[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY, HARVARD UNIVERSITY]

Substitution and Elimination Rate Studies on Some Deutero-isopropyl Bromides

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The rates of the bimolecular substitution and elimination reactions of α-deutero- and β-hexadeutero-isopropyl bromides in *ca.* 1 *N* alcoholic sodium ethoxide have been determined. These are compared with the rates observed for ordinary isopropyl bromide. The substitution rate is the same for all three compounds. The elimination rate is the same for the ordinary and the α-deutero compounds while the β-deutero one eliminates more slowly than the protium analog by a factor of 6.7. It is concluded that these results are in full accord with the predictions of the familiar S_N2 and E2 mechanisms.

It has been proposed by Hughes, Ingold and coworkers[2] that the bimolecular elimination reaction (E2) proceeds by a rate-determining attack of the base on a β-situated hydrogen atom while the electronegative group X separates simultaneously with its bonding electrons

$$\text{Y:} + \text{H-CR}_2\text{—CR}_2\text{-X} \longrightarrow \text{YH}^+ + \text{CR}_2\text{CR}_2 + \text{X}^-$$

This scheme has enabled the considerable body of evidence collected on this reaction to be consistently explained.

An obvious corollary of this mechanism is that the bimolecular elimination and the bimolecular substitution (S_N2) which generally accompanies it are two competing, concurrent, independent reactions. It appeared that interesting evidence concerning the validity of the E2 mechanism could be obtained by determining the isotope effect on the reaction rate when the α- or β-hydrogen atoms were replaced by deuterium. It has been established from theoretical considerations and amply demonstrated by a number of experimental examples[3-5] that a reaction which involves the removal of a hydrogen atom in its rate-determining step will show a marked difference in rate for removal of protium, deuterium or tritium. This consideration arises from the difference in zero point energies of bonds involving the isotopically different atoms. Thus the E2 mechanism predicts that the rate of the elimination reaction of β-hexadeutero-isopropyl bromide will be slower than the corresponding rate for the protium analog. However, the rate effect of an α-deuterium substitution should be negligible. The accompanying substitution reaction rate should be essentially independent of any deuterium substitution.

Acetone-d_6 was made by exchanging acetone with successive samples of deuterium oxide. This material was then reduced to β-hexadeutero-isopropyl alcohol and converted to the alkyl bromide. α-Deutero-isopropyl alcohol was made by the reduction of acetone with lithium aluminum deuteride. From the analyses and the infrared spectra of the various compounds together with the kinetic behavior of the bromides, it seems certain that no spurious isotope exchanges took place in the reduction and bromination reactions.

The method of kinetic analysis was essentially that described by Dhar, Hughes and Ingold.[6] The reaction was carried out in sealed tubes at 25.0°. The total reaction was followed by titration of developing bromide ion using the Volhard method. At the end of the reaction the olefin fraction was determined by the reaction with bromine in chloroform. The over-all bimolecular rate constant obtained for isopropyl bromide (2.82×10^{-6} l./mole/sec.) agreed well with that observed by Dhar, Hughes and Ingold[6] (2.95×10^{-6}). However the olefin fraction here reported (0.625) is definitely smaller than that observed by the above authors (0.82) although it seems to be more in line with the value obtained at 55° (0.79) by Hughes, Ingold, Masterman and McNulty.[7]

The correction factor for losses in the extraction analytical procedure for propylene was determined by analyzing sealed vials of known volume containing pure propylene gas. Some sealed vials containing propylene were analyzed also by direct reaction with bromine in chloroform. This method always gave within 1% of the value obtained from volume calculations. The correction factor for extraction losses was 1.07 which is essentially the same as that used by Dhar, Hughes and Ingold.[6]

Table I gives the deuterium analyses in atoms of deuterium per molecule for the isopropyl bromides and the intermediates isolated in their preparation. Experiment number 1 was done on only partially exchanged acetone, while in number 2 acetone which had been equilibrated six times with three molar equivalents of deuterium oxide was used. In experiment number 3, ordinary acetone was reduced with lithium aluminum deuteride.

