[CONTRIBUTION FROM THE CHEMISTRY DIVISION, ARGONNE NATIONAL LABORATORY]

Isotope Effects in the Chromic Acid Oxidation of 2-Propanol-2-*t*[1]

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The relative rates of oxidation of 2-propanol and 2-propanol-2-*t* by aqueous chromic acid have been measured by a competitive method. In the presence of manganous ion, added to isolate the rate-determining oxidation by acid chromate ion, the discrimination factor, $k_T/k_H = 0.04 \pm 0.02$, is consistent with the ratio of rate constants, $k_D/k_H = 1/7$, previously obtained by Westheimer and his co-workers. In the absence of manganous ion, the observed discrimination factor varies with perchloric acid concentration from $k_T/k_H = 0.13$ in 0.3 M acid to $k_T/k_H = 0.26$ in 2 M acid. From the results it has been possible to estimate the magnitude of the isotope effects for the oxidation of 2-propanol by lower valence states of chromium. It is concluded that C–H bond rupture, which occurs in the rate-determining step of the attack by acid chromate ion, must likewise occur, at least predominantly, in the slow steps of the subsequent oxidations by the lower-valent species. Attack at the hydroxyl hydrogen may, however, occur to a significant extent at high acid concentrations.

The oxidation of 2-propanol by chromic acid has been investigated[2] in considerable detail by Westheimer and his co-workers, who have clarified many aspects of the reaction mechanism. The reaction, which results in the quantitative formation of acetone,[2b] is, in aqueous solution, first order in alcohol and in acid chromate ion, and second order in hydrogen ion. The oxidation is inhibited by manganous ion, the oxidation of the latter to manganese dioxide being induced.[2c] Substitution of deuterium for protium on the carbinol carbon results[2d,2h] in a sevenfold reduction in reaction rate.

The reaction occurs in two distinct stages.[2a,2c] In the first stage, which determines the over-all rate, a molecule of 2-propanol is oxidized to acetone by an acid chromate ion, which is reduced to a chromium(IV) species (equation I).

$$HCrO_4^- + (CH_3)_2CHOH \longrightarrow Cr(IV) + (CH_3)_2CO \quad (I)$$

In the second stage, the stoichiometry of which may be expressed as

$$Cr(IV) + Cr(VI) + 2(CH_3)_2CHOH \longrightarrow 2(CH_3)_2CO + 2Cr(III) \quad (II)$$

two additional molecules of the alcohol are oxidized. Manganous ion, by reducing chromium(IV) to chromium(III), suppresses the second stage. The detailed mechanism of the first stage is rather well understood. The carbinol C–H bond is broken[2d] in the slow step, which is probably the decomposition of monoisopropyl chromate.[2e,2f] With respect to the second stage, it has been possible only to restrict to four[2a,2c] the number of sequences of reaction steps which are consistent with the experimental results and with a set of reasonable assumptions. These four sequences have in common the oxidation of a molecule of alcohol by a chromium(V) species; they differ in that another molecule of alcohol is attacked either by chromium(V), by chromium(IV) (in one of two different ways), or by a hydroxyl free radical. The detailed nature of these possible reaction steps is not specified.

Mosher has proposed,[3] largely on the basis of the formation of cleavage products during the oxidation of certain secondary alcohols, that oxidations of alcohols by chromic acid proceed *via* removal of the hydroxyl hydrogen as hydride ion. Such a mechanism has been ruled out for the first stage of the 2-propanol oxidation by the observed[2d,2h] difference in the rate constants for the deuterium and protium compounds but, as Leo has pointed out,[2h] has not been ruled out for the faster reactions of the second stage. In the present paper, *competitive* measurement of the relative rates of oxidation of 2-propanol-2-*t* and 2-propanol by chromic acid in aqueous solution is employed to obtain information which does apply to the latter reactions.

