

of isochondrodendriline¹¹ in benzene-methanol, gave arnepavine oxalate, mp 211–213° (lit. mp 211–212° uncor⁵ and mp 209°⁶).

Demerarine.—Demerarine hydrochloride¹ had $[\alpha]^{25}_D - 181^\circ$, $[\alpha]^{25}_{5461} - 219^\circ$ (*c* 1.0, water). Treatment of an aqueous solution with ammonium hydroxide gave demerarine which crystallized in needles from methanol: mp 222–223°; $[\alpha]^{25}_D - 162^\circ$ (*c* 0.35, 5% methanol in chloroform). The mass spectrum exhibited a molecular ion peak at *m/e* 594 ± 1 in accord with the molecular formula C₃₆H₃₈N₂O₆. Other important peaks were at *m/e* 168, 191, 381, and 382.

N-Methyl demerarine.—Demerarine (100 mg) in 0.5 ml of formic acid and 0.5 ml of formalin was heated in a steam bath for 4 hr. Treatment with water and ammonia gave a precipitate which on drying weighed 91 mg. The infrared spectrum in a KBr pellet was the same as that of a sample of repandine. In thin layer chromatographic comparisons on silica gel (Ad-sorbosil-1), using 12 different solvent systems, N-methyl demerarine and repandine had the same *R_f* values. The mass spectra of the two alkaloids were identical showing a molecular ion peak at *m/e* 608 ± 1 in accord with the molecular formula C₃₇H₄₀N₂O₆.

Oxyacanthine Hydrochloride.—The addition of saturated sodium sulfate solution to a solution of commercial "oxyacanthine hydrochloride tetrahydrate" (Fluka AG, Buchs, Switzerland) gave platelets of oxyacanthine sulfate. The product was recrystallized from water and was converted into oxyacanthine hydrochloride by the addition of hydrochloric acid to an aqueous solution: $[\alpha]^{25}_D + 188^\circ$ (*c* 1.0, water); *K* = 2.36.

Hydroepistephanine-A Hydrochloride.—A sample of epistephanine in sulfuric acid and ethanol was reduced with zinc dust by the method of Tomita and Watanabe.⁴ Hydroepistephanine-A hydrochloride was obtained in small, long rods: $[\alpha]^{25}_D + 300^\circ$ (*c* 0.27, water) (lit.⁴ $[\alpha]^{25}_D + 298^\circ$, *c* 0.24, water); *K* = 1.03; *R_f* 0.58 for the free alkaloid with the system amyl alcohol-pyridine-water (110:110:90) on buffered paper.¹⁰

Registry No.—II, 6787-93-5; VIII, 15353-21-6; N-methylcocotamine HCl, 15352-74-6; O-methylcocotamine HCl, 15352-75-7; N-methyl demerarine, 15352-76-8.

Acknowledgments.—The authors wish to thank Dr. Yasuo Watanabe, First College of Pharmacy, Fukuoka City, for a sample of epistephanine, Dr. I. R. C. Bick, University of Tasmania, for a sample of repandine, and Dr. M. F. Grundon, The Queen's University, Belfast, for a sample of sepeperine. M. S. wishes to acknowledge financial support from the National Institutes of Health through Grant GM-10608.

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Solvent Effects in the Chlorination of Isobutyl Chloride and *t*-Butyl Chloride¹

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Received July 31, 1967

Russell² reported that in the photochlorination of 2,3-dimethylbutane at 25° the relative reactivities of the primary and tertiary hydrogen atoms varied from 4.2 in pure carbon tetrachloride to 225 in 12 *M* carbon disulfide. The relative reactivities of covalently

bound hydrogen atoms to photochlorination in different solvents have been determined for other compounds such as *n*-pentane,³ *n*-butyl chloride,⁴ hexanoyl chloride,⁵ *n*-heptane,⁶ octanoyl chloride,⁶ and chlorocyclopentane;⁷ relationships between the nature of the solvent and the relative reactivities of the hydrogen atoms being abstracted have been developed. Our purpose in this investigation was to apply these principles to the chlorination of isobutyl chloride in order to obtain a better understanding of the transition state.

