

A STUDY OF HYDROGEN EXCHANGE IN BENZENE AND
SEVERAL ALKYL BENZENES

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1960

Submitted to the faculty of the Graduate School of
the Oklahoma State University
in partial fulfillment of the requirements
for the degree of
DOCTOR OF PHILOSOPHY
August, 1965

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A STUDY OF HYDROGEN EXCHANGE IN BENZENE AND
SEVERAL ALKYL BENZENES

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ACKNOWLEDGMENTS

Grateful acknowledgment is made to Dr. E. M. Hodnett, research adviser, for his patience, guidance, and assistance throughout this work; to Dr. O. C. Dermer, head of the Chemistry Department, for his reading of the manuscript prior to its being typed; to Mr. C. R. Williams, formerly in the Chemistry Department, for his assistance in the early phases of the computer programming; to Mr. Preston Gant, Central Research Division of the Continental Oil Company, for helpful suggestions on the tritium assays; and to Mr. Prem S. Juneja for his helpful suggestions concerning experimental details which arose from time to time.

Acknowledgment is made of financial assistance in the form of a graduate teaching assistantship in the Chemistry Department. Also, a research assistantship from the Atomic Energy Commission, Contract No. AT(11-1)-1049, through the Research Foundation is appreciated. Research done during the term of the latter assistantship provided material for this thesis.

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CHAPTER I

INTRODUCTION

The object of this research is to gain a clearer knowledge of hydrogen exchange in aromatic molecules and of aromatic electrophilic substitution in general. For some time it has been known that a hydrocarbon substituted with a heavy hydrogen isotope will, in a strongly acid medium, undergo exchange of protium in the acid for deuterium or tritium in the hydrocarbon. This reaction is thought to be an electrophilic reaction just as nitration, halogenation, and sulfonation are.

If hydrogen exchange is electrophilic then the partial rate factors relating the reactivity of each ring position of any other aromatic hydrocarbon to that of benzene should be about the same as for nitration, etc., of the same compound. Frequently any decrease in reactivity at an ortho position relative to that at the para position is attributed to steric effects between the substrate and the approaching electrophile. If the steric requirement of the electrophile in hydrogen exchange is less than that for the other, more common electrophilic substitutions, the partial rate factors found for this exchange should tell us the importance of the "steric hindrance argument" and, if steric effects are unimportant, give a more meaningful measure of ortho reactivity.

In this study various aromatic hydrocarbons, in the presence of benzene, were allowed to exchange their hydrogen atoms with tritium

atoms initially present in a solvent of sulfuric and trifluoroacetic acids. Substitution is known to occur at all positions on the ring, and at the tracer level, determination of the tritium content at each of the individual positions on the ring is not possible from an ion-current measurement of the tritium in the hydrocarbon. The only measurement of radioactivity that can be made is the total radioactivity; therefore, after the rate equations were set up, it was necessary to relate the overall specific radioactivity to the unknown parameters, the independent variable being time. The equation so derived was non-linear in the parameters so a considerable amount of time was spent resolving the mathematical difficulties.

The experimental procedure follows:

1. Benzene and another hydrocarbon were mixed with an acid solvent and water-t and sealed in glass reaction tubes.
2. The contents of these tubes were allowed to react in a constant-temperature bath.
3. An aliquot of the reaction mixture was removed at predetermined times, and the reaction was stopped by neutralizing the acid.
4. The hydrocarbons were separately assayed for their total tritium content.
5. The data of specific radioactivity versus time were analyzed for the partial rate factors using a digital computer.

CHAPTER II

HISTORICAL

For many years aromatic compounds such as benzene and toluene have been known to undergo substitution reactions. Typical of these substitutions are halogenation, sulfonation, and nitration. The active species for each of these reactions has been shown to be electrophilic, i.e., the attacking reagent in each reaction is electron-deficient. It is this deficiency which allows the reagent to interact with the π -electron system of the aromatic ring.

One reaction of the aromatic nucleus not mentioned above is the substitution of a hydrogen atom by another hydrogen atom. Obviously, to observe the replacement of a protium atom by a protium atom would be impossible. However, the exchange of a protium atom with a hydrogen atom having a mass different from one could be observed.

In 1936, soon after the discovery of deuterium and tritium, Ingold (16) observed the substitution of ring protium atoms in benzene by deuterium. Strong acid was required to effect the substitution, or exchange as the reaction is now known since it is a special kind of substitution. For a given substrate, the exchange went more readily as the acid strength was increased. In a weak acid, relatively reactive substrates were found to undergo the same degree of exchange as a less reactive substrate in a stronger acid. Substituent effects and reactivities were observed to be similar to those for the familiar

electrophilic substitutions such as nitration, halogenation, and sulfonation. This qualitative work led Ingold to suggest that the exchange was electrophilic.

For the exchange to be electrophilic, deuteration of substituted benzene molecules should follow known rules of orientation and velocity as observed in other electrophilic aromatic substitutions. Also, the deuteration efficiency of an acid reagent should increase with its proton-donating ability, i.e., with its tendency to ionize. To test these points the phenolate ion, dimethylaniline, anisole, benzene, and benzenesulfonic acid were used as substrates; the hydronium ion, water, phenol, sulfuric and selenic acids were used as acids. The rate of deuteration varied with the ionization constant of the acid. Qualitatively, deuteration of benzene molecules which were substituted with electron-donating groups proceeded much faster than deuteration of those which were substituted with electron-withdrawing groups. Furthermore, the rate was proportional to the ease of this electron donation. Also, as the substrate molecule became less reactive, i.e., had less tendency for electron donation, the acid causing the exchange had to be more highly ionized.

Exchange is known to be acid catalyzed and, in general, to be specific-acid catalyzed. For extremely activated aromatic compounds, substances not normally considered acidic might readily cause exchange. Kresge and Chiang (18) have shown that exchange of tritium in 1,3,5-trimethoxybenzene-2- t occurs in acids as weak as water. Satchell (29) observed similar results in exchange studies with 1,2,3-trimethoxybenzene-4,6- t_2 using potassium hydrogen sulfate, dichloroacetic acid, and trichloroacetic acid.

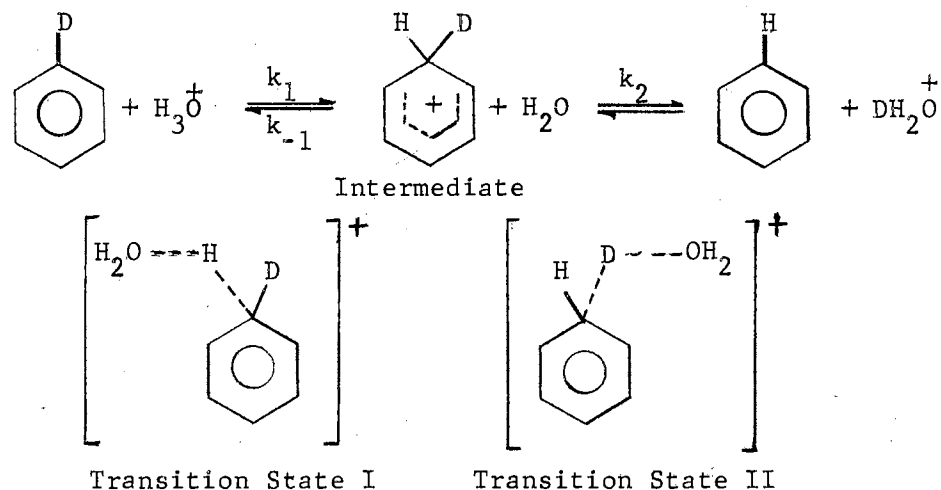
More recently Satchell (30) has found that the rate for hydrogen exchange is proportional to the sum of the stoichiometric concentrations of all acidic species present. Hydrogen exchange was studied using mixtures of stannic chloride as the Lewis acid and either acetic acid, hydrochloric acid, or water as the Brönsted acid. In each of these cases the rate of the exchange reaction increased as the stannic chloride and/or the Brönsted acid concentration was increased. With trifluoroacetic acid containing stannic chloride as the acid mixture, the exchange was slower than for any of the other Brönsted acids tried. This behavior was attributed to the fact that no complex can form between the trifluoroacetic acid and stannic chloride.

How long does this exchange go on? In other electrophilic aromatic substitutions, e.g., nitration of benzene, the presence of a nitro group after the first substitution greatly slows further substitution. However, monodeuteration of benzene yields a substance which, in the absence of a secondary deuterium kinetic isotope effect, should be as reactive as benzene toward further ring substitution. Then for benzene, if sufficient deuterium were present, one could obtain a mono- or polydeuterated compound depending on the length of reaction time.

In a substance such as toluene where the 2, 4, and 6 positions are approximately equally reactive but much more reactive than the 3 and 5 positions, where would deuteration occur? In 1938 Best and Wilson (2) answered this question. With sodium phenolate and deuterium oxide at 100° for 96 hours and aniline hydrochloride and deuterium oxide at 100° for 30 hours, the 2,4,6-trideutero compound was formed in both cases. That deuterium was present at only these positions was proved by treating the resulting compound with bromine water and showing that no

deuterium then remained in the molecule. We now know that deuteration would have occurred at the two remaining positions if the exchange had been allowed to proceed longer.

Olsson (26) postulated the following mechanism for hydrogen exchange:



Others have assumed that originally the proton becomes involved with the aromatic system by a " π -complex" with the π electrons of the ring (10,11). Once formed, this π -complex rearranges to the intermediate, which is σ -bonded. The departing deuterium is then assumed to pass through an analogous π -complex before the aromatic system is finally restored.

After Ingold's original work, no more was done with the hydrogen exchange reaction until about 1954. By this time the effects of various substituents on other electrophilic aromatic substitutions had been determined. If the exchange really were electrophilic a quantitative study of substituent effects would be of interest.

Melander and Olsson (27) were the first to make such a study.

When their work was reported in 1954, tritium had become rather plentiful and cheap; furthermore, the assay for tritium is simpler in the laboratory than for deuterium. Toluene successively labeled with tritium at the tracer level in the ortho, meta, para, and alpha positions was prepared. Each of these hydrocarbons was separately mixed with about 80 per cent sulfuric acid forming a heterogeneous system, and the loss of tritium at 25° was measured as a function of time. For the ortho and para compounds the half-reaction time was about one hour while that for the meta was about thirty-two hours. For a maximum reaction time of two days, less than 2 per cent of the tritium was lost from toluene- α -t. However, due to an insufficient shaking speed, the first reported relative rates for detritiation of toluene were in error. In 1956, the detritiation experiment was repeated and also the analogous dedeuteration was studied (23). For detritiation, the ortho/meta/para ratio was 47:1:41 and for dedeuteration it was 51:1:46. The kinetic isotope effect k_T/k_D had a value of the order of 0.55 to 0.60.

When tritium was initially present in the acid, approximately the same relative rates were found from the growth curve of the radioactivity in toluene although no distinction could be made between ortho and para reactivity (27). For long exchange times permitting approach to equilibrium, the heavier isotope preferred the position in the aromatic nucleus to that in the acid.

Tiers (32) reported the dedeuteration of toluene in aqueous 70.8 per cent perchloric acid--a heterogeneous system--and also in anhydrous heptafluorobutyric acid. A difference in the ortho/para ratio was found when these acids were used. For the perchloric acid, the ortho/para ratio was 1.09 and the meta/para was 0.065. Tiers assumed that the

attacking species in the perchloric acid experiments was the hydronium ion. The exchange was repeated with anhydrous heptafluorobutyric acid. In this medium the ortho/para ratio was 0.4 and the meta/para about the same as for perchloric acid. These results were explained on the assumption that the attacking species for the perchloric-acid-induced exchange has a much smaller steric requirement than that for the heptafluorobutyric acid. However, steric effects probably have not been completely eliminated in this comparison.

Partial rate factors for the exchange were first studied by Gold and Satchell (12). A partial rate factor for any reaction in an aromatic compound is defined as the rate of substitution of a particular nuclear position in a substituted benzene molecule relative to a single position in benzene. Partial rate factors had previously been determined for aromatic nitrations and halogenations. If the reaction were truly electrophilic and operating under a similar mechanism, one might expect partial rate factors for the exchange similar to those for other aromatic substitution reactions. Partial rate factors for hydrogen exchange in toluene have been determined by several research groups and are shown in Table I.

In electrophilic substitutions the ortho/para ratio has been of interest in that variations in the ratio might be due to changes in the steric requirement of the attacking electrophile. Various values found for the ortho/para ratio in hydrogen exchange are shown in Table IIa and IIb. On comparing the ortho/para ratio for exchange with the same ratios for bromination and nitration, Gold and Satchell (12) found a value between those reported for bromination and nitration. They interpreted these results to mean that steric requirements for the

TABLE I
PARTIAL RATE FACTORS FOR HYDROGEN EXCHANGE IN TOLUENE

Medium Composition ^{a, b}	Partial Rate Factor			Reference
	ortho	meta	para	
CF ₃ CO ₂ H (62) ^{c, d}	250	4	420	21
H ₂ SO ₄ (81) ^e	135	2.6	121	26
H ₂ SO ₄ (81) ^f	117	2.6	97	26
CF ₃ CO ₂ H - H ₂ SO ₄ (0.25 molal in sulfuric) ^e	238	3.1	350	22
H ₂ SO ₄ (71) ^f	250	5	250	7
H ₂ SO ₄ (40) - CH ₃ CO ₂ H (26) ^f	305	5	313	7
H ₂ SO ₄ (2.5) - CF ₃ CO ₂ H (95.3) ^f	541	9.2	702	7
HClO ₄ (2.5) - CF ₃ CO ₂ H (92) ^f	330	7.2	313	7
H ₂ SO ₄ (68) ^e	83	1.9	83	12

^aNumbers in parentheses are weight per cent unless otherwise stated

^bWater is the remainder of the solvent

^cReaction temperature is 70°

^dDeuteration studies

^eDedeuteration studies

^fDetritiation studies

TABLE IIa

VARIATION IN THE ORTHO/PARA RATIO IN HYDROGEN EXCHANGE
WITH CHANGES IN THE CATALYZING ACID

Medium Composition ^a					Ortho/Para Ratio ^b	
H ₂ SO ₄	HClO ₄	CF ₃ CO ₂ H	C ₃ F ₇ CO ₂ H	H ₂ O	Toluene	<u>tert</u> -Butylbenzene
	2.51	92.04		5.45	1.05	1.02
2.48		95.31		2.21	0.77	-
1.88		93.00		5.12	0.73	0.72
		62.00		38.00	0.60 ^c	0.40 ^c
		100.00			0.49	0.45
			100.00		0.39	0.37

^aWeight per cent

^bDetritiation studies, unless otherwise indicated

^cDeuteration studies

TABLE IIb

VARIATION OF THE ORTHO/PARA RATIO WITH SULFURIC ACID
CONCENTRATION FOR HYDROGEN EXCHANGE IN TOLUENE

Sulfuric Acid Concentration ^a	Ortho/Para Ratio	Reference
81.0 ^b	1.11	26
81.0	1.20	26
74.8	1.06	1
73.2	1.04	1
71.3	1.00	7
70.7	1.00	1
69.0	0.99	1
64.5	0.98	1

^aWeight per cent

^bDedeuteration studies; all other entries in the table are from detritiation studies

exchange are intermediate to those for bromination and nitration.