TABLE I

DEUTERIUM ANALYSES (IN ATOMS PER MOLECULE)

Expt. no.	Acetone	Isopropyl alcohol	Isopropyl bromide Uncor.	Isopropyl bromide Corrected[a]	Position
1	3.02(?)	3.21[b]	3.30	3.40	β
2	5.84	5.24[b]	5.54	5.91	β
3	0.00	0.970	0.977	0.977	α

[a] Corrected in cases 1 and 2 for the presence of a small amount of ethyl bromide (see text). [b] Not corrected for the presence of a small amount of ethyl alcohol.

As is shown in Table II the kinetic runs gave good second-order rate constants. The zero point

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[2] For the latest discussion, with complete references, of the present state of elimination reaction theory see M. L. Dhar, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Maw and L. I. Woolf, *J. Chem. Soc.*, 2094 (1948).

[3] O. Reitz, *Z. physik. Chem.*, **A179**, 119 (1937); **A184**, 429 (1939).

[4] For an interesting example of a large negative isotope effect see H. Gilman, G. E. Dunn and G. S. Hammond, THIS JOURNAL, **73**, 4499 (1951).

[5] F. H. Westheimer and N. Nicolaides, *ibid.*, **71**, 25 (1949).

[6] M. L. Dhar, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.* 2058 (1948).

[7] E. D. Hughes, C. K. Ingold, S. Masterman and B. J. McNulty, *ibid.*, 899 (1940).

TABLE II

KINETIC DATA FOR THE BIMOLECULAR REACTIONS OF ORDINARY AND DEUTERATED ISOPROPYL BROMIDES IN ALCOHOLIC SODIUM ETHOXIDE

Run	1	2	3	4
Number of atoms of D	3.40	5.91	0.98	0.00
Position of D	β	β	α	
(NaOEt) in mole/l.	1.09	1.05	1.11	0.997
Total bimolecular reaction rate constants (units, 10^{-6} l./mole/sec.) for each point up to 70% completion	1.95	1.10	2.78	2.83
	1.91	1.20	2.76	2.83
	1.92	1.26	2.73	2.80
	1.89	1.24	2.72	2.78
	1.94	1.21	2.76	2.72
	2.05	1.23	2.77	2.88
	1.97	1.23	2.76	2.78
	1.92	1.25	2.68	2.79
	1.97	1.31	2.68	2.94
	1.84		2.74	2.82
	1.84		2.72	2.93
	2.04			
Average k_2	1.92	1.23	2.74	2.82
Olefin fraction	0.461	0.24	0.612	0.625
$k_{S_{N2}}$	1.03	.94	1.06	1.06
k_{E_2}	0.89	.29	1.68	1.76

for each run was determined from the intercept of the best straight line from the plot of $\frac{1}{(\text{NaOEt})} \log \frac{(\text{Br}^-)_{\text{inf}}}{(\text{Br}^-)_{\text{inf}} - (\text{Br}^-)_t}$ *versus* time. In runs 1 and 2 this intercept showed a small but appreciable deviation from the corresponding zero titration. Purification of the solvent, diethyl carbitol, used in the lithium aluminum hydride reductions in runs 3 and 4, by vacuum distillation from a slight excess of lithium aluminum hydride eliminated the deviation of the zero point in those runs. It is probable therefore that the deviation observed in runs 1 and 2 was due to the presence of a small amount of acetaldehyde or ethyl alcohol in the diethyl carbitol. This led to contamination of the final product in runs 1 and 2 with some ethyl bromide which, due to its very rapid rate of reaction relative to isopropyl bromide,[6] would only result in the displacement of the intercept from zero. Using this deviation of the intercept from the zero point the amounts of ethyl bromide impurity were calculated to be (in moles per cent.): sample 1, 3.8; sample, 2, 8.3. Since ethyl bromide gives a very low olefin fraction[6] the observed value for the olefin fraction in run 2 (0.224) was corrected to 0.24. As is indicated in Table I, it was necessary to correct the deuterium analyses of bromides 1 and 2 for the presence of the indicated amount of ethyl bromide.