Experimental

2-Propanol-2-*t*.—Into a 50-ml. long-necked flask with a standard taper joint were introduced 0.273 g. (7.2 mmoles, 83 mc. T) of lithium aluminum hydride-*t*[4] and a small glass-enclosed magnet. The flask was attached to a vacuum line, 20 ml. of dry ether was distilled in, and the mixture was stirred at room temperature for one hour. The flask was cooled with liquid nitrogen and evacuated, and 3.0 ml. of dry acetone was distilled in. It was then brought to −20° for one-half hour and then stirred at room temperature for one hour. The ether and excess acetone were removed in a high vacuum, and 1.1 g. of water was distilled onto the residue. After two hours at room temperature, the volatile material was distilled onto 15 g. of Drierite and subsequently distilled off at 0°. The yield of product, which had a vapor pressure of 10 mm. at 0°, was 1.38 g. (80% of theory, based on $LiAlH_4$); analysis after dilution showed it to contain 64 mc. of tritium (77%). A portion of the product, diluted 130-fold with ordinary 2-propanol, was fractionally distilled through a wire-wound column, and the fraction distilling at 81.5–81.6° at 747 mm. was used in the subsequent experiments.

To determine how much tritium might have been incorporated in the methyl groups of the 2-propanol, a 60-mg. aliquot (19.0 μc. per mmole) was oxidized at room temperature for 16 hr. with 110 mg. of $KMnO_4$ in 5 ml. of water containing 110 mg. of $MgSO_4 \cdot 7H_2O$. The acetone and water were removed by distillation *in vacuo* and added to a solution of dinitrophenylhydrazine in 2 N HCl. The precipitated dinitrophenylhydrazone, filtered off immediately and recrystallized four times from ethanol, contained only 0.0028 μc. T per mmole corresponding to 0.015% of that in the 2-propanol. That methyl tritium was not lost by exchange during the permanganate oxidation was demonstrated by similarly oxidizing ordinary isopropyl alcohol in tritiated water. In this case the dinitrophenylhydrazone contained 0.026 μc. per mmole compared with 15.1 μc. per mmole of water. As a demonstration that much tritium

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[1] Work performed under the auspices of the U. S. Atomic Energy Commission.

[2] (a) F. H. Westheimer, *Chem. Revs.*, **45**, 419 (1949); (b) F. H. Westheimer and A. Novick, *J. Chem. Phys.*, 11, 506 (1943); (c) W. Watanabe and F. H. Westheimer, *ibid.*, **17**, 61 (1949); (d) F. H. Westheimer and N. Nicolaides, THIS JOURNAL, **71**, 25 (1949); (e) F. Holloway, M. Cohen and F. H. Westheimer, *ibid.*, **73**, 65 (1951); (f) A. Leo and F. H. Westheimer, *ibid.*, **74**, 4383 (1952); (g) M. Cohen and F. H. Westheimer, *ibid.*, **74**, 4387 (1952); (h) A. J. Leo, Ph.D. Thesis, University of Chicago, 1952.

[3] W. A. Mosher and F. Whitmore, THIS JOURNAL, **70**, 2544 (1948); W. A. Mosher and E. O. Langerak, *ibid.*, **71**, 286 (1949); **73**, 1302 (1951); W. A. Mosher and D. M. Preiss, *ibid.*, **75**, 5605 (1953).

[4] K. E. Wilzbach and L. Kaplan, *ibid.*, **72**, 5795 (1950).

was not lost during preparation or purification of the dinitrophenylhydrazone, acetone labeled with tritium by base-catalyzed exchange with tritiated water (15.1 μc. per mmole) yielded a dinitrophenylhydrazone containing 34.1 μc. per mmole.

Analytical Procedures.—Tritium was determined by ion-current measurement[5] on the gas produced by heating the compound with zinc and nickel oxide.[6] Decay corrections were made using $t_{1/2}$ = 12.4 yr. The mean deviation of replicate analyses was less than 1%.

Isopropyl alcohol was determined by oxidation to acetone with excess dichromate in sulfuric acid solution. To an aliquot containing 0.2 to 0.5 meq. of alcohol were added an excess of standard potassium dichromate, sufficient water to make a volume of 20 ml., and 15 ml. of 18 N H_2SO_4. After standing for one-half hour at room temperature and one-half hour at 65°, the solution was diluted, and the excess dichromate titrated with ferrous ammonium sulfate to a Ferroin endpoint. Duplicate analyses agreed within 1% and were not affected by the presence of acetone. Samples of pure isopropyl alcohol subjected to distillation as in the oxidation experiments gave recoveries of 99–100%.