Mackor, Smit, and van der Waals (22) reported the dedeuteration of deuterated benzene, toluene, ethylbenzene, tert-butylbenzene, m- and p-xylene, and mesitylene. A mixture of trifluoroacetic and sulfuric acids (0.1-0.25 molal) made a good solvent which was also strong enough to effect the exchange. Addition of sulfuric acid accelerated the reaction and kept it within experimentally accessible limits. For less reactive hydrocarbons sulfuric acid at concentrations up to 2 molal was used. Deuterium analyses were done by mass spectrometry.

The only case of hydrogen exchange in which the heavy hydrogen isotope was not originally present in the hydrocarbon was reported by Lauer, Matson, and Stedman (21). Trifluoroacetic acid was used as the solvent, and the deuterium was introduced as deuterium oxide. The exchange was followed in benzene, toluene, and several other mono- and polyalkylbenzenes. Partial rate factors determined in this study are shown in Table III. Determination of the deuterium content at each of the nuclear positions was necessary since all possible monodeutero hydrocarbons were produced. As an example of their analytical approach, the 2-nitro, 4-nitro, and the 2,4,6-trinitro derivatives of toluene were made. Each of these nitro compounds was then analyzed for deuterium, and by proper mathematical manipulation of the results of these analyses, the deuterium content at the 2, 3, and 4 positions was determined by difference.

With 70-80 per cent aqueous sulfuric acid, Eaborn and Taylor (6) found that on detrutiation of toluene-3-t and -4-t, the partial rate factor varied with the concentration of sulfuric acid used. The rates of detrutiation of benzene-t, toluene-2-t, -3-t, and -4-t, and tert-butylbenzene-2-t, -3-t, and -4-t were determined using as acids sulfuric,

TABLE III
PARTIAL RATE FACTORS FOR HYDROGEN-DEUTERIUM EXCHANGE
FOR THE MONOALKYLBENZENES

Compound	Partial Rate Factor		
	ortho	meta	para
Toluene	253	3.5	421
Ethylbenzene	257	6.9	449
Cumene	259	-	493
<u>n</u> -Propylbenzene	-	6.8	-
<u>sec</u> -Butylbenzene	202	8.4	478
<u>tert</u> -Butylbenzene	198	7.0	490

trifluoroacetic containing aqueous perchloric, and trifluoroacetic containing aqueous sulfuric (7). A large spread in rates was observed as the medium was varied, and this spread increased as the solvating power of the medium decreased. The 4-tert-butyl group was found to be either more or less activating than the 4-methyl group, this difference appearing as the medium was varied. The 3-tert-butyl group was always more activating than the 3-methyl group.

In a study by Baker, Eaborn, and Taylor (1), the detritiation of toluene-2-t and -4-t and tert-butylbenzene-2-t and -4-t was followed using several acids of different solvating powers. The acids used were aqueous sulfuric, trifluoroacetic and either sulfuric or perchloric, anhydrous trifluoroacetic, and anhydrous heptafluorobutyric. If the spread in rates were truly due to differences in the solvating powers of the media, then the spread of rates should be very marked with the substrates and acids used. The ortho and para relative reactivities in the several acids were found to vary in a closely similar way so the effect must not originate in steric hindrance from the ortho alkyl groups.

CHAPTER III

INTRODUCTION TO THE EXPERIMENTAL WORK

Objectives and Plan of the Study

The purpose of this section is to present the plan of this study and to discuss these plans in the light of past work. The desired goal is to assess more accurately the reactivity at the ortho position. What are felt to be better means to achieve this goal are presented. Most of the points covered here have been briefly discussed in Chapter II. They will again be discussed and, in general, the various points which the results of this study are hoped to clarify will be emphasized.

Much of the earlier exchange work was done in 75-85 per cent sulfuric acid, a medium in which the hydrocarbons are practically insoluble. This low solubility led to a two-phase, heterogeneous reaction mixture in which the reaction rate was a function of the contact area of the two phases. Several workers have followed the exchange in sulfuric acid saturated with the deuterated or tritiated hydrocarbon, but the solubilities are low and difficult to measure (25). Exchange has also been accelerated by shaking or stirring the medium, but invariably, duplication of these conditions has been impossible. At the concentration of sulfuric acid which has been used, sulfonation becomes a serious side reaction, and seldom has the observed exchange rate constant been corrected for the sulfonation which is simultaneously occurring.

With an unlabeled hydrocarbon as the starting material, there is only one case, as already noted, where the exchange was followed by measuring the uptake of deuterium with increasing time (21). Lauer et al., studied the deuteration of benzene, toluene, and heavier alkylbenzenes in the presence of deuterium oxide and trifluoroacetic acid. The deuterium content was determined by nitration of the hydrocarbon, subsequent combustion of the nitro compounds, and collection of the water so formed. The results from the determination of the density of the water are a measure of the deuterium present. This method of analysis seems questionable in that during the nitration process the hydrocarbon is in contact with a mixture of nitric and sulfuric acids, conditions under which loss of deuterium could occur. Also, deuterium in the meta position is determined by difference of two large numbers, so that the accuracy of the meta deuterium content is questionable.

There seemed to be several areas of the previous work which needed clarification, and these are briefly summarized below:

1. In a homogeneous system factors such as surface contact area would not be relevant. Also, any correction for hydrocarbon solubility would be unnecessary.
2. Competitive exchange with another hydrocarbon as a reference has not been reported to date. Slight differences in reactant composition, temperature, and other variables would cancel since both hydrocarbons would be reacting under identical conditions. Results from separate experiments should be more readily comparable with the "internal standard" present.
3. Constant medium composition should rule out such variables as solvation of intermediates which earlier workers have used to

explain their results. Exchange of hydrogen in the various compounds will be followed at the same temperature so that the results will be comparable.

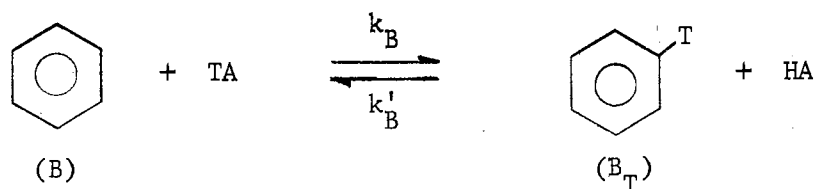
4. An attempt will be made to do the tritiation experiment analogous to Lauer's deuteration studies. Benzene will be present in each of the runs so the exchange will be competitive. The tritium content will be determined by a completely different analytical method than Lauer used.
5. Toward electrophilic substitution the meta position in an alkylbenzene is much less reactive than either the ortho or para position. In the experiments on dedeuteration and detritiation of the hydrocarbon, one would expect little deuterium or tritium, once removed from the ortho or para position and in the acid, to substitute back in the meta position. However, loss of the heavy isotope from the meta position is relatively much slower and any deuterium or tritium once removed might readily substitute back in an ortho or para position. This situation would result in an apparent value for the meta rate constant smaller than it truly is.
6. The lower reactivity of the ortho position in alkylbenzenes in electrophilic substitutions has generally been attributed to steric hindrance to the incoming electrophile. The hydrocarbons used for this study--benzene, toluene, ethylbenzene, etc.--have an increasing steric requirement for the alkyl group since each of the alpha hydrogen atoms in toluene is successively replaced by a methyl group until tert-butylbenzene is obtained. The importance of the steric hindrance argument

will be determined. If steric effects are unimportant, a more accurate measure of ortho reactivity will be obtained.

Experimentally, aliquots of an exchange mixture of two hydrocarbons were removed from a constant-temperature bath at predetermined times, the reaction stopped by neutralizing the acid with sodium hydroxide, and the hydrocarbons separated and assayed several times for their total tritium content. After all aliquots from the run were assayed for tritium, the data were analyzed for the parameters using an IBM 1410 digital computer. These partial rate factors were compared with those from other electrophilic substitutions as well as those from previously reported hydrogen exchanges.

Kinetics of the Exchange

The substitution of protium on benzene by labile tritium of an acid solvent can be represented by the following equation:



The exchange is bimolecular and second-order (18). The rate of formation of tritiated benzene (B_T) is given in Equation [1]¹.

$$\frac{d[B_T]}{dt} = k_B[B][TA] - k'_B[B_T][HA] \quad [1]$$

¹To avoid ambiguity, equations are numbered in brackets and references in parentheses.

The concentration of hydrocarbon $[B]$ is assumed to be constant since at the tracer level, only a minute amount of it becomes tritiated. The mole fraction of acid is made so large that even at equilibrium, the amount of tritium lost from the acid to the hydrocarbon is of the order of only 5 per cent. Therefore, both $[TA]$ and $[HA]$ are regarded as constant. Equation [1] can be rewritten as

$$\frac{d[B_T]}{dt} + k'_B[B_T][HA] = 6k_B[B][TA] \quad [2]$$

Equation [2] is a linear differential equation of the form

$$\frac{dy}{dx} + Py = Q$$

where the integrating factor, as given by Cohen (5), is

$$e^{\int P dx}$$

Integration of such an equation yields

$$ye^{\int P dx} = \int Qe^{\int P dx} dx + \text{constant} \quad [3]$$

Applying this general solution to Equation [2],

$$[B_T]e^{k'_B[HA]t} = 6 \frac{k_B}{k'_B} [B] \frac{[TA]}{[HA]} e^{k'_B[HA]t} + \text{constant} \quad [4]$$

Dividing both sides by $[B]$ and integrating between the limits of $t = 0$ ($[B_T] = 0$) and $t = t$ ($[B_T] = [B_T]$),

$$\frac{[B_T]}{[B]} e^{k'_B[HA]t} = 6 \frac{k_B}{k'_B} \cdot \frac{[TA]}{[HA]} e^{k'_B[HA]t} - 6 \frac{k_B}{k'_B} \cdot \frac{[TA]}{[HA]} \quad [5]$$

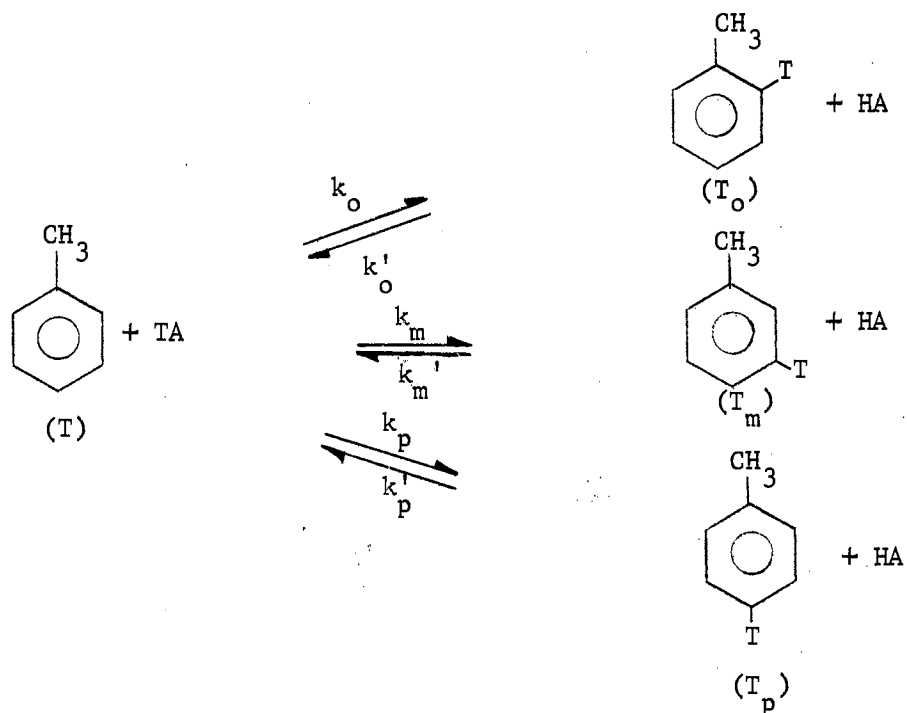
Factoring the right-hand side of the equation and dividing both sides by the exponential,

$$\frac{[B_T]}{[B]} = 6 \frac{k_B}{k'_B} \cdot \frac{[TA]}{[HA]} \left[1 - e^{-k'_B [HA] t} \right] \quad [6]$$

$[TA]/[HA]$ represents the molar radioactivity of the labile tritium present in the acid solvent, and $[B_T]/[B]$ the molar radioactivity of the benzene. Qualitatively, this expression indicates that the specific radioactivity of the benzene increases exponentially and that at equilibrium, it is $6 k_B/k'_B$ times the specific radioactivity of the acid solvent.

For monosubstituted benzene molecules such as toluene, the hydrogen exchange becomes somewhat more complicated. Here there are five positions at which reaction can and does occur. However, one cannot assume that reactions at all of these positions occur at equal rates, as was the case for benzene. Experience from other electrophilic reactions leads one to expect reaction in the meta position to proceed much more slowly than those for either the ortho or para position.

Toluene is used as an example of a hydrocarbon where hydrogen in three chemically different positions undergoes simultaneous exchange. What is said here concerning toluene is applicable to any other monosubstituted hydrocarbon with three chemically different labile hydrogen atoms. When toluene is mixed with a tritiated acid, the following equations represent the overall result. It must be emphasized that all three reactions are simultaneously occurring.



The rates of formation of the three isomers of tritiated toluene are

$$\frac{d[T_o]}{dt} = 2k_o [T][TA] - k'_o [T_o][HA] \quad [7]$$

$$\frac{d[T_m]}{dt} = 2k_m [T][TA] - k'_m [T_m][HA] \quad [8]$$

$$\frac{d[T_p]}{dt} = k_p [T][TA] - k'_p [T_p][HA] \quad [9]$$

On rewriting, these equations become

$$\frac{d[T_o]}{dt} + k'_o [T_o][HA] = 2k_o [T][TA] \quad [10]$$

$$\frac{d[T_m]}{dt} + k'_m [T_m][HA] = 2k_m [T][TA] \quad [11]$$

$$\frac{d[T_p]}{dt} + k'_p [T_p][HA] = k_p [T][TA] \quad [12]$$

By making the same assumptions as was done for benzene, these differential equations can be solved in a similar manner. With Equation [10] as an example, integration between the limits of $t = 0$ ($[T_o] = 0$) and $t = t$ ($[T_o] = [T_o]$) yields, on rearrangement,

$$\frac{[T_o]}{[T]} = 2 \frac{k_o}{k'_o} \cdot \frac{[TA]}{[HA]} \left[1 - e^{-k'_o[HA]t} \right] \quad [13]$$

Similarly, Equations [14] and [15] result from [11] and [12], respectively.

$$\frac{[T_m]}{[T]} = 2 \frac{k_m}{k'_m} \cdot \frac{[TA]}{[HA]} \left[1 - e^{-k'_m[HA]t} \right] \quad [14]$$

$$\frac{[T_p]}{[T]} = \frac{k_p}{k'_p} \cdot \frac{[TA]}{[HA]} \left[1 - e^{-k'_p[HA]t} \right] \quad [15]$$

Experimentally, all three reactions are occurring simultaneously. Since the exchange is conducted at the tracer level, determination of the specific radioactivities $[T_o]/[T]$, $[T_m]/[T]$, and $[T_p]/[T]$ is not possible unless one further substitutes the hydrocarbon as other workers have done (21). From an ion-current measurement of the tritium in the hydrocarbon, the overall specific radioactivity can be determined. Theoretically the overall specific radioactivity is equal to the sum of the specific radioactivities for each chemical position. Thus,

$$\text{Overall specific radioactivity} = \frac{[T_o]}{[T]} + \frac{[T_m]}{[T]} + \frac{[T_p]}{[T]} \quad [16]$$

Substituting from above and factoring out common terms,

$$\text{Overall specific radioactivity} = \frac{[\text{TA}]}{[\text{HA}]} \left\{ 2 \frac{k_o}{k_o'} \left[1 - e^{-k_o' [\text{HA}] t} \right] + \right. \\ \left. 2 \frac{k_m}{k_m'} \left[1 - e^{-k_m' [\text{HA}] t} \right] + \frac{k_p}{k_p'} \left[1 - e^{-k_p' [\text{HA}] t} \right] \right\} \quad [17]$$

If the equilibrium distribution of tritium between the hydrocarbon and the acid solvent is assumed to be the same at the ortho, meta, and para positions, Equation [17] predicts that at equilibrium the specific radioactivity of the hydrocarbon will be $5 k_o/k_o'$ times the specific radioactivity of the acid. Although the growth curve of the radioactivity in toluene is the same in principle as the curve for benzene, the former is more complex since it is the sum of three growth curves each similar to the latter.

