Co., for the sample of perfluoromethylcyclohexane, and the Office of Naval Research for financial support of this research.

Summary

Liquid–liquid solubility curves have been determined for binary mixtures of perfluoromethylcyclohexane with five other liquids, giving the following results for the critical solution temperatures in °C. and the mole fractions of the second components: carbon tetrachloride, 26.8°, 0.70; chloroform, 50.3°, 0.74; benzene, 85.3°, 0.73; toluene, 88.8°, 0.69; chlorobenzene, 126.8°, 0.69.

These values agree within the usual limits of error with those calculated by aid of the equations for regular solutions and the value 6.0, previously derived by Scott for the "solubility parameter" (the square root of the energy of vaporization per cc.) of the fluorocarbon.

BERKELEY, CALIF. RECEIVED AUGUST 23, 1948

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Kinetics of the Oxidation of 2-Deuteropropanol-2 by Chromic Acid

BY F. H. WESTHEIMER AND NICHOLAS NICOLAIDES

The rate of the chromic acid oxidation of isopropyl alcohol to acetone has been shown to be proportional to the concentrations of isopropyl alcohol and the acid chromate ion, and proportional to the square of the concentration of hydrogen ion.[1] Although these kinetics fix the composition of the activated complex in the oxidation, they leave unanswered many questions concerning the mechanism. Specifically, they do not show whether the oxidative attack upon the alcohol molecule is at the secondary hydrogen atom, at the hydroxyl hydrogen atom,[2] or elsewhere. This question can be answered by studying the rate of oxidation of 2-deuteropropanol-2.

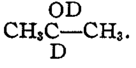
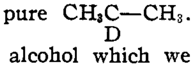
Both experimental and theoretical considerations show that, if the deuterium atom of 2-deuteropropanol-2 is removed in the rate-controlling step of the oxidation, the 2-deuteroalcohol will be oxidized much less rapidly than the corresponding hydrogen compound. On the other hand, if the rate determining step does not involve the removal of this deuterium atom, the oxidation rates for the hydrogen and deuterium compounds should be almost if not exactly identical. This test for the direct removal of a hydrogen atom depends upon the fact that C–H and C–D bonds differ in their zero-point energies. The method is completely general[3]; it has been strikingly applied by Reitz[4] in a study of the rate of enolization of acetone and of the deuteroacetones. In the present work, it has been found that 2-deuteropropanol-2 is oxidized by chromic acid only about one-sixth as fast as is ordinary isopropyl alcohol; it follows unambiguously that the secondary hydrogen atom is removed during the rate controlling step of the reaction.

Experimental

Deuterium.—The deuterium for these experiments was made by vaporizing 12.1 g. of Norwegian heavy water (Norsk Hydro Elektrish Kvaelstofaktieselskat 99.73% D_2O; $d^{20}{}_4$ 1.10516) over Grignard magnesium heated electrically to 490 ± 25° in a heavy-walled combustion tube.[5] The resulting deuterium gas was passed through alkaline permanganate and stored over a saturated solution of sodium sulfate.

2-Deuteropropanol-2.—2-Deuteropropanol-2 was made by the catalytic deuteration of acetone according to the directions of Anderson and MacNaughton.[6] Eighty-six grams of acetone (J. T. Baker reagent grade, previously dried with potassium carbonate and distilled) was deuterated with 10.8 liters of deuterium gas, by means of 1.62 g. of Adams catalyst promoted with a few crystals of ferrous chloride. The deuteration required five days, during which time the catalyst was reactivated several times by briefly stirring the reaction mixture in air.

