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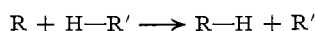
Use of Substituent Effects on Isotope Effects to Distinguish between Proton and Hydride Transfers. Part I. Mechanism of Oxidation of Alcohols by Bromine in Water¹⁻³

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Differences between proton and hydride transfers are discussed. Theoretical reasons are given for expecting k_H/k_D isotope effects to increase markedly on introduction of electron-attracting substituents for proton transfers, but to be much less sensitive to substituents for hydride transfers. Experimental data support this conclusion. Therefore it is applied as a tool for distinguishing between proton and hydride transfers in the oxidation of 0.01–1 *M* 2-propanol by 0.001–0.008 *M* bromine in water solution at 50°. This reaction is first order in each reactant, independent of bromide ion and acidity from *pH* 1–3, and exhibits CH and OH isotope effects of 2.94 and 1.49. These results exclude a hypobromite intermediate. The oxidation of 1-fluoro-2-propanol is kinetically similar but exhibits CH and OH isotope effects of 2.83 and 2.06. These changes in isotope effect are inconsistent with a proton transfer from carbon and a hydride transfer from oxygen, but consistent with a hydride transfer from carbon and a proton transfer from oxygen.

Proton vs. Hydride Transfers.—The transition state R---H---R' for a proton or hydride transfer from one atom or group (R') to another (R)



is stabilized by overlap of orbitals on R, H and R'. Each R or R' groups furnishes a *p*-orbital or some hybrid of *s*- and *p*-orbitals (if the atom bonded to H is C, N, O, S or halogen) while hydrogen contributes its *s*-orbital. These three orbitals combine to give three molecular σ -orbitals.

In a hydride transfer between two electron-deficient atoms, the two electrons contributed by the hydride are accommodated in the σ -orbital of lowest energy. These two electrons cement the three nuclei together in a strong, short, highly covalent and relatively non-polarizable bond. This bonding orbital is shown as σ_1 in Fig. 1 for the particular example of pure *p*-orbitals on R and R' and an exactly linear bond. The signs refer to the signs of the component atomic orbital wave functions, not to charge, which is always negative except at the three nuclei. Boranes have similar (but non-linear and more stable) bonds with a bridging hydride between two borons.

In a proton transfer, two additional electrons must be fitted in, as in hydrogen difluoride ion or other hydrogen bonds, because R is now a nucleophilic center supplying another pair. Because there is no more room in the bonding orbital, they must occupy what would be a non-bonding orbital if repulsion between the orbitals on R and R' were negligible. Actually it is an antibonding orbital (σ_2 of Fig. 1) because R---H and H---R' bonds are short compared to bonds not involving hydrogen; hence the R-R' distance is generally less than the sum of van der Waals radii of the two closest atoms in R and R'. The resulting repulsion of these two electron clouds when σ_2 is occupied should lead to weaker, longer, more ionic and more polarizable bonding between R, H and R'.⁴

(1) Supported in part by the National Institutes of Health under Research Grant RG-3711 (C2), the Atomic Energy Commission under Contract No. AT(30-1)-905, and an Ethyl Corporation Fellowship to R. A. W.

(2) Cf. Part II, C. G. Swain, R. F. W. Bader, R. M. Esteve, Jr., and R. N. Griffin, *J. Am. Chem. Soc.*, **83**, 1951 (1961).

(3) For complete experimental data, cf. R. A. Wiles, Ph.D. Thesis in Organic Chemistry, M.I.T., October, 1957.

Measured O—O bond distances for various O---H—O hydrogen bonds are generally greater than the sum of two normal covalent OH bonds ($2 \times 1.00 = 2.00$ Å.) but less than twice the van der Waals radius of oxygen ($2 \times 1.40 = 2.80$ Å.). There are wide variations: cf. 2.40 Å. in acetamide hemihydrochloride and 2.76 Å. in ice.⁵ In contrast, covalent OH or CH bonds are generally constant to ± 0.04 Å. This extreme variability in over-all length is characteristic of proton bonds between two nucleophilic atoms. Because these bonds are long and relatively ionic (as a result of σ_2 antibonding) the changes in bond length and force constant with structure are large. Electron supply to either end shortens the over-all length because increased electron density decreases inter-nuclear repulsions, and the bonding of σ_2 outweighs the antibonding of σ_2 . With strong electron-supplying substituents a proton bond between two electron-rich atoms may even have higher force constants for its bending vibrations than a corresponding hydride bond between two electron deficient atoms. This would be a stronger bond in spite of being a longer bond. Hydride- and proton-transfer transition states in similar systems with the same force constants and hydrogen isotope effect have different electron distributions. In a proton transfer transition state, the electron density is higher both relatively and absolutely on R and R', these groups are farther apart, and the distance and force constants are much more sensitive to substituents because the antibonding makes energy a weak function of distance.⁶

(4) P. D. Bartlett and F. A. Tate, *J. Am. Chem. Soc.*, **75**, 91 (1953) previously suggested that most proton bonds are relatively weak and largely coulombic compared to hydride bonds.

(5) For refs., cf. K. Nakamoto, M. Margoshes and R. E. Rundle, *ibid.*, **77**, 6480 (1955), and L. Pauling, "The Nature of the Chemical Bond, 3rd. ed., Cornell Univ. Press, Ithaca, N. Y., 1960, p. 485.

