as the oxidant, and suggests that the reaction sequence is

$$Cr^4 + Ce^3 \longrightarrow Cr^3 + Ce^4 \qquad (6)$$

When reaction 6 intervenes in place of reaction 4, the total rate of consumption of chromic acid is decreased. Although the study of the induced oxidation is very much less complete than that for the oxidation of isopropyl alcohol,[4] the result is similar, and suggests that the rate-controlling reaction produces tetravalent chromium. If this is so, then the chromic acid oxidation of benzaldehyde is a two-electron process, such as that shown in equations 2, 3, 4 and 5.

CHICAGO, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WASHINGTON]

The Deuterium Isotope Effect in the Side Chain Halogenation of Toluene[1]

BY KENNETH B. WIBERG AND LYNN H. SLAUGH

RECEIVED DECEMBER 12, 1957

The intramolecular deuterium isotope effect obtained in the side chain halogenation of toluene and some of its derivatives has been determined. Factors which decreased the energy of activation decrease the isotope effect. This observation may be interpreted by a consideration of the potential energy curves for the dissociation of reactants and products. The magnitude of the isotope effect is used as a criterion in considering the mechanisms of some halogenation reactions.

Introduction

The isotope effects obtained in the side chain halogenation of toluene and some of its derivatives have been examined previously.[2] The more extensive of these investigations gave, however, the value for a mixture of an inter- and an intramolecular isotope effect. In order to obtain data which may be consistently interpreted throughout a series, we have measured the pure intramolecular isotope effect for a number of these reactions. The method involved in this work was to carry out the halogenation to a known extent (usually about 50% of completion) and then to isolate the unchanged reactant and the product. Whenever possible, the product was converted back to the reactant by reduction. Mass spectrometric analysis of the starting material, the unchanged reactant and the product, along with the extent of reaction gave the data necessary for the calculation of the intramolecular isotope effect.

Experimental

Reactants.—Most of the α-deuteriotoluenes were prepared by the reduction of the appropriate side-chain halogenated compound. Three procedures were used: zinc and deuterioacetic acid reduction (method A),[3] treatment of the Grignard reagent with deuterium chloride (method B)[4] and treatment of the halide with lithium aluminum deuteride (method C).[5] The results are summarized in Table I.

Ethylbenzene-α-d_1 was kindly supplied by Drs. H. J. Dauben and L. L. McCoy and had a composition 1.37% d_0 and 98.63% d_1. The other compounds were prepared as follows.

***p*-Methylacetophenone-d_3.**—To a solution of 28.5 g. (0.35 mole) of toluene-d_3 in 120 ml. of dry carbon disulfide was added 89.6 g. (0.67 mole) of anhydrous aluminum chloride. The mixture was heated on the steam-bath to reflux and 24.5 g. (0.24 mole) of acetic anhydride was added slowly while stirring over a period of one hour. Heating was continued for an additional hour. The solvent was removed by distillation from a steam-bath. The reaction mixture was cooled and slowly poured into a well stirred ice–hydrochloric acid mixture. The mixture was extracted several times with 200–300-ml. portions of ether, and the combined extracts were washed twice with water, once with 10% sodium hydroxide and twice more with water. The extract was dried over calcium chloride, filtered and the solvent removed. Distillation gave 25.7 g. (63%) of *p*-methylacetophenone-d_3, b.p. 100–100.5° at 12–13 mm.

***p*-Cresyl Acetate-d_3.**—A solution of peroxytrifluoroacetic acid prepared by the addition of trifluoroacetic anhydride (0.36 mole, 50.8 ml.) to 8.3 ml. of 90% hydrogen peroxide in 50 ml. of methylene chloride at 0° was added slowly to a mixture of 130 g. of dibasic sodium phosphate and 25.7 g. (0.19 mole) of *p*-methylacetophenone-d_3 in 150 ml. of methylene chloride over a period of 30 minutes. The reaction mixture was heated to reflux for one hour, cooled, and filtered. The filtrate was washed once with 50 ml. of 10% sodium carbonate and dried over anhydrous magnesium sulfate. Upon filtering and distilling, 23.7 g. (83%) of *p*-cresyl acetate-d_3 was obtained, b.p. 90–91° at 10 mm.

***p*-Cresol-d_3.**—A solution of 23.7 g. of *p*-cresyl acetate-d_3 in 150 ml. of ether was added to a suspension of 0.2 mole (7.6 g.) of lithium aluminum hydride and 1.0 g. of lithium hydride in 400 ml. of anhydrous ether at such a rate as to cause gentle reflux. Heating was continued for one hour, the mixture was cooled and the excess reagent was destroyed by the dropwise addition of water. The mixture was added to a 10% sulfuric acid–ice mixture. After the aluminum salt had dissolved, the layers were separated and the ether was washed with water and dried over calcium sulfate. The ether was removed leaving an oil which was not purified before the next reaction.

***p*-Methoxytoluene-d_3.**—To a solution of 6.6 g. (0.16 mole) of sodium hydroxide and the crude *p*-cresol-d_3 prepared above in 65 ml. of water was added 0.19 mole of dimethyl sulfate over a period of one hour with the solution maintained at 5–10°. It was stirred an additional 45 minutes at 10° and 30 minutes at 50–60°. An additional 2.5 g. of sodium hydroxide was added in 15 ml. of water and the mixture was heated to reflux with stirring for 7 hours. After cooling the mixture, it was extracted several times with benzene. The benzene solution was dried over anhydrous calcium chloride and distilled giving 15.9 g. (85%) of *p*-methoxytoluene-d_3 b.p. 168–175°. Careful distillation through an efficient column gave the pure compound (14.5 g.), b.p. 177.0–177.1°, n^{25}D 1.5100.