The reaction mixture was then fractionated through a small Podbielniak column (about 25 theoretical plates) to remove the large excess of acetone. When all the acetone had been removed, 54 cc. of water was added in order to exchange the hydroxylic deuterium of the isopropyl alcohol with the hydrogen of the water. Then the distillation (through the same column) was resumed. The fraction collected was 15 g. of the azeotropic mixture of isopropyl alcohol and water. Some of this azeotrope was used directly for rate measurements; some was re-equilibrated with water. The latter portion was prepared by adding 8.5 g. of the azeotrope to 100 g. of water, and then redistilling the mixture through the same Podbielniak column. The composition of the azeotrope was calculated as 90.1% deuteroisopropyl alcohol and 9.9% water from the combustion analysis of the material. (Microanalysis by Wm. Saschek, C, 53.40; H, 12.82.) Both portions of the azeotrope (that equilibrated once and that equilibrated twice) had the same rate of oxidation.

The work of Anderson and MacNaughton[6] suggests that in the deuteration all the deuterium gas is taken up at the carbonyl group, and the resulting product should be pure  $CH_3\overset{OD}{\underset{D}{C}}—CH_3$. If this were the fact, the product after equilibration with water should have been pure  $CH_3\overset{OH}{\underset{D}{C}}—CH_3$. Regrettably, however, the isopropyl alcohol which we prepared was a mixture containing only about 55% of the desired 2-deuteroalcohol. Fortunately the qualitative

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(1) Westheimer and Novick, *J. Chem. Phys.*, **11**, 506 (1943).

(2) Mosher, Abstracts, September, 1947, meeting of the American Chemical Society. Mosher and Whitmore, THIS JOURNAL **70**, 2544 (1948).

(3) Urey and Teal, *Rev. Mod. Phys.*, **7**, 34 (1935); *cf.* Taylor and Eyring, *Proc. Am. Phil. Soc.*, **72**, 255 (1933).

(4) Reitz, *Z. physik. Chem.*, **A179**, 119 (1937); *ibid.*, **A184**, 429 (1939); *cf.*, however, Wynne-Jones, *J. Chem. Phys.*, **2**, 381 (1934); Reitz, *Z. physik. Chem.*, **A176**, 363 (1936); and Maron and LaMer, THIS JOURNAL, **60**, 2588 (1938).

(5) Knowlton and Rossini, *Bur. Standards J. Research*, **19**, 605 (1937).

(6) Anderson and MacNaughton, THIS JOURNAL, **64**, 1456 (1942); see also Carothers and Adams, *ibid.*, **46**, 1675 (1924).

TABLE I

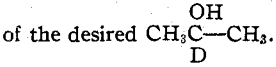
RATE OF OXIDATION OF 55% 2-DEUTEROPROPANOL-2

Experiment[a]	Concn. CrO_3, mole/l.	Concn. alcohol, mole/l.	Concn. H^+, mole/l.	Ionic strength	k, min.$^{-1}$ (mole/l.)$^{-1}$ k_H	k_{DI}[b]	k_H/k_{DI}
I	0.005480	0.2072	0.3143	0.40	2.04		1.88
D-I	.005520	.2139	.3140	.40		1.09	
II	.001059	.2061	.3120	.40	2.30		1.90
D-II	.001059	.2139	.3120	.40		1.21	
III	.005480	.02960	.3143	.40	1.73		1.91
D-III	.005520	.03059	.3140	.40		.907	
IV	.005591	.2046	.1083	.40	2.77		1.89
D-IV	.005520	.2138	.1082	.40		1.47	

[a] In those experiments prefixed with the letter "D," the isopropyl alcohol used contained 55% deuterium on the central carbon atom. [b] The symbol k_{DI} represents the rate constant for the isotopically impure 2-deuteropropanol-2.

conclusions here reached (see the discussion) do not depend upon the isotopic purity of the alcohol used. (The mixture of isopropyl alcohol and deuteroisopropyl alcohol used for the oxidations is hereafter called isotopically impure deuteroisopropyl alcohol, or, when the meaning is clear, simply "2-deuteropropanol-2"). The material was analyzed for deuterium by burning a sample in air on a sintered glass wick and determining by a float method the density of the water formed. The procedure of Brown and Eberly[7] was followed, and was found to be reliable to within 0.01 mole per cent. of the deuterium oxide in the water analyzed. In one experiment 0.4855 g. of the azeotrope was mixed with 1.3085 g. of pure, dry, ordinary isopropyl alcohol; before combustion the mixture was dried over lime and distilled. The water formed contained 2.01 mole per cent. deuterium oxide, corresponding to 0.65 gram atom of deuterium per mole of the (isotopically impure) 2-deuteropropanol-2.