(6) An alternative description may be given in terms of the treatment of proton affinities by Longuet-Higgins.⁷ His approach considers the change in energy Φ as a positive charge (λ) is built up by degrees from zero to +1 at the point where the hydrogen is to be placed. The imaginary R---R' system of a hydride transition state can be shown by perturbation theory to have a proton affinity even though it is neutral. However the value of $\partial\Phi/\partial\lambda$ will be very slight corresponding to a "tight" transition state with little variation of isotope effect with structure. The R---R' system of a proton transition state has a much larger $\partial\Phi/\partial\lambda$ because of its negative charge and extra pair of electrons, and the possibilities of further electron supply from R and greater electronic reorganization. This corresponds to a wide range

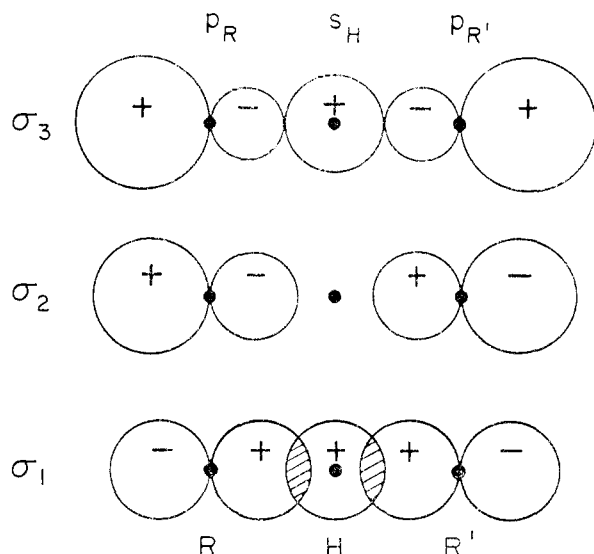


Fig. 1.—Molecular orbitals for proton or hydride transfers.

A k_H/k_D (or k_H/k_1) isotope effect which is strongly affected by introduction of electron-supplying or electron-attracting substituents in R or R' indicates that a polar hydrogen transfer is a proton transfer; an isotope effect almost independent of substituents in R or R' indicates a hydride transfer.

Experimental data on hydrogen transfer reactions at the present time support this proposed distinction between proton and hydride transfers on the basis of variability of hydrogen isotope effect with structure. Proton transfer isotope effects vary over a wide range, from 0.84 to 11.7 for k_H/k_D for transfers between C and O.⁹ For simple hydride transfers from C to C, the values observed in several systems range only from 1.8 to 2.6.^{10,11} Values of 7 for the oxidation of alcohols by diazonium ions¹² were cited¹³ to show that larger values can occur. However these values are for tritium, not deuterium, and it is not certain whether these are hydride transfers or hydrogen atom transfers.

The experimental results to be reported in this and the following paper also appear to be sufficiently extreme to warrant the distinctions drawn between proton and hydride mechanisms, since the variation of hydrogen isotope effect with substituents in each case is either unexpectedly large or else so small as to be within experimental error. This measurement of sensitivity of isotope effect to substituents may in time prove to be a useful general tool if results continue to fall into two distinct groups. Of course, the utility of any dual classification can be undermined by borderline cases. When R and R' are conjugated systems,

of electron densities about the proton and of isotope effects. Correlations between electron density and the force constant for a bond involving a hydrogen atom are well supported.⁸

(7) H. C. Longuet-Higgins, *Rec. trav. chim.*, **75**, 825 (1956).

(8) J. R. Platt, *J. Chem. Phys.*, **18**, 932 (1950); H. C. Longuet-Higgins and L. H. Brown, *J. Inorg. & Nuclear Chem.*, **1**, 60 (1955).

(9) K. B. Wiberg, *Chem. Revs.*, **55**, 723 (1955); R. P. Bell, "The Proton in Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1959, p. 201.

(10) K. B. Wiberg, *J. Am. Chem. Soc.*, **76**, 5371 (1954).

(11) P. D. Bartlett and J. D. McCollum, *ibid.*, **78**, 1441 (1956).

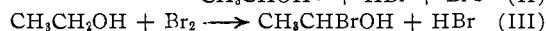
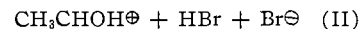
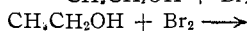
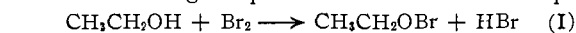
(12) L. Melander, *Arkiv. Kemi*, **3**, 525 (1951).

(13) K. B. Wiberg, *Chem. Revs.*, **55**, 727 (1955).

additional bonding and antibonding orbitals are involved, and these may possibly lead to smaller differences between proton and hydride transfers. If in the future a substantial number of intermediate sensitivities are found experimentally, this approach must be abandoned for distinguishing between proton and hydride transfers. However, the Hammett ρ for the isotope effect may then still serve as a measure of the *proton character* of hydrogen in a transition state in the way that bond energies are used to measure ionic character of a particular bond or the Hammett ρ for the rate is used to measure SN1 character of a particular solvolysis of a benzyl or trityl compound.

Previous Work on Oxidation of Alcohols by Bromine.—Previous kinetic studies have been concerned primarily with ethanol ($Z = H$, $R = H$). Bugarszky found that the oxidation of a 1% solution of ethanol in water at 25° gave acetic acid.¹⁴ The reaction was first order in ethanol and first order in free bromine; tribromide ion was unreactive. The reaction was markedly slower in less polar solvents (carbon tetrachloride or carbon disulfide).

