[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

A Study of the Decomposition of *p*-Nitrophenethyltrimethylammonium Iodide by Means of the Hydrogen Isotope Effect[1]

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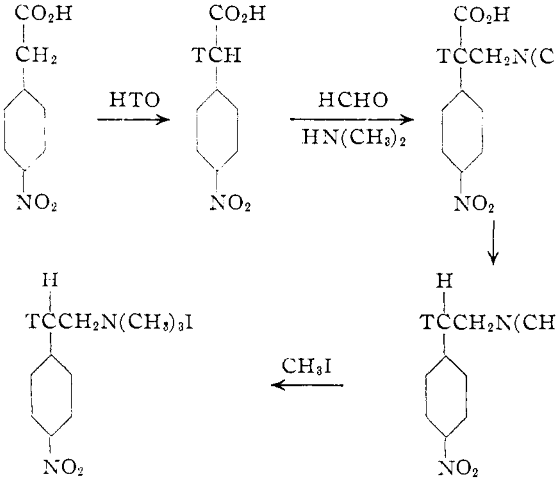
The hydrogen isotope effect in the decomposition of *p*-nitrophenethyl-β-*t*-trimethylammonium iodide in water at 100° has been measured. A hydrogen atom on the carbon adjacent to the ring is removed from a labeled molecule 7.4 times as rapidly as a tritium atom in the same position. A hydrogen atom in this same position in an inactive molecule is removed 15% faster than a hydrogen atom in the corresponding position of the labeled molecule. The existence of these differences in rate of reaction establishes the mechanism of the decomposition as being that of an attack on the hydrogen atom in the β-position to the ammonium group.

Hughes and Ingold[2] reported that the decomposition of phenethyltrimethylammonium hydroxide in water at 100° is first order in hydroxide ion as well as in the cation. *p*-Nitrophenethyltrimethylammonium iodide and the corresponding bromide each decompose in water at 100° with unimolecular kinetics. These latter decompositions are retarded by acids, unaffected by neutral salts and accelerated by bases although the rate constants were not reported. The kinetics of decomposition of *p*-nitrophenethyltrimethylammonium hydroxide were not studied.

Hughes, Ingold and Patel[3] attributed these differences to increased polarization of the β-hydrogen atom of the cation and decreased proton affinity of the anion in the case of *p*-nitrophenethyltrimethylammonium bromide or iodide. Although this explanation seems satisfactory on the basis of present knowledge of other decompositions, the possibility exists that the rate-determining step of the reaction is the breaking of the carbon–nitrogen bond of the cation and that the rate of removal of β-hydrogen atom has no effect on the rate of the reaction. Therefore the hydrogen isotope effect in the decomposition of *p*-nitrophenethyl-β-*t*-trimethylammonium iodide has been studied to elucidate further the mechanism of the reaction.



p-Nitrophenethyl-β-*t*-trimethylammonium iodide was prepared by the reactions.

Aqueous solutions of the *p*-nitrophenethyl-β-*t*-trimethylammonium iodide were sealed in tubes and held at 100° for various times. The remaining ammonium salt was precipitated as the sparingly soluble picrate and the latter dried and assayed for tritium. For low extents of reaction the product of the reaction was isolated by formation of the dibromide of the *p*-nitrostyrene which was purified and assayed. From these data it was possible to calculate the various isotope effects in the reaction.

Experimental

Preparation of *p*-Nitrophenethyltrimethylammonium Iodide.—Ten grams of phenethylamine was added during 1.5 hr. to 50 ml. of fuming nitric acid at −10°. Nitration occurred immediately; the mixture was allowed to warm slowly to 0° at which point ice and sodium hydroxide were added. The mixture of amines was extracted with ether and isolated as their hydrochlorides. A single crystallization from alcohol gave 6 g. of almost colorless plates of *p*-nitrophenethylamine hydrochloride,[4] m.p. 209–210°.

To the *p*-nitrophenethylamine obtained from 2 g. of the corresponding hydrochloride by neutralization with a base, extraction with ether and evaporation of the ether was added 5 g. of sodium carbonate, 5 ml. of absolute ethyl alcohol and with care 7 ml. of methyl iodide. After the initial vigorous reaction had subsided, it was completed by refluxing the mixture on a water-bath. The carbonate was removed by filtration, washed with ether and neutralized with 47% hydriodic acid. The quaternary ammonium iodide was collected by filtration, washed with acetone and ethyl ether and crystallized from 95% ethyl alcohol. Two grams of feathery lemon-yellow leaflets melting at 206° was obtained. The melting point reported[2] for *p*-nitrophenethyltrimethylammonium iodide is 199°.