Evidently the "2-deuteropropanol-2" contained a fairly large proportion of ordinary isopropyl alcohol, with hydrogen rather than deuterium on the center carbon atom. This hydrogen could not have come from the heavy water, which was of good quality (the residual heavy water left over from the investigation had a density, $d^{20}{}_4$, of 1.1040, corresponding[8] to 98.7 mole per cent. deuterium oxide); neither could the hydrogen have come from water vapor in the deuterium gas, since the latter was dried over calcium chloride before use. But hydrogen–deuterium exchange does occur between acetone or isopropyl alcohol and deuterium gas at room temperature in the presence of platinum black,[9] and therefore this exchange may have occurred here in the presence of Adams catalyst. A small amount (0.1 g. atom per mole) of deuterium was observed (see below) in the acetone obtained by oxidation of the deuterated isopropyl alcohol here prepared. If exchange occurred with all the acetone used in the hydrogenation to the extent of 0.1 g. atom per mole, this exchange would be sufficient to supply the hydrogen needed to form the isotopically impure isopropyl alcohol actually obtained. Extensive further research will be needed to decide whether the method of preparation of the catalyst and other experimental details control the extent of the exchange, or whether such exchange is inevitable in hydrogenations over Adams catalyst, although, because of the limited extent of exchange, it sometimes escapes notice. In any event, it was necessary to find how much of the deuterium was attached to the secondary carbon atom, and how much occurred in the methyl groups. The isotopically impure 2-deuteropropanol-2 was therefore oxidized to acetone. The oxidation method of Anderson[10] (where rather concentrated sulfuric acid is employed) was abandoned in favor of the gentler Oppenauer method.[11] Four and two-tenths cc. of the deuteroisopropyl alcohol and 16 g. of fluorenone (Eastman Kodak Co. m. p. 80.5–81.5°) were refluxed for six hours with 1.7 g. of aluminum tertiary butoxide[12] in 70 cc. of dry toluene. The reaction mixture was fractionated through a 50-theoretical plate Piros-Glover micro still. The resulting acetone was burned, and found to contain 0.105 gram atom of deuterium per mole. The deuteroisopropyl alcohol used therefore contained about 65.0 − 10.5 = 54.5% of the desired



$CH_3\overset{OH}{\underset{D}{C}}—CH_3$.

The calculation just given is based on the assumption that little or no exchange occurs during Oppenauer oxidation. To test this assumption, ordinary acetone (6.9 g.) was put back into the reaction mixture from which the (deuterium-containing) acetone and isopropyl alcohol had been removed by fractionation. The mixture was refluxed and distilled under the conditions employed in the oxidation of the isopropyl alcohol. The recovered acetone contained only 0.01 gram atom of deuterium per mole. This finding indicates that the exchange with deuterium during the Oppenauer reaction is negligible.

Rate Determinations.—The oxidation rates for isopropyl alcohol and the (isotopically impure) 2-deuteropropanol-2 were determined at 40° by the methods and equations of Westheimer and Novick.[1] The analytical method, however, differed from theirs. Instead of titrating the unreacted chromic acid, the quantity remaining in solution was determined spectrophotometrically with a Beckman Quartz Spectrophotometer, model DU. It was found that all the chromic acid solutions used had an absorption maximum close to 3500 Å.; at this wave length, chromic ion absorbs hardly at all. Despite the equilibrium[1,13] between $HCrO_4^-$ and $Cr_2O_7^=$ ions, solutions of chromic acid within the range of acidity used very nearly obey Beer's law. Nevertheless, an empirical standardization curve was prepared. The samples withdrawn from the reaction mixture were pipetted into a standard solution of sodium acetate such that the resulting buffer had an acetic acid–acetate ion ratio of one to 0.18. Blank experiments showed that, in this buffer, the rate of oxidation of isopropyl alcohol was negligible. These buffered solutions were then examined spectrophotometrically.