Each of the positions on toluene is a certain number of times as reactive as one position of benzene. This number relating the reactivities is the partial rate factor and is one of the points of interest in this study. The following relationships are defined:

$$k_o' = \alpha k_B' \quad k_m' = \beta k_B' \quad k_p' = \gamma k_B' \quad [18]$$

α , β , and γ are the partial rate factors for the ortho, meta, and para positions, respectively. Making these substitutions in Equation [17]

$$\text{Overall specific radioactivity} = \frac{[\text{TA}]}{[\text{HA}]} \left\{ 2 \frac{k_o}{k_o'} \left[1 - e^{-\alpha k_B' [\text{HA}] t} \right] + \right. \\ \left. + 2 \frac{k_m}{k_m'} \left[1 - e^{-\beta k_B' [\text{HA}] t} \right] + \frac{k_p}{k_p'} \left[1 - e^{-\gamma k_B' [\text{HA}] t} \right] \right\} \quad [19]$$

Mathematically, this study involves fitting some n overall specific radioactivity values at n times t to this model [19] so the parameters, α , β , and γ , can be determined. Equation [19] is obviously non-linear in the parameters. The various methods which were tried to fit the experimental data to the model are described in detail in Chapter VI.

Instrumentation Applicable for the Assay for Tritium

Tritium is an unstable isotope and decays to helium-3 with emission of a beta particle. Tritium has a half-life of 12.5 years; its emitted beta particle has an average energy of 0.018 Mev. (14). This low beta energy makes the assay for tritium more difficult than that for most other isotopes. The loss in energy of the beta particle on passing through the window of a counter tube becomes appreciable at this energy level and, therefore, counting by such methods is impractical.

A more efficient method of counting is realized when the sample is introduced into the detection area of the counter. Here the particle from the isotopic decay does not have to pass through any window with the consequent loss of energy. Two "internal counting" instruments, a vibrating-reed electrometer and a liquid-scintillation spectrometer, were available for this study. The latter was used in some of the preliminary work but no reproducibility was found; therefore, its use was discontinued. The vibrating-reed electrometer was used routinely and a brief description of the instrumentation will be given.

The vibrating-reed electrometer used was an Applied Physics Corporation Model 30. To measure an ion current with an electrometer, the sample is introduced into an ionization chamber in the gaseous state along with a gas, such as methane, which has a relatively low ionization

potential. The ionization chamber has a central electrode which is electrically insulated from the outer metallic shell. A potential of 90-360 volts d.c., depending on the ionization chamber, is applied across these two electrodes. The energy made available by the decay of the atom is sufficient to ionize the methane. The ionized particles, essentially between the plates of a charged condenser, experience a force which produces what is commonly referred to as an ion current. This current, though only 10^{-13} - 10^{-16} amperes, is impressed across a resistance of 10^{10} - 10^{12} ohms. The potential drop across this resistance is then measured on a strip-chart recorder. This method is rather sensitive and is reproducible to $\pm 1\%$. The ionization chamber can be of several types; each is discussed in the appropriate place in Chapter IV.

CHAPTER IV

CHEMICAL ASPECTS OF THE EXPERIMENTAL WORK

The details of the chemical experimentation are discussed in this chapter. This discussion includes the selection of a solvent appropriate for the study, the separation of the hydrocarbons, the preparation and assay of the hydrocarbon standards, the methods tried for the tritium assays, the method for starting and following a run, and finally, the oxidation of cumene and tert-butylbenzene.

Choice of Solvent and Acid

When this work was started the common solvent-acid system for exchange in the literature was 70-80 per cent sulfuric acid, a concentration at which aromatic hydrocarbons are almost insoluble. This heterogeneity is one of the points to be eliminated in this study. Also, sulfonation becomes a significant side reaction at the concentrations needed to effect exchange. Therefore, a different solvent system was necessary in order to achieve one of the goals of this study. This solvent should have the following characteristics:

- 1) The acid must be strong enough to effect exchange.
- 2) Aromatic hydrocarbons should be soluble in the acid.
- 3) The acid should not react with the hydrocarbon in any manner such as sulfonation by sulfuric acid.

- 4) The acid should not cause any degradation, such as oxidation, of the hydrocarbon.

With these preferred acid characteristics in mind, various other strong, inorganic acids were tried. Concentrated (37.5%) hydrochloric acid was the first acid tried. Although aromatic hydrocarbons are insoluble in this acid and a heterogeneous exchange was not desired, it was felt that the data would still be useful since the exchange could be made competitive with that in benzene. Two methods of stirring, a screw-type vertical stirrer and also a magnetic stirrer, were tried but neither was very effective. With each of these methods of stirring, benzene and toluene showed no measurable exchange in hydrochloric acid at room temperature in one week.

After these conditions failed to effect any exchange, several emulsifying agents were tried in the hope that exchange would be measurable since the hydrocarbon and acid would be more intimately mixed. Tween 40 and Dreft detergent were both used as emulsifying agents. The experiment yielded the same result as before--no measurable exchange at room temperature after one week. In consideration of these findings, exchange using hydrochloric acid alone was discontinued.

Concentrated phosphoric acid (85%) was next tried. This acid also forms a heterogeneous system with arenes. No exchange was realized at room temperature, and on refluxing the mixture for three days at 77°, still there was no exchange. Work with phosphoric acid was consequently discontinued. The only other strong, inorganic acid which was considered--perchloric acid--was never tried due to its strong tendency to act as an oxidizing agent and its sometimes unstable behavior.

An alternative was to try organic acids. Immediately one would

expect solubility problems, if they still exist, to be less. In the literature several cases were found where acetic acid and trifluoroacetic acid had been used separately, each with small amounts of sulfuric acid present (7,20,22). It was decided that these two acids might be used without any sulfuric acid. Preliminary studies showed that exchange using trifluoroacetic acid went much more rapidly under the same conditions than when acetic acid was used. Acetic acid, though weaker than hydrochloric acid, gave a measurable degree of exchange, probably because of the homogeneity of the reaction medium. Various ratios of acid to benzene and toluene were used. The reaction was stopped after four days, and the hydrocarbons were assayed for their total tritium content. The results, assuming no equilibrium isotope effect, are shown in Table IV. The percentage of equilibrium attained, based on a statistical distribution of tritium in the reactants, was calculated by assuming that only aromatic hydrogen is labile under the reaction conditions used. These exchange rates, although considerably higher than in the two heterogeneous systems studied, were still too small to be practical.

Lauer and Day (20) reported the dedeuteration of phenyl alkyl ethers such as anisole and phenetole with a 50:1 mixture of glacial acetic and sulfuric acids. For these very reactive substrates, the half-reaction time at 100° was found to be 40-75 minutes. However, a mixture of hydrochloric and glacial acetic acids failed to effect hydrogen exchange in benzene and toluene at 40° in a two-week period. With trifluoroacetic acid containing either sulfuric or perchloric acid to increase the acidity, Mackor, et al. (22) found appreciable exchange in various alkylbenzenes. Substitution of hydrochloric acid for either

sulfuric or perchloric acid to increase the acidity proved unsuccessful, probably because hydrochloric acid is not a stronger acid than trifluoroacetic acid. Work with these two organic acids in conjunction with hydrochloric acid was therefore discontinued.

TABLE IV

EFFICIENCIES OF ACETIC AND TRIFLUOROACETIC ACIDS IN CATALYZING
HYDROGEN EXCHANGE IN AROMATIC HYDROCARBONS

Benzene	Relative Volumes, ml.				Calculated	
	Toluene	$\text{CF}_3\text{CO}_2\text{H}$	$\text{CH}_3\text{CO}_2\text{H}$	$\text{H}_2\text{O} \pm$	Equilibrium Attained, % Benzene	Toluene
1	1	4		0.05	0.23	16.0
1	1		4	0.05	0.40	1.7
1	1	5		0.05	0.35	17.3
1	1		5	0.05	0.32	1.65
2	2	2		0.05	0.46	4.3

After all other acid pairs failed to give the desired results, a decision was made to use small amounts of sulfuric acid with trifluoroacetic acid as the solvent. Preliminary work was done to determine the degree of exchange in media of varying sulfuric acid concentration. The reaction temperature was increased from 40 to 50° to accelerate the reaction. The results, after fourteen days of reaction, are shown in Table V. The percentage of equilibrium attained was calculated as before. That sulfuric acid markedly influences the rate is evident in these results. The results from tube C may appear inconsistent with those from tube B. However, some of the 0.5 ml. of sulfuric acid in C did not dissolve so the reported concentration is actually high.

TABLE V
SULFURIC ACID CATALYSIS OF HYDROGEN EXCHANGE
IN BENZENE AND TOLUENE

Tube	Volume of Reactants, ml.					Calculated	
	Benzene	Toluene	$\text{CF}_3\text{CO}_2\text{H}$	H_2SO_4	$\text{H}_2\text{O} \pm$	Equilibrium Attained, % Benzene	Toluene
A	4	4	25	0.0	0.1	0.11	18.2
B	4	4	25	0.3	0.1	17.8	30.1
C	4	4	25	0.5	0.1	26.5	63.1

Either of the systems represented by tubes B or C in Table V might seem good enough. However, one other factor must be taken into account. In the derivation of the equation relating overall radioactivity to time, the specific radioactivity of the acid was assumed to remain constant and equal to its initial value. While this situation cannot be realized experimentally, the system must be arranged so the error introduced is as small as possible, preferably five per cent or less. From the number of exchangeable hydrogen atoms in each reactant and the number of moles of each reactant, an equilibrium distribution of tritium can be calculated using statistical principles. Despite earlier thinking to the contrary, the equilibrium distribution of tritium is independent of the amount of it initially present. To state this in another way: in two exchanges having the same mole fraction of reactants but different amounts of tritium, a given hydrocarbon will accumulate the same fraction of total tritium at equilibrium. Increasing the amount of tritium in the reaction mixture does not have any bearing on the change in the specific radioactivity of the acid. Increasing the mole fraction of trifluoroacetic acid keeps the change in the specific

radioactivity of the acid at a minimum. This point is illustrated in Table VI. N_H is the calculated mole fraction of labile hydrogen. The figures shown in the first part of the table represent values from a hypothetical experiment using the same ratio of reactants as in tube C, Table V. Those in the second part represent conditions of a run actually done in the laboratory. The exchange is so slow for benzene that exchange of ring hydrogens in toluene is essentially at equilibrium before benzene starts to react. Therefore, only the N_H value for toluene need be considered in determining the change in the acid specific radioactivity. From the first and second parts of Table VI the N_H values for toluene are 0.218 and 0.0659, respectively. At equilibrium, 21.8 and 6.59 per cent of tritium initially in the acid will be in toluene. These percentages also represent the decrease in specific radioactivity of the acid. An experiment designed with mole fractions like those in the second part of the table would be in closer agreement with the assumption of constant tritium content of the solvent. Therefore, this acid pair and these mole fractions were the conditions finally chosen for the experimental work.

Separation of the Hydrocarbon Mixtures

Since this study involves a competitive exchange in which more than one hydrocarbon is present, one of the early problems was that of separating the hydrocarbons. The first method tried was fractional distillation. The hydrocarbons studied have boiling points relatively close together, which makes fractional distillation of some of the pairs of compounds difficult. The ratio of hydrocarbon to acid solvent must be kept as small as possible as discussed in the previous section.

TABLE VI
CALCULATED VARIATION IN THE SPECIFIC RADIOACTIVITY OF
THE ACID WITH A CHANGE IN THE MOLE FRACTION
OF TRIFLUOROACETIC ACID

Compound	Moles	Moles Exchangeable Hydrogen ^a	N _H
<u>Reaction Mixture A</u>			
Benzene	0.630	3.780	0.314
Toluene	0.526	2.630	0.218
Water- <u>t</u>	0.083	0.166	0.014
Sulfuric acid	0.134	0.268	0.022
Trifluoroacetic acid	5.20	5.20	0.432
<u>Reaction Mixture B</u>			
Benzene	0.120	0.720	0.0949
Toluene	0.100	0.500	0.0659
Water- <u>t</u>	0.0555	0.111	0.0146
Sulfuric acid	0.0510	0.102	0.0134
Trifluoroacetic acid	6.156	6.156	0.812

^a Assuming only aromatic hydrogen is labile

This restriction in practice necessitates distillation of a very small volume, a difficult task since the total volume used must also allow for holdup in the flask and column. For the necessary tritium assays, one-fourth milliliter of each pure hydrocarbon should be available. A vacuum-jacketed fractionating column sixteen inches long with a metal spiral to increase the surface area was available in this laboratory. No provision was made to apply external heat to this column. There was sufficient heat loss in this column to cause flooding; however, the flooding could be prevented by allowing the distillation to proceed at its own rate, a procedure which was very time-consuming. Separation of a 1:1 mixture of benzene and toluene was tried repeatedly with a reflux ratio of 30:1 or greater. Never was the separation successful and at least for this work, fractional distillation proved not to be a feasible method.

Vapor-phase chromatography was another available method of separation. Gas chromatography was used on both the preparative and analytical scales. The preparative column, a commercial model one inch in inside diameter and 6.5 feet long, was prepared by Perkin-Elmer. It had a liquid phase of silicone oil (Dow Corning #200). The separation of mixtures of benzene and toluene was tried with this column, and the column temperature which seemed best was 143° . Nitrogen was used as the carrier gas and the flow rate was $1100 \text{ cm}^3/\text{min}$. This column was not particularly efficient in separating aromatic hydrocarbons, so it was necessary to take small cuts during trapping. Although the cuts were small it was found that each recovered hydrocarbon contained up to 10 per cent of the other one.