Isobutyl chloride in mixed solvents of different compositions was allowed to react photochemically with a small amount of chlorine and the products were separated and measured quantitatively by gas chromatography. The results are shown in Table I.

TABLE I
SOLVENT EFFECTS IN THE CHLORINATION OF ISOBUTYL CHLORIDE^a

Solvents	Concn of second solvent, mol/l.	$(\text{CH}_3)_2\text{CHCH}_2\text{Cl} + \text{Cl}_2 \begin{cases} \xrightarrow{k_1} (\text{CH}_3)_2\text{CClCH}_2\text{Cl} \\ \xrightarrow{2k_2} (\text{CH}_3)_2\text{CHCHCl}_2 \\ \xrightarrow{6k_3} \text{CH}_3\text{CH}(\text{CH}_2\text{Cl})_2 \end{cases}$		
		<i>k</i> ₁ / <i>k</i> ₂ ^b	<i>k</i> ₁ / <i>k</i> ₃ ^b	<i>k</i> ₂ / <i>k</i> ₃ ^b
CCl ₄	...	4.5	6.1	1.35 ^c
CCl ₄ -CS ₂	1.2	8.8	8.7	0.99
CCl ₄ -CS ₂	2.2	11.4	10.2	0.90
CCl ₄ -CS ₂	3.8	14.4	11.6	0.81
CCl ₄ -CS ₂	6.2	19.7	13.6	0.69
CCl ₄ -CS ₂	8.5	24.3	14.6	0.60
CCl ₄ -CS ₂	9.2	24.3	14.8	0.61
CCl ₄ -CS ₂	11.2	27.2	15.0	0.55
CS ₂	...	29.1	15.3	0.53
CCl ₄ -C ₆ H ₆	1.3	8.4	9.2	1.10
CCl ₄ -C ₆ H ₆	2.5	11.2	10.6	0.95
CCl ₄ -C ₆ H ₆	3.7	13.3	11.7	0.88
CCl ₄ -C ₆ H ₆	5.0	15.7	12.5	0.80
CCl ₄ -C ₆ H ₆	6.3	17.4	12.6	0.72
CCl ₄ -C ₆ H ₆	7.4	19.6	<i>d</i>	<i>d</i>

^a Each solution contained 0.87 g of isobutyl chloride and 0.024 g of chlorine in a total volume of 4.2 ml. ^b Each value is the result of four or five determinations; the average deviation of each value is ±3%. ^c E. M. Hodnett and P. S. Juneja, *J. Org. Chem.*, **32**, 4114 (1967). ^d Not determined because of experimental difficulties.

For further comparison, mixtures of isobutyl chloride and *t*-butyl chloride were chlorinated in the same solvents under the same conditions; the results are shown in Table II.

Russell^{2,8} has suggested that relative reactivities that are determined mainly by the availability of electrons in the carbon-hydrogen bond are not particularly sensitive to solvent effects while relative reactivities that are determined mainly by the stabilities of the incipient free radicals are very sensitive to changes in solvent. This is because in solvents which complex chlorine atoms the transition state has more radical character and therefore is influenced

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(1) Abstracted in part from the Ph.D. dissertation of P. S. J., Oklahoma State University, May 1967.