Preparation of *p*-Nitrophenethyl-β-*t*-trimethylammonium Iodide.—*p*-Nitrophenylacetic acid (1.8 g., 0.01 mole) was placed in a tube with 1 ml. of tritiated water (7.13 mc./g.). The tube was sealed and placed in a bath at 100° for four days. The tritiated water was recovered by distillation on the vacuum line, and the acid was recrystallized once from water, dried and assayed. With an activity of 77.7 μc./mmole of acid and a recovery of 78%, the activity in the acid was 8.5% of that in the original water, but the actual loss in activity was negligible.

This *p*-nitrophenylacetic-α-*t* acid was shaken with 2 ml. of water and neutralized with a concentrated solution of dimethylamine. One milliliter of formalin was added and the solution was allowed to stand at room temperature for four days. The solid which crystallized on standing was separated by filtration. Unreacted *p*-nitrophenylacetic-α-*t* acid was recovered by acidifying the mixture with hydrochloric acid. The α-(*p*-nitrophenyl)-β-dimethylaminopropionic-α-*t* acid[5] after crystallization from water melted at 164°. The yield was 1 g. or 54% of the theory. The radioactivity of the acid was 54 μc./mmole, representing retention of 69.5% of the initial specific activity. Since on a statistical basis

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[2] E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 523 (1933).

[3] E. D. Hughes, C. K. Ingold and C. S. Patel, *ibid.*, 526 (1933).

[4] R. R. Gross, W. Hanhart and C. K. Ingold, *ibid.*, 255 (1927).

[5] C. Mannich and L. Stein, *Ber.*, **58**, 2659 (1925).

one-half of the tritium atoms would be lost in the reaction, this recovery represents a favorable isotope effect.

The amino acid was mixed with 50 mg. of copper carbonate and 1 ml. of pyridine. The mixture was refluxed until evolution of gas had stopped. Water was added to the mixture until a reddish-brown oil separated. The oil layer was washed with water and extracted with ether. Evaporation of the ether gave *p*-nitrophenethyl-*β*-*t*-dimethylamine.

This amine was treated with 3 ml. of methyl iodide in a water-bath for 1 hr. *p*-Nitrophenethyl-*β*-*t*-trimethylammonium iodide, which crystallized out on cooling, was filtered off, recrystallized from 95% ethyl alcohol and dried. The yield from 1 g. of the aminopropionic acid was 0.3 g. (21% of theory). The activity was 50 μc./mmole and the melting point was 197°.[2]

Determination of the Isotope Effect.—A solution buffered at *p*H 7 was prepared[6] by diluting a mixture of 29.63 ml. of 0.1 *N* sodium hydroxide and 50 ml. of 0.1 *M* diacid potassium phosphate to 100 ml. Three grams of *p*-nitrophenethyl-*β*-*t*-trimethylammonium iodide was dissolved in 30 ml. of this buffer solution. Two 1-ml. portions were removed for confirmation of the initial concentration. Two 1-ml. portions and one 2-ml. portion were removed and sealed in small tubes for study of the reaction mixture at 50, 65 and 80% of complete reaction. The remaining solution (24 ml.) and the latter three portions were placed in an oil-bath at 100°. After 45 min. the 24-ml. portion was taken from the bath, and two 1-ml. portions were removed for determination of the extent of the reaction by precipitation of the picrate of the remaining reactant.

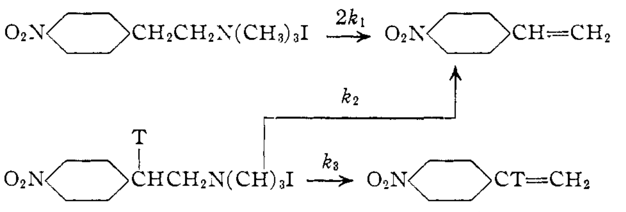
The remainder of the 24-ml. portion of the reaction solution was shaken with petroleum ether to extract *p*-nitrostyrene. The petroleum ether was then evaporated and the residue dissolved in 1 ml. of carbon tetrachloride and treated with 5 drops of bromine. The mixture was heated in a water-bath for 5 min. and the liquid evaporated off with a stream of nitrogen. The residue after recrystallization from aqueous methyl alcohol melted at 71°; m.p. reported[7] for *p*-nitrostyrene, 72–73°.

The other reaction mixtures were removed from the bath at the proper times and the extents of reaction determined by precipitation of the remaining reactant as the picrate. The picrates were assayed for tritium to obtain the molar activity of the remaining reactants.