With the flow rate this large the trapping system had to be extra

efficient. The trap found most effective was made from Pyrex glass tubing about 4-5 mm. in inside diameter. This tubing was wound into a four-coil spiral about one and three-fourths inches in diameter. The total length of a trap was about two feet. A number of trap-coolant temperatures were tested to find the most efficient trapping conditions. The following liquids were used as coolants: air at room temperature, ice water, ice-salt bath, dry ice-acetone slush, and liquid nitrogen. Experience showed that the recovery of hydrocarbon was greatest in traps at or near room temperature. The hydrocarbons had a great tendency to form aerosols when they came into contact with the traps, and this aerosol formation seemed to increase as the trap-coolant temperature was lowered. Even at room temperature there was some aerosol formation.

Gas chromatography was used routinely on the analytical scale for separation of the hydrocarbon mixtures. In all cases helium was used as the carrier gas. During the preliminary parts of this work a Perkin-Elmer Model 154 C gas chromatograph was used. For the latter routine work, an Aerograph gas chromatograph, Model A 90 P-3, was used. The column, generously made available by the Continental Oil Company, had 30 weight-per cent Resoflex-728 as the liquid phase on 42/60 mesh firebrick. This column, one-fourth inch in inside diameter and fifteen feet long, proved very efficient for separating the aromatic hydrocarbons. Table VII shows the optimum operating conditions for separation of benzene from the hydrocarbon shown. In all cases the temperature of the injection block was maintained at 60-75° above column temperature, and the detector and collector temperatures were 50° above column temperature.

TABLE VII
OPTIMUM CONDITIONS FOR GAS CHROMATOGRAPHIC SEPARATION
OF BENZENE FROM THE HYDROCARBON SHOWN

Compound	Column Temperature, °C	Flow Rate, ml./min.
Toluene	142	80
Ethylbenzene	155	90
Cumene	165	100
<u>tert</u> -Butylbenzene	175	120

Preparation of the Hydrocarbon Standards

Benzene-t-Eastman white-label bromobenzene was distilled through a fractionating column one inch in diameter and two feet long. The column was packed with glass helices and was so constructed that external heat could be applied to compensate for heat lost by the vapor to the surroundings. The fraction boiling at 153.7-154.1⁰/735 mm. Hg (uncorrected) was collected. This redistilled bromobenzene (31.5 g.) was mixed with 25 ml. of absolute ether, and the mixture was placed in a pressure-equalizing dropping funnel. To a three-neck round-bottom flask fitted with the dropping funnel, two reflux condensers, and a ground-glass stirring assembly were added 4.8 g. of dried magnesium turnings and 50 ml. of absolute ether. The ether solution of bromobenzene was added over a period of one hour while the reaction mixture was vigorously stirred. After all the bromobenzene had been added, the mixture was left to stir for another thirty minutes.

Hydrolysis of the Grignard reagent was effected by adding water-t to the mixture. Three ml. of water-t (79 mc./g.) was added very slowly

while the mixture was vigorously stirred. Some insoluble magnesium compounds formed during the addition but partially dissolved on continued stirring. The mixture was heated to reflux and another 3 ml. of the water-t was added. The magnesium compounds were finally dissolved by adding 25 ml. of concentrated hydrochloric acid followed by water. After stirring, the mixture cleanly separated into two layers. The aqueous phase was washed with 3 ml. of ether and this extract was added to the organic phase, which was subsequently dried over anhydrous calcium chloride. This mixture was distilled through a heated fractionating column which was three feet long and was packed with glass helices. The fraction boiling at 79.0-80.5°/741 mm. Hg (uncorrected) was collected.

Toluene-t-Toluene-t was not prepared for this work. There was available in the laboratory some toluene- α -t made by hydrolysis of the benzyl Grignard reagent with water-t. The position of tritium in the molecule is irrelevant for use of the material as a standard.

Ethylbenzene-t--Preparation of tritiated compounds by hydrolysis of the appropriate Grignard reagent is a time-consuming operation. Moreover, the radioactivity yield is generally 25 per cent or less (24). Since no specific tritiated isomer of the hydrocarbon was needed, a decision was made to prepare tritiated standards of ethylbenzene, cumene, and tert-butylbenzene by exchange. Since it was unnecessary to keep the specific radioactivity of the acid constant, the mole fraction of the hydrocarbon was made large and 40 per cent or more of the tritium was incorporated into the hydrocarbon. The method of preparation was simple since the reaction mixture was left to react for a week or more and required no attention. Work-up of the reaction mixture

from the exchange was simpler than hydrolysis of the Grignard reagent.

Into a 100-ml. volumetric flask were placed 10.6 g. of ethylbenzene, 1.3 g. of water-t (65.2 mc./g.), 5 drops of concentrated sulfuric acid, and 45 g. of trifluoroacetic acid. The reactants formed a homogeneous medium when shaken. The flask was sealed and placed in a constant-temperature bath at 40°. After ten days the flask was removed from the bath, and the contents were poured into a 250-ml. Erlenmeyer flask containing 20 ml. of water and surrounded by an ice-salt bath. Just sufficient water was added to make the solution heterogeneous. The acid was neutralized to pH 5-6 by the slow addition of a concentrated sodium hydroxide solution. The contents of the flask were then transferred to a 125-ml. separatory funnel and the organic phase was saved. This material was dried over anhydrous calcium chloride overnight and then distilled under vacuum. The fraction boiling at 50-53°/45 mm. Hg (uncorrected) was saved. Gas chromatography showed less than 0.1 per cent of benzene, toluene, or cumene in the ethylbenzene.

Cumene-t--The commercial cumene available showed no more than 0.2 per cent impurities by gas chromatography. Therefore, it was felt that distillation of the cumene after exchange was unnecessary since the products from probable side reactions would be removed by sodium hydroxide extraction. Into a 20 x 250 mm. test tube were placed 0.19 g. of water-t (171.8 mc./g.), 2.4 g. of cumene, about 18 g. of trifluoroacetic acid, and 4 drops of concentrated sulfuric acid. The tube was sealed, shaken well, and placed in a constant-temperature bath at 40°. After eighteen days the tube was removed from the bath, and its contents were poured into a 250-ml. Erlenmeyer flask containing 10 ml. of water and surrounded by an ice-salt bath. The acid was neutralized to

pH 7 by the slow addition of a concentrated sodium hydroxide solution. The contents of the flask were then transferred to a 125-ml. separatory funnel and the organic phase was saved. This material was washed with two 5-ml. portions of water and finally placed in a 25-ml. vial to dry over anhydrous calcium chloride. Gas chromatography showed this compound to contain less than 0.3 per cent impurities.

tert-Butylbenzene-t--The tert-butylbenzene standard was prepared like cumene-t. Into a 20 x 250 mm. test tube were placed 0.16 g. of water-t (167.8 mc./g.), 2.7 g. of tert-butylbenzene, about 20 g. of trifluoroacetic acid, and 5 drops of concentrated sulfuric acid. The tube was sealed, shaken well, and placed in a constant-temperature bath at 40°. After seven days the tube was removed from the bath, and the reaction mixture was worked up in a manner analogous to that for cumene-t. Gas chromatography showed the tert-butylbenzene-t to contain less than 0.3 per cent impurities.

Assay of the Hydrocarbon Standards for

Total Tritium Content

The static ionization chamber for the vibrating-reed electrometer was used to assay the hydrocarbon standards. The use of this ionization chamber requires that the sample be introduced into the chamber in the gaseous state. Wilzbach, et.al., (33,34) have described a procedure for preparing such samples, and the method used for the preparation will be described.

Five to ten milligrams of a liquid compound to be assayed is drawn up into a heated, tared ampoule. One end of the ampoule was previously drawn into a very fine break-off tip. The open end of the ampoule is

then sealed in a micro flame, and the ampoule is again weighed on a micro balance. The sample weight, to three significant figures, is obtained by difference. Five to six milligrams of water is sealed in a similar ampoule. One end of a reaction tube of 1720 Pyrex was drawn into a break-off tip. These two ampoules are placed inside a tube of 1720 Pyrex 11 mm. in outside diameter along with 1 g. of zinc (40 mesh) and 0.1 g. of powdered nickel(III) oxide. A solid sample was weighed in a zinc boat and directly introduced into the tube on a boat. The inside wall of the tube was brushed clean with a large pipe cleaner, and the tube was constricted to an inside diameter of 1 mm. or less. This tube was joined with rubber tubing to a vacuum system and evacuated to 5 microns or less. While evacuated the tube was sealed at the constriction in such a manner that as few thermal strains as possible remained. When cool, the tube was shaken in order to break the tips of the two ampoules. The 1720 tube was carefully placed horizontally in a furnace at $640 \pm 10^\circ$ and left for three hours. Regulation of the temperature was very important in that this temperature was about the limit of the glass. If the furnace is too hot, the tube will swell and make further use of it impossible. It is important that the seals on the 1720 tube be as free of thermal strains as possible; otherwise, the tube usually breaks immediately after being placed in the furnace. After three hours the tube was removed from the furnace and allowed to cool. Under the conditions of this reduction, all carbon in the molecule is reduced to methane.

The 1720 tube is then placed inside another tube just enough larger in diameter to allow free movement of the 1720 tube. The apparatus is illustrated in Figure 1. Stopcocks 2 and 3 are arranged so that

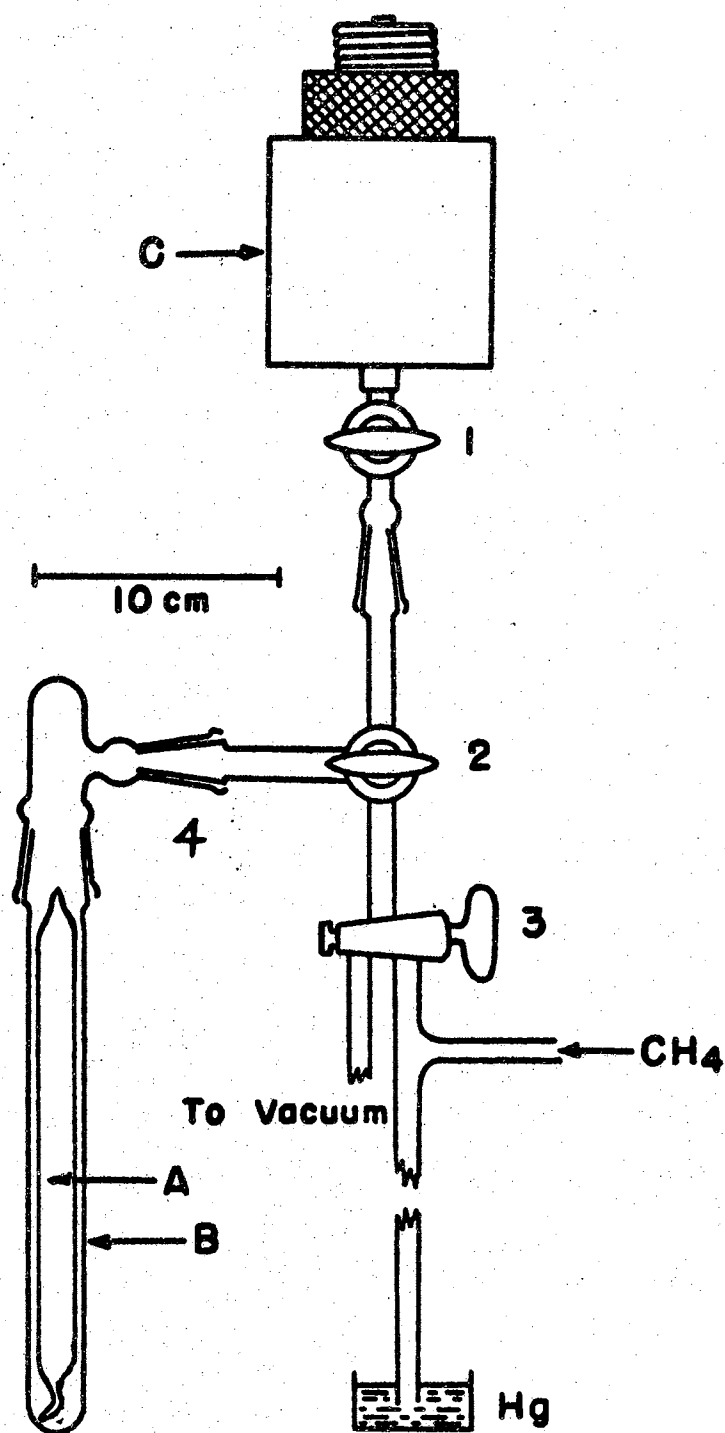


Figure 1. Apparatus for Transferring Tritiated Gases from a 1720 Pyrex Tube to an Ionization Chamber

systems B and C are open to the vacuum pump, and the system is evacuated to 2 microns. Stopcock 2 is positioned to isolate system B, and system B is turned about the standard-taper joint 4 so B is in a horizontal position. When B is quickly returned to the vertical position, the tip of the 1720 tube breaks and the gases in A expand into B. Stopcock 2 is then turned to connect B with only the system containing the ionization chamber. About thirty seconds is allowed for the gases to diffuse completely. During this time stopcock 3 is turned to connect stopcock 2 to the methane supply. With the methane supply so arranged that a large gas flow is possible, stopcock 2 is turned to connect stopcocks 1 and 3 and any gas between stopcocks 1 and 2 is quickly swept into the ionization chamber. Just as soon as atmospheric pressure is registered on the manometer, stopcock 1 is closed.

The ionization chamber is then removed from the vacuum line and assembled on the preamplifier head of the vibrating-reed electrometer. A potential of 360 volts is applied across the chamber and an appropriate resistance, usually 10^{10} ohms, is used to give a measurable reading on the strip-chart recorder. The recorder reads directly in millivolts. A background count is determined in a similar manner so the reading due to the tritiated material is the difference of these two numbers. The experimentally determined radioactivity must be multiplied by a number representing the ratio of the total volume of systems B and C to that of B since the transfer of gas from B to the ionization chamber was not complete. The radioactivity of a sample can be calculated from the following equation:

$$\text{Specific radioactivity, } \frac{\mu\text{c.}}{\text{mmole}} = \frac{8.75 \times 10^{11} \frac{\mu\text{c.}}{\text{amp.}} \times \frac{\text{mv. reading}}{\text{ohms in resistor}}}{\frac{\text{sample wt., mg.}}{\text{millimolecular weight}}} \times \text{volume factor}$$

The $8.75 \times 10^{11} \mu\text{c./amp.}$ factor is the reciprocal of the product of the number of coulombs per disintegration and the value for the microcurie. The volume factor is determined by measurement of the volumes involved.

When these techniques were applied in assaying the hydrocarbon standards, inconsistent results were obtained at first. After considerable time was spent ruling out such errors as faulty seals, etc., calculations were made to see if the 5-6 mg. of water used, the amount prescribed by the authors, was sufficient to provide the hydrogen necessary for complete reduction since the water is the only outside source of hydrogen (33,34). The results of these calculations are shown in Table VIII. When 20 mg. of water was used in the assays instead of 5 mg. the assays became consistent. The procedure was modified to use 20 mg. of water in all of the assays. The results of the radioactivity measurements of the standards are shown in Table IX.