Cumene-d_1.—To a solution of 15 g. of methyl 2-phenyl-2-propyl ether in 300 ml. of anhydrous ether was added 10 ml. of liquid sodium–potassium alloy (prepared under benzene from 3 parts potassium and 1 part of sodium). The mixture was stirred for four hours. After this time, a stream of warm, dry nitrogen which had been passed through deuterium oxide was passed into the reaction mixture until the red color of the carbanion had been discharged. Ethanol was then added to decompose the excess alloy. The solution was treated with water and the organic layer was sepa-

---

[1] This is taken from a thesis submitted by L. H. Slaugh to the University of Washington in partial fulfillment of the requirements for the Ph.D. degree, 1956.

[2] H. C. Brown and G. A. Russell, THIS JOURNAL, **74**, 3995 (1952); W. H. Urry, Abstracts Twelfth National Symposium, Denver, Colo., June, 1951, p. 30.

[3] R. Renaud and L. C. Leitch, *Can. J. Chem.*, **34**, 98 (1956).

[4] H. C. Brown and G. A. Russell, THIS JOURNAL, **74**, 3995 (1952)

[5] E. Eliel, *ibid.*, **71**, 3970 (1949).

TABLE I

PREPARATION OF LABELED TOLUENES

Compound	Reactant, chloride	Method	Yield, %	B.p., °C.	d_0, %	d_1, %	d_2, %	d_3, %
Toluene-d_1	Benzyl	A	35–45	108.5–109	6.18	93.82		
		B	70		6.03	93.97		
		C	75		2.30	97.70		
Toluene-d_2	Benzal	A	34	108.5–109.4	0.86	14.12	85.01	
Toluene-d_3	Benzotrichloride	A	33–41	108.5–109.4	0.00	0.75	13.98	85.26
p-Chlorotoluene-d_1	*p*-Chlorobenzyl	A	57	156.9–157	10.26	89.74		
p-Chlorotoluene-d_2	*p*-Chlorobenzal	A	60	156.8–157	0.35	9.77	89.89	
p-Methoxytoluene-d_1	*p*-Methoxybenzyl	A	0					
		C	62	172	1.87	98.13		

rated and washed with water. After drying over anhydrous sodium sulfate, distillation gave 6.4 g. (53%) of cumene-d_1, b.p. 145–155°. This was diluted with cumene-d_0 and redistilled (b.p. 152°) before being used.

Analysis.—The isotopic analysis of the samples was performed using mass spectra. The spectra were obtained at a low ionizing voltage (7–10 volts) which is above the ionization potential of the molecule, but below the potential for removing a hydrogen.[6] This permits the appearance of only the parent peaks for each isotopic molecule. A determination of the discrimination between isotopically labeled molecules in the mass spectrometer was performed by preparing mixtures of toluene-d_1 (prepared by the lithium aluminum deuteride–lithium deuteride reduction of benzyl chloride and having the highest percentage of toluene-d_1) with toluene-d_0. The calculated and observed percentages of toluene-d_1 were compared and this indicated a discrimination of 1% from 0–28% toluene-d_0 and 2% from 28–34% toluene-d_0. This amount of discrimination will result in a 1 or 2% error in the isotope effects which are calculated. Since the error caused by discrimination was less than the experimental error in determining the isotope effects, the analyses were not corrected and all isotopic compositions in this paper are calculated directly from the mass spectra. In the calculation of the isotopic compositions correction was first made for the normal abundance of C^{13}. Then the isotopic compositions were taken as the intensity of the peak for a given species divided by the sum of all the intensities. The reproducibility of the mass spectra was very good and a typical result is shown in Table II.

Procedures Used in Effecting the Halogenations. A. Bromination of Deuteriotoluenes (Toluene-d_2 as an Example).—A 500-ml., three-necked flask was equipped with a Dry Ice–acetone cooled condenser, a 125-ml. Hershberg dropping funnel and a nitrogen inlet tube that extended to the bottom of the flask. All joints were lubricated with Dow silicone grease to prevent loss of bromine.

In the flask was placed 3.8857 g. of toluene d_2 (0.04135 mole) in 60 ml. of carbon tetrachloride (dried over calcium chloride and distilled). Dry Ice and acetone were placed in the condenser and 4.3717 g. of bromine (0.02735 mole) was placed in the dropping funnel. While gently refluxing and irradiating with ultraviolet light, the bromine was added over a period of 15 minutes as nitrogen gas was bubbled (2–5 bubbles per second) through the refluxing solution. The excess Dry Ice was removed from the condenser allowing the refluxing carbon tetrachloride to wash down the condensed bromine. The Hershberg dropping funnel was rinsed several times to ensure complete addition of all the bromine. The reaction flask was cooled quickly and the contents washed several times with dilute sodium bicarbonate solution. The above procedure was completed in less than 20 minutes. The reaction mixture was worked up as described below for each labeled compound.

Bromination of Deuteriotoluenes with N-Bromosuccinimide.—The N-bromosuccinimide was purified by rapidly dissolving it in boiling water (10 ml. of water for each gram of NBS), filtering while hot and cooling to allow crystallization. After filtration, it was washed with water and dried over phosphorus pentoxide for several days. The purity was determined by iodometric analysis.

In a 200-ml. flask equipped with a condenser were placed 6.2042 g. of N-bromosuccinimide (98.42% pure) and 50 ml. of carbon tetrachloride. After adding 4.5642 g. of toluene-d_1, refluxing was begun and the solution was irradiated with ultraviolet light. The reaction appeared to be completed in less than 20 minutes. However, the irradiation and refluxing were continued for an additional hour to ensure complete reaction. After cooling, the succinimide was removed by filtration and the products were isolated as described below.

Chlorination of Deuteriotoluenes (Toluene-d_2 as an Example).—Dried chlorine was bubbled through 200 ml. of carbon tetrachloride (purified by shaking with concentrated sulfuric acid, washing with dilute sodium bicarbonate solution and with water, drying over calcium chloride and distilling) in a gas bubbler until saturated. Care was taken to exclude moisture. The solution was diluted with twice its volume of carbon tetrachloride and analyzed iodometrically.