Results.—The kinetic results obtained as described are shown in Table I. The figures for isopropyl alcohol agree well with those of Westheimer and Novick. The ratio of the oxidation rates for isopropyl alcohol and the isotopically impure 2-deuteropropanol-2 was uniformly about 1.9.

In all the experiments hitherto cited, the concentration of alcohol greatly exceeded that of the chromic acid, and the former was therefore essentially constant during any individual rate determination. For this reason, the rate constant during any one experiment did not "drift," despite the fact that isotopically impure material (55% 2-deuteropropanol-2 and 45% isopropyl alcohol) was used. A few experiments were made with equivalent concentrations of ordinary isopropyl alcohol (or isotopically impure 2-deuteropropanol-2) and chromic acid. Here the rate constant for the oxidation of ordinary isopropyl alcohol was

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(7) Brown and Eberly, THIS JOURNAL, **62**, 113 (1940).

(8) Wirtz, *Physik. Z.*, **43**, 465 (1942).

(9) Farkas and Farkas, THIS JOURNAL, **61**, 1336 (1939); Friedman, Dissertation, Princeton University, 1947

(10) Anderson, private communication.

(11) Baker and Adkins, THIS JOURNAL, **62**, 3305 (1940).

(12) Wayne and Adkins, "Organic Syntheses," **21**, 8 (1941).

(13) Neuss and Rieman, THIS JOURNAL, **56**, 2238 (1934).

essentially constant, whereas that for the oxidation of the isotopically impure deuteroisopropyl alcohol decreased during the course of the experiment. This drift was to be expected. Since isopropyl alcohol reacts faster than does the corresponding deutero compound, the latter forms the bulk of the residual material left toward the end of any oxidation.

It was possible to calculate for this latter type of experiment the chromic acid concentration anticipated at various reaction times (see Appendix and Table II). The first column of the table gives the times at which samples were withdrawn; the observed chromic acid concentrations of these samples are given in column three. The second column gives the fourth order rate constants, determined by the equation of Westheimer and Novick; the drift is obvious. Column four gives the chromic acid concentrations computed for various times on the basis of an assumed ratio (4.5) for the rate constants of the oxidations of ordinary and 2-deuteropropanol-2; column five gives the concentrations similarly computed on the basis of another assumed ratio (6). A few readings taken very early in the experiments and a few taken beyond the point of 90% reaction were erratic; these have been omitted from the table.

TABLE II

RATE OF OXIDATION OF ISOTOPICALLY IMPURE 2-DEUTEROPROPANOL-2

Initial concentration in moles/1:2-deuteropropanol-2, 0.0537; chromic acid, 0.0693; isopropyl alcohol, 0.0433; H^+, 0.4944

Time in minutes	"k," min.$^{-1}$ (m./l.)$^{-3}$	Chromic acid reacted, m./l. Exp.[a]	Calculated with k_H/k_D 4.5	6.0
11.4	0.88	0.00420	0.0042	0.0042
27.4	.92	.00952	.0095	.0093
56.5	.92	.01647	.0163	.0152
106.4	.86	.02371	.0236	.0221
204	.79	.0318	.0314	.0282
352	.70	.0379	.0379	.0358
661	.60	.0445	.0445	.0442
1146	.52	.0492	.0500	.0475
1851	.45	.0528	.0535	.0511
2785.	.41	.0556	.0561	.0541
3645.	.40	.0574	.0579	.0560

[a] Average values from two duplicate experiments.

