340. *Prototropy in Relation to the Exchange of Hydrogen Isotopes. Part II. A Comparison of the Velocities of Dissociation of a Proton and a Deuteron from a ψ-Acid.*

By CHRISTOPHER L. WILSON.

CONSIDERABLE interest attaches to comparisons of the rates of corresponding reactions involving the hydrogen isotopes, since the factors responsible for the differences of rate can usually be theoretically specified in at least a semi-quantitative manner. This paper deals with the relative rates of ionisation of an ordinary hydrogen acid and the corresponding deuteracid, *i.e.*, with the relative rates of transference of proton and deuteron respectively from the compounds HA and DA to a common solvent S :

$$\left.\begin{array}{l} \mathrm{HA} + \mathrm{S} \longrightarrow \overset{-}{\mathrm{A}} + \mathrm{H}\overset{+}{\mathrm{S}} \\ \mathrm{DA} + \mathrm{S} \longrightarrow \overset{-}{\mathrm{A}} + \mathrm{D}\overset{+}{\mathrm{S}} \end{array}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (\mathrm{I})$$

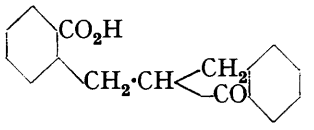
It is only for very weak acids, such as ψ-acidic ketones and nitro-compounds, that ionisation in hydroxylic solvents is slow enough for measurement, but it is just these slow ionisations which play so fundamental a part in prototropy and several other general reactions of organic chemistry. These reactions are being investigated, in this series *inter alia*, by the use of protium–deuterium exchange as an indicator for hydrogen ionisation; yet no such investigation can be developed on quantitative lines without taking account of the different rates of transference which, for known reasons, the bound proton and deuteron exhibit; this was made clear in Part I (Ingold, De Salas, and Wilson, this vol., p. 1328).

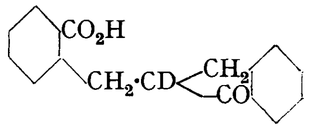
It is known that with aliphatic nitro-compounds (Wynne-Jones, *J. Chem. Physics*, 1934, **2**, 381; Reitz, *Z. physikal. Chem.*, 1936, *A*, **176**, 363; *Z. Elektrochem.*, 1936, **42**, 582) and with *cyclo*hexenylacetonitrile (Part I, *loc. cit.*) the proton is ionised several times faster than the deuteron in hydroxylic solvents. These examples are complicated by multiple replacements, isomeric changes, or both, and it seemed desirable to attempt a direct measurement of the rates of a pair of isolated reactions of type (I).

In these experiments HA takes the form of a ketone with only one α-hydrogen atom : $>CH{\cdot}CO-$. By well-known general results relating to the halogenation of ketones, the rate of bromination in aqueous solvents under conditions of basic catalysis must give the rate of ionisation of the proton; and the rate of bromination of the deutero-ketone, $>CD{\cdot}CO-$, will give the corresponding rate of ionisation of the deuteron.

The truth of these assertions has been specifically supported for the example studied and the conditions chosen in a recent investigation by Hsü and Wilson (this vol., p. 623). The ketones were 2-*o*-carboxybenzylindan-1-one (II) and its 2-deutero-analogue (III); the solvent was aqueous acetic acid and the basic catalyst acetate ions :

(II.)





(III.)

$$\left.\begin{array}{l} >CH{\cdot}CO- + [OAc]^- \longrightarrow [>\overset{\frown}{C}-C-\overset{\frown}{O}-]^- + HOAc \\ >CD{\cdot}CO- + [OAc]^- \longrightarrow [>\overset{\frown}{C}-C-\overset{\frown}{O}-]^- + DOAc \end{array}\right\} \quad . \; . \; . \quad (IV)$$

In the paper cited it is shown that the rate of bromination of ketone (II) under these conditions is independent of the concentration of halogen, that it is dominated by the single basic catalyst, and that it is equal to the rate of the racemisation which obtains under corresponding conditions when the ketone is optically active.

The following table contains the first-order velocity constants for the bromination of the ketones (II, k_1^H) and (III, k_1^D) each at three temperatures; the composition of the aqueous acetic acid solvent and the concentration of acetate ions are specified on p. **1553**.