To a 17-mm. Pyrex tube sealed at one end and cooled in a Dry Ice-acetone-bath was added 69.27 ml. of 0.697 *N* chlorine in carbon tetrachloride. Toluene-d_2 (4.0331 g., 0.04292 mole) was added and the walls were washed down with carbon tetrachloride. After sealing the tube, it was placed in a water-bath at 77–80° and irradiated with a mercury lamp for several hours. The chlorine color had disappeared after 15 minutes. After freezing the contents of the tube, it was opened and allowed to warm to room temperature as the hydrogen chloride escaped. The carbon tetrachloride solution was washed with dilute sodium bicarbonate solution and dried over calcium chloride. An infrared spectrum of the product did not indicate the presence of benzal chloride when compared with the spectrum of an authentic sample of the latter. The product was isolated as described below.

Chlorination of Toluene-d_1 with N-Chlorosuccinimide at 110°.—A mixture of 4.5288 g. of N-chlorosuccinimide (96.08% pure as determined by iodometric analysis) and 15.1181 g. of toluene-d_1 was heated to gentle reflux and irradiated with ultraviolet light for 24 hours. The reaction was then complete as indicated by a negative starch–iodide test. Carbon tetrachloride was added, the mixture was cooled and the succinimide removed by filtration. The isolation procedure is described below. The reaction could not be carried out in carbon tetrachloride as a solvent because of the exceedingly low rate of reaction.

Bromination of Toluene-d_1 with N-Bromosuccinimide at 110°.—A mixture of 5.9227 g. of N-bromosuccinimide (97.45% pure) and 16.4851 g. of toluene-d_1 was heated to gentle reflux and irradiated with ultraviolet light for one or two hours to complete the reaction. Carbon tetrachloride was added, the mixture was cooled and the succinimide removed by filtration. The isolation of the product is described below.

Chlorination of Toluene-d_1 with Sulfuryl Chloride at 77°.—To a 100-ml. flask equipped with two condensers was added 4.9146 g. of toluene-d_1, 3.3091 g. of sulfuryl chloride (purified by distilling reagent grade sulfuryl chloride through a glass packed column), 30 mg. of benzoyl peroxide (0.5 mole %) and 60 ml. of carbon tetrachloride (purified as described above). The solution was refluxed gently until the evolution of hydrogen chloride and sulfur dioxide had ceased. The condenser was washed down to return any volatilized sulfuryl chloride or toluene-d_1 to the reaction flask. Refluxing was continued for an additional two hours to ensure complete reaction as was indicated by a negative starch–iodide test. The solution was washed with dilute sodium bicarbonate and dried over potassium carbonate. The product was isolated as described below.

Another chlorination of toluene-d_1 was carried out in a sealed tube using benzoyl peroxide as a catalyst and carbon tetrachloride as a solvent. However, the reaction would

---

[6] A Consolidated Electrodynamics Corp. model 21-103 mass spectrometer was used.

not go to completion even after heating at 80° and irradiating with ultraviolet light for 40 hours. This procedure was not used in determining the isotope effect.

Chlorination of Toluene-d_1 with Sulfuryl Chloride in the Absence of Solvent.—In a 60-ml. flask equipped with a condenser were placed 4.7338 g. of sulfuryl chloride, 15.1970 g. of toluene-d_1 and 30 mg. of benzoyl peroxide (0.4 mole per cent.). The mixture was heated to gentle reflux until the reaction was complete and then boiled vigorously to permit the toluene-d_1 to wash down any sulfuryl chloride that might have volatilized and condensed on the condenser. Ether was added and the solution was washed with sodium bicarbonate and dried over potassium carbonate. The isolation is described below.

Chlorination of Toluene-d_1 with Sulfuryl Chloride in Carbon Tetrachloride in the Presence of Sulfur Dioxide.—In a 200-ml. flask with a side-arm inlet and reflux condenser were placed 5.1811 g. of toluene-d_1, 3.7490 g. of sulfuryl chloride, benzoyl peroxide (0.5 mole %) and 100 ml. of carbon tetrachloride. Sulfur dioxide was bubbled through the solution for several minutes and the solution was then heated to reflux and irradiated with ultraviolet light until the reaction had gone to completion. The carbon tetrachloride solution was washed with dilute sodium bicarbonate and dried over potassium carbonate.

Isolation of Products. Toluene-d_1 and Toluene-d_2.—After the halogenation, the excess carbon tetrachloride was carefully removed by distillation. The infrared spectrum of the remaining oil was examined to see if a significant amount of benzal halide had been formed. The latter was not present in sufficient amount to be detected. The mixture was distilled carefully through a concentric tube column under a nitrogen atmosphere. Only the middle fraction of toluene-d_1 or toluene-d_2 (80% recovery) and the last fraction of the benzyl halide (65% yield) were collected at their correct boiling points to ensure a good separation. The recovered toluene was analyzed for its isotopic composition.

In a 100-ml. three-necked flask equipped with a reflux condenser, stirrer and dropping funnel were placed 1.0 g. of lithium aluminum hydride, 0.3 g. of lithium hydride and 15–20 ml. of tetrahydrofuran (purified by refluxing with potassium and distilling from lithium aluminum hydride). While stirring and maintaining the temperature at 25°, the benzyl halide (1.0–2.4 g.) in 10 ml. of tetrahydrofuran was added slowly. The mixture was heated to reflux for 14 hours and then the excess reagent was destroyed by the dropwise addition of a water–tetrahydrofuran mixture. The aluminum salts were dissolved by adding the reaction mixture to a 10% sulfuric acid–ice mixture. The ether solution was washed with dilute sodium bicarbonate solution, dried over calcium chloride and distilled giving "product" toluene (40–60%), b.p. 108–110°.