There is about a nine per cent difference observed in the radioactivity values obtained using either the 10^{10} - or the 10^{12} -ohm and the 10^{11} -ohm resistors in the preamplifier head of the electrometer. The 10^{11} -ohm resistor has a tolerance of one per cent, and the results of the assays of the hydrocarbons reported in Tables XV through XXII were determined using that resistor. Since keeping the system internally consistent was desirable, all of the values in Table IX are converted to a value which would have been obtained if the 10^{11} -ohm resistor had been used.

TABLE VIII

HYDROGEN AVAILABLE FOR THE SEALED-TUBE REDUCTION OF AROMATIC HYDROCARBONS
FROM TWO DIFFERENT AMOUNTS OF WATER

Compound	Sample Wt., mg.	Total Millimoles of Hydrogen				
		Needed	Available from Hydrocarbon	Needed from Water	Available from Water	
					5 mg.	20 mg.
Benzene	10	1.15	0.38	0.77	0.28	1.10
Toluene	10	1.08	0.43	0.65	0.28	1.10
Ethylbenzene	10	1.04	0.47	0.57	0.28	1.10
Cumene	10	1.00	0.50	0.50	0.28	1.10
<u>tert</u> -Butylbenzene	10	0.97	0.52	0.45	0.28	1.10

TABLE IX
SPECIFIC RADIOACTIVITY OF HYDROCARBON STANDARDS

Compound	Specific Radioactivity, $\mu\text{c./mmole}$	Date Determined
Benzene	60.06 60.52 Ave. 60.29	4-1-64
Toluene	81.07 81.83 Ave. 81.45	1-15-64
Ethylbenzene	31.38 31.55 31.32 31.57 Ave. 31.46	3-22-64
Cumene	33.39 33.28 33.05 Ave. 33.24	1-20-65
<u>tert</u> -Butylbenzene	12.56 12.58 12.66 Ave. 12.60	3-13-65

Tritium Assays of the Hydrocarbon Mixtures

Several methods were tried for assaying the hydrocarbon samples which were taken as the exchange reaction proceeded. These methods are discussed in this section.

A single instrument designed to perform the quantitative analysis and the radioassay of tritium-labeled volatiles seemed highly desirable. Such an instrument has been in use at the Central Research Division of Continental Oil Company at Ponca City, Oklahoma, and is described by Gant (9). The instrument is essentially a standard gas chromatograph with an ion chamber in series after the thermal-conductivity cell. Basically the method involves separating the hydrocarbon mixture in an analytical gas chromatography column and passing the effluent gases, while still separated, through the ionization chamber.

With a flow chamber kindly made available by the Continental Oil Company, preliminary experiments were started in order to gain experience in the use of the system and to provide information concerning the accuracy and precision of the method. The volume of the chamber is about 7 ml. The chamber was attached to the outlet of the gas chromatograph by a line as short and small in diameter as possible. As the vapors of radioactive material passed through the chamber, the response was indicated on a strip-chart recorder. The chamber was not linked directly to the head of the vibrating-reed electrometer but was connected by means of a coaxial cable. Mounting the chamber in such a way that all mechanical strains were out of the system was difficult. Such strains showed up as noise on the recorder and made accurate work difficult, if not impossible. Also, the chamber had a mass of metal

great enough that keeping it warm with only the gas stream from the chromatograph was impossible. This chamber with no external heat applied proved too effective in condensing the vapors of tritiated material. Such tritiated material retained in the chamber lessened the resolution of the once well-separated and resolved components. Attempts to heat the chamber with either an infrared heat lamp or a heating tape were unsuccessful. Similar results were obtained when the chamber, connected to the head of the instrument with a longer coaxial cable, was placed in an oven. This combination gave results with little reproducibility and use of the method was discontinued.

Another method that was tried made use of the static ionization chamber for the vibrating-reed electrometer. The hydrocarbon mixture was separated by preparative gas chromatography and trapped using equipment and methods discussed in a previous section. Separation of the hydrocarbons to a state pure enough to suffice for this work was difficult. Also, routine assays using the reduction method of Wilzbach et al., are time consuming. When no method was found suitable to separate the hydrocarbons on the preparative scale, use of this assay method was discontinued.

The Applied Physics Corporation makes a flow ionization chamber for their electrometer and this chamber was commercially available about the time the previous two methods were found to fail. In a discussion with Mr. Gant, he expressed the feeling that this chamber was the answer to our needs and kindly loaned us one. This chamber was spherical and had a volume of 250 ml. The spherical shell was electrically insulated from the preamplifier of the electrometer with a standard-taper ceramic adapter and from the gas chromatograph with an aluminum fitting sealed

in glass. A potential of 90 volts d.c. was used to collect the ionized particles. The chamber was mounted on a rigid steel tube, and the circuit was completed by an insulated rod down through the middle of the tube. This rigid mounting eliminated most of the noise which was encountered with the smaller chamber previously used. Probably the greatest advantage of this chamber was that it could be heated to 300° without damage to the head of the electrometer. Heat was applied to the chamber by means of two 250-ml. hemispherical heating mantles fitted tightly against it. The temperature of the chamber, measured with an iron-constantan thermocouple, was maintained 25-50° higher than the temperature of the chromatography column.

Experimentally, the use of this chamber differs from that of the smaller flow chamber previously used. With a chamber volume of about 7 ml. and a gas flow rate of 60-70 ml. per minute, the gas in the smaller chamber was changed 9-10 times per minute. This number of changes was found to be sufficient because of the cylindrical design of the chamber. No two pairs of compounds studied had retention times closer than one minute. In the case of the 250-ml. spherical chamber, the helium flow rate, at about 100 ml. per minute, was certainly insufficient to change the gas in the chamber 8-10 times in a minute or less. Obviously it was necessary to remove one substance from the chamber before another came through. Therefore, the helium flow was supplemented with argon between the gas chromatograph and the ionization chamber. Argon was used because of its low ionization potential; the counting efficiency of the electrometer is greater with such gases. The design of this spherical chamber necessitates an even greater number of gas changes than in the former case. An argon flow rate of about 3.5 liters per

minute was used, the exact rate being immaterial as long as it was constant. A flow meter was placed in the argon line ahead of the chamber. The pressure-reduction valve on the argon tank was adjusted as necessary during an assay period to maintain a constant flow rate.

The beauty of the flow method of radioassay lies in its ease and speed. No more than 2 μ l. of a hydrocarbon mixture was injected into the gas chromatograph. As the components were separated, they passed through the ionization chamber and their radioactivity was registered on the recorder. At most, five minutes were required with this method so that many assays could be made on a given sample with a minimum of time and effort.

The specific radioactivity of a hydrocarbon from the exchange was determined by comparison with a standard of the same material. For example, assume that the specific radioactivity of toluene in a benzene-toluene mixture was to be determined. To achieve this, a tritiated toluene standard of known specific radioactivity was injected into the gas chromatograph. The ratio of the peak area on the electrometer recorder to the corresponding peak area on the gas chromatograph recorder is proportional to the specific radioactivity of the sample. Multiple assays were done to minimize the error in the method. After the standard had been assayed, the sample from the exchange was treated in the same manner. Column temperature, flow rate, and other variables must be kept constant to use this method. If the specific radioactivity of a sample differed substantially from that of its standard, the sample size was changed in order to keep the electrometer recorder on scale. To keep such a change from increasing the error of the peak-height measurement, the attenuation of the gas chromatograph was changed to

keep the peak height as near full scale as possible. The error of the resistors in the conductivity bridge on the gas chromatograph is well within that of the rest of the system.

The peaks obtained on both recorders were always good, sharp, symmetrical peaks. One method often used to measure the area of such peaks treats them as triangles (17). The area is computed from the product of peak height and the width of the peak at half its height (half-width). In this study peak width on both recorders was in the order of 6 mm., but the measurements were only accurate to ± 0.3 mm. at best. Considerable error was immediately introduced into the calculation of the area so other methods were tried. The chart speeds on both recorders were increased to their maximum, about 3 in. per minute, and the area under the curve was determined by numerical integration using Simpson's Rule (28b). Very little more consistency was realized this way, and the time and effort expended on the method far outweighed any good points. Use of this method was discontinued. In another method the peaks were cut out and the paper fragments accurately weighed on an analytical balance. This method assumes chart paper of very even density, a condition not strictly obeyed in this case. This method, besides being time consuming, was not as good as the ones previously discussed. The last method tried, and the one finally adopted, requires that gas flow rate and column temperature be maintained constant, conditions under which the peak height is proportional to the area (17). The ratio of peak height on the electrometer recorder to that on the gas chromatograph recorder is also proportional to the specific radioactivity of the sample. Peak heights average 200 mm. and the measurements are accurate to ± 0.5 mm. so this measurement error is insignificant.

Typically, 6-12 assays can be run on the standard and on 2-3 samples within a four-hour period. With care, all variables mentioned earlier can be held constant for this length of time, and all samples assayed during this time can be directly compared with the standard. The average of the peak-height-ratio values for a sample is then compared with the same average for the standard. The results of the assays reported in Tables XV through XXII were determined by this method.

Procedure for Starting a Run

Previously described work indicated that this reaction would be relatively slow. A decision was made to run the exchange at above room temperature. The first temperature tried was 50°. A preliminary run was started in which the mole fraction of each reactant was essentially the same as shown in Table X. Exchange was rapid at this temperature. At 50°, the initial increase in tritium content in toluene was so great that considerable error was introduced into the time axis due to the uncertainty of zero-time. The temperature of the bath was lowered to 40° with the hope that this decrease in reaction rate would remove some of the difficulties in the regression method. This aspect is discussed in a later section.

The procedure used in starting a kinetic run will now be described in detail; however, only one of the runs will be discussed since the procedure for all others is analogous. As an example, the first run of the benzene-toluene exchange will be described. The quantity of each reactant is shown in Table X. Similarly, the reactant quantities in each run for the other pairs of compounds studied are shown in Tables XI through XIII.

TABLE X
REACTANTS USED IN THE COMPETITIVE EXCHANGES
BENZENE-TOLUENE

Compound	Weight, g.	Mmoles	Milligram-atoms of Hydrogen ^a	Mole Fraction	N _H ^b
<u>First Run</u>					
Benzene	9.371	120.0	720.0	0.01861	0.09535
Toluene	9.213	100.0	500.0	0.01551	0.06621
Water-t (189.2 mc./g.)	1.003	55.66	111.3	0.00863	0.01473
Sulfuric acid	4.997	50.94	101.9	0.00790	0.01349
Trifluoroacetic acid	697.4	6118.	6118.	0.9493	0.8102
<u>Second Run</u>					
Benzene	9.374	120.0	720.0	0.01850	0.09484
Toluene	9.213	100.0	500.0	0.01542	0.06586
Water-t (186.7 mc./g.)	1.000	55.49	111.0	0.00855	0.01462
Sulfuric acid	5.003	51.00	102.0	0.00786	0.01343
Trifluoroacetic acid	702.0	6158.	6158.	0.9497	0.8112

^a Actually the number of mg.-atoms of hydrogen labile under the reaction conditions used assuming only aromatic hydrogen exchanges

^b N_H is the calculated "mg.-atom fraction" of exchangeable hydrogen

TABLE XI
REACTANTS USED IN THE COMPETITIVE EXCHANGES
BENZENE-ETHYLBENZENE

Compound	Weight, g.	Mmoles	Milligram-atoms of Hydrogen ^a	Mole Fraction	N _H ^b
<u>First Run</u>					
Benzene	9.373	120.0	720.0	0.01863	0.09540
Ethylbenzene	10.62	100.0	500.0	0.01552	0.06625
Water-t (189.2 mc./g.)	1.001	55.54	111.1	0.00862	0.01472
Sulfuric acid	5.000	50.97	101.9	0.00791	0.01350
Trifluoroacetic acid	697.0	6114.	6114.	0.9494	0.8101
<u>Second Run</u>					
Benzene	9.373	120.0	720.0	0.01860	0.09528
Ethylbenzene	10.62	100.0	500.0	0.01550	0.06617
Water-t (186.7 mc./g.)	1.002	55.60	111.2	0.00862	0.01471
Sulfuric acid	5.002	50.99	102.0	0.00790	0.01349
Trifluoroacetic acid	698.0	6123.	6123.	0.9493	0.8103

^a Actually the number of mg.-atoms of hydrogen labile under the reaction conditions used assuming only aromatic hydrogen exchanges

^b N_H is the calculated "mg.-atom fraction" of exchangeable hydrogen

TABLE XII
REACTANTS USED IN THE COMPETITIVE EXCHANGES
BENZENE-CUMENE

Compound	Weight, g.	Mmoles	Milligram-atoms of Hydrogen ^a	Mole Fraction	N _H ^b
<u>First Run</u>					
Benzene	9.370	120.0	720.0	0.01853	0.09496
Cumene	12.02	100.0	500.0	0.01544	0.06594
Water-t (186.7 mc./g.)	1.000	55.49	111.0	0.00856	0.01463
Sulfuric acid	5.001	50.98	102.0	0.00787	0.01345
Trifluoroacetic acid	701.0	6149.	6149.	0.9496	0.8110
<u>Second Run</u>					
Benzene	9.373	120.0	720.0	0.01863	0.09541
Cumene	12.02	100.0	500.0	0.01553	0.06626
Water-t (185.0 mc./g.)	0.9997	55.47	110.9	0.00861	0.01469
Sulfuric acid	5.001	50.98	102.0	0.00791	0.01351
Trifluoroacetic acid	696.9	6113.	6113.	0.9494	0.8101

^a Actually the number of mg.-atoms of hydrogen labile under the reaction conditions used assuming only aromatic hydrogen exchanges

^b N_H is the calculated "mg.-atom fraction" of exchangeable hydrogen

TABLE XIII

 REACTANTS USED IN THE COMPETITIVE EXCHANGES
 BENZENE-TERT-BUTYLBENZENE

Compound	Weight g.	Mmoles	Milligram-atoms of Hydrogen ^a	Mole Fraction	N _H ^b
<u>First Run</u>					
Benzene	9.373	120.0	720.0	0.01864	0.09544
<u>tert</u> -Butylbenzene	13.42	100.0	500.0	0.01553	0.06627
Water- <u>t</u> (185.0 mc./g.)	1.000	55.49	111.0	0.00862	0.01471
Sulfuric acid	5.000	50.97	101.9	0.00791	0.01350
Trifluoroacetic acid	696.7	6111.	6111.	0.9494	0.8100
<u>Second Run</u>					
Benzene	9.374	120.0	720.0	0.01860	0.09527
<u>tert</u> -Butylbenzene	13.42	100.0	500.0	0.01550	0.06616
Water- <u>t</u> (185.0 mc./g.)	0.9997	55.47	110.9	0.00860	0.01467
Sulfuric acid	5.001	50.98	102.0	0.00790	0.01349
Trifluoroacetic acid	698.1	6124.	6124.	0.9494	0.8104

^aActually the number of mg.-atoms of hydrogen labile under the reaction conditions used in assuming only aromatic hydrogen exchanges

^bN_H is the calculated "mg.-atom fraction" of exchangeable hydrogen

Into separate, tared, glass-stoppered Erlenmeyer flasks were weighed 9.371 g. of benzene, 9.213 g. of toluene, 1.003 g. of water-t (189.2 mc./g.), and 4.997 g. of concentrated sulfuric acid. The flask size was kept at a minimum to make the sensitivity of the weighings as great as possible. Each reagent was kept in its respective container until time to start the reaction. A 500-ml. glass-stoppered volumetric flask was also tared. Benzene and toluene were quantitatively transferred to the volumetric flask with trifluoroacetic acid from a polyethylene wash bottle. Before any sulfuric acid was added, approximately 400 ml. of trifluoroacetic acid was added to the flask to decrease the probability of sulfonation of the aromatic hydrocarbons. The sulfuric acid was next transferred to the flask by the same technique. When necessary, sufficient trifluoroacetic acid was added to bring the total volume to within 10-20 ml. of the mark on the volumetric flask. The flask was stoppered and placed in a previously prepared beaker of water at 20°. While being frequently shaken, the flask remained in the water for 15-20 minutes. When the reactants were at 20°, the water-t was similarly transferred to the flask and trifluoroacetic acid was added to make the total volume 500 ml. The tritiated water was always the last reagent added. The flask was dried externally and quickly weighed on a triple-beam balance.