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TABLE II
SOLVENT EFFECTS IN THE COMPETITIVE CHLORINATION
OF ISOBUTYL CHLORIDE AND *t*-BUTYL CHLORIDE^a

$$\begin{array}{l}
 (\text{CH}_3)_2\text{CHCH}_2\text{Cl} + \text{Cl}_2 \xrightarrow{2k_2} (\text{CH}_3)_2\text{CHCHCl}_2 \\
 \phantom{(\text{CH}_3)_2\text{CHCH}_2\text{Cl} + \text{Cl}_2} \xrightarrow{6k_3} \text{CH}_3\text{CH}(\text{CH}_2\text{Cl})_2 \\
 (\text{CH}_3)_3\text{CCl} + \text{Cl}_2 \xrightarrow{9k_2} (\text{CH}_3)_2\text{CClCH}_2\text{Cl}
 \end{array}$$

Solvents	Concn of second solvent, mol/l.	k_2/k_3^b	k_2/k_6^b
CCl ₄	...	2.25 ^c	1.78 ^c
CCl ₄ -CS ₂	2.1	2.09	2.33
CCl ₄ -CS ₂	4.2	2.38	3.12
CCl ₄ -CS ₂	6.3	2.18	3.19
CCl ₄ -CS ₂	8.4	1.83	3.30
CS ₂	...	1.98	3.94
CCl ₄ -C ₆ H ₆	1.2	2.12	1.97
CCl ₄ -C ₆ H ₆	2.5	2.05	2.13
CCl ₄ -C ₆ H ₆	3.7	1.91	2.18
CCl ₄ -C ₆ H ₆	5.0	1.98	2.50

^a Each solution contained 0.42 g of *t*-butyl chloride, 0.44 g of isobutyl chloride, and 0.017 g of chlorine in a total volume of 4 ml. ^b Each value is the result of four or five determinations; the average deviation of each value is $\pm 3\%$. ^c See footnote c, Table I.

by the stability of the incipient radicals. These principles seem to have been observed in other investigations of solvent effects³⁻⁷ and have been applied to the results of this study.

The reactivities of the hydrogen atoms of isobutyl chloride in photochlorination in mixed solvents are compared with one another in Table I and with the reactivity of the hydrogen atoms of *t*-butyl chloride in Table II. The absolute reactivity of the hydrogen atoms of *t*-butyl chloride may change with each solvent. It is possible that the chlorine atom of *t*-butyl chloride may participate in the stabilization of the incipient radical $(\text{CH}_3)_2\text{CCl}\dot{\text{C}}\text{H}_2$.⁹ The results given in Tables I and II are summarized in Table III.

TABLE III

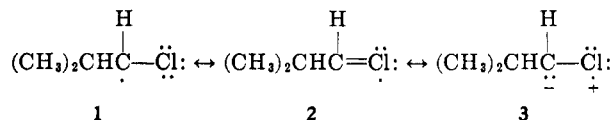
CH ₃ -CH-CH ₂ Cl			CH ₃ -CCl-CH ₂		Solvent
2.25	8.02	1.78	1.00 ^a		Carbon tetrachloride
1.98	31.2	2.50	1.00 ^a		Benzene (5.0 M) and carbon tetrachloride
1.98	60.3	3.94	1.00 ^a		Carbon disulfide

^a Assumed value.

The greatest solvent effect is demonstrated by the tertiary hydrogen atom of isobutyl chloride; the relative reactivity varies from 8.02 in carbon tetrachloride to 60.3 in carbon disulfide solutions. This large effect probably results from the stability of the radical $(\text{CH}_3)_2\dot{\text{C}}\text{CH}_2\text{Cl}$ which is formed by abstraction of the tertiary hydrogen atom; that is, hyperconjugative stabilization of the incipient radical rather than polar effects probably determines the reactivity of this hydrogen atom.