***p*-Chlorotoluene-d_1 and *p*-Chlorotoluene-d_2.**—After the chlorination of the toluenes, the carbon tetrachloride was removed by distillation. The residue was fractionally distilled through a concentric tube column, collecting the middle fraction of the *p*-chlorotoluene and the latter part of the *p*-chlorobenzyl chloride fraction. The recovered *p*-chlorotoluene was analyzed mass spectrometrically for its isotopic composition. The *p*-chlorobenzyl chloride was reduced to *p*-chlorotoluene with lithium aluminum hydride as described above, and the "product" *p*-chlorotoluene was analyzed for its isotopic composition.

After the bromination of the *p*-chlorotoluene, the solvent was removed and the unreacted *p*-chlorotoluene was recovered by distillation through a concentric tube column under reduced pressure. The crude *p*-chlorobenzyl bromide remaining in the distilling flask was poured into a 100-ml. beaker and allowed to crystallize. Two recrystallizations from petroleum ether gave white crystals, m.p. 50–50.5°. The bromide was reduced with lithium aluminum hydride as described above and the *p*-chlorotoluene thus obtained was analyzed for its isotopic composition.

***p*-Methoxytoluene-d_1 and *p*-Methoxytoluene-d_3.**—After the bromination, the solvent was removed under reduced pressure. The residue was added to a solution of 5 g. of sodium in 130 ml. of anhydrous methanol and the solution was stirred for 10 min. at 35–45°. The solution was diluted with water, extracted with ether several times, and the ether solution was washed with water and dried over calcium chloride. The ether solution gave a negative silver nitrate test indicating completeness of reaction. The ether was removed and the residue was distilled through a concentric tube column giving 1.8 g. of unreacted *p*-methoxytoluene (82%, b.p. 74–75° at 15 mm.) and 4.8 g. of *p*-methoxybenzyl methyl ether (81%, b.p. 112–113° at 15 mm.). The recovered *p*-methoxytoluene and the methyl ether were analyzed for their isotopic compositions.

Ethylbenzene-d_1.—In the bromination using N-bromosuccinimide as previously described, equal molar quantities of ethylbenzene-d_1 and N-bromosuccinimide were used so as to permit all the ethylbenzene-d_1 to be converted to 1-bromoethylbenzene-d_1. After the solvent had been removed, the bromide was reduced to ethylbenzene using lithium aluminum hydride, and this product was analyzed. In one case, the bromination was carried to 91.7% completion, and the ethylbenzene was separated from the bromide by fractional distillation. The recovered ethylbenzene and that formed by the reduction of the bromide were analyzed for their isotopic compositions.

Cumene-d_1.—After the bromination using N-bromosuccinimide, the solvent was removed by vacuum distillation, and the residue was added to 40 ml. of methanol and allowed to stand overnight. This converted the bromide to the methyl ether. *n*-Pentane and excess dilute sodium bicarbonate solution were added to the methanol solution and the two layers were separated. The aqueous layer was washed with *n*-pentane and the combined pentane solutions were washed with sodium bicarbonate. After drying over calcium chloride, the solvent was removed and the product was distilled giving unreacted cumene-d_1. The ether was not isolated since it was not required for the calculation of the isotope effect. The recovered cumene was analyzed for its isotopic composition.

Deuterium–Hydrogen Exchange between Toluene-d_1 and Hydrogen Bromide.—Dry hydrogen bromide was bubbled through carbon tetrachloride in a gas bubbler until saturated. Fifty milliliters of the hydrogen bromide–carbon tetrachloride solution and 0.75 g. of toluene-d_1 were placed in a 17-mm. Pyrex tube and the tube was sealed. The tube was heated at 80° for eight hours, cooled and opened. After washing the solution and drying over calcium chloride, the toluene-d_1 was recovered by distillation. The reactant and the recovered toluene-d_1 were analyzed in the mass spectrometer for their isotopic composition. The toluene-d_1 (before reaction) had an isotopic composition of 17% toluene-d_0, 83% toluene-d_1 and 0% toluene-d_2, and the recovered toluene-d_1 had an isotopic composition of 29% toluene-d_0, 68% toluene-d_1 and 3% toluene-d_2. These results clearly show that deuterium–hydrogen exchange does occur when deuteriotoluenes are brominated in a sealed tube as described in the previous section.

A similar result was obtained when *p*-chlorotoluene-d_2 was allowed to react with hydrogen bromide under the above conditions. However, when *p*-thiocresol was added to the reaction mixture, no exchange was noted.

Bromination of a Mixture of *p*-Methoxytoluene-d_3 and *p*-Methoxytoluene-d_0 with N-Bromosuccinimide.—A mixture of *p*-methoxytoluene-d_0 and *p*-methoxytoluene-d_3 was brominated with N-bromosuccinimide (0.6 equiv.), the bromide converted to *p*-methoxybenzyl methyl ether and separated from the unreacted *p*-methoxydeuteriotoluene as described in the previous section. The isotopic composition for the reactant was *p*-methoxytoluene-d_0, 50.52%; *p*-methoxytoluene-d_1, 0.34%; *p*-methoxytoluene-d_2, 6.86%, *p*-methoxytoluene-d_3, 42.29%. If the *p*-methoxybenzyl radicals had reacted with *p*-methoxytoluene to generate new radicals the concentration of *p*-methoxytoluene-d_1 should have increased considerably; however, it only increased slightly (0.78%), largely as a result of its lower concentration and lower reactivity as compared to *p*-methoxytoluene-d_0. This type of exchange is therefore negligible during the halogenation reactions.

Percentage Side Chain Halogenation in the Bromination of Toluenes.—The bromination was carried out as described above and after the reaction had gone to completion, the bubbling of dry nitrogen through the solution was continued for two hours under reflux. This removed the hydrogen bromide present. To the solution was added silver nitrate in methanol. The precipitate was allowed to stand one hour and then was filtered. The precipitate was washed with water and methanol and dried to constant weight. The yield of silver bromide was 99.27% of the theoretical amount assuming complete side chain bromination by the bromide present.