Table II also gives the average over-all rate constant for each compound with the olefin fractions observed. The total rates are resolved into S_N2 and E2 rates in each case and the amount and position of deuterium substitution is given. The deviation of the points from the average value is over 0.05 rate unit in only about 20% of the cases including, in all runs, reaction to over 70% of completion. The variation of the values between different runs, including those due to the salt effect of slight changes in concentration of sodium ethoxide, should be less than 0.1 rate unit. The olefin fractions were reproducible to within ±2%. It is obvious that within these limits the α-deutero compound gives the same results as ordinary isopropyl bromide. Also, the substitution rate constants are experimentally the same in all four cases studied. It is not thought that the apparent slight effect of β-deuteration on the substitution rate is significant enough to allow speculation as to its origin. This very interesting question is one of the objects of further experiments now under way. On the other hand it is clear that the elimination rate constant is cut down severely by β-deuteration. If one makes the assumption that each protium and deuterium atom was eliminated at its own characteristic rate regardless of whether the other β-hydrogens were protium or deuterium, then it is possible to calculate the elimination rates for partially deuterated bromides. From the E2 rate for isopropyl bromide the rate for elimination of one hydrogen was 1.76/6 or 0.293. Then by subtracting the E2 rate due to the 0.09 atom of protium (0.03) in the bromide of run 2, 0.26 is obtained as the E2 rate for 5.91 deuterium atoms. This is 0.044 for each deuterium atom. This gives a rate ratio of 0.293/0.044 or 6.7 for the relative reactivity of protium and deuterium in the elimination reaction. This is very close to the rate ratio of about six reported by Westheimer and Nicolaides[5] for the oxidation of isopropyl and α-deutero-isopropyl alcohols.

Using the rate constants for hydrogen and deuterium elimination and combining them in the proper proportion one can calculate the expected rate for the partially deuterated bromide used in run 1

$$\begin{array}{lcl} \text{D elimination rate} + \text{H elimination rate} & = & \text{total E2 rate} \\ (3.40 \times 0.044) \quad + (2.60 \times 0.293) & = & 0.92 \end{array}$$

This figure compares as favorably as could be expected with the 0.89 actually observed for the E2 rate in run 1.

It being established that the β-hydrogen is involved in the rate-determining step of the elimination it is interesting to see what evidence there is that the bromide ion is lost in this same step. Skell and Hauser[8] have shown, in the elimination of HBr from β-phenylethyl bromide by sodium ethoxide, that the loss of the bromide ion is not preceded by a fast step involving the loss of a proton because the bromide did not undergo isotope exchange with ethanol-*d* in the presence of sodium ethoxide. This evidence means of course that each molecule that loses a proton must also lose the bromide ion, but it does not make it certain that both ions are lost simultaneously. It is still admissible under the evidence that the proton could be lost in a slow step with the bromide ion being lost in a subsequent fast step. However, in the cases being considered this behavior would not seem likely because there is little reason to believe that the beta proton would be labile if its loss were not assisted by simultaneous olefin formation. It is also inherent in the theory of the effect of alkyl substitution on the rate of elimination, including the orienting effects summarized by the Saytzeff

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(8) P. S. Skell and C. R. Hauser, THIS JOURNAL, **67**, 1661 (1945).

rule, that the double bond be partially developed in the transition state of the rate-determining step.

The conclusion that, in the case of bimolecular hydrogen halide elimination from alkyl halides, the two ions are lost simultaneously in the rate-determining step seems therefore to be fairly well founded. It is also clear from this work that the bimolecular substitution and elimination are essentially independent reactions proceeding simultaneously.

The predictions of the familiar Hughes-Ingold S_N2 and E2 mechanisms for these reactions are therefore borne out in detail.