After the contents of the flask were thoroughly mixed, about 50 ml. of the mixture was carefully but quickly added to each of ten 25 x 250 mm. test tubes. Because of the volatility of trifluoroacetic acid, some fuming of the acid always occurred and, therefore, the hood was used during this transfer process. Admittedly, some of the acid was lost during the transfer but the amount was very small. The

trifluoroacetic acid concentrations shown in Tables X through XIII are subject to less error due to this loss than are other parts of the experimental work. The reaction tubes were quickly sealed in the flame of a methane-oxygen torch and placed in a constant-temperature oil bath at $40 \pm 0.02^{\circ}$. Temperature control was maintained by a Sargent Thermometer, an instrument which proved very successful in maintaining the temperature within these limits for a period of 8-12 months or longer. During the first five minutes the reaction tubes were in the bath, they were shaken several times to hasten thermal equilibration. The time from the addition of the tritiated water until attainment of thermal equilibrium of the reactants in the constant-temperature bath varied from 15-20 minutes. At the temperature prevailing in the room before the tubes were placed in the bath, the amount of exchange was negligible.

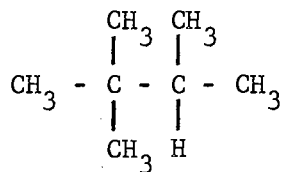
At predetermined times a tube was removed from the bath, and its contents were poured into a 250-ml. Erlenmeyer flask containing about 20 ml. of water and surrounded by an ice-salt bath. Just sufficient water was added to make the solution heterogeneous. The acid was neutralized to pH 5-6 by the slow addition of a concentrated sodium hydroxide solution. The contents of the flask were then transferred to a 125-ml. separatory funnel and the organic phase was saved. This material was stored in a 5-dram vial containing anhydrous potassium carbonate and anhydrous calcium chloride. Assays were done with the flow ionization chamber technique previously described. The results of the assays, shown in Tables XV through XXII, are corrected for isotopic decay when the correction is 1 per cent or more. Tritium decays about 0.5 per cent per month.

Oxidation of Cumene and *tert*-Butylbenzene

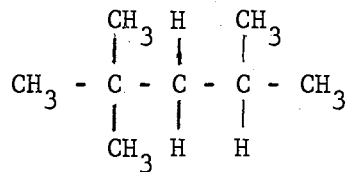
No case of hydrogen exchange in the side chain of an alkylaromatic compound has ever been reported. Olsson (24) checked for exchange in toluene- α -t. The material was mixed with about 80 per cent aqueous sulfuric acid, but less than a two per cent loss of tritium was observed in forty-nine hours while 57 per cent of the tritium in toluene-3-t was lost in 13.5 hours under the same conditions. Similar results were found by Lauer et al. (21). Therefore, it has generally been believed that no side-chain exchange of hydrogen occurs in alkylbenzenes under acidic conditions.

In this study it was possible, by knowing the number of moles of each reactant present and the number of labile hydrogen atoms per molecule, to calculate a statistical equilibrium distribution of tritium in the hydrocarbon if no equilibrium isotope effect was assumed. The samples of cumene and *tert*-butylbenzene, after being subjected to exchange for more than 3,000 hours, were assayed for tritium content, and the average specific radioactivities at 3,000 plus hours were found to be 138 and 189 per cent, respectively, of the calculated values. Moreover, for toluene and ethylbenzene the corresponding values were 73.4 and 73.2 per cent of the calculated.

Burwell and Gordon (4,13) have reported hydrogen exchange in aliphatic systems but no alkylaromatic hydrocarbons were studied. They followed the incorporation of deuterium into 2,2,3-trimethylbutane(I) and 2,2,4-trimethylpentane(II). Initially seven of the sixteen hydrogen atoms in I and nine of the eighteen hydrogen atoms in II were replaced by deuterium in sulfuric acid. In longer times all of the hydrogen



I



II

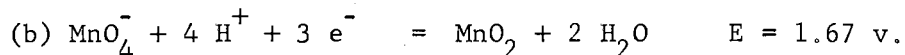
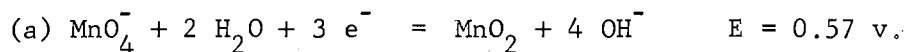
atoms in both compounds were exchanged. Studies with these two compounds and others led to the following conclusions: 1) When the molecule contains both a tertiary and a quaternary carbon atom, hydrogen is replaced in that part of the molecule up to the quaternary carbon atom. 2) No exchange occurs at a primary or secondary carbon. 3) Exchange at a quaternary carbon atom occurs with a simultaneous rearrangement of the carbon skeleton.

The probability seemed good that the unexpectedly high tritium content in the cumene and tert-butylbenzene previously mentioned was present in the side chain since compounds I and II each have a unit common to cumene and tert-butylbenzene. Therefore, if the side chain could be transformed by some reaction such as oxidation to a carboxylic acid group, one could arrive at the tritium content on the ring by a comparison of the molar radioactivities of the hydrocarbon and the derived benzoic acid.

The oxidizing agent must not require strong acid for its oxidizing strength. Conditions no more acid than pH 4-5 could be used. A dichromate oxidation using concentrated sulfuric acid was ruled out since the latter is known to be very effective in catalyzing hydrogen exchange. The possibility was good that tritium would be lost from the more reactive ring positions in the hydrocarbon before oxidation using dichromate could occur, and this loss would certainly lead to erroneous

results. No significant oxidation potentials exist for chromium(VI) in weakly acid to basic solution.

The oxidizing agent of choice was permanganate. In neutral and basic solution several reduction potentials of permanganate are known (19). Reaction (b) is that which occurs in a weakly acidic



solution such as acetic acid. For a reaction started in water, equation (a) is followed. The solution becomes increasingly more basic as reaction proceeds. A permanganate oxidation begun in basic solution is less vigorous than one begun in water.

Since the oxidation of cumene should be easier than that of tert-butylbenzene, experimental oxidation procedures were started first with the latter. The oxidation was attempted in basic solution, neutral solution, and acidic solution. Preliminary oxidations were carried out on non-tritiated compounds. In the basic oxidation 1 ml. (6.5 mmole) of tert-butylbenzene was added to about 80 ml. of water containing 3 grams of potassium permanganate. One pellet of sodium hydroxide was added, and the mixture was heated under reflux. At the end of six hours no oxidation had occurred as evidenced by lack of solid manganese dioxide on the walls of the flask above the liquid level.

The reaction of tert-butylbenzene and aqueous potassium permanganate became very vigorous when acetic acid was added. All of the permanganate was consumed and more was added, and consumed, up to twice the theoretical amount. No products were recovered on work-up of the reaction mixture. The only partially successful degradation of

tert-butylbenzene in the literature (Kuhn-Roth conditions) gives pivalic acid in 10 per cent yield, some of which further oxidizes to acetic acid (59).

For neutral oxidations Fieser and Fieser (8) describe a procedure to buffer the solution to prevent the accumulation of hydroxide ions during the reduction. This buffering results in increased oxidizing ability. The hydroxide ion produced can be precipitated from solution by a metal ion such as magnesium. The amount of magnesium ion used is sufficient to react with any hydroxide ion above that which is neutralized by the benzoic acid. Under these conditions no oxidation of tert-butylbenzene was realized in twenty-four hours. With these findings work with the compound was temporarily discontinued.

Cumene was subjected to oxidation under the three sets of conditions just described. In no case was benzoic acid isolated. A search of the literature revealed that there is no clean oxidation of cumene to benzoic acid but that a mixture of products is most generally obtained. The common products isolated are cumene hydroperoxide and the products of its decomposition, phenol and acetone, acetophenone, α,α -dimethylbenzyl alcohol, and a small amount of benzoic acid. On the semimicro scale isolation of the benzoic acid is virtually impossible.

In an attempt to decrease the reactivity of the benzylic carbon atom, cumene was photobrominated with bromine in strong ultraviolet light. The benzylic hydrogen atom reacted first. Additional bromine substituted with a longer reaction time and increased temperature. Experimentally, the cumene was placed in a 12-ml. centrifuge tube fitted with a F 19/22 joint. A six-inch tube was attached to serve as an air condenser. The centrifuge tube was placed in a beaker of water on a

hot plate and the water was heated to about 90° . The ultraviolet source was placed within six inches of the setup. Bromine in a 3:1 molar ratio to cumene was carefully added to the cumene. Under these conditions three atom equivalents of bromine substituted on the hydrocarbon in about ten minutes. There was no further reaction with bromine.

This brominated cumene was subjected to the neutral oxidation for three hours. The reaction mixture was filtered to remove manganese dioxide and magnesium hydroxide, and the excess permanganate was removed with solid sodium bisulfite. The solution was acidified to pH 3 with concentrated sulfuric acid and extracted with three 20-ml. portions of ether. The benzoic acid was removed from the neutral components of the ether extract with three 20-ml. portions of a sodium bicarbonate solution. This bicarbonate wash was carefully acidified as above and similarly extracted with ether. The ether was evaporated, and the remaining benzoic acid was recrystallized from about 10 ml. of water. The overall yield of benzoic acid from cumene was about 55 per cent. The problem of converting cumene to benzoic acid was solved.

One other point had to be investigated before oxidation was started on the samples from the runs: that there was no loss of tritium from the ring during the bromination and oxidation steps needed to be established. Previously some toluene-4-t had been prepared. This material was assayed, and its specific radioactivity (using the vibrating-reed electrometer and the Wilzbach reduction) was $2.36 \mu\text{c./mmole}$ with a standard deviation of 0.02. This material was brominated as before (only one equivalent of bromine was used) and the bromo compound oxidized to benzoic acid. This benzoic acid was assayed in the same way and was found to have a specific radioactivity of $2.36 \mu\text{c./mmole}$ with

a standard deviation of 0.016. It was concluded that there was no loss of tritium during the bromination and oxidation steps.

Each of the samples from the first run of the benzene-cumene exchange was brominated and subsequently oxidized to benzoic acid. These oxidations yielded only a very small amount of benzoic acid from the ether extraction. Recrystallization of this material was difficult but was accomplished using no more than 3 ml. of water. These samples were all assayed for tritium, and the results were very inconsistent. The benzoic acid-4-t previously mentioned was reassayed, and the results showed nothing wrong with the reduction or assay method. It was concluded that some impurity remained in the acid which poisoned the catalyst in the system. The specific radioactivity of the benzoic acid from the last sample of cumene showed ring tritium content the same, within experimental error, as did the last samples from benzene-toluene and benzene-ethylbenzene exchanges. Since the only objective in oxidizing the samples of cumene was to determine the equilibrium distribution, it was unnecessary to oxidize the material from the duplicate benzene-cumene exchange. The equilibrium distribution of tritium in the aromatic ring was thus considered to be the same for all of the alkylbenzenes.

No further work was done with the samples of tert-butylbenzene. If skeletal rearrangement of the alkyl group occurs during exchange, as has been suggested, one would expect rearrangement of tert-butylbenzene to an isomeric butylbenzene. Commercial samples of sec-butylbenzene and isobutylbenzene (both of greater than 99.5 per cent purity) were mixed with tert-butylbenzene. This mixture was subjected to gas-chromatographic separation, but no separation was realized even fifty

degrees below the boiling point. The three compounds boil at about 170° with only a three-degree spread from low to high. Detection of any isomerization was not possible using gas chromatography.

Nuclear magnetic resonance spectra were taken on the three pure isomeric butylbenzenes mentioned.¹ The three isomers were clearly distinguishable. A spectrum was similarly taken on the last sample from both benzene versus tert-butylbenzene exchanges. However, these samples were extracted from the neutralization mixture using ether, and their spectra were complicated by the presence of the ether. The pertinent information from these spectra is recorded in Table XIV. Clearly no isomeric butylbenzene was present.

If the equilibrium distribution of tritium in tert-butylbenzene is the same as that for toluene, ethylbenzene, etc., the amount of tritium found in tert-butylbenzene at greater than 3,000 hours is sufficient for complete equilibration of the side chain hydrogen atoms. Also, if isomerization is occurring before the hydrogen exchanges, then the butylbenzene must be completely isomerized to account for these findings. No isomer was found so exchange must proceed without isomerization.

On the assumption that the presence of a tritiated methyl group in tert-butylbenzene shows no secondary isotope effects on further exchange, the data were analyzed by incorporating into the computer program another exponential term to account for exchange of the methyl hydrogen atoms.

¹The nuclear magnetic resonance spectra were very graciously taken by Mr. George Cabat, Oklahoma State University. A Varian Model A-60 nuclear magnetic resonance spectrometer was used. Tetramethylsilane was used as an internal standard.

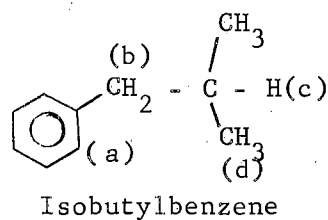
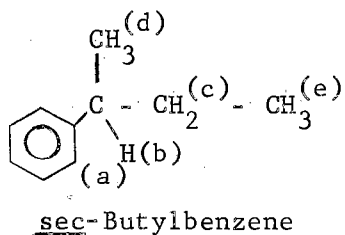
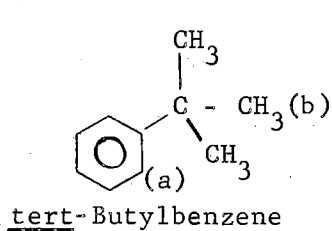
TABLE XIV

RESULTS FROM THE NUCLEAR MAGNETIC RESONANCE SPECTRA OF
THE ISOMERIC BUTYLBENZENES

Compound	Hydrogen Type ^a	Chemical Shift, δ	Relative Number of Hydrogen Atoms
<u>tert</u> -Butylbenzene	a	7.27	5
	b	1.24	9
<u>sec</u> -Butylbenzene	a	7.15	5
	b	2.50	1
	c	1.50	5
	d	1.17	5
	e	0.80	3
Isobutylbenzene	a	7.19	5
	b	2.43	2
	c	1.82	1
	d	0.86	6
Sample No. 10 ^b (first run) ^b	a	7.29	-
	b	1.22	-
Sample No. 10 ^b (second run) ^b	a	7.31	-
	b	1.24	-

^aThe letters refer to the hydrogen atoms labeled in the particular compound at the bottom of this table.