Percentage Deuterium on the Ring of Toluene-d_2 and Cumene-d_1.—In order to determine the true isotope effect of reactions involving deuteriotoluenes and halogens, it is necessary to know the percentage deuterium on the ring. To determine this in a typical case, toluene-d_2 was oxidized to benzoic acid and decarboxylated giving benzene which was analyzed on the mass spectrometer for deuterium content. Fifty-five milliliters of a solution containing 6.0 g. of potassium permanganate (0.038 mole) and 1.0 g. of potassium hydroxide (0.018 mole) was placed in a small flask equipped with a condenser, and 1.48 g. of toluene-d_2 (0.016 mole) was added. The solution was heated on the steam-bath for one hour and then refluxed while stirring until the permanganate color disappeared. After filtering, the yellow solution was decolorized using Norite. Acidification gave 0.54 g. of benzoic acid (30%) which was dissolved in base and reprecipitated by acidification.

The benzoic acid was decarboxylated using quinoline and copper powder. The benzene obtained was collected and washed with dilute hydrochloric acid. After drying over anhydrous calcium sulfate, the benzene was analyzed using a mass spectrometer with an ionization potential of 70 volts. The ratio of the mass numbers 79 and 78 for the two benzene samples were both 6.54%. This is the normal C-13 content indicating that no deuterium was attached to the aromatic ring.

Russell[7] has found that the cumene-*d* prepared by the reaction of α-cumylpotassium with deuterium chloride contained a considerable amount of ring-deuterated material. The material prepared in this work, using deuterium oxide rather than deuterium chloride, was therefore examined for ring deuteration. A comparison of the mass spectra of this material at ionizing potentials of 20 and 70 v. with that of cumene and of cumene-d_1 which had been shown to contain no deuterium in the ring (prepared by the alkylation of benzene with 2-propyl-2-d_1 alcohol and kindly supplied by Dr. A. Streitwieser) indicated that no significant amount of deuterium was attached to the ring. A further difference between the products obtained by the use of deuterium chloride and deuterium oxide is that the former has considerable cumene-d_2 and -d_3 whereas the latter contained neither of these species.

Results and Discussion

Before considering the results of this investigation, it is necessary to distinguish between the intermolecular and intramolecular isotope effects. Using reactions proceeding at the methyl group of toluene as an example, the former will be the ratio of the rate of hydrogen abstraction from toluene to that of deuterium abstraction from a deuterium labeled toluene and the effect arises from the difference in ground state zero-point energies between the two molecules undergoing reaction. Correspondingly, the intramolecular isotope effect is the ratio of the rates of hydrogen to deuterium abstraction from a given molecule. Here the ground state energy will be the same for either reaction since the same molecules will be involved, and the difference in rate arises from the difference in zero-point energies in the two different activated complexes formed by removal of hydrogen or deuterium. It is the latter effect which is measured in the present case.

A typical example of the data obtained is shown in Table II, for the reaction of toluene-α-d_1 with N-bromosuccinimide. The compositions of the reactant toluene, the toluene recovered from the reaction and of the toluene formed by lithium aluminum hydride reduction of the benzyl bromide formed were determined mass spectrometrically using an ionizing potential (~ 9 v.) which was sufficient to produce $C_6H_5CH_3^+$ ions but would not result in fragmentation. The accuracy of the analyses was determined by comparing the composition of known mixtures of toluene and toluene-d_1 with that obtained from the mass spectra. A discrimination between the two species of 1% was found for mixtures having 72–100% toluene-d_1, and for those having 65–72%, a discrimination of 2% was noted. These errors will cause a proportionate error in the isotope effects, but since the error produced would be within the experimental error, the discrimination has been neglected in calculating the isotope effects.

TABLE II

REACTION OF TOLUENE-d_1 WITH N-BROMOSUCCINIMIDE

	Run 1		Run 2	
Reactant	6.18% d_0[a]	93.82% d_1	15.79% d_0	84.21% d_1
	6.19	93.83	15.84	84.16
Recovd. reactant	4.41	95.60	11.25	88.75
	4.36	95.64		
Product (as toluene)	15.94	84.06	25.52	74.48
	15.96	84.04	25.50	74.50
Reaction, %	60.33		69.82	
k_H/k_D	4.89		4.83	

[a] Composition calculated from duplicate mass spectral determinations.

The amounts of toluene-d_0 and -d_1 which were used in the reaction were calculated from the compositions of the reactant and recovered reactant, and the percentage conversion. The amount of toluene-d_0 which reacted was subtracted from the amount of unlabeled material in the product, and the ratio of labeled to unlabeled product, corrected for statistical effects, gave the k_H/k_D ratio. This method is believed to be superior to those in which the deuterium content of product formed in the abstraction of the hydrogen (*e.g.*, a hydrogen halide) is determined since exchange reactions are not as likely to introduce an error, and since exchange between the reactant and the product will immediately become evident as an unusual composition of the recovered reactant.

The results obtained in determining the isotope effects for the halogenation of several deuterium-labeled toluenes are given in Table III. All of the results were obtained in carbon tetrachloride solution at 77°. The results will be compared first with those obtained by previous investigators. The bromination of toluene was found by the previous investigators to give an isotope effect of 3.3[2] and this value is much lower than that obtained here. It has now been found that considerable hydrogen–deuterium exchange occurs between toluene and the product, hydrogen bromide, if the latter is not removed from the reaction mixture as it is formed, and this type of exchange probably accounts for the lower isotope effect observed by the previous workers. The exchange is readily apparent since the toluene recovered from the bromination of toluene-d_1 contains a considerable amount of toluene-d_2 if the hydrogen bromide is not swept out of the reaction flask. In a separate experiment, toluene-d_1 was found to exchange with hydrogen bromide, and the exchange was inhibited by thiocresol. This suggests that benzyl radicals are formed and that they react with hydrogen bromide at an appreciable rate to form toluene and bromine radicals, and is in accord with the kinetic data which have been obtained on the bromination of

---

(7) G. A. Russell, THIS JOURNAL, **79**, 3871 (1957).