Velocity of Bromination of Ketones (II) *and* (III) *in Aqueous Acetic Acid Containing Acetate Ions.*

Temp.	$10^6 k_1^H$ (sec.$^{-1}$).	$10^6 k_1^D$ (sec.$^{-1}$).	k_1^H/k_1^D.
25·00°	11·5	2·62	4·4
35·00	37·0	10·50	3·5
45·00	100·0	33·70	3·0

It will be seen that the rate of reaction of the ordinary ketone (II) is several times greater than that of the deutero-ketone (III). Throughout any individual experiment with the deutero-ketone the first-order velocity coefficient remained sensibly constant, proving that no protium–deuterium exchange with the medium could have occurred by any unknown mechanism ahead of the measured reaction; for any such prior conversion of (III) into (II) would have shown itself in a rise of the rate constant as reaction proceeded.

If the "temperature independent factor" of the Arrhenius equation is assumed to be the same for reactions (IV), the difference of rates corresponds to a difference in energies of activation amounting to 0·9 kg.-cal. The separate energies of activation (kg.-cals.), calculated by means of the Arrhenius equation from the temperature coefficients of the rate constants, are 20·4 ± 1·0 for (II) and 24·0 ± 2·0 for (III). In view of the errors, these figures are not inconsistent with the assumed difference of 0·9 kg.-cal.

Theoretically, the most important single contribution to the difference of the activation energies should be the difference between the zero-point energies of the C–H and the C–D stretching vibrations; this effect contributes 1·2 kg.-cals. in the direction of the observed energy difference. To this we have to add two contributions arising from orthogonal bending vibrations of the C–H and the C–D bonds, and subtract three contributions corresponding to the vibratory degrees of freedom of the migrating atoms in the transition state.* Making estimates of the magnitude of these minor contributions, we may say

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* This statement neglects the intramolecular coupling of the active vibrations, and also the tunnel effect.

that the difference of critical energy is likely to be of the order of 1 kg.-cal., and this accords satisfactorily with the observed rate ratios and temperature coefficients.

EXPERIMENTAL.

2-*o*-Carboxybenzylindan-1-one (II), prepared as described by Ingold and Wilson (J., 1934, 773), was recrystallised twice from benzene and had m. p. 142·5° (Found: C, 76·5; H, 5·3. Calc.: C, 76·7; H, 5·3%).

Preparation of the Deutero-ketone (III).—It was assumed that isotopic hydrogen exchange with the α-position in the ketone would occur only under conditions of racemisation of the *d*-ketone. The latter (for preparation, see *idem, ibid.*), dissolved in a mixture of dioxan (5 c.c.) and water (1 c.c.), racemised slowly at 20°, as indicated by the following rotations [time (mins.) is given in parentheses]: 1·16° (0), 1·09° (50), 1·01° (120), 0·92° (215). When the solution was heated to 100° in a sealed bulb, complete racemisation occurred in less than 10 minutes.

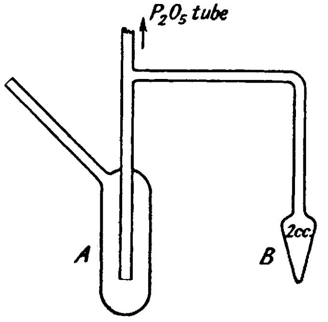
The pure racemic ketone (2·66 g.) was heated to 100° in a sealed bulb with dioxan (sodium-dried and distilled, 5 c.c.) and deuterium oxide (99·6%, 1 c.c.). After 30 minutes, the bulb was cooled, and the solvent distilled off in a vacuum. Repetition of the experiment with fresh deuterium oxide gave a final product which was thoroughly dried in a vacuum at 100° and then recrystallised once from benzene (previously dried over phosphoric oxide and distilled). The *deutero-ketone* was analysed (Found: C, 76·7; H, 5·6. $C_{17}H_{12}D_2O_3$ requires C, 76·2; H, 5·3%).

Isotopic Analysis of the Deutero-ketone.—Under the above conditions, two hydrogen atoms in the ketone are replaced by deuterium, one in the α-position to the carbonyl group as desired, and one in the carboxyl group. Normalisation of the latter with respect to hydrogen isotopes was unnecessary prior to bromination, since the increase in the deuterium of the acetic acid solvent caused by the relatively instantaneous distribution of the carboxyl deuterium could not be greater than 0·1%: this would not affect the velocity of halogenation.

Before combustion, however, normalisation of the carboxyl hydrogen was carried out by shaking an ethereal solution of the ketone with tap water, conditions which were shown to cause no racemisation of the *d*-ketone and were therefore assumed to result in no isotopic exchange with the α-position.