Farkas and co-workers established that acetaldehyde is formed as an intermediate, but has a larger rate constant for oxidation than ethanol.¹⁵ The rate of oxidation of ethanol was independent of acidity and no significant amount of organically bound bromine was produced from pH 1 to 3; at higher acidities, bromination of the intermediate (acetaldehyde) became a serious side reaction. They proposed three mechanisms, which may be characterized simply by giving their respective rate-determining steps. Mechanism I was pre-



ferred because alkyl hypochlorites were known to decompose to give aldehyde or ketone and hydrochloric acid.¹⁶ Ethyl hypochlorite had earlier been proposed as an intermediate in the formation of chloral from ethanol and chlorine.¹⁷ More recently mechanism I was also advocated by Levitt, who suggested that the oxidation of alcohols by a large number of oxidizing agents always proceeds with such esters as intermediates between the alcohol and the aldehyde or ketone.¹⁸

Kaplan proved that mechanism I is incorrect for oxidation of ethanol by bromine by showing that ethanol was oxidized 4.3 times more rapidly than ethan-1,1- d_2 -ol.¹⁹ Agreement between kinetically measured and competitively measured isotope effects was observed. Therefore the CH bond is broken in the rate-determining step and ethyl hypobromite plays no role in the oxidation of ethanol, either as the precursor of acetaldehyde or

(14) S. Bugarszky, *Z. physik. Chem.*, **38**, 561 (1901); **42**, 545 (1902); **71**, 705 (1910).

(15) L. Farkas, B. Perlmutter and O. Schächter, *J. Am. Chem. Soc.*, **71**, 2827, 2829, 2833 (1949).

(16) F. D. Chattaway and O. G. Backeberg, *J. Chem. Soc.*, **123**, 3000 (1923).

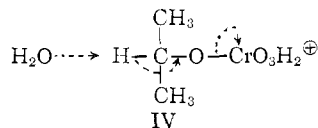
(17) F. D. Chattaway and O. G. Backeberg, *ibid.*, **125**, 1097 (1924).

(18) L. S. Levitt, *J. Org. Chem.*, **20**, 1297 (1955); L. S. Levitt and E. R. Malinowski, *J. Am. Chem. Soc.*, **77**, 4517 (1955).

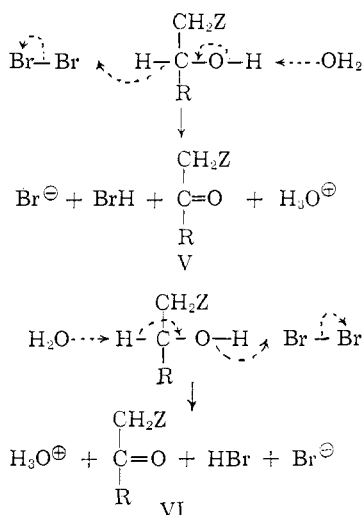
(19) L. Kaplan, *ibid.*, **76**, 4645 (1954); **80**, 2639 (1958).

as the oxidant of a second ethanol molecule. Kaplan favored mechanism II.

This assumption that a hydride rather than a proton was removed from the α -carbon contrasted sharply with the opinion of Westheimer and co-workers²⁰ that when 2-propanol (isopropyl alcohol) is oxidized with chromic acid in water at 25° it is a proton which is removed from carbon, as in mechanism IV.



The present problem is to distinguish between mechanisms V and VI ($Z = \text{H}$, $R = \text{H}$ or CH_3).



Mechanism V is intended to represent either a rate-determining *hydride transfer from carbon* followed by a fast proton removal from oxygen as in II or a partly concerted process in which the proton removal is not a completely separate subsequent step. VI is the closest analog of the chromic acid mechanism (IV) consistent with all of the data so far described. It is a concerted *proton transfer from carbon* and hydride transfer from oxygen. Neither the kinetic equation, isotope effects on a single alcohol (Z), nor the effect of substituents (Z) on the over-all rate distinguishes between V and VI. However, determining the effect of substituents on the isotope effect of the two alcoholic hydrogens one at a time does permit a distinction as shown below.

Substituent Effects on Isotope Effects in Oxidation of Alcohols by Bromine.—Tables I and II summarize our results. We used 2-propanol ($Z = \text{H}$, $R = \text{CH}_3$) rather than ethanol to avoid kinetic complications from a second stage of oxidation (from aldehyde to acid). The results con-

(20) F. H. Westheimer and Y. W. Chang, *J. Am. Chem. Soc.*, **63**, 438 (1959); G. T. E. Graham and F. H. Westheimer, *ibid.*, **80**, 3030 (1958), and eight earlier papers cited in their references 3-7 and 19; cf. also W. A. Mosher and D. M. Preiss, *ibid.*, **75**, 5605 (1953); J. Schreiber and A. Eschenmoser, *Helv. Chim. Acta*, **38**, 1529 (1955); H. Kwart and P. S. Francis, *J. Am. Chem. Soc.*, **77**, 4907 (1955); **81**, 2116 (1959); L. Kaplan, *ibid.*, **77**, 5469 (1955); J. Rocek and J. Krupicka, *Coll. Czech. Chem. Commun.*, **23**, 2068 (1958); W. A. Waters, *Quart. Revs. (London)*, **12**, 284 (1958); A. C. Chatterji and V. Anthony, *Z. physik. Chem. (Leipzig)*, **210**, 50 (1959).