The inductive effect of a chlorine atom normally results in deactivation of the hydrogen atoms on the same and adjacent carbon atoms as shown by the

relative reactivities of the hydrogen atoms on carbons 1 and 4 of *n*-butyl chloride.^{4,10} However, the hydrogen atoms on carbon 1 of isobutyl chloride are more reactive than the hydrogen atoms of *t*-butyl chloride in carbon tetrachloride and become even more reactive in carbon disulfide. Although the solvent effect on the reactivity of the hydrogen atoms on carbon 1 of isobutyl chloride is not so great as that for the tertiary hydrogen atom of isobutyl chloride, these hydrogen atoms do become more reactive in the solvent which is more capable of complexing with chlorine. The incipient free radical, $(\text{CH}_3)_2\text{CH}\dot{\text{C}}\text{HCl}$, is significantly stabilized by conjugation of the forms¹¹



Structure 3 may also be stabilized by dipole-induced dipole interaction with solvents having easily polarizable π electrons. Thus to the extent that structure 3 contributes to the resonance hybrid of the incipient radical one would expect some solvent stabilization. Walling and Wagner¹² have suggested that the solvation of the organic free radical which is being formed is an important factor in determining the selectivity of the reaction.

The relative reactivity of the hydrogen atoms on carbon 3 of isobutyl chloride varies least of all with changes in solvents. This is to be expected since it is most like the hydrogen atoms of *t*-butyl chloride with which it is being compared. The greater reactivity of the hydrogen atoms on carbon 3 of isobutyl chloride compared to those of *t*-butyl chloride may be due to (1) hyperconjugative stabilization of the incipient radical $\text{CH}_2\text{CH}(\text{CH}_3)\dot{\text{C}}\text{H}_2\text{Cl}$ (not possible for *t*-butyl chloride) or (2) the inductive effect of the chlorine atom of *t*-butyl chloride (which is closer to the reaction site than the chlorine atom of isobutyl chloride).

Experimental Section

Materials.—The benzene used in this work was obtained from J. T. Baker Co. as their reagent grade; gas chromatography showed that it contained no more than 0.4% impurities, of which 0.33% was toluene. Carbon disulfide was also a reagent grade from J. T. Baker Co. and was gas chromatographically pure. The sources and purities of other materials used were described previously.¹³

Procedure.—The procedures were also described previously.¹³ The solutions contained known quantities of the compound or compounds to be chlorinated, a limiting amount of chlorine, and known ratios of solvents. After the reaction mixture was degassed it was irradiated at room temperature with an incandescent light until all the chlorine had reacted. The reaction mixture was shaken with solid sodium bicarbonate, dried with Drierite, and analyzed quantitatively by gas chromatography; the peak area (peak height times width at half-peak height) was assumed to be proportional to the concentration of products.¹⁴ The three dichloro isomers from isobutane were considered to have the same thermal conductivity response and hence no calibration was employed.¹³

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Identification of Products.—The products of the reaction were identified by nmr spectra and retention times on the gas chromatograph.¹³

Registry No.—Isobutyl chloride, 513-36-0; *t*-butyl chloride, 507-20-0.

Acknowledgments.—We thank Dr. Stuart Scheppele for helpful discussions in the interpretations of these results. This work was supported financially by the U. S. Atomic Energy Commission under Contract AT(11-1)-1049 and by the Research Foundation of Oklahoma State University.

A β Secondary Isotope Effect in the Photochlorination of 2-Methylpropane-2-*t*¹

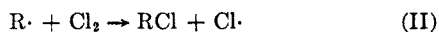
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The primary hydrogen atoms of 2-methylpropane-2-*t* are removed by photochlorination less rapidly than are the primary hydrogen atoms of isobutane. This difference in rates indicates that tritium has a β -secondary isotope effect in this free-radical chlorination. Secondary β -isotope effects of deuterium have been reported,²⁻⁹ but few of these are for reactions with free-radical mechanisms.¹⁰⁻¹²

The photochlorination of hydrocarbons occurs by a chain reaction. For the chlorination of methane, the



calculated heat of reaction of step I is -1 kcal/mole and that of step II is -23 kcal/mole;¹³ step I is probably rate determining. The rate of chlorination of a mixture of isobutane and tracer amounts of 2-methylpropane-2-*t*, therefore, is determined by the first step of each of the four reactions given in Scheme I.