Manganese dioxide was estimated by reduction with excess ferrous ammonium sulfate in dilute sulfuric acid and back titration of the excess ferrous ion with dichromate.

Competitive Oxidations.—In a glass-stoppered flask were placed the calculated amounts of water, 5 N perchloric acid and a stock aqueous solution of 2-propanol-2-*t*. The flask was thermostated at 25.0°, and the desired amount of a 1 N solution of chromic acid was added rapidly with swirling; the total volume of solution was 50 ml. The reaction mixtures were kept in the thermostat for one to two weeks, after which time there was no visual evidence of unreacted chromic acid. Each solution was neutralized with NaOH to *p*H 7 and was then subjected to distillation through a Vigreux column until about half of the original volume had distilled. The pot residue was acidified and analyzed for the small amount of residual chromium(VI). The distillate, after removal of aliquots for alcohol determination, was saturated with potassium carbonate and extracted with several portions of benzene. The benzene solution was treated with pyridine and excess *p*-nitrobenzoyl chloride and heated at 60–70° for one hour. The solvent was removed in a stream of nitrogen, the residue was taken up in water, and the *p*-nitrobenzoate was filtered off, washed with 1 N potassium hydroxide and water, and recrystallized four times from hexane. After drying *in vacuo*, the samples of 2-propyl *p*-nitrobenzoate used for tritium determination melted at 108.5–109.0°.

For the run carried out in the presence of manganous sulfate, the reaction mixture, which contained 5 g. of $MnSO_4 \cdot H_2O$ in a total volume of 200 ml., was kept at 25.0° for 24 hrs. and then filtered through an asbestos mat, taking precautions to avoid loss of alcohol by evaporation. The filtrate was neutralized and treated as above; the precipitate was analyzed for MnO_2.

Calculations

In these experiments, 2-propanol containing a minute concentration of 2-propanol-2-*t* was oxidized with a deficiency of chromic acid. In such a competitive system the relative rates of consumption of the isotopic molecules can be determined[7,8] from the amount and isotopic content of unreacted material. For the over-all reactions

$$(CH_3)_2CHOH + (O) \xrightarrow{k_H} (CH_3)_2C{=}O + H_2O$$

$$(CH_3)_2CTOH + (O) \xrightarrow{k_T} (CH_3)_2C{=}O + HTO$$

the ratio k_T/k_H is given by the equation

$$\frac{k_T}{k_H} = \frac{\log (AT)/(AT)_0}{\log (AH)/(AH)_0} \qquad (1)$$

where (AT) and (AH) are the concentrations of tritiated and ordinary 2-propanol, respectively. In terms of specific activity

$$\frac{k_T}{k_H} = 1 + \frac{\log N_A/N_A^0}{\log (A)/(A_0)} \qquad (2)$$

where N_A^0 and N_A are, respectively, the specific activities of the initial 2-propanol and of the fraction $(A)/(A_0)$ which remains unreacted.

If the alcohol is consumed by several processes having different isotopic discrimination factors, $(k_T/k_H)_I$, $(k_T/k_H)_{II}$, etc., the experimental ratio k_T/k_H, calculated by equation 1, is a resultant of the individual ratios and the amounts reacting by each process. For the case, as here, that the concentration of tritium compound is very much smaller than that of protium compound, the total amount of tritium compound consumed in an interval dt is expressed by

$$\frac{-d(AT)}{dt} = -\frac{(AT)}{(AH)}\frac{d(AH)}{dt}\,\Sigma\left(\frac{k_T}{k_H}\right)_i x_i \qquad (3)$$

where x_i is the fraction of d(AH) reacting by process i with the discrimination factor $(k_T/k_H)_i$. This equation is valid regardless of the kinetic orders or relative rates of the various processes. If the fractions x_i remain constant throughout the reaction, equation 3 can be integrated to give