TABLE I

OXIDATIONS OF 2-PROPANOL WITH BROMINE IN WATER AT 50°

$\text{C}_2\text{H}_5\text{OH}$, mM	Br_2 , mM	HClO_4 , mM	NaClO_4 , mM	NaBr , mM	$k \times 10^4$, $M^{-1} \text{sec.}^{-1}$
100	2.94	1.00	99	..	5.90
80	3.09	1.00	99	..	5.91
50	4.18	1.00	99	..	5.82
40	2.96	1.00	99	..	5.98
20	4.37	1.00	99	..	6.08
10	4.15	1.00	99	..	6.14
50	8.16	1.00	99	..	5.73
50	4.18	1.00	99	..	5.82
50	1.34	1.00	99	..	6.16
50	3.92	..	100	..	5.68
50	4.16	10.0	90	..	5.92
50	3.30	100	5.85
50	3.79	1.00	9	..	5.70
50	4.27	1.00	999	..	7.08
50	3.50	1.00	89	10	5.28
50	3.64	1.00	..	99	2.61
100 ^a	4.17	1.00	99	..	1.90 ^a
80 ^a	3.35	1.00	99	..	2.17 ^a
50 ^a	4.08	1.00	99	..	2.05 ^a
40 ^a	3.91	1.00	99	..	1.96 ^a
20 ^a	4.23	1.00	99	..	2.05 ^a
10 ^a	4.34	1.00	99	..	2.03 ^a
100 ^b	6.02	1.00	99	..	3.80 ^b
80 ^b	3.42	1.00	99	..	4.06 ^b
50 ^b	4.98	1.00	99	..	3.83 ^b
40 ^b	4.47	1.00	99	..	4.00 ^b
20 ^b	5.35	1.00	99	..	4.06 ^b
10 ^b	3.27	1.00	99	..	4.29 ^b

^a 2-Propan-2-*d*-ol. ^b 2-Propanol-*d* in D_2O .

TABLE II

OXIDATIONS OF 1-FLUORO-2-PROPANOL WITH BROMINE IN WATER AT 50°

C_2FH_5 OH , mM	Br_2 , mM	HClO_4 , mM	NaCl_4 , mM	NaBr , mM	$k \times 10^4$, $M^{-1} \text{sec.}^{-1}$
100	3.15	1.00	99	..	5.61
80	3.15	1.00	99	..	6.00
50	2.69	1.00	99	..	5.92
40	3.01	1.00	99	..	5.92
50	9.23	1.00	99	..	5.39
50	1.93	1.00	99	..	6.25
50	2.26	1.00	100	..	5.75
50	2.90	10	90	..	5.82
50	2.89	100	6.00
50	3.68	1.0	9	..	5.75
50	3.08	1.0	999	..	5.89
50	3.49	1.0	89	10	5.30
50	3.90	1.0	..	99	3.14
100 ^a	3.95	1.0	99	..	2.12 ^a
80 ^a	3.70	1.0	99	..	2.05 ^a
50 ^a	3.99	1.0	99	..	2.06 ^a
40 ^a	3.70	1.0	99	..	2.04 ^a
100 ^b	1.83	1.0	99	..	2.94 ^b
80 ^b	3.54	1.0	99	..	2.69 ^b
50 ^b	3.74	1.0	99	..	2.78 ^b
40 ^b	3.87	1.0	99	..	2.94 ^b

^a 1-Fluoro-2-propan-2-*d*-ol. ^b 1-Fluoro-2-propanol-*d* in D_2O .

firm previous results with ethanol in respect to kinetic order in alcohol and bromine (first order in each), and independence of rate on bromide ion (except insofar as it lowers the concentration of

bromine by forming tribromide ion) or hydrogen ion (from pH 1-3). The rate is also independent of ionic strength from 0.01 to 0.1 *M*. 1-Fluoro-2-propanol ($Z = F$, $R = CH_3$) is quite similar kinetically, indicating that it also proceeds by the same mechanism.

Note that all concentrations are given in millimoles per liter and that 2-propanol reacts about one thousand times faster than 1-fluoro-2-propanol. This substituent effect on the over-all rate shows that fluorine retards the hydride removal much more than it aids the proton removal, but does not indicate which hydrogen is which as is needed to distinguish between mechanisms V and VI. However, the substituent effect on the isotope effect can distinguish because it is possible to examine one hydrogen at a time.

The CH isotope effect (2.94 ± 0.1 for $Z = H$) is much larger than 1.0, showing that this bond is broken during the rate-determining step. With the substitution of the strongly electron-attracting fluorine atom for one of the methyl hydrogens, the CH isotope effect is unchanged within experimental error (2.83 ± 0.1 for $Z = F$); it certainly is not markedly affected by the fluorine. As discussed in the Introduction, this insensitivity is incompatible with mechanism VI but in accord with mechanism V. We conclude that this hydrogen is transferred as a hydride rather than as a proton.²¹

The OH isotope effect rises considerably with fluorine (1.49 for $Z = H$, 2.06 for $Z = F$). This change is not attributable to steric differences because H and F are of nearly the same size. It cannot be attributed to differences in zero-point vibrational energy in the ground state because the OH and CH stretching vibrations, which make the major contribution to the internal energy, are practically unchanged on introduction of the fluorine. For example, the difference in unassociated OH stretching frequencies of 2-propanol and 1-fluoro-2-propanol is less than 10 cm.^{-1} in 1% solution in CCl_4 and so could account for no more than a 2% change in rate. Furthermore the same small difference is observed in the OH stretching frequencies of the corresponding CD compounds. As discussed in the Introduction, this large change in isotope effect is incompatible with mechanism VI, but in accord with mechanism V. We conclude that this hydrogen is transferred as a proton rather than as a hydride.