No exchange of hydrogen atoms occurred between *p*-nitrophenethyl-*β*-*t*-trimethylammonium iodide and water under the same conditions at which decomposition occurred. This was demonstrated by heating *p*-nitrophenethyltrimethylammonium iodide in tritiated water until one-half of the former had decomposed. Assay of the remaining reactant showed no radioactivity.

Discussion of Results

Three reaction rate constants are involved in the process studied



The intermolecular isotope effect, $2k_1/(k_2 + k_3)$, can be derived from the equation

$$(k_2 + k_3)/2k_1 = 1 + (\log N_1/N_2)/\log (1 - f)$$

where f is the fraction reacted, and N_1/N_2 is the ratio of molar activity of the reactant at a given time to that of the initial reactant.

The secondary isotope effect, k_3/k_1, can be found from

$$k_3/2k_1 = N_3/N_1 \text{ (as } f \rightarrow 0)$$

where N_3 is the molar activity of the first product of the reaction.

The intramolecular isotope effect, k_3/k_2, can be determined from the above ratios.

The data obtained in this investigation are summarized in Table I; each figure represents from 2 to 5 assays for which the average deviation is not greater than ±0.5%.

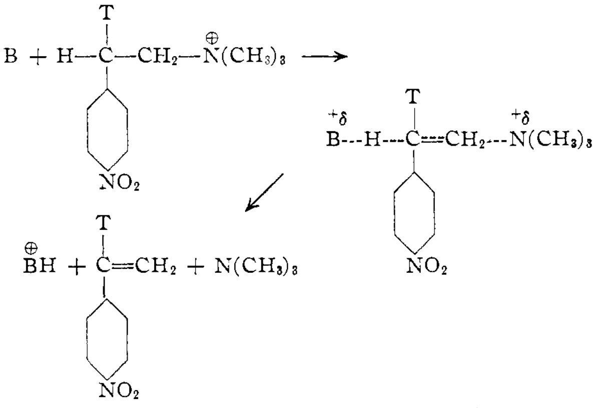
TABLE I

DECOMPOSITION OF *p*-NITROPHENETHYL-*β*-*t*-TRIMETHYLAMMONIUM IODIDE IN WATER AT 100°

Run	Extent of reacn., %	Activity of picrate, μc./mmole	Activity of *p*-nitrostyrene dibromide, μc./mmole	$\frac{k_3}{2k_1}$	$\frac{k_2 + k_3}{2k_1}$
I	0	11.53			
	17.3	12.33	5.43	0.455	
	43.7	14.95			0.550
	61.8	19.42			.458
II	0	12.33			
	8.6	12.70	5.18	0.414	
	82.6	29.58			0.500
III	0	12.64			
	50.0	18.07			0.484
	65.4	22.43			.459
	71.1	22.80			.510

From these results, the following values for the isotope effects have been calculated together with the average deviations, intermolecular isotope effect, $2k_1/(k_2 + k_3)$, 2.03 ± 0.11; intramolecular isotope effect, k_3/k_2, 7.4 ± 2.8; secondary isotope effect, k_3/k_1, 0.868 ± 0.04.

These ratios show beyond doubt that the decomposition of *p*-nitrophenethyl-*β*-*t*-trimethylammonium iodide in water at 100° occurs at a rate different from that of the normal compound. This difference proves that the bond between the hydrogen atom and the carbon atom which is adjacent to the ring is broken in the rate-determining step of the reaction. The point of attack on the molecule is therefore a hydrogen atom on the carbon atom beta to the ammonium group, as shown in the reaction scheme



Although Hughes and Ingold[2] found unimolecular kinetics for this reaction, it must be only pseudo-unimolecular.

It seems likely that the hydrogen atoms on the carbon atom adjacent to the ring are activated by the nitro group by the inductive effect as well as by conjugation. These hydrogen atoms may be ac-

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(6) W. M. Clark, "The Determination of Hydrogen Ions," 2nd ed., William and Wilkins, Baltimore, Md., 1922, pp. 106–107.

(7) A. Basler, *Ber.*, **16**, 3006 (1883).

tivated enough to react with molecules as weakly basic as water molecules, thereby producing a pseudo-unimolecular reaction. The exact nature of the attacking molecule, if any, is the subject of further investigation.