TABLE III

ISOTOPE EFFECTS IN THE SIDE CHAIN HALOGENATION OF TOLUENES IN CARBON TETRACHLORIDE SOLUTION AT 77°

Reagent	Toluene-d_1	Toluene-d_2	*p*-Chlorotoluene-d_1	*p*-Chlorotoluene-d_2	*p*-Methoxytoluene-d_1
N-Bromosuccinimide	4.86 ± 0.03[a]	5.11 ± 0.02	5.08 ± 0.14	5.54 ± 0.10	3.22 ± 0.12
Bromine	4.59 ± .03	5.15 ± .27	5.22 ± .17	5.73	
Chlorine	1.30 ± .01	1.38 ± .09	1.44 ± .08	1.33 ± .10	
Sulfuryl chloride	1.42 ± .02				

[a] The deviations given are based on duplicate determinations.

toluene.[8] All of the experiments reported in this work were done under conditions which would minimize this exchange.

The isotope effect for the chlorination of toluene has been found to be appreciably lower than the values obtained by previous investigators.[2] The reason for this difference is not clear, but it does not appear to be due to exchange or to discrimination in the mass spectrometer since the former would have been detected by an abnormal composition of the unreacted toluene, and the latter could not cause an error greater than 0.1 in the isotope effect. It should be noted that the isotope effects for chlorination obtained in this investigation were reproducible, and that about the same value was obtained for a series of compounds. The difference between our results and the previous ones may in part result from the use of toluene as a solvent in most of the previous work, whereas it is now known that chlorine atoms show greater selectivity in aromatic solvents.[9] Also, in some of the previous work, a mixture of inter- and intramolecular isotope effects was measured, and there may be some difference between the two isotope effects. Finally, the previous workers determined the isotope effect by converting the hydrogen chloride formed in the reaction to water using silver oxide, followed by analysis of the water. A small amount of extraneous water introduced in this operation would lead to a high value for the isotope effect.

If one reads across the table, one finds that the isotope effect is largest with *p*-chlorotoluene, intermediate with toluene and smallest with *p*-methoxytoluene. Also, reading down the table, it may be observed that the isotope effect is less for chlorination than for bromination, and that bromination using N-bromosuccinimide or bromine give about the same (although significantly different) isotope effect. We have suggested that in any series of reactions, the one with the highest activation energy should have the highest isotope effect, and have interpreted this in terms of the potential energy curves for the dissociation of products and reactants (*i.e.*, $C_6H_5CH_3 \rightarrow C_6H_5CH_2\cdot + H\cdot$ and $HX \rightarrow X\cdot + H\cdot$).[10] If these curves are assumed to intersect at approximately the points given by the activation energies for the forward and reverse reactions, then the extent of C–H bond breaking is a function of the activation energy and, correspondingly, the magnitude of the isotope effect will parallel the change in activation energy for a series of related reactions.

The results obtained in this investigation are in accord with this, for the chlorination of hydrocarbons in the gas phase has been found to have a very low activation energy (~ 1 kcal.)[11] and it cannot be much higher in the liquid phase. The bromination of toluene has been found to have an activation energy of 7.2 kcal.[8] and the activation energy for the propagation step in the reaction with N-bromosuccinimide[12] will probably be about as large.

Correspondingly, the Hammett ρ-value for hydrogen abstraction by bromine, chlorine or other radicals has been found always to be negative,[13] and if it is assumed that the entropy factor will be essentially constant for the reactions of a series of substituted toluenes with a given reagent, then the activation energy will be largest for electron-withdrawing substituents and lowest for electron-releasing substituents. Here again, the largest isotope effect is obtained with the substituent giving the highest activation energy.

The energy of activation for hydrogen abstraction may be changed in another way, that of introducing α-methyl substituents which change the type of hydrogen being abstracted from primary to secondary and to tertiary. The isotope effects observed in the bromination by N-bromosuccinimide are given in Table IV, and are compared with the selectivity ratios obtained in the reaction of these compounds with peroxy radicals.[14] It must first be noted that the value given for cumene is of necessity the intermolecular isotope effect. However, the data to be presented subsequently indicate that the inter- and intramolecular isotope effects for these reactions are not much different, and therefore the isotope effect for the reaction of cumene is significantly less than that for ethylbenzene. It is reasonable to conclude that the activation energies would decrease going down the series, thus accounting for the selectivity ratios, and therefore the isotope effect again shows a parallelism with activation energies. All of the available data appear to be in accord with the postulate of a parallelism between activation energy and the deuterium isotope effect, and it should be mentioned

TABLE IV

EFFECT OF α-METHYL SUBSTITUTION ON THE ISOTOPE EFFECT

Compound	k_H/k_D	Selectivity ratio
Toluene	4.86 ± 0.03	1
Ethylbenzene	2.67 ± .04	7.9
Cumene	1.81 ± .05	13

---

[8] H. R. Anderson, Jr., H. A. Scheraga and E. R. Van Artsdalen, *J. Chem. Phys.*, **21**, 1258 (1953).

[9] G. A. Russell, THIS JOURNAL, **79**, 2977 (1957).

[10] K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955). A similar suggestion has been made by G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

[11] H. O. Pritchard, J. B. Pyke and A. F. Trotman-Dickenson, *ibid.*, **77**, 2628 (1955).

[12] *Cf.* E. Youngham, Ph.D. Thesis, University of Washington, 1952, on the reaction of N-bromosuccinimide with cyclohexene.

[13] C. Walling and B. Miller, THIS JOURNAL, **79**, 4181 (1957), and referenced cited therein.