The timing of the proton transfer from oxygen is indicated by the smallness of the OH isotope effect (1.49 for $Z = H$). If the proton were transferred during the rate-determining step, it would be difficult to explain such a small value. A primary hydrogen isotope effect can be this small only if the transition state is very asymmetric with respect

to the hydrogen. If the proton were practically completely transferred to the water, the isotope effect should be not less than about 2.8, the isotope effect associated with conversion of three HO bonds to HO^+ bonds.²² It should be greater than this to an extent depending on the partial negative charge on bromine and the contribution of the primary isotope effect. However, if the hydrogen is still on the alcohol, we have mechanism II, for which 1.49 is reasonable. Complete formation of bromide ion (solvated by three water molecules) should give a factor of 1.5; development of a full positive charge on the alcoholic oxygen should give a factor of 1.4.²² The resulting k_{H_2O}/k_{D_2O} isotope effect would be 2.1. Lesser charge development at the transition state would give an isotope effect nearer 1.0, as observed. With fluorine the isotope effect is enough larger (2.06 for $Z = F$) to suggest that the proton may have just begun to transfer to a water molecule at the transition state. Thus we conclude that proton transfer has not begun or has only barely begun at the transition state, corresponding to the extreme of mechanism V represented by mechanism II.

In the sense that it involves hydride rather than proton removal from carbon, mechanism V is similar to that of several previously studied oxidations, including (1) the Oppenauer oxidation of alcohols by ketones,²³ (2) the disproportionation of 2-propanol by aluminum chloride,²⁴ (3) the oxidation of alcohols by carbonium ions¹¹ and (4) the oxidation of benzhydrol by permanganate ion.²⁵

Two other oxidizing agents of high electrode potential, ceric and persulfate ions, have been shown²⁶ to oxidize alcohols in water solution by free radical mechanisms, which are excluded for all of the oxidations previously mentioned in this paper. In the presence of light the oxidations with bromine are accelerated, presumably also by a free radical mechanism (see end of Experimental section).

Experimental

Reactants.—The light water used in preparing the solutions was distilled from alkaline potassium permanganate. The heavy water was 99.5% D_2O from Stuart Oxygen Co.

The 2-propanol was Mallinckrodt analytical reagent grade and was distilled from calcium oxide before use; b.p. 82.5° , n_D^{25} 1.3739.

Because the physical properties of our fluorinated compounds disagreed with those reported in the literature, the details of our work are given below in some detail.

Epifluorohydrin was prepared as follows. A Pyrex 100-ml. 3-necked flask was fitted with a dropping funnel, a stirrer and a small distilling column with 6 in. of Podbielniak Heligrad packing, about 10 theoretical plates. In this flask was placed 58 g. (1 mole) of finely powdered potassium fluoride which had been dried for 1 week at 240° and 20 ml. of diethylene glycol which had been dried over calcium oxide and distilled; b.p. $244-245^\circ$. The mixture was heated to $170-180^\circ$ with an oil-bath and 70 g. of epi-

(21) It is a still unsolved question whether the bromine, hydride and carbon are roughly linear in the transition state, or triangularly arranged as suggested by E. S. Lewis and M. C. R. Symons, *Quart. Revs. (London)*, **12**, 246 (1958). Prof. A. Eschenmoser has suggested that bromine may complex with the alcoholic oxygen, followed by a 1,2-hydride shift from carbon to oxygen in the slow step. Another possibility is a hydride transfer from carbon to one of the bromine atoms within the complex. There is insufficient evidence to decide whether this complex is an intermediate or only a reversibly formed minor by-product. Therefore we favor the simpler mechanism without this extra intermediate.

(22) C. G. Swain and R. F. W. Bader, *Tetrahedron*, **10**, 182 (1960); C. G. Swain, R. F. W. Bader and E. R. Thornton, *ibid.*, **10**, 200 (1960); C. G. Swain and E. R. Thornton, two papers submitted for publication. These calculated values are for 25° rather than 50° , but would be expected to be less at 50° by less than a factor of two.

(23) W. Hüchel and H. Naab, *Ber.*, **64**, 2137 (1931); W. E. Doering and R. W. Young, *J. Am. Chem. Soc.*, **72**, 631 (1950).

(24) G. Baddeley and W. Pickles, *J. Chem. Soc.*, 3726 (1953).

(25) R. Stewart, *ibid.*, **79**, 3057 (1957).

(26) M. Ardon, *J. Chem. Soc.*, 1811 (1957); P. D. Bartlett and J. D. Cotman, Jr., *J. Am. Chem. Soc.*, **71**, 1419 (1949); K. B. Wiberg, *ibid.*, **81**, 252 (1959).

chlorohydrin (0.76 mole), b.p. 114–116°, was added at such a rate that the head temperature of the distilling column remained between 85 and 95° throughout the addition. The total time of addition was 3 hr. The product was collected as it formed. After all the epichlorohydrin had been added and the head temperature had dropped to 70°, 10 ml. of xylene was added to the reaction mixture to drive over the last trace of epifluorohydrin. The crude distillate was redistilled using the same column to give 21 g. of epifluorohydrin, b.p. 86–88° (lit.²⁷ b.p. 82–87°), n_{25}^{25}, d_{25}^{25} 1.3708, $d_{25}^{25}, 1.088$.