$$\frac{\log (AT)/(AT)_0}{\log (AH)/(AH)_0} = \Sigma\, x_i \left(\frac{k_T}{k_H}\right)_i$$

which, combined with equation 1, yields

$$(k_T/k_H)_{expt.} = \Sigma x_i\, (k_T/k_H)_i \qquad (4)$$

Results

The results of a number of oxidations, at perchloric acid concentrations ranging from 0.3 to 2.0 N, are summarized in Table I. The blank runs, 17 and 18, demonstrate the quantitativeness of alcohol recovery as well as the absence of hydrogen exchange with the solvent. The values of k_T/k_H are calculated from equation 2; the tabulated uncertainties are those associated with 1% errors in $(A)/(A)_0$ and N_A/N_A^0. At a given acid concen-

TABLE I

ISOTOPE EFFECT IN OXIDATION OF 2-PROH-2-*t* AT 25°

Run	$HClO_4$ initial, M[a]	2-PrOH, meq. Initial $(A)_0$	Final (A)	CrO_3, meq. Initial	Final	Specific activity,[d] μc./mmole N_A	k_T/k_H[e]
17	0.3	7.36	7.42	0		19.45	
18	2.0	7.36	7.33	0		19.35	
19	0.3	12.25	4.12	8.23	0.00	48.9	0.152 ± 0.017
14	0.3	12.50	3.31	9.42	.23	61.8	.128 ± .015
20	0.3	12.25	2.28	10.16	.09	83.9	.130 ± .011
3	0.4	7.54	2.80	4.77	.00	45.8	.134 ± .019
2	1.0	12.64	6.42	6.25	.00	33.6	.190 ± .027
4	1.0	12.65	4.45	8.13	.00	44.0	.215 ± .018
5	1.0	12.65	2.65	10.00	.00	67.2	.207 ± .011
11	2.0	12.50	3.25	9.42	.12	53.6	.246 ± .012
21	2.0	12.25	2.17	10.10	.00	68.1	.275 ± .010
23	1.0[b]	7.36	2.03	7.62	1.00[c]	66.7	.04 ± .02

[a] Total volume of solution 50 ml., except where noted. [b] Contained in addition 5 g. of $MnSO_4 \cdot H_2O$, total volume 200 ml. [c] Plus 1.41 meq. MnO_2. [d] The *p*-nitrobenzoate prepared directly from the initial 2-propanol-2-*t* contained 19.13 μc./mmole. [e] Calculated with equation 2. The indicated error is the maximum which would be produced by 1% errors in $(A)/(A)_0$ and N_A/N_A^0.

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(5) K. E. Wilzbach, A. R. Van Dyken and L. Kaplan, *Anal Chem.*, **26**, 880 (1954).

(6) K. E. Wilzbach, L. Kaplan and W. G. Brown, *Science*, **118**, 522 (1953).

(7) J. Bigeleisen, *ibid.*, **110**, 14 (1949).

(8) L. Kaplan, THIS JOURNAL, **76**, 4645 (1954).

tration the results agree, within the estimated error, for conversions varying from 50 to 82%. The isotopic rate ratio does, however, change with acidity, the values becoming closer to unity at higher perchloric acid concentrations.

Run 23 was carried out in the presence of manganous sulfate in order to obtain an estimate of k_T/k_H for reaction I. Reaction II could not be completely suppressed by manganous ion under conditions which would permit reliable chemical and radiochemical analysis of the residual 2-propanol. The induction factor[2c] found in this experiment was 0.27 compared with the theoretical value of 0.50 which has been observed[2c] at very low 2-propanol concentrations. Although the value of k_T/k_H found in this experiment is not an accurate measure of the isotope effect for reaction I, there is no doubt that the true value is much lower than the values obtained in the absence of manganous ion.