Discussion

The experiments here reported prove beyond doubt that 2-deuteropropanol-2 reacts with chromic acid much more slowly than does ordinary isopropyl alcohol. Since the deuterated material here used contained only 55% of 2-deuteropropanol-2, the exact ratio of the oxidation rates must be calculated on the (almost certain) assumptions (1) that the isopropyl alcohol and the 2-deuteropropanol-2 react independently, and (2) that deuterium in the methyl groups has little if any effect upon the oxidation rate. Calculations made on this basis indicate that pure isopropyl alcohol should be oxidized about 6.7 times as rapidly as pure 2-deuteropropanol-2; this value is roughly consistent with the rate ratio of about 5 obtained from the data (presented in Table II) for experiments in which the initial chromic acid and alcohol concentrations were equivalent. The rate ratio calculated from experiments with 55% 2-deuteropropanol-2 is likely to be somewhat in error. Although the probable error in the rate constants is small (of the order of 2%), the possible errors in the deuterium analysis and the questionable distribution of deuterium between the secondary carbon atom and the methyl groups make the computed oxidation rate for 2-deuteropropanol-2 somewhat uncertain. This uncertainty is such that the ratio of the rate of oxidation of the pure 2-deuteropropanol-2 to that of isopropyl alcohol should probably be written as 0.17 ± 0.05. Such uncertainty is, however, irrelevant for the conclusion here drawn. For if 2-deuteropropanol-2 is oxidized much more slowly than is ordinary isopropyl alcohol, it follows that the carbon to secondary hydrogen bond (or carbon to secondary deuterium bond) is broken in the rate determining step of the reaction.

Appendix

The data in Table II were obtained by use of the equations derived below. In these equations, the symbols b', c', K' have the meanings previously[1] assigned to them. The initial concentration of the ordinary isopropyl alcohol is represented by a_H, that which has reacted is represented by x; the initial concentration of the 2-deuteropropanol-2 is represented by a_D, that which has reacted is represented by y. The fourth order rate constant for the decrease in concentration of chromic acid during the oxidation of ordinary isopropyl alcohol is represented by k_H rather than by k. The corresponding constant for decrease during the oxidation of the deuteroalcohol is k_D. Since the stoichiometry of the reaction demands that three molecules of alcohol react for every two of chromic acid, the rate constants for the decrease of the concentration of isopropyl alcohol and deuteropropanol-2 are respectively $3/2\ k_H$ and $3/2\ k_D$. It follows that

$$dx/dt = 3/8\ k_H\ (a_H - x)\ \{-K' + \sqrt{K'^2 + 8K'\ [b' - 2/3\ (x + y)]}\}\ [c - 8/3\ (x + y)]^2 \quad (1)$$

$$dy/dt = 3/8\ k_D\ (a_D - y)\ \{-K' + \sqrt{K'^2 + 8K'\ [b' - 2/3\ (x + y)]}\}\ [c - 8/3\ (x + y)]^2 \quad (2)$$

$$dy/dx = k_D\ (a_D - y)/k_H\ (a_H - x) \quad (3)$$

Equation (3) when integrated yields (4)

$$y = a_D - \frac{a_D}{\left(1 - \frac{x}{a_H}\right)^{k_H/k_D}} \quad (4)$$

From eqn. (4), the value of y corresponding to any value of x can be found for any assumed value of k_H/k_D. When the values of y corresponding to various values of x are inserted into eqn. (1), this equation can be graphically integrated. This graphical integration gives the theoretical relation between the amount of alcohol (or chromic acid) consumed and the reaction time for the particular value of k_H/k_D used. The values thus computed are presented in Table II.

Summary

1. When Adams catalyst, activated by ferrous chloride, is used, the deuteration of acetone is accompanied by some hydrogen–deuterium exchange. The product here obtained was a mixture containing 55% of 2-deuteropropanol-2.

2. The rate of chromic acid oxidation of this product was only 52% of that of ordinary isopropyl alcohol. On the basis of this result, it is calculated that the rate of chromic acid oxidation of pure 2-deuteropropanol-2 should be about one-sixth that of pure isopropyl alcohol.

3. The lower rate of oxidation of the 2-deutero compound (which arises from differences between the zero point energies of the C–H and C–D bonds) proves that the secondary hydrogen (or deuterium) in isopropyl alcohol is removed in the rate controlling step of the chromic acid oxidation.