1-Fluoro-2-propanol was prepared from epifluorohydrin. Epifluorohydrin (20 g., 0.276 mole) was placed in a 500-ml., 3-necked flask along with 25 ml. of dry ether. The flask was fitted with a dropping funnel, stirrer and reflux condenser protected with a drying tube. The mixture was cooled with an ice-water-bath. Lithium aluminum hydride (0.071 mole) in 70 ml. of dry ether was added slowly. Total time of addition was 45 min. After the addition was complete the mixture was stirred for 15 min. The reaction mixture was hydrolyzed with 14 g. of sulfuric acid mixed with 50 g. of ice. The ether layer was separated and the water layer was extracted with three 25-ml. portions of ether. The combined ether layers were dried first over magnesium sulfate and finally over Drierite. Distillation through the small 6-in. column described earlier gave 9.38 g. of 1-fluoro-2-propanol, b.p. 99.7–100°, n_{25}^{25}, d_{25}^{25} 1.3727, $d_{25}^{25}, 1.017$. Gas chromatography indicated no 2-propanol to be present in the forerun nor 3-fluoro-1-propanol in the pot residue from the distillation.

Anal. Calcd. for C_3H_7FO : C, 46.15; H, 8.97. Found: C, 45.89; H, 9.11.

The α -naphthylurethan was recrystallized from 90–100° petroleum ether and melted at 107.8–108.4°.

Anal. Calcd. for $C_{14}H_{14}FNO_2$: C, 68.02; H, 5.67. Found: C, 68.07; H, 6.03.

A small sample of 1-fluoro-2-propanol gave 1-fluoro-2-propanone when oxidized with chromic acid. The ketone was isolated as its 2,4-dinitrophenylhydrazone, m.p. 132.8–134.0°. The melting point was undepressed when mixed with the 2,4-dinitrophenylhydrazone of 1-fluoro-2-propanone prepared in the next section.

1-Fluoro-2-propanone was prepared using the same apparatus as in the preparation of epifluorohydrin. The flask was charged with 58 g. (1 mole) of dry, finely powdered potassium fluoride and 20 ml. of diethylene glycol. This mixture was heated to 170–180° with an oil-bath and 35 g. (0.38 mole) of 1-chloro-2-propanone was added at such a rate that the head temperature of the distilling column remained between 75–90° throughout the addition. The total time of addition was 30 min. The product was collected as it formed. After all the 1-chloro-2-propanone had been added and the head temperature had dropped to 65°, 10 ml. of xylene was added to the reaction mixture to drive over the last traces of 1-fluoro-2-propanone. The crude distillate was redistilled using the same column to give 10–12 g. of 1-fluoro-2-propanone, b.p. 74–78°. The combined 1-fluoro-2-propanone collected from several of these reactions (53 g.) was distilled through a 12-in., vacuum jacketed column packed with sixteenth-inch single-turn stainless steel helices. About 20 g. of material boiled at 73°. This material separated into two phases. The remainder of the material boiled at 78–79°. Both fractions were combined again and dried over magnesium sulfate. Upon distilling through the same column no material distilled at 73°. Twenty-five grams of 1-fluoro-2-propanone was collected, b.p. 78–79°, n_{25}^{25}, d_{25}^{25} 1.3645, $d_{25}^{25}, 1.054$. The 2,4-dinitrophenylhydrazone recrystallized from 2-propanol melted at 134.2–135.4° (lit.²⁸ 118–120°, 134–135°).

Anal. Calcd. for $C_3H_5FN_4O_4$: C, 42.19; H, 3.52. Found: C, 42.46; H, 3.78.

The semicarbazone melted at 138–144° dec. (lit.²⁹ 132° dec.).

(27) G. Olah and A. Paulath, *Acta Chim. Acad. Sci. Hung.*, **3**, 431 (1953); *C. A.*, **49**, 2384 (1955).

(28) G. Olah and S. Kuhn, *Chem. Ber.*, **89**, 864 (1956); E. D. Bergmann and R. Ikan, *Chemistry & Industry*, 394 (1957); E. D. Bergmann and S. Cohen, *J. Chem. Soc.*, 2259 (1958).

(29) P. C. Ray, H. C. Goswami and A. C. Ray, *J. Indian Chem. Soc.*, **12**, 93 (1935); N. Fukuhara and L. A. Bigelow, *J. Am. Chem. Soc.*, **63**, 788 (1941).

1-Fluoro-2-propanol was also prepared from 1-fluoro-2-propanone. Sixteen grams (0.211 mole) of 1-fluoro-2-propanone in 30 ml. of dry ether was placed in a 200-ml., 3-necked flask fitted with a dropping funnel, a stirrer and a reflux condenser protected with a drying tube. The reaction vessel was cooled in an ice-water-bath and 1.5 g. (0.0395 mole) of lithium aluminum hydride dissolved in 70 ml. of ether was added over a period of 20 min. After being stirred for an additional 10 min., the mixture was hydrolyzed with a mixture of 7.5 g. of sulfuric acid and 50 g. of ice. The ether layer was separated and the water layer extracted with two 25-ml. portions of ether. The combined ether layers were dried over magnesium sulfate. The magnesium sulfate was removed and the product finally dried over Drierite. The ether was removed by distillation and the product was distilled through the small 6-in. column described earlier. The yield of 1-fluoro-2-propanol boiling at 99.8–100° was 5.3 g., n_{25}^{25}, d_{25}^{25} 1.3725, $d_{25}^{25}, 1.015$. This was the material used for kinetic runs. The α -naphthylurethan recrystallized from 90–100° petroleum ether melted at 108.6–110°. The mixed m.p. with α -naphthylurethan of the 1-fluoro-2-propanol prepared from epifluorohydrin was 107.2–108.8°. The 3,5-dinitrobenzoate recrystallized from water-ethanol melted at 108.6–109.8°.

