn}^{-}} \arrow[r, shift left, "k_{34}"] \arrow[u, shift right, "k_{31}"'] & \underset{\mathrm{IV}}{\mathrm{Me}^{+2} + \mathrm{ADPH}^{-2} + \mathrm{In}^{-2}} \arrow[l, shift left, "k_{43}"] \arrow[u, shift right, "k_{42}"']
\end{tikzcd}$$

Reactants	k_{34} × 10^{-1} M^{-1} sec.$^{-1}$	k_{43} × 10^{-1} M^{-1} sec.$^{-1}$	k_{35} × 10^{-4} M^{-1} sec.$^{-1}$	k_{53} × 10^{-11} M^{-1} sec.$^{-1}$	k_{43}/k_{34}[a]
ADP + PR	3.4	7	0.06	3.0	21
ADP + CPR	20	1	1.9	2.3	0.53
ATP + PR	4.8	7	0.06	3.0	15
ATP + CPR	20	0.8	1.9	2.3	0.39

[a] Determined from the equilibrium constants of ADP, ATP^{-4} and the indicators (measured by pH and spectrophotometric titration).

In calculating the relaxation time, the presence of the indicator must be taken into account and the complete expression given previously must be used to evaluate the data. By varying the concentration and pH (5.7–6.1) and utilizing the equilibrium constants determined by Martell and Schwarzenbach[4] (which refer to the conditions of our experiments, *cf.* also ref. 5), k_{13}, k_{31}, k_{24} and k_{42} could be obtained. These results together with data obtained previously for ATP are summarized in Table II. The precision of the rate constants is about ± 35% for the ADP reactions.

Since only one relaxation time is observed when Ca^{++} is substituted for Mg^{++}, the relaxation time characteristic of the Ca^{++}–ADP reaction must be shorter than 5 μsec. and a lower bound can be obtained for k_{31} and k_{13} (see ref. 1 for details of this procedure). These minimum values (which do not differ greatly from the upper limits for these rate constants) also are presented in Table II.

TABLE II

The temperature was 26° (+2°) and the ionic strength 0.1 M (KNO$_3$).

Reactants	k_{13} × 10^{-3} sec.$^{-1}$	k_{31} × 10^{-7} sec.$^{-1}$	k_{24} × M^{-1} sec.$^{-1}$	k_{42} × 10^{-6} M^{-1} sec.$^{-1}$	k_{31}/k_{13}[4] M^{-1}	k_{42}/k_{24}[4] M^{-1}
Mg^{++} + ADP	2.5	0.3	3	1	$10^{3.1}$	$10^{1.0}$
Mg^{++} + ATP	1.2	1.2	3	3	$10^{4.0}$	$10^{2.0}$
Ca^{++} + ADP	>400	> 25	..	..	$10^{2.8}$	..
Ca^{++} + ATP	>250	>100	..	..	$10^{3.6}$	$10^{1.8}$

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