Experimental

Kinetic Method.—A series of twenty-five 15 × 125-mm. clean, dry Pyrex test-tubes were drawn down near the open end to a diameter of about 6 mm. Each of these tubes was flushed out with dry nitrogen before a sample of 2.00 ml. of an approximately 0.1 molar solution of isopropyl bromide in absolute ethanol was measured in with an automatic pipet. Each tube was then in turn cooled to −80° while 2.00 ml. of a sample of *ca.* 2 *N* sodium ethoxide in ethyl alcohol was slowly run in, and then the tube was quickly sealed off. The tubes were successively placed in wire holders and stored at −80°. At zero time for the kinetic run the tubes were immersed in the 25° bath with vigorous initial shaking to mix the reactants and reduce the warm-up time. The zero titration was obtained by analyzing two or three tubes which were not previously taken from the −80° bath. At appropriate time intervals the tubes were removed and analyzed by titration for bromide ion. The total amount of alkyl bromide present was determined by averaging the results of several "infinity" tubes which had been allowed to stand 12 to 24 hours at 100°. The concentration of sodium ethoxide was determined by titrating several aliquots of the ethanol solution. The base was present in more than tenfold excess so that the reactions were pseudo-first order. The plot of $\frac{1}{(\text{NaOEt})} \log \frac{(\text{Br}^-)_{\text{inf}}}{(\text{Br}^-)_{\text{inf}} - (\text{Br}^-)_t}$ (where (NaOEt) is the concentration of sodium ethoxide in moles per liter, $(\text{Br}^-)_{\text{inf}}$ is the concentration of bromide ion in the infinity tubes and $(\text{Br}^-)_t$ is the concentration of bromide ion in the tube removed at time *t*) *versus* time gave good straight lines.

Determination of Bromide Ion.—The tube was removed from the 25° bath and wire holder and cleaned with distilled water. It was then placed in a 250-ml. heavy-walled Pyrex separatory funnel with 100 ml. of 2.5 *N* nitric acid and 60 ml. of reagent grade ether. Vigorous shaking of the funnel caused the tube to shatter and quenched the reaction. The nitric acid layer was run into a known amount of standard silver nitrate solution always present in excess. The amount of excess was determined by back titration with sodium thiocyanate using ferric ammonium sulfate as the indicator. The concentration of the bromide ion or the total amount of alkyl bromide reacted was then the difference between the amount of silver nitrate solution which reacted with the sample and that which reacted with the zero sample. This figure is most easily expressed in the equivalent number of ml. of standard sodium thiocyanate.

Olefin Determinations.—When the kinetic run was 70 to 100% complete six to eight tubes were removed and chilled to −80°. The total reaction at this time was determined by estimation of bromide ion in two or three tubes. The amount of olefin present was determined for four or five samples as follows. The tube was cleaned and placed in a 250-ml. heavy-walled Pyrex separatory funnel with 100 ml. of reagent grade chloroform and 30 ml. of 1 *N* aqueous hydrochloric acid which had been cooled below 0°. The tube was smashed by shaking the funnel and then the chloroform layer was run into a 250-ml. glass-stoppered bottle containing 5 g. of powdered C.P. anhydrous calcium chloride. The chloroform was dried by shaking the bottle. The solution was cooled to *ca.* −15° and then 10.00 ml. of an approximately 0.06 *N* standard bromine in CCl_4 solution was added. The bottle was allowed to stand in an ice-bath for one-half hour before 20 ml. of 2 *N* hydrochloric acid and 2 g. of C.P. potassium iodide were added. The liberated iodine was titrated with standard sodium thiosulfate solution. The amount of olefin present was calculated from the difference between the amount of bromine used by the sample and that used by the zero sample. This quantity divided by the total amount of reaction gave the olefin fraction.

Chloroform, instead of carbon tetrachloride, was used as a solvent because bromine additions seem to be favored by the medium of higher dielectric constant. Standard bromine solutions were made up in carbon tetrachloride because this solution is much more stable than bromine in chloroform. Experience showed that best results were obtained when the blank reaction (determination using no sample except 4 ml. of ethanol) consumed no bromine. If this condition was not met, new chloroform and a new bromine solution were used.