Discussion

The isotopic rate ratio, k_D/k_H, obtained from the rate constants for the oxidation of 2-deutero-2-propanol and ordinary 2-propanol by chromic acid is one-seventh.[2d,2h] The rate ratio for tritium, k_T/k_H, would, if it could be determined in the same way, be about 0.06.[9] These values refer to the first stage of the oxidation (equation I); under conditions designed to isolate this stage by addition of manganous ion (run 23, Table I) the experimental value of $k_T/k_H = 0.04 \pm 0.02$ agrees, within its rather large uncertainty, with that expected. In the absence of manganous ion, two additional molecules of 2-propanol are oxidized in the subsequent fast stage, as indicated in equation II, for each molecule oxidized in the first stage. Competitive measurement of k_T/k_H in such a system gives a value which is the weighted mean, as shown in equation 4, of the isotopic discrimination factors pertaining to each process by which some of the 2-propanol is oxidized in the particular system. On the reasonable assumption that one-third of the total 2-propanol oxidized is consumed in the first stage with a discrimination factor of 0.06, it is possible to calculate, for each experiment recorded in Table I, the mean value of k_T/k_H for the two-thirds of the alcohol consumed in the second stage. The values thus calculated are 0.17 in 0.3 *M* perchloric acid, 0.28 in 1 *M* acid, and 0.36 in 2 *M* acid.

The dependence of k_T/k_H on perchloric acid concentration suggests that the mechanism by which 2-propanol is oxidized in the second stage of the reaction may change with the acidity of the medium. The nature of such a change is highly speculative. One possibility is that the presumably oxygenated chromium (V) (or chromium(IV)) species taking part in the oxidation varies with hydrogen ion concentration, and that the variously oxygenated species discriminate to a different extent between C–H and C–T bonds. Another possibility is that more than one of the proposed[2a,2c] reaction sequences may be operative, the fraction of alcohol oxidized by each process varying with the acidity. Differences in isotopic discrimination factors in the reactions of the various possible oxidants, even though the slow step of the attack by each reagent involved C–H bond rupture, might then account for the experimental results; such differences might reflect the difference between an ionic and a free radical reaction,[10] or simply a difference in oxidation potential between chromium(V) and chromium(IV). Similar considerations may also account for the fact that less isotopic discrimination occurs in the second stage of the oxidation, even at low acid concentration, than in the first stage.

Although the experimental results may well be consistent with the assumption that all of the alcohol is oxidized by processes involving C–H bond rupture, it is necessary to consider the alternative hypothesis that some attack occurs with rupture of the O–H bond, along the lines of the Mosher hydride ion mechanism,[3] a process which would be rather insensitive to the substitution of tritium for protium on carbon. If the discrimination factors for the two types of process were known, it would be possible to calculate, from equation 4, the fraction of the alcohol consumed by each process. For the purpose of this calculation the value of k_T/k_H for C–H bond rupture in the second stage of the reaction will be taken equal to that in the first stage, namely, 0.06, and that for O–H bond rupture will be taken equal to unity. Then of the two molecules of alcohol consumed according to equation II, 0.23 molecule is oxidized, in 0.3 *M* acid, by a process involving O–H bond rupture; the corresponding values in 1 and 2 *M* acid are 0.47 and 0.64 molecule, respectively. These values would, of course, be increased by selecting lower values of k_T/k_H for the individual processes, but any reasonable choice would leave unchanged the conclusion that at the lowest acid concentration not more than a small fraction of the alcohol is oxidized by attack at the hydroxyl hydrogen. Such a conclusion is less certain for the 2 *M* acid; it is conceivable that here as much as one of the two molecules of alcohol is oxiized by such an attack. It should be emphasized that these are essentially maximum values, and that the experimentally observed discrimination factors do not prove that any process involving O–H bond rupture does occur in the second stage of the oxidation, but rather that such a process cannot be the predominant one in the systems studied.

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[9] Calculated on the assumption that the isotope effects result from the differences in zero point energy associated with the C–H stretching vibration, using $\nu_{CH}/\nu_{CD} = 1.36$, $\nu_{CH}/\nu_{CT} = 1.61$.

[10] P. D. Bartlett and F. A. Tate, THIS JOURNAL, **75**, 91 (1953).