2-Propanol-2-*d* was prepared by a method already described.³⁰ Use of 1.5 g. of lithium aluminum deuteride and 12 g. of acetone gave 5.98 g. of 2-propanol-2-*d*, b.p. 81.1–82.5°, n_{25}^{25}, d_{25}^{25} 1.3741.

Anal. Calcd. for C_3H_7DO : 12.50 atom-% D. Found: 11.56 atom-% D.

1-Fluoro-2-propanol-2-*d* was prepared by the same method as 1-fluoro-2-propanol. Use of 1.5 g. of lithium aluminum deuteride and 16 g. of 1-fluoro-2-propanone gave 4.20 g., b.p. 99.8–100.2°, n_{25}^{25}, d_{25}^{25} 1.3724.

Anal. Calcd. for C_3H_5DOF : 14.28 atom-% D. Found: 13.27 atom-% D.

Because of the widely differing properties of the 1-fluoro-2-propanol prepared here and that described in the literature, 2-fluoro-1-propanol was prepared for comparative purposes.

Ethyl α -fluoropropionate was prepared by combining 50 g. (0.275 mole) of ethyl α -bromopropionate, 25 g. (0.43 mole) of dry potassium fluoride and 25 g. of acetamide in a 200-ml., 2-necked flask. One neck was fitted with the small 6-in. distilling column described earlier and the other neck with a stirrer. The mixture was heated to 170°. The material distilled rapidly at 100–120° giving 21 g. of crude product. Redistillation through the same column gave 164 g. of ethyl α -fluoropropionate, b.p. 120–122° (lit.³¹ b.p. 122.5–123.0°), n_{25}^{25}, d_{25}^{25} 1.3747.

2-Fluoro-1-propanol was prepared by combining 16.4 g. (0.137 mole) of ethyl α -fluoropropionate with 25 ml. of dry ether in a 500-ml., 3-necked flask fitted with a dropping funnel, a stirrer and a reflux condenser protected with a drying tube. The solution was cooled with an ice-water-bath and 0.0685 mole of lithium aluminum hydride in 250 ml. of dry ether was added slowly over a period of 1 hr. Then water was added to the mixture to precipitate lithium aluminate and the ether layer separated. The lithium aluminate was washed with ether. The ether solutions were combined and dried over magnesium sulfate. Distillation through a 12-in. Holzman³² column gave 4.82 g. of 2-fluoro-1-propanol, b.p. 109–110°, n_{25}^{25}, d_{25}^{25} 1.3723, $d_{25}^{25}, 1.019$. The α -naphthylurethan recrystallized from 90–100° petroleum ether melted at 93.2–94.1°.

Anal. Calcd. for $C_{14}H_{14}FNO_2$: C, 68.02; H, 5.67. Found: C, 68.03; H, 6.19.

The 3,5-dinitrobenzoate recrystallized from water-ethanol melted at 68.9–69.9°.

The 1-fluoro-2-propanol described in the literature had a b.p. of 106–108°³³ or 107–108°³⁴ and gave a α -naphthyl-

(30) A. Leo and F. H. Westheimer, *J. Am. Chem. Soc.*, **74**, 4383 (1952).

(31) E. Gryszkiewicz-Trochimowski, A. Sporzynski and J. Wnuk, *Rec. trav. chim.*, **66**, 413 (1947).

(32) C. W. Gould, G. Holzman and C. Niemann, *Anal. Chem.*, **20**, 361 (1948).

(33) E. Gryszkiewicz-Trochimowski, *Rec. trav. chim.*, **66**, 428 (1947).

(34) I. L. Knunyants, O. V. Kildasheva and I. P. Petrov, *J. Gen. Chem., USSR*, **19**, 87 (1949).

urethan with m.p. 81–83°. Since these properties agree much more closely with those of our 2-fluoro-1-propanol, it seems likely that the opening of propylene oxide with anhydrous hydrogen fluoride in ether solution containing a trace of water gave 2-fluoro-1-propanol rather than the 1-fluoro-2-propanol reported.³⁴

Isolation of Products.—The oxidation of 2-propanol with bromine gives acetone. The reaction mixture was prepared by placing 100 ml. of water, 0.785 g. (0.013 mole) of 2-propanol, 1.22 g. (0.010 mole) of sodium perchlorate and 1 ml. (0.000119 mole) of 0.119 *M* perchloric acid in a 100-ml. flask. The reaction mixture was placed in the 50° bath and 0.156 g. of bromine was added. After the bromine color had disappeared, sodium hydroxide was added until the brom phenol blue end-point was reached. This sequence was repeated until 0.780 g. (0.0048 mole) of bromine had been added. After the last of the bromine had disappeared, 29 ml. of 2-propanol was added and the product was distilled through a 5-ft. Podbielniak Heligridd-packed column with about 100 theoretical plates. The fraction boiling at 72–79.5° was collected and added to 2,4-dinitrophenylhydrazine reagent.³⁵ The crystals were dried and weighed 0.8862 g. After one recrystallization from 2-propanol-water the crystals melted at 125.4–126.8°. The melting point when mixed with an authentic sample of acetone 2,4-dinitrophenylhydrazone was undepressed. The yield of acetone actually isolated as the 2,4-dinitrophenylhydrazone was 77%. After correcting for the solubility of the hydrazone in the solution in which it was made the yield was 93%.