Preparation of the Isopropyl Bromides.—A sample of 5 g. of acetone was mixed with 5 g. of deuterium oxide and 0.1 g. of sodium hydroxide and allowed to stand for 36 hours at room temperature. Then the acetone was fractionally distilled into another sample of basic deuterium oxide and the process was repeated until the acetone had been exchanged with six successive samples of deuterium oxide. The first sample of acetone was followed down the series by a second and a third. The first sample of acetone, 4.0 g. (0.069 mole), after recovery from the sixth exchange was reduced by a slurry of 1.0 g. (0.025 mole) of lithium aluminum hydride in 50 ml. of diethyl carbitol.[9] The isopropyl alcohol, 3.0 g. (0.05 mole), which was distilled from the reduction reaction mixture was treated with 8 g. (0.03 mole) of phosphorus tribromide dropwise at −10°. After standing overnight, 3.6 g. (0.03 mole) of isopropyl bromide was recovered by distillation, washed twice with cold sulfuric acid, dried with potassium carbonate, redistilled and used for kinetic run 2. The third sample of acetone was recovered after the third exchange and converted to isopropyl bromide in the manner described above. This was the material used in kinetic run 1. The α-deutero-isopropyl bromide used in run 3 was made by reducing ordinary acetone with lithium aluminum deuteride and converting the product to the alkyl bromide by the above procedure.

Deuterium Analyses.—The deuterium analyses were done by combustion of the compounds and purification of the resulting water by the method of Keston, Rittenberg and Schoenheimer.[10] The deuterium oxide concentration of the pure combustion water was determined in a gradient density tube which was set up and used as described by Anfinsen.[11] The standard samples were stored under hypodermic stopples and withdrawn for use with a hypodermic needle attached by means of a Leur joint to the dropping pipet. The gradient covered the 0 to 14 mole per cent. deuterium oxide range. Samples more concentrated than this were diluted with the corresponding protium compound before combustion and a dilution factor was used in calculating the

TABLE III

INFRARED BANDS IN THE C–D STRETCHING REGION SHOWN BY SEVERAL DEUTERATED ORGANIC COMPOUNDS

Compound	Bands Wave length, μ	Intensity
Acetone-d_6	4.50	Weak
	4.60	Weak
β-Hexadeutero-isopropyl alcohol	4.55	Strong
	4.75	Medium
	4.90	Medium
α-Deutero-isopropyl alcohol	4.70	Strong
	4.80	Strong
β-Hexadeutero-isopropyl bromide	4.55	Strong
	4.75	Medium
	4.90	Medium
α-Deutero-isopropyl bromide	4.50	Very weak
	4.62	Medium
	4.70	Very weak

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[9] R. F. Nystrom, W. H. Yanko and W. G. Brown, THIS JOURNAL, **70**, 441 (1948).

[10] A. S. Keston, D. Rittenberg and R. Schoenheimer, *J. Biol. Chem.*, **122**, 227 (1937).

[11] C. Anfinsen in O. W. Wilson, A. O. C. Nier and S. R. Reimann's "Preparation and Measurement of Isotopic Tracers," J. W. Edwards, Ann Arbor, Michigan, 1946, pp. 61–65.

results. The analytical results were in atoms per cent. deuterium in the compound and were converted into atoms of deuterium per molecule by dividing by 100 and multiplying by the total number of hydrogen and deuterium atoms in the molecule.

Infrared Measurements.—Infrared spectrograms were taken on carbon tetrachloride solutions of all of the organic deuterium compounds used with a Baird double-beam recording infrared spectrophotometer. Table III gives a summary of the bands observed in the C–D stretching region.

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CAMBRIDGE, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND LABORATORY FOR NUCLEAR SCIENCE AND ENGINEERING, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

A Molecular Orbital Treatment of the Ionization Equilibria of Triarylchloromethanes

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The experimental free energies of ionization of triarylchloromethanes in liquid sulfur dioxide were found to be a smooth function of the increase in resonance energies attending the ionization as calculated by the simple LCAO molecular orbital method.