[14] G. A. Russell, *ibid.*, **78**, 1047 (1956).

that this has been observed recently for a C-13 isotope effect.[15]

The data also indicate the effect of α-deuterium substitution on the magnitude of the isotope effect. For the brominations recorded in Table III, the average ratio of the isotope effect for the monodeuterio- to that for the dideuteriocompound is 0.92 ± 0.02, indicating that in the activated complex the remaining carbon–hydrogen or carbon–deuterium bonds are strengthened as compared to the ground state. This effect probably accounts in large measure for the difference in isotope effect in the bromination of p-methoxytoluene-d_1 (k_H/k_D 3.22, intramolecular) and p-methoxytoluene-d_3 (k_H/k_D 4.32, intermolecular). Here the ratio of isotope effects is 0.75, whereas if there were no difference between the two types of isotope effects, one might estimate a value of about 0.85 based on the previously determined effect of α-deuterium substitution (*i.e.*, 0.92^2). This suggests that the intermolecular isotope effect may be slightly higher than the intramolecular isotope effect.

Some data on the difference between the two types of isotope effects may be obtained directly from the isotopic compositions for the runs given in Table II. If the rate constant for the abstraction of a hydrogen from toluene-d_0 is k_1, that for removing a hydrogen from toluene-d_1 is k_2, and that for removing a deuterium from the latter is k_3, then the rate expressions for the reaction of toluene-d_0 (D_0) and toluene-d_1 (D_1) are

$$v_0 = 3k_1[D_0][X]$$
$$v_1 = 2k_2[D_1][X] + k_3[D_1][X]$$

where X is the attacking radical. Dividing one expression by the other and rearranging the terms gives

$$\frac{k_D}{k_H} = \frac{k_3}{k_1} = 3\left(\frac{v_1D_0}{v_0D_1}\right) - 2\frac{k_2}{k_1}$$

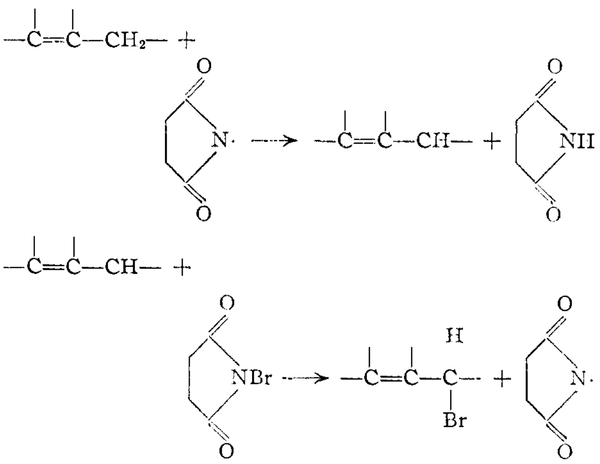
Substituting $-dD_0/dt$ for v_0 and $-dD_1/dt$ for v_1 and integrating gives

$$\frac{k_D}{k_H} = 3\ [(\log D_1^i/D_1^f)/(\log D_0^i/D_0^f)] - 2\frac{k_2}{k_1}$$

If the values given in Table II are substituted into this expression and k_2/k_1 is assumed to be between 0.95 and 1.0, the isotope effect, k_B/k_D, is found to be 4.8 ± 0.8. Although the accuracy of this value is not high, it does indicate that the inter- and intramolecular isotope effects are quite similar in this reaction.

In all of these reactions a possible, but somewhat unlikely, reaction which would give hydrogen–deuterium exchange is the reaction of a benzyl radical with toluene, transferring either a hydrogen or a deuterium. A test for this type of reaction was made by brominating a mixture of p-methoxytoluene and p-methoxytoluene-d_3 and examining the recovered reactant for mono- and dideuterated compounds in excess of that originally present. No enrichment of these species was found, indicating that this type of exchange is not important in these reactions.

We now wish to turn our attention to the use which may be made of the magnitude of the isotope effect. The halogenations by chlorine and bromine have been shown clearly to involve the abstraction of a hydrogen atom by a chlorine or bromine radical. The available kinetic data on allylic bromination by N-bromosuccinimide, that the reaction is first order with respect to the olefin, half order in initiator (azo-bis-isobutyronitrile) and zeroth order in N-bromosuccinimide,[12] along with other evidence, shows that the reaction follows the path proposed by Bloomfield[16]



The chlorination by N-chlorosuccinimide has, however, been reported to proceed *via* another course, namely, by the formation of chlorine which then effects the halogenation in the usual fashion.[17] This may be tested easily by determining the isotope effect for the reaction with toluene, for the values which are expected for abstraction of hydrogen by the N-succinimidyl radical and by a chlorine atom are now known. The reaction of N-chlorosuccinimide does not proceed readily in carbon tetrachloride solution, but an essentially quantitative reaction is obtained when toluene is used as the solvent. The isotope effects for some halogenations carried out in toluene solution at 110° are given in Table V.

TABLE V

ISOTOPE EFFECTS FOR HALOGENATION IN TOLUENE SOLUTION AT 110°

Reagent	k_H/k_D
N-Bromosuccinimide	3.59 ± 0.05
N-Chlorosuccinimide	1.59 ± .05
Chlorine	1.47 ± .02
Sulfuryl chloride	1.73 ± .05

It is immediately apparent that the N-chlorosuccinimide reaction does not involve an N-succinimidyl radical, and therefore probably does involve a chlorine radical. The isotope effect for the reaction with N-bromosuccinimide observed here is smaller than that found at 77° and this is expected since the isotope effect is temperature dependent. However, an activation energy difference for hydrogen and deuterium abstraction should not be calculated from these data since Russell[9] has shown that the selectivity of a chlorine radical is

---

(15) C. A. Ropp, C. J. Danby and D. A. Dominey, THIS JOURNAL, **79**, 4944 (1957).

(16) G. F. Bloomfield, *J. Chem. Soc.*, 114 (1944).