Equations 1-3 may be used to compare the four reaction rate constants with each other: eq 1

$$\frac{\log N_A/N_{A_0}}{\log A/A_0} = \frac{9k_4 + k_2}{9k_1 + k_2} - 1 \quad (1)$$

(1) These results were presented at the Oklahoma Tetrasectional Meeting of the American Chemical Society, Tulsa, Okla., March 1967; abstracted from a portion of the Ph.D. dissertation of P. S. J., Oklahoma State University, May 1967.

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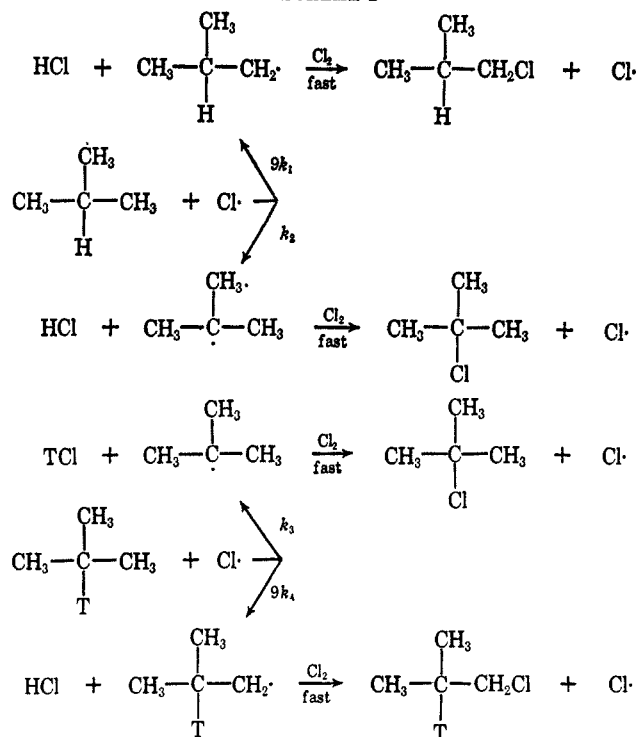
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SCHEME I



where N_{A_0} and N_A are the specific radioactivities of the isobutane-*t* at the start and at the end of the experiment and A/A_0 is the fraction of isobutane remaining at the end of the experiment; eq 2 shown below

$$k_2/9k_1 = B/C \quad (2)$$

where B/C is the ratio of *t*-butyl chloride and isobutyl chloride formed in the reaction (under these conditions k_2/k_1 has a magnitude¹⁴ of 3.5); and eq 3

$$k_1/k_4 = N_{A_0}/N_B \quad (3)$$

(for low extents of reaction) where N_B is the specific activity of the isobutyl chloride formed at low extents of reaction. Equation 3 assumes that the specific radioactivity of the isobutane-*t* does not change for low extents of reaction. However, if one assumes that the primary isotope effect has a magnitude¹⁵ of 5 and the β secondary isotope effect has a magnitude of 1.04, the radioactivity of the remaining isobutane-*t* after 1.5% reaction can be calculated by eq 1 to have increased by 0.37%. Since the isobutyl chloride was formed from isobutane-*t* with an initial radioactivity of 59.92 μ curies/mole and a final one of 60.14 μ curies/mole, an average value of 60.03 μ curies/mole is used in the calculations of the β secondary isotope effect shown in Table I.

2-Methylpropane-2-*t*, prepared from *t*-butylmagnesium chloride and tritiated water, was treated in carbon tetrachloride solution with enough chlorine to react with 1.5% of the isobutane. The reaction mixture was irradiated at room temperature until the chlorine color disappeared and the hydrogen chloride and part of the remaining isobutane were removed. Samples of the remainder were injected into a gas chromatograph which was attached to an ionization chamber. The components of the mixture were sep-

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(15) Preliminary work by E. M. Hodnett, S. Scheppele, and P. S. Juneja indicates that the magnitude of the primary isotope effect in this reaction under these conditions is between 4 and 5.