^bThese two samples contained benzene which would make the integration of no value. The integration was not done.



CHAPTER V

EXPERIMENTAL DATA

Competitive hydrogen-exchange experiments between benzene and alkylbenzenes were studied. The concentrations of the reactants were shown in Tables X through XIII. After appropriate time intervals these hydrocarbons were separately assayed for their total tritium content, and the results of those assays are shown in Tables XV through XXII.

The hydrocarbons from the exchange experiments were assayed by the flow-ionization-chamber technique. The 10^{11} -ohm resistor in the pre-amplifier head of the electrometer was used in all of those assays. The hydrocarbon standards were assayed with either the 10^{10} - or 10^{12} -ohm resistor, resistors less precise than the 10^{11} -ohm resistor. The results of the following tables have been corrected for this difference. The hydrocarbon standards were not restandardized each time they were used so that a correction for isotopic decay of the tritium in the standards had to be made. Also, isotopic decay in the hydrocarbon samples from the exchange after 3000 hours amounts to about 2 per cent. All of the following data were corrected for the decay.

TABLE XV

ASSAYS OF BENZENE FROM BENZENE:TOLUENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$			Average Value
	Individual Assays			
	<u>First Run</u>			
96	9.04	9.86	9.67	9.59
	10.20	9.17		
337	19.82	19.96	20.51	20.13
	20.42	19.95		
672	28.09	26.82	27.17	27.36
	27.08	27.64		
3245	51.40	52.36	52.70	52.41
	52.96	51.60	52.07	
	52.51	52.95	53.14	
	<u>Second Run</u>			
48	5.13	5.60	5.16	5.16
	5.51	4.57	4.97	
96	9.13	8.86	8.28	8.45
	8.79	8.41	7.56	
		8.12		
336	17.52	17.58	17.00	17.22
	17.34	17.69	16.12	
	17.77	16.76		
3007	49.15	49.05	49.30	49.38
	50.04	49.05	49.01	
	49.76	50.34	49.01	
		49.14		

TABLE XVI

ASSAYS OF BENZENE FROM BENZENE:ETHYLBENZENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$			Average Value
	Individual Assays			
	<u>First Run</u>			
97.5	8.74	9.62	8.65	8.89
	8.99	8.44		
336	16.87	18.09	17.15	17.58
	18.09	17.51	17.76	
672	23.97	23.85	24.00	23.64
	24.12	24.22	24.12	
	22.36	23.02	23.09	
3173	45.18	43.50	43.70	44.83
	45.39	45.50	44.62	
	44.38	45.61	45.77	
	43.50	45.99		
	<u>Second Run</u>			
48.5	5.36	4.87	5.12	4.68
	4.71	4.19	4.17	
		4.31		
96.5	7.56	7.04	8.65	7.73
	7.35	7.62	7.53	
		8.36		
336.5	17.67	15.92	16.43	16.28
	16.99	15.55	16.86	
		14.57		
701	22.17	23.37	23.84	23.24
	23.39	23.51	23.39	
	23.64	22.62		
3008	42.50	41.12	44.56	44.38
	46.95	44.45	44.78	
	43.98	46.57	45.47	
	43.99	43.76		

TABLE XVII

ASSAYS OF BENZENE FROM BENZENE:CUMENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$		
	Individual Assays		Average Value
	<u>First Run</u>		
47	5.49	5.64	4.72
	4.31	4.21	4.52
	5.41	4.63	4.87
94.5	7.71	8.38	7.82
	8.43	7.18	6.63
		7.22	7.62
335	14.31	14.24	14.32
	14.66	14.95	14.50
698.8	20.34	20.75	20.72
	19.83	20.50	19.99
		20.10	20.32
3006	39.68	39.07	39.57
	40.08	40.21	40.73
	40.35	39.28	39.90
		39.32	39.82
	<u>Second Run</u>		
49	4.96	4.70	5.33
	4.24	4.36	4.55
	5.06	5.41	4.27
		4.36	4.72
98	7.00	7.35	7.92
	8.03	6.04	8.00
	7.62	7.34	6.71
	6.24	6.68	7.18
338	13.95	13.75	14.58
	14.17	14.08	13.46
	14.04	13.46	13.69
		13.79	13.90
991	25.80	25.92	25.86
3679	47.60	48.82	49.74
	47.90	47.46	49.28
		47.17	48.28

TABLE XVIII

ASSAYS OF BENZENE FROM BENZENE:TERT-BUTYLBENZENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$		
	Individual Assays		Average Value
	<u>First Run</u>		
48	6.42	5.66	6.12
	5.60	5.80	6.01
	6.22	6.05	5.63
			5.94
98	9.55	9.91	8.94
	9.15	10.06	9.80
	9.65	9.20	
			9.53
337	19.41	20.33	20.26
	19.32	20.58	
			19.98
3678	54.92	53.80	55.75
		55.81	
			55.07
	<u>Second Run</u>		
48	5.08	5.34	5.19
	5.09	5.62	5.74
	4.84	4.55	5.37
		5.14	
			5.20
98.5	9.28	9.17	9.60
	8.79	9.21	9.07
	9.28	9.45	8.54
		9.72	
			9.21
337.75	19.33	19.78	20.11
	20.30	20.09	19.92
	19.76	19.69	20.54
			19.95
3678	54.83	55.81	56.78
	56.33	54.94	55.43
	55.43	56.52	56.29
		56.83	
			55.92

TABLE XIX

ASSAYS OF TOLUENE FROM BENZENE:TOLUENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$		
	Individual Assays		Average Value
	<u>First Run</u>		
2	52.75	53.19	53.06
	54.54	53.06	
4	66.62	63.78	64.30
	63.45	64.58	
	63.07	65.76	
		63.69	
8	76.32	75.74	74.53
	75.52	74.38	
	72.35	73.70	
		70.82	
15	78.64	74.32	78.10
	77.51	78.42	
	79.36	77.36	
		78.88	
25.5	81.10	82.30	82.10
	82.99	81.82	
48	87.38	85.36	85.86
	87.22	84.58	
96	88.66	90.21	91.03
	89.78	93.72	
337	101.7	104.7	103.6
	106.4	99.89	
672	107.3	109.7	107.9
	106.7	107.5	
3245	109.8	110.7	111.4
	112.2	112.3	
	111.8	112.5	

TABLE XIX (Continued)

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$			Average Value
	Individual Assays			
	<u>Second Run</u>			
1	30.58	31.25	30.86	31.31
	31.18	31.92	31.64	
		31.77		
2	49.91	49.19	48.79	49.27
	49.78	48.83	49.10	
4	68.23	69.65	70.75	69.49
	68.63	70.90	70.90	
		67.38		
8	80.93	79.77	83.16	81.92
	81.66	84.42	81.60	
24	76.12	75.02	80.12	77.75
	78.40	79.74	76.44	
	78.04	76.02	79.84	
48	82.59	85.73	84.36	84.78
	84.95	84.97	86.10	
96	88.67	90.62	92.02	89.59
	89.54	87.51	89.17	
336	101.4	101.8	101.9	101.5
	100.2	102.2	101.9	
		101.3		
3007	109.8	108.4	113.9	111.4
	111.3	113.6	112.3	
	109.0	109.2	114.6	
	112.2	111.5		

TABLE XX

ASSAYS OF ETHYLBENZENE FROM BENZENE:ETHYLBENZENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$			
	Individual Assays			Average Value
	<u>First Run</u>			
2	52.57	50.87	51.19	52.48
	53.18	53.67	53.43	
4	68.12	66.90	68.79	67.39
	67.35	68.31	64.88	
8	74.90	77.34	76.34	76.60
	76.84	77.48	76.90	
		76.42		
16	77.34	76.10	76.17	78.15
	79.21	78.40	81.68	
24	85.48	85.53	85.00	83.92
	81.73	83.91	81.86	
53.5	93.45	91.22	92.46	91.68
	89.95	91.46	91.54	
97.5	93.33	93.18	94.76	93.91
	94.47	95.49	95.00	
		91.16		
336	110.2	108.8	106.1	108.1
	107.2	108.2		
672	109.7	112.5	113.0	109.4
	109.2	108.4	104.6	
	104.7	113.0		
3173	107.8	109.6	107.3	109.6
	112.3	108.7	109.2	
	111.5	109.5	110.1	
	109.6	109.8		

TABLE XX (Continued)

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{C./mmole}$		
	Individual Assays		Average Value
	<u>Second Run</u>		
1	27.10	27.89	27.76
	29.00	32.63	31.48
		30.53	29.48
2	49.03	47.92	48.37
	48.25	48.46	49.49
		50.23	48.82
4	66.05	65.80	64.69
	65.14	65.55	65.45
8	70.44	72.66	71.88
	72.62	71.63	72.95
		72.95	72.16
24.25	83.77	86.54	83.40
	85.71	86.70	83.57
48.5			84.95
	79.99	82.98	83.71
	84.06	82.93	81.92
96.5		84.18	81.28
	88.90	86.75	89.24
	88.84	88.65	90.75
336.5		91.17	89.18
	96.73	98.97	102.9
	104.0	100.2	103.1
701		99.12	100.7
	105.6	104.7	108.7
	109.2	112.8	109.0
3008	107.4	112.2	108.7
3008	109.4	113.5	113.2
	111.2	114.2	113.7
	116.0	116.6	113.5

TABLE XXI

ASSAYS OF CUMENE FROM BENZENE:CUMENE:ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c.}/\text{mmole}$		
	Individual Assays		Average Value
	<u>First Run</u>		
1	31.20	30.66	29.36
	28.80	29.11	31.91
	29.73	29.98	30.09
2	42.98	44.08	44.56
	45.59	45.68	46.07
		44.85	44.83
4	58.62	56.39	57.27
	59.04	59.34	60.93
		60.85	58.92
8.25	67.04	65.91	68.25
	68.05	67.07	65.15
		67.01	66.93
24	70.02	66.72	66.76
	68.91	68.48	68.42
		69.78	68.44
47	82.84	75.10	74.81
	75.46	79.34	80.12
94.5			77.94
	88.20	89.05	89.78
	86.48	89.46	92.99
		89.13	89.30
335	109.0	109.8	109.8
	110.6	108.2	109.9
			109.6
698.8	137.5	129.9	137.5
	133.6	135.4	132.1
			134.3
3006	186.1	186.0	184.4
	185.3	183.4	187.0
		184.6	185.2

TABLE XXI (Continued)

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$		
	Individual Assays		Average Value
	<u>Second Run</u>		
1	25.73	24.86	25.17
	25.23	24.23	25.03
	25.13	25.20	24.26
		25.90	25.07
2	40.03	39.16	40.33
	40.49	40.20	39.93
	39.86	39.62	40.93
		40.69	40.12
4	57.46	57.59	58.26
	58.06	58.60	58.26
	58.12	58.53	57.83
		57.66	58.04
8	55.94	58.30	56.76
	57.23	59.38	58.78
	61.00	60.76	60.15
		60.59	58.89
24	67.31	69.36	67.92
	69.77	68.85	69.29
	70.36	69.66	69.66
			69.13
49	79.80	81.92	83.90
	82.51	82.38	82.10
98	101.6	103.8	103.2
	97.62	99.50	97.16
	99.14	100.7	100.7
			100.4
338	113.4	115.5	119.1
	115.5	118.8	111.2
	115.7	113.5	116.5
		116.0	115.5
991	148.1	149.8	149.8
	142.7	157.7	151.5
	155.6	149.4	151.6
		148.1	150.4
3679	211.4	216.3	203.8
	210.3	212.6	201.8
	205.9	203.1	204.0
		206.4	207.6

TABLE XXII

ASSAYS OF TERT-BUTYLBENZENE FROM BENZENE:TERT-BUTYLBENZENE:
ACID MIXTURES

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{C./mmole}$		
	Individual Assays		Average Value
	<u>First Run</u>		
1	26.70	26.02	26.67
	27.37	26.96	27.82
	26.42	26.42	26.65
			26.78
2	42.88	42.57	41.73
	41.36	42.88	42.12
	44.91	43.22	43.31
		43.38	
			42.84
4	63.18	61.76	64.25
	63.25	62.86	62.44
	63.48	63.32	
			63.07
8	81.79	79.59	77.74
	77.60	79.10	78.15
	81.10	80.52	82.57
		79.84	
			79.80
24	94.97	93.21	96.11
	93.37	94.11	94.50
	95.16	91.66	91.80
			93.88
48	102.2	106.2	106.0
	102.3	104.8	102.6
	108.5	105.2	108.1
			105.1
98	120.9	126.6	123.8
	124.3	126.2	127.0
	126.1	123.2	
			124.8
337	164.6	161.6	166.3
	167.2	166.0	165.9
		167.6	
			165.6
3678	272.8	284.4	282.3
	272.3	278.9	292.4
		283.3	
			280.9

TABLE XXII (Continued)

Reaction Time, hrs.	Specific Radioactivity, $\mu\text{c./mmole}$		
	Individual Assays		Average Value
	<u>Second Run</u>		
1	23.98	24.17	24.85
	24.80	25.06	25.00
	24.87	25.34	24.76
2	42.68	41.26	42.05
	42.01	40.37	42.39
	41.24	41.30	41.14
		41.58	41.60
4	62.67	61.22	62.63
	61.80	61.46	62.58
		61.29	61.95
8	78.40	77.24	76.41
	77.43	79.19	75.79
	77.02	78.09	76.96
24			77.39
	90.98	92.95	92.97
	90.78	92.14	91.65
48	92.38	90.61	92.76
			91.91
	101.3	106.7	99.41
98.5	103.8	103.4	106.6
	103.1	102.9	104.9
		101.0	103.3
337.75	120.6	124.4	124.7
	128.5	125.0	126.9
	127.3	120.6	124.4
3678			124.7
	162.2	162.1	164.0
	171.5	163.8	168.9
	166.9	169.2	171.3
		169.2	166.9
3678	281.4	280.2	281.6
	287.3	284.5	289.1
	285.4	283.0	292.1
			285.0

CHAPTER VI

MATHEMATICAL ASPECTS OF THE EXPERIMENTAL WORK

The discussion in this chapter concerns the various methods which were tried to extract from the experimental data the parameters in the overall radioactivity-versus-time relationships derived in Chapter III. Data for exchange of hydrogen on benzene must be treated differently from those for the alkylbenzenes. Exchange is so slow on benzene that an experimental determination of the ratio of forward to reverse rate constants was not possible within a reasonable length of time. For the alkylbenzenes, the exchange reaction was fast enough that the value of this ratio was determined by allowing the exchange to proceed essentially to equilibrium.