(17) P. A. Goldfinger, P. A. Gosselain and R. H. Martin, *Nature*, **168**, 30 (1951).

increased when it is introduced into an aromatic solvent, and the same may hold true for an N-succinimidyl radical. The effect of solvent on the isotope effect for chlorination was noted here also, the value obtained at 110° in toluene solution (1.47) being significantly larger than that obtained at 77° in carbon tetrachloride (1.30).

There is also a question as to whether the chlorination by sulfuryl chloride involves a chlorine radical or a $SO_2Cl\cdot$ radical.[18] If the latter were involved, and it had a significantly different reactivity difference for H and D than does the chlorine radical, this would be observed in the isotope effects of the two reactions. The reaction with N-chlorosuccinimide gives, within the experimental error, the same isotope effect as does the reaction with chlorine, and the chlorination by sulfuryl chloride gives a significantly larger isotope effect. This adds weight to the idea that another species than the chlorine radical is to at least a small extent involved in the hydrogen abstraction step for the latter reagent. It should be noted that in carbon tetrachloride solution only a small difference was found in the isotope effects for the reactions with chlorine and with sulfuryl chloride (Table III).

Acknowledgment.—We wish to thank the National Science Foundation for their support of this work, and the Atomic Energy Commission for assistance in obtaining certain equipment for the mass spectrometer. We also wish to thank Mr. B. J. Nist for his invaluable assistance in obtaining the mass spectra.

SEATTLE, WASHINGTON

---

[18] G. A. Russell and H. C. Brown, THIS JOURNAL, **77**, 4031 (1955).

[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY]

Effect of Various Friedel–Crafts Catalysts on the Rates and Kinetics of the Reaction of Benzoyl Chloride with Aromatics[1,2]

BY FREDERICK R. JENSEN[3,4] AND HERBERT C. BROWN

RECEIVED OCTOBER 30, 1957

The metal chloride-catalyzed Friedel–Crafts acylation of aromatics in benzoyl chloride as solvent proceeds far faster with gallium chloride, ferric chloride and antimony pentachloride than does the corresponding reaction with aluminum chloride. On the other hand, the catalysis by stannic chloride, boron chloride and antimony trichloride is far smaller than that by aluminum chloride. The observed effects of the metal halides on the rate of the benzoylation reaction at 25° ($SbCl_5$, 1300; $FeCl_3$, 570; $GaCl_3$, 500; $AlCl_3$, 1; $SnCl_4$, 1/350; BCl_3, 1/1600; $SbCl_3$, very small) does not correspond to the relative strengths of these Lewis acids. Instead of the simple second-order kinetics exhibited by the aluminum chloride reaction, the fast reactions follow the alternative kinetic expression: rate = $(k_3/[MCl_n]_0)[MCl_n]^2[ArH]$. On the other hand, the slow reaction with stannic chloride and boron chloride appears to follow the alternative kinetic expression (similar to that previously observed with aluminum chloride): rate = $k_2[MCl_n][ArH]$. The similarity in the isomer distributions realized in the benzoylation of toluene argues for a common reaction intermediate, presumably the acylonium ion, $C_6H_5CO^+$, in the substitution stage. The difference in the reaction kinetics can be rationalized in terms of the role of the metal halide in ionizing the benzoyl chloride.

Aluminum chloride is by far the most commonly used Friedel–Crafts catalyst for the acylation of aromatics.[5] However, numerous other metal halides have been utilized as catalysts for this reaction.

Attempts have been made to ascertain the relative effectiveness of various catalysts in the acylation reaction by comparing the yields of ketones realized in these reactions.[6,7] Such methods can provide only rough qualitative information. The recent observation that the benzoylation of aromatics by aluminum chloride in benzoyl chloride proceeds by clean second-order kinetics[8] suggested that a kinetic approach might provide a more quantitative understanding of the effect of the metal halide on this reaction. Such information should be of value in guiding the selection of the most favorable catalyst in acylations and in furthering our understanding of the role of the metal halide catalyst in Friedel–Crafts reactions. For this reason we undertook a study of the rates and kinetics of the benzoylation reaction in benzoyl chloride solution utilizing the chlorides of antimony(III, V), gallium(III), iron(III), boron(III) and tin(IV).

We had anticipated that all of these metal halides would exhibit the simple second-order kinetics of the aluminum chloride reaction

$$\text{rate} = k_2[AlCl_3][ArH] \qquad (1)$$
$$\text{or rate} = k_2[C_6H_5COCl\cdot AlCl_3][ArH]$$

with the magnitudes of the rate constants reflecting the strengths of the metal halides as Lewis acids. However, we observed markedly different kinetics for some of the metal halides studied, with some of the catalytic activities being far greater than that of aluminum chloride, presumably the strongest Lewis acid in the group.

Results

Gallium Chloride.—Gallium halides have received only limited attention as Friedel–Crafts catalysts, probably because of the cost and scarcity

---

[1] The Catalytic Halides. XXII.

[2] Based upon a thesis submitted by F. R. Jensen in partial fulfillment of the requirements for the Ph.D. degree.

[3] Department of Chemistry, University of California, Berkeley, California.

[4] Research assistant on a project supported by the Atomic Energy Commission, 1953–1954; National Science Foundation Predoctoral Fellow, 1954–1955.

[5] C. A. Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941.

[6] N. O. Calloway, *Chem. Revs.*, **17**, 327 (1935).

[7] O. C. Dermer, D. M. Wilson, F. M. Johnson and V. H. Dermer, THIS JOURNAL, **63**, 2881 (1941); O. C. Dermer and R. A. Billmeier, *ibid.*, **64**, 464 (1942); O. C. Dermer, P. T. Mori and S. Suguitan, *Proc. Oklahoma Akad. Sci.*, **29**, 74 (1948).

[8] H. C. Brown and F. R. Jensen, THIS JOURNAL, **80**, 2291, 2296 (1958).