CHICAGO, ILLINOIS RECEIVED MAY 13, 1948

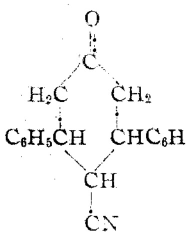
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

1-Cyano-2,6-diphenyl-4-hydroxycyclohexane and Some Related Compounds[1]

BY C. S. MARVEL AND ALLEN C. MOORE[2]

1-Cyano-2,6-diphenyl-4-hydroxycyclohexane (VI) was needed for another synthetic problem and it seemed probable that it could be produced readily by the addition of ethyl cyanoacetate to dibenzalacetone followed by hydrolysis, decarboxylation and reduction.

Kohler and Helmkamp[3] have prepared 1-cyano-2,6-diphenyl-4-cyclohexanone (I) by the addition of methyl cyanoacetate to dibenzalacetone followed by hydrolysis and decarboxylation of the addition product (II, R = CH_3). In our work the addition of ethyl cyanoacetate to dibenzalacetone ran smoothly in the presence of sodium ethoxide to give an 88% yield of the cyclic cyanoester (II R = C_2H_5). Difficulty was experienced in hydrolysis of the ethyl ester although the methyl ester had not been difficult to hydrolyze.[3] It seemed probable that reduction of the carbonyl group would stabilize the cyclohexane ring so no reversal of the Michael reaction would occur under the conditions of alkaline hydrolysis. Accordingly, the keto ester (II, R = C_2H_5) was reduced by the Meerwein–Ponndorf–Verley method.[4] This reduction did not give the simple hydroxy compound but two other products. One was crystalline and proved to be a lactone (III). The other was a noncrystalline polyester (IV). The formation of lactones in this reaction is not unusual.[4] The lactone (III) was undoubtedly formed from the hydroxy ester intermediate with the *cis*-configuration for these groups and the polyester therefore was probably derived from the *trans*-isomer. Hydrolysis of this glassy material gave a 63% yield of the free acid (V) which did not readily form a lactone and this further confirms its *trans*-structure with respect to hydroxyl and carboxyl groups.



I

When the cyanolactone (III) was refluxed for three hours with 40% aqueous sodium hydroxide, the lactone ring was opened and decarboxylation occurred, giving an 80% yield of the hydroxy nitrile (VI). Decarboxylation of the free acid (V) also gave the hydroxynitrile (VI), in 50% yield. By continuing the alkaline hydrolysis of the cyanolactone for a total of thirty-one hours, there was obtained a 94% yield of 2,6-diphenyl-4-hydroxycyclohexane-1-carboxylic acid (VII).

It became evident, from examination of the hydroxy acid (VII) derived from the hydroxynitrile (VI), that the acid had the *cis*-configuration. Thus, the hydroxy acid formed a second lactone (VIII) with ease, in 79% yield, when heated at its melting point. The action of such reagents as acetic anhydride, acetyl chloride and *p*-toluenesulfonyl chloride also brought about lactone formation. By contrast, the strictly analogous *trans*-4-hydroxycyclohexane-1-carboxylic acid prepared by Perkin[5] showed no tendency to yield a lactone when distilled, or when treated with hot 25% sulfuric acid.

When it is considered that the hydroxyl and carboxyl groups of the precursor of the cyanolactone (III) must have been *cis* with respect to one another, it follows that the nitrile and hydroxyl groups must have been in the *trans* configuration originally. It is clear then, that an inversion must have occurred to give a product (VII) of *cis* configuration. This inversion might have occurred during the opening of the lactone ring,[6,7] during

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[1] This investigation was carried out under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

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[3] Kohler and Helmkamp, THIS JOURNAL, **46**, 1018 (1924).

[4] Wilds, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 178 (1944).

[5] Perkin, *J. Chem. Soc.*, **85**, 416 (1904).

[6] Olson and Miller, THIS JOURNAL, **60**, 2687 (1938).

[7] Kohler and Jansen, *ibid.*, **60**, 2142 (1938).