The correlation of experimental reactivities of π-electron systems with molecular orbital calculations has recently been reviewed by Brown.[2] The simple Linear Combination of Atomic Orbitals (LCAO) molecular orbital method has found qualitative success in the treatment of such systems as orientation in aromatic substitution,[3] relative rates of Diels–Alder reactions[4] and the reaction of double bond systems with osmium tetroxide.[2,5]

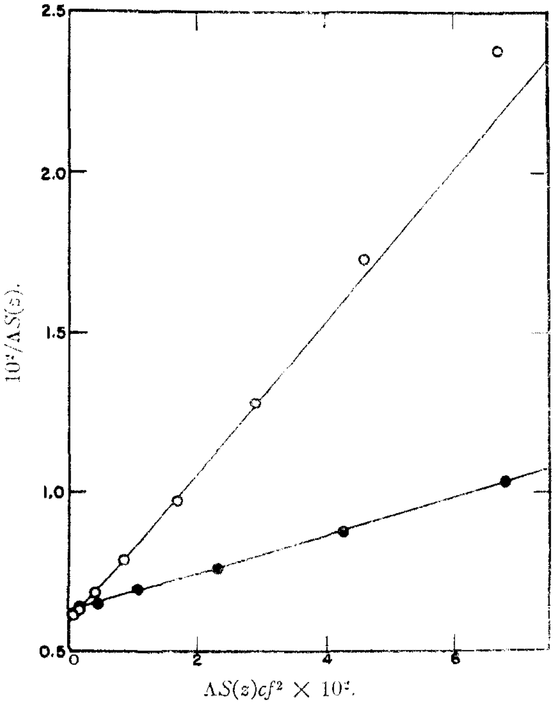

Fig. 1.—Shedlovsky plots for α-naphthyldiphenylchloromethane, ●, and β-naphthyldiphenylchloromethane, O, from the data of Ziegler and Wollschitt.[8]

Unfortunately, there has been a lack of suitable experimental data for quantitative comparison with the results of molecular orbital calculations. However, the recent work of Lichtin and Bartlett[6] and of Lichtin and Glazer[7] provides an excellent opportunity for an experimental test: these authors measured the extent of ionization of triarylchloromethanes in liquid sulfur dioxide, expressing their results in terms of an experimental free energy. While these free energy values are not those of the true equilibrium, $R_3CCl \rightleftarrows R_3C^+ + Cl^-$, because of significant ion-pair association, the dissociation of the ion pairs is approximately constant for a related series of compounds and the experimental free energies are quantitative measures of the tendency of the triarylchloromethanes to ionize. Among the compounds measured, those which are amenable to simple LCAO calculation are triphenylchloromethane and its mono-*m*-phenyl and mono-*p*-phenyl derivatives. In addition, the earlier data of Ziegler and Wollschitt[8] were used to calculate the experimental free energies for di-*p*-biphenylylphenyl-,[7] tri-*p*-biphenylyl-[7] and tri-*m*-biphenylylchloromethanes.[9] The data of Ziegler and Wollschitt were used to construct Shedlovsky plots for α-naphthyldiphenylchloromethane and β-naphthyldiphenylchloromethane in the manner detailed by Lichtin and Bartlett.[6] The second approximation Shedlovsky plots for these compounds are reproduced in Fig. 1. All of the experimental free energies (ΔF) are listed in Table I.

Because of its extended conjugated system, a triarylmethyl cation possesses greater resonance energy than its derived chloride. One would expect, *a priori*, that as this difference in resonance energy increased, the extent of ionization would increase and that the experimental free energy

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(2) R. D. Brown, *Quart. Rev.*, **6**, 63 (1952).

(3) G. W. Wheland, THIS JOURNAL, **64**, 900 (1942); J. D. Roberts and A. Streitwieser, J., *ibid.*, **74**, 4723 (1952).

(4) R. D. Brown, *J. Chem. Soc.*, 691 (1950), 3129 (1951).

(5) R. D. Brown, *ibid.*, 3249 (1950).

(6) N. N. Lichtin and P. D. Barltett, THIS JOURNAL, **73**, 5530 (1951).

(7) N. N. Lichtin and H. Glazer, *ibid.*, **73**, 5537 (1951).

(8) K. Ziegler and H. Wollschitt, *Ann.*, **479**, 108 (1930).

(9) Private communication from N. N. Lichtin.