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Studies in Stereochemistry. XXII. The Preparation and Reactions of Trimesitylborane. Evidence for the Non-localized Nature of the Odd Electron in Triarylborane Radical Ions and Related Free Radicals[1]

BY HERBERT C. BROWN AND VANCE H. DODSON

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Trimesitylborane has been synthesized and its chemical behavior compared with that of triphenyl- and tri-α-naphthylboranes. In contrast to the latter compounds, trimesitylborane is far less reactive toward oxygen and water. Moreover, it fails to add either ammonia or sodium alkoxides. It is concluded that the steric effects of the three mesityl groups are so large as to hinder greatly the approach of a reacting molecule to the central atom. On the other hand, sodium reacts with trimesitylborane to form sodio derivatives analogous to those previously reported for triphenyl- and tri-α-naphthylborane. Since the vacant *p*-orbital of the boron atom is so completely blocked by the three mesityl groups, the ready formation of sodio derivatives in the case of trimesitylborane argues strongly for the entrance of the electron from the sodium atom into a non-localized orbital of the trimesitylborane molecule.

Differences in the chemical behavior of certain trialkylboranes can be correlated with the steric requirements of the alkyl groups in the boron derivative. Thus, trimethylamine forms a more stable addition compound with trimethylborane than does ammonia, whereas the reverse is true in the case of tri-*t*-butylborane.[2] Indeed, in this case trimethylamine exhibits no tendency to unite with the boron component.

It appeared of interest to examine the behavior of a borane derivative which might be expected to be even more hindered than tri-*t*-butylborane. Accordingly, the synthesis of trimesitylborane was undertaken and a study made of its chemical properties. For purposes of comparison, triphenyl- and tri-α-naphthylborane were included in the study. The behavior of these three compounds toward ammonia, sodium methoxide and *t*-butoxide, oxygen, water, sodium hydroxide and sodium metal was compared.

Results

Triphenylborane[3] and tri-α-naphthylborane[3] were prepared by treating phenylmagnesium bromide and α-naphthylmagnesium bromide, respectively, with boron trifluoride, according to the procedures previously described.[4,5] Utilization of a similar procedure for the preparation of trimesitylborane[3] resulted in the formation of dimesitylfluoroborane. Trimesitylborane could be obtained only by the use of a large excess of mesitylmagnesium bromide and forcing conditions.

Treatment of the three triarylboranes in ether solution with gaseous ammonia led to the precipitation of white crystalline addition compounds in the case of TPB and TNB (TPB:NH_3 and TNB:NH_3). However, under the same conditions TMB showed no tendency to react with ammonia. The data are summarized in Table I.

TABLE I

REACTIONS OF TPB, TNB AND TMB WITH AMMONIA

Triaryl-boron R_3B	Wt. of R_3B, g.	Wt. of combined ammonia, g.	Wt. of ammonia calcd. for $R_3B:NH_3$, g.
TPB	0.4380	0.0293	0.0308
	0.6753	.0471	.0473
TNB	1.2131	.0518	.0527
	0.5162	.0218	.0224
TMB	.1902	.0004	.0088
	.4458	.0007	.0206

Benzene solutions of TPB and TNB could be titrated stoichiometrically by standard solutions of sodium methoxide in methanol, using phenolphthalein as indicator. In the case of TNB it was demonstrated that the neutralization reaction involved the reaction of a sodium methoxide molecule with the TNB molecule by isolating the product, TNB·$NaOCH_3$, presumably $Na^+[(\alpha\text{-}C_{10}H_7)_3BOCH_3]^-$. Water hydrolyzed the salt with the formation of naphthalene and di-α-naphthylborinic acid. However, the addition of anhydrous hydrogen chloride to the salt (in benzene solution) permitted the regeneration and recovery of TNB. The reactions are

$$Na^+[(\alpha\text{-}C_{10}H_7)_3B:OCH_3]^- + 2H_2O \longrightarrow C_{10}H_8 + (\alpha\text{-}C_{10}H_7)_2BOH + NaOH + CH_3OH$$

$$Na^+[(\alpha\text{-}C_{10}H_7)_3B:OCH_3]^- + HCl \xrightarrow{\text{benzene}} (\alpha\text{-}C_{10}H_7)_3B + NaCl + CH_3OH$$

In titrations of TPB and TNB with sodium *t*-butoxide in *t*-butyl alcohol the indicator changed color when less than 50% of the stoichiometric quantity of base had been added. However, benzene solutions of TMB failed to react with either base. The results of several typical titrations are summarized in Table II.

The reactivities of the triarylboranes toward oxygen were examined in α-bromonaphthalene solution. Both TPB and TNB were found to

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(1) Based upon a thesis submitted by Vance H. Dodson in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) H. C. Brown, THIS JOURNAL, **67**, 374 (1945).

(3) For convenience the following abbreviations will be used: triphenylborane, TPB; tri-α-naphthylborane, TNB; trimesitylborane, TMB.

(4) E. Krause and R. Nitsche, *Ber.*, **55**, 1261 (1922).

(5) H. C. Brown and S. Sujishi, THIS JOURNAL, **70**, 2793 (1948).