Combustion of the ketone followed the lines of a macro-estimation of carbon and hydrogen, and this was followed by pyknometric density determination of the combustion water (cf. J., 1934, 493, 1593; 1935, 492; this vol., p. 1328).

Certain experimental modifications require mention. The organic material was contained in a boat of clean copper foil; the combustion tube, heated electrically, was of Jena glass (15 mm. internal diameter), the exit end of which was drawn out obliquely and fixed, by means of a short sleeve of rubber, inside the side tube of a Pyrex apparatus shown in the figure. As an alternative to diluting the combustion water with tap water, it was found more convenient to burn a mixture of the deutero-ketone with a known amount of either the ordinary ketone or pure naphthalene. The quantities of organic materials taken are determined by the size of the pyknometer and the accuracy desired.



Bulb *A* was maintained at − 78°, and if the oxygen supply is continued until all the copper becomes reoxidised (a little water appears at this stage) the yield of water is quantitative. After the addition of a little silver oxide the side arm is sealed, the water allowed to stand a few hours, then repeatedly frozen with evacuation to 0·1 mm. and thawed until gas-free, and finally evacuated and sealed off. Complete distillation without ebullition into *B*, using the temperature gradient between 0° and 25°, takes about 3 hours.

Organic material is economised by the shape of *B*, which enables the pyknometer to be filled with ease when only very little more than the necessary volume of water is available.

A pyknometer of 0·6 c.c. capacity was used. It was of Pyrex glass, which has the advantage of reducing the progressive loss in weight due to solubility. The scratch arm had a capillary bore of 0·1 mm. radius, and the tip was provided with a tapering cap (1·5 cm. long), which, although not essential in the present instance, is invaluable when dealing with more volatile liquids (*e.g.*, benzene, alcohol, etc.; this vol., p. 918).

Counterpoise and pyknometer had the same external volume (to within 0·05 c.c.); this obviates a correction due to buoyancy which varies with changing density of the air. An accuracy in density measurement to ± 1·5 p.p.m. was attainable.

Isotopic analysis of the ketone was performed before and after normalisation of the carboxyl group. Expressed as an atomic percentage of deuterium in the substituted positions, the figures were 71·7 and 76·7 respectively. This percentage would have been over 90 if the equilibrium constant for the exchange had been unity; it must therefore be considerably less (cf. Reitz, *loc. cit.*; Hamill and La Mer, *J. Chem. Physics*, **1936**, **4**, 395). Some loss of deuterium from the carboxyl group might be expected during experimental manipulation.

Bromination.—The halogenations were carried out exactly as previously described by Hsü and Wilson (*loc. cit.*) in 16*M*-acetic acid containing 2% of sodium acetate crystals. Only one bromine concentration (0·01*M*) was employed.

For the ordinary ketone, tables giving all the measurements are omitted, since they are similar to those published previously (*idem, ibid.*). The mean values of the velocity constants in the foregoing table are subject to a possible error not greater than ± 5%.

For the deutero-ketone, one specimen experiment is set out below, to illustrate the method of allowing for the 23·3% of ordinary ketone present. Col. 3 gives the total bromine absorption, $x_{(D+H)}$, as determined by titration of 5 c.c. of the reaction mixture, x_H is the absorption calculated for the ordinary ketone present, its velocity of reaction being known (k_1^H). The difference between these figures represents the absorption (x_D) due to the pure deutero-ketone, and corresponds with the velocity coefficients of the last column (k_1^D).

Bromination of the Deutero-ketone at 35°.

$k_1^H = 37{\cdot}0 \,.\, 10^{-6}$ (sec.$^{-1}$); $[Br_2] \sim 0{\cdot}01M$; [Ketone III] = 0·03835*M*; [Ketone II] = 0·01165*M*.

t (mins.).	Titre (c.c. *N*/50-$Na_2S_2O_3$).	$10^5 x_{(H-D)}M$.	$10^5 x_H M$ (calc.).	$10^5 x_D M$ (by diff.).	$10^6 k_1^D$ (sec.$^{-1}$).
0	4·65*	0	0	0	—
2	4·61	9	5	4	—
22	4·01	108	55	53	10·7
70	2·92	346	165	181	11·5
93	2·44	442	217	225	10·9
122	1·90	550	276	274	10·2
141	1·56	618	313	305	9·8
172	1·07	716	370	346	9·2
					Mean 10·4 ± 1·0

* Extrapolated.

The average constants from several experiments are collected in the first table; the possible error is greater, however, than for k_1^H owing to the calculation involved, and is set at a maximum of ± 10%.

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