1-Fluoro-2-propanol (1.56 g., 0.02 mole) was oxidized with 2.44 g. (0.020 mole) of bromine and 200 ml. of water in a 200-ml. flask, sealed and placed in a 50° bath in the dark for 7 days. The reaction mixture was mixed with 20 ml. of 2-methyl-2-butanol and distilled through the 5-ft. 100-plate Podbielniak column. The product boiling at 86–87.5° was collected until the distillate no longer gave a precipitate with 2,4-dinitrophenylhydrazine reagent. The dried crystals of 1-fluoro-2-propanone 2,4-dinitrophenylhydrazone weighed 0.1651 g. After two recrystallizations from 2-propanol the crystals melted at 131.3–133.6°. The melting point when mixed with an authentic sample of 1-fluoro-2-propanone 2,4-dinitrophenylhydrazone was undepressed. The yield of 1-fluoro-2-propanone actually isolated as the 2,4-dinitrophenylhydrazone was 66% of theory. After correcting for the solubility of the hydrazone in the solution in which it was made, the yield was 79%.

Kinetic Procedure.—The kinetic runs were all carried out at 49.95 ± 0.05°. Each kinetic run was made up in a 10-ml. volumetric flask from appropriate stock solutions. For runs containing 2-propanol, acetone and 1-fluoro-2-propanone, the flask containing the alcohol or ketone, sodium perchlorate, perchloric acid and enough water to make about 9 ml. of solution was placed in the constant temperature bath at least 15 min. before the reaction was started. To start the reaction, enough bromine water containing 0.002 ml. of bromine per ml., also at bath temperature, was drawn into a syringe and introduced into the reaction flask (final volume, 10 ml.). The time of addition of the bromine water was less than 1 second. The syringe used to introduce the bromine had a glass needle attached to the syringe by polyethylene tubing. The reactions were conducted in a darkroom with only a General Electric 100-watt 115–125 volt yellow incandescent bulb for light.

(35) N. D. Cheronis in A. Weissberger, "Technique of Organic Chemistry," Vol. VI, Interscience Publishers, Inc., New York, N. Y., 1954, p. 506.

In those runs containing 1-fluoro-2-propanol the runs were made up including the bromine at room temperature. The solutions were drawn into a syringe which was surrounded by an ice-water-bath. This syringe also had a glass needle attached to the syringe with polyethylene tubing. After the solution had cooled, 0.6-ml. samples were placed in cooled 1-ml. ampoules. It was found that in order to reduce the experimental error the ampoules had to be filled by inserting the glass needle all the way to the bottom of the ampoule before the solution was introduced. The ampoules were sealed and placed in bottles which had been wrapped in aluminium foil. These bottles were then placed in the constant temperature bath. Samples were removed from these bottles in the dark.

All of the runs were followed by taking samples from time to time. These samples were quenched by adding them to a 1% potassium iodide solution. The iodine thus formed was titrated to a starch-iodide end-point with sodium thiosulfate using a Gilmont ultramicroburet (Emil Greiner Co., no. G15395B). The sodium thiosulfate solution was stabilized with *n*-amyl alcohol and was standardized frequently against a standard solution of potassium iodate.

Some of the oxidations of 2-propanol were so fast that a sample withdrawn 30–50 sec. after the start had already undergone significant reaction. To determine the initial concentration of bromine in such cases, a plot of log (Br₂) vs. time was extrapolated back to zero time. Second-order rate constants were then evaluated by plotting log [(alcohol)/(Br₂)] vs. time and multiplying the slope of this line by 2.303/[(alcohol)₀ - (Br₂)₀] where subscript zero refers to zero time.

The loss of bromine by bromination of the ketones formed was negligible under most of the conditions used. From direct measurements of the rate of bromination of 0.125 *M* acetone and 0.137 *M* 1-fluoro-2-propanone, each with 0.100 *M* perchloric acid in water at 50°, the rate constants (*k*₂) corresponding to the equation

$$-d(\text{Br})_2/dt = k_2(\text{ketone})(\text{H}^+)$$

where 4.32 × 10⁻⁴ and 2.75 × 10⁻⁵ *M*⁻¹ sec.⁻¹, respectively. However, this bromination did prevent use of data on the oxidation of <0.040 *M* 1-fluoro-2-propanol (initial concentration) or the use of late points on some of the runs at higher concentrations.

The equilibrium constant for formation of tribromide ion from bromide and bromine ion appears to be about 10 *M*⁻¹ at 50°. It is 16.7 *M*⁻¹ at 25°.³⁶ Although the tribromide ion was unreactive, no correction was made for it because the initial concentration of bromine was sufficiently low in most cases so that the error introduced was 4% or less. This error nearly disappears when ratios of rate constants at approximately the same initial concentration of bromine are compared.

Addition of 0.4 g. of no. 7740 Pyrex glass wool to typical runs with 2-propanol and 1-fluoro-2-propanol failed to change the rate constants (5.92 × 10⁻² and 5.87 × 10⁻³), indicating absence of heterogeneous catalysis by glass.

Photocatalysis of the oxidation of ethanol by bromine led to erratic and non-reproducible results in preliminary work, especially at low concentrations (0.01 *M*) of ethanol. The catalysis was greatest in the daytime and almost disappeared at night under fluorescent lights. To avoid it, the runs that followed were done in a dark room where only a yellow incandescent bulb was used.

(36) R. O. Griffith, A. McKeown and A. G. Winn, *Trans. Faraday Soc.*, **28**, 101 (1932); D. B. Scaife and H. J. V. Tyrrell, *J. Chem. Soc.*, 386 (1958).