Analysis of Data for Exchange in Toluene, Ethylbenzene, and Cumene

Exchange at each position of the ring in an alkylbenzene occurs simultaneously. Determination of the tritium content at each of the individual ring positions is not possible from a measurement on the hydrocarbon. In Chapter III an equation was derived relating the overall specific radioactivity to time. This relationship [1] has the form of the summation of three exponential growth curves where the parameters sought, α , β , and γ , form a part of the exponents of the exponential terms. $[TA]/[HA]$ is the specific radioactivity of labile tritium in

$$\begin{aligned} \text{Overall specific radioactivity} = \frac{[TA]}{[HA]} & \left\{ \frac{k_o}{k_o'} \left[1 - e^{-\alpha k_B' [HA] t} \right] \right. \\ & \left. + \frac{k_m}{k_m'} \left[1 - e^{-\beta k_B' [HA] t} \right] + \frac{k_p}{k_p'} \left[1 - e^{-\gamma k_B' [HA] t} \right] \right\} \quad [1] \end{aligned}$$

the acid solvent. The ratios k_o/k_o' , k_m/k_m' , and k_p/k_p' are essentially equilibrium constants for the ortho, meta, and para positions. The value of the equilibrium constant is assumed to be the same for the three ring positions. α , β , and γ are the ortho, meta, and para partial rate factors, respectively. k_B' is the exchange rate constant for one position in benzene.

Determination of these parameters involves a non-linear regression treatment of the data. There is no general method to approach such a regression but a common technique, when possible, is to express the non-linear portions of the equation as a power series (31). The Taylor's series for the expansion of $y(x+h)$ about x , as given by Salvadori and Baron (28a), is

$$y(x+h) = y(x) + \frac{h}{1!} y'(x) + \frac{h^2}{2!} y''(x) + \dots + \frac{h^n}{n!} y^{(n)}(x)$$

When this general formula is applied to an exponential, $e^{(x_o+\Delta x)}$ becomes

$$\begin{aligned} e^{(x_o + \Delta x)} &= e^{x_o} + \Delta x e^{x_o} + \frac{\Delta x^2}{2!} e^{x_o} + \dots + \\ &= e^{x_o} \left[1 + \Delta x + \frac{\Delta x^2}{2!} + \dots + \right] \end{aligned}$$

Similarly,

$$\begin{aligned}
e^{-(x_o + \Delta x)} &= e^{-x_o} - \Delta x e^{-x_o} + \frac{\Delta x^2}{2!} e^{-x_o} - \dots + \\
&= e^{-x_o} \left[1 - \Delta x + \frac{\Delta x^2}{2!} - \dots + \right]
\end{aligned}$$

With initial estimates of α_o , β_o , and γ_o , the following relations can be incorporated into Equation [1]

$$\alpha = \alpha_o + \Delta a$$

$$\beta = \beta_o + \Delta b$$

$$\gamma = \gamma_o + \Delta c$$

$$\begin{aligned}
\text{Overall specific} &= \frac{[TA]}{[HA]} \cdot \frac{k_o}{k_o'} \left\{ 5 - 2e^{-(\alpha_o + \Delta a)k_B'[HA]t} \right. \\
\text{radioactivity} &\quad \left. - 2e^{-(\beta_o + \Delta b)k_B'[HA]t} - e^{-(\gamma_o + \Delta c)k_B'[HA]t} \right\} \quad [2]
\end{aligned}$$

Specifically for this case, each of the three exponential terms in Equation [2] was expressed as a Taylor's power series about an initial estimate point. Then as an approximation, the series was truncated to include only those terms up to and including the term linear in the correction to the parameter. Thus,

$$\begin{aligned}
\text{Overall specific} &= \frac{[TA]}{[HA]} \cdot \frac{k_o}{k_o'} \left\{ 5 - 2e^{-\alpha_o k_B'[HA]t} (1 - \Delta a k_B'[HA]t) \right. \\
\text{radioactivity} &\quad - 2e^{-\beta_o k_B'[HA]t} (1 - \Delta b k_B'[HA]t) \\
&\quad \left. - e^{-\gamma_o k_B'[HA]t} (1 - \Delta c k_B'[HA]t) \right\} \quad [3]
\end{aligned}$$

On rearranging, [3] becomes [4].

$$\begin{aligned}
& \frac{\text{Overall specific radioactivity}}{\frac{[TA]}{[HA]} \cdot \frac{k_o}{k'_o}} = \frac{5 + 2e^{-\alpha_o k'_B [HA]t} + 2e^{-\beta_o k'_B [HA]t} + e^{-\gamma_o k'_B [HA]t}}{k'_B [HA]t} \\
& \frac{\overline{2\Delta a} e^{-\alpha_o k'_B [HA]t} + \overline{2\Delta b} e^{-\beta_o k'_B [HA]t} + \overline{\Delta c} e^{-\gamma_o k'_B [HA]t}}{k'_B [HA]t} = [4]
\end{aligned}$$

In the limit, where the estimates of the parameters approach the true values, i.e., as $\alpha_o \rightarrow \alpha$ and $\Delta a \rightarrow 0$, etc., Equation [4] becomes more exact. This situation immediately suggests an iterative type process whereby each successive iteration, it is hoped, improves on the previous values for the parameters. The improved value obtained for the parameter is then regarded as an initial estimate in the next iteration.

Equation [4] is to be obeyed by all of the data. For a given run ten samples were taken and assayed. Ten of these equations each linear in the same three unknowns resulted. However, only three equations are needed to solve for the three unknowns. The total number of ways in which the ten equations can be grouped three at a time is one hundred twenty. Obviously an iterative process for solving one hundred twenty sets of simultaneous equations in three unknowns would be a very time-consuming process even on an electronic computer. One could choose to solve only selected sets of the equations but bias enters when such choices are made.

The general method for the solution of such sets of equations follows. The form of the equations has been changed to make the meaning clearer and to simplify writing. The n equations become

$$\left. \begin{aligned}
 b_1)_1 x + b_2)_1 y + b_3)_1 z &= m_1 \\
 b_1)_2 x + b_2)_2 y + b_3)_2 z &= m_2 \\
 b_1)_3 x + b_2)_3 y + b_3)_3 z &= m_3 \\
 \cdot &\cdot \\
 \cdot &\cdot \\
 \cdot &\cdot \\
 b_1)_n x + b_2)_n y + b_3)_n z &= m_n
 \end{aligned} \right\} \quad [5]$$

The \underline{m} 's represent the time-variable but known left-hand side of Equation [4]. The x , y , and z represent the unknown corrections on the parameters and the \underline{b} 's the coefficients of these corrections. The \underline{n} equations in [5] can be transformed into a set of three simultaneous linear equations [6] in the same three unknowns by the transformations [7].

$$\left. \begin{aligned}
 a_{11}x + a_{12}y + a_{13}z &= p_1 \\
 a_{21}x + a_{22}y + a_{23}z &= p_2 \\
 a_{31}x + a_{32}y + a_{33}z &= p_3
 \end{aligned} \right\} \quad [6]$$

$$a_{ij} = \sum_{k=1}^n b_i)_k \cdot b_j)_k \quad p_l = \sum_{k=1}^n m_k \cdot b_l)_k \quad [7]$$

$$i = 1, 2, 3$$

$$l = 1, 2, 3$$

$$j = 1, 2, 3$$

$$k = 1, 2, \dots, n$$

$$k = 1, 2, \dots, n$$

This regression method was programmed for the IBM 650 digital computer. Synthetic data were used in an attempt to test the method, but answers near the correct values never were obtained. Negative answers resulted frequently, but could not be accepted because of their

lack of physical significance. The parameters are, in effect, rate constants and cannot assume negative values.

After several months of trying to find where the method went astray, it was found that the determinant of the coefficients of the three equations was zero. Solution of simultaneous equations ultimately involves division by this number and, of course, fails when it is zero. When the value of the determinant differed only very slightly from zero, i.e., when it was of the order of 10^{-20} , the division resulted in very large changes in the parameters. Frequently no more than one iteration was necessary for the correction to move the parameters out of the correct region in parameter space and even into an octant where one or more of the parameters was negative.

The method was changed so only some of the data points were used and was reprogrammed for the computer. Previously the n specific radioactivity versus time relationships [5] were manipulated [7] so only three equations were the result. In this revised program only three of the points were used at a time. More synthetic data were generated, but this time the data were for a slower reaction than before. The method worked very nicely on most of these data although the initial estimates were considerably in error. Some of the results are shown in Table XXIII.

A comparison of entries (e) and (i) with the others in Table XXIII shows that the regression method works fine as long as the initial estimates are of the same order as the true values. In other words, since the ortho partial rate factor is smaller than that for the para position, the initial estimates of these parameters must also be in this same order. Actually (e) and (i) fit the data just as well as do

TABLE XXIII

SOME RESULTS OF THE REGRESSION ON SYNTHETIC DATA

	Time, hrs.	ST/SA ^a
Data 1	87.5	1.9733450
	100.0	2.1449316
	1000.0	4.3472989
Data 2	6.5	0.2105288
	32.0	0.9182724
	69.5	1.6891798
Data 3	14.0	0.05684870
	56.0	0.22159700
	94.0	0.36346930

		Initial Estimate			Final Answer			Correct Answer		
		α_o	β_o	γ_o	α	β	γ	α	β	γ
Data 1	(a)	500	50	600	600	70	750	600	70	750
	(b)	400	40	880	600	70	750	600	70	750
Data 2	(c)	500	50	600	600	70	750	600	70	750
	(d)	400	40	880	600	70	750	600	70	750
	(e)	800	100	500	702	71	546	600	70	750
Data 3	(f)	50	1	145	70.7	7.93	98.7	70.5	8.0	99.0
	(g)	63	7	75	70.4	8.02	99.1	70.5	8.0	99.0
	(h)	100	12.6	129	70.6	7.98	98.9	70.5	8.0	99.0
	(i)	92	12	88	90.1	8.36	59.0	70.5	8.0	99.0

^aST/SA is the ratio of the specific radioactivity of the hydrocarbon to that of the acid.

the other entries in the table. The only drawback in the method lies in the fact that the order of magnitude and the relative size of the partial rate factors must be known.

When experimental data were analyzed by the method just described, no convergence to an answer was obtained. The rate constant found for hydrogen exchange in benzene was one order of magnitude greater than that assumed in the synthetic data. After a considerable time it was discovered that the method failed because the approximation of the exponential by only two terms of the series was greatly in error. To illustrate this, assume that k'_B for the synthetic data is 1×10^{-6} and is 1×10^{-5} liter mole $^{-1}$ hr. $^{-1}$ for the experimental data, $[HA] = 10$ moles liter $^{-1}$, and $t = 1000$ hours. Also, assume that α is 50, $\alpha_o = 30$, and $\Delta a = 20$. In general, the ortho and para partial rate factors can be estimated only to this accuracy. For the synthetic data, the approximation becomes

$$e^{-\alpha k'_B [HA]t} \doteq e^{-\alpha_o k'_B [HA]t} \left[1 - \overline{\Delta a} k'_B [HA]t \right]$$

$$e^{-0.5} \stackrel{?}{=} e^{-0.3} [1 - 0.2] = 0.7408(0.8)$$

$$0.6065 = 0.5926$$

For the experimental data, the approximation becomes

$$e^{-5} = e^{-3} [1 - 2] = -e^{-3}$$

$$0.006738 \neq -0.04979$$

Clearly the exponential cannot be accurately approximated by a series in the case of experimental data. The rate of exchange must be reduced in order to come within the limits of the synthetic data, but then the reaction is too slow to be followed conveniently in the laboratory. After an initial period of jubilation over having made the regression method work, it was concluded that the method would not apply to the experimental data and that some other method had to be devised to analyze these data.

A second method tried, and the one finally adopted, is much less elegant than the regression method just described. The parameters that are sought must be positive to have physical significance, so the space in which the parameters lie was immediately reduced to one octant. If three ranges could be established, each of which contained the correct value for one of the parameters, these ranges could be systematically searched by a trial-and-error method. The value of the dependent variable, the specific radioactivity, was calculated at each datum time using the trial value for each of the parameters. Each of these calculated values could then be compared with the corresponding experimentally observed values. The sum of the squares of the differences between the calculated and observed values of the specific radioactivity was calculated for each set of trial parameters. The set of parameters giving the least value for the sum of the squares of the differences was assumed to give the best fit to the data since the least-squares method was used as a criterion for goodness of fit.

The method can become very time consuming if the grid is made too small. Assume p parameters are to be fitted and that the range for each is divided into n parts. It can be shown that there are $(n + 1)^p$

different possible combinations of the parameter values. For each of these combinations the calculated value of the function must be compared with the observed value and the sum of the squares of their differences must be calculated for each of the data points.

There are several drawbacks to this method besides the length of time required. One must be sure that the correct value for each of the parameters lies within the range being searched. If not, the apparent best fit is obtained for the set of partial rate factors in the end of the range nearest the correct values. Due to the nature of Equation [1], two or more sets of values might give fits to the data nearly equivalent. One cannot get the fit any better than the grid will allow. The results in Table XXIV, obtained from a trial-and-error analysis on some experimental data, illustrate these various drawbacks.

Analysis of Data for Exchange in tert-Butylbenzene

The data for specific radioactivity versus time for exchange in tert-butylbenzene cannot be analyzed by the regression method previously discussed. Exchange occurs at the ring positions and also at the methyl groups, and all attempts to convert tert-butylbenzene to benzoic acid failed. The trial-and-error computer program which was used for toluene, ethylbenzene, and cumene was modified to include a fourth exponential term for exchange of the methyl hydrogen atoms.

The increase in specific radioactivity in tert-butylbenzene due to exchange of hydrogen in the methyl groups can be derived by the methods shown in Chapter III. The contribution from the methyl hydrogen atoms is given by

TABLE XXIV
SOME RESULTS FROM THE TRIAL-AND-ERROR ANALYSIS OF
EXPERIMENTAL DATA FOR EXCHANGE IN TOLUENE

Assumed Set of Partial Rate Factors			Overall Least-Squares Fit
<u>ortho</u>	<u>meta</u>	<u>para</u>	
50	2	50	231.305
50	2	60	252.308
50	4	50	269.035
50	2	70	269.334
60	2	50	274.559
50	2	80	283.304
50	4	60	292.397
50	2	90	294.884
60	2	60	298.058
50	2	100	304.562
50	4	70	311.043
70	2	50	311.399
50	2	110	312.706
60	4	50	317.007
60	2	70	317.071
50	2	120	319.596
50	2	130	325.451
50	4	80	326.180
50	2	140	330.446
60	2	80	332.643
50	2	150	334.719
70	2	60	336.885
50	4	90	338.631
80	2	50	342.783
60	4	60	342.866
60	2	90	345.528
50	4	100	348.977

$$\begin{array}{l} \text{Overall specific} \\ \text{radioactivity in} \\ \text{methyl groups} \end{array} = 9 \frac{[\text{TA}]}{[\text{HA}]} \cdot \frac{k_c}{k_c'} \left[1 - e^{-k_c' [\text{HA}] t} \right]$$

where k_c/k_c' is the ratio of forward to reverse rate constants for methyl hydrogen exchange. The value of the ratio is assumed to be the same as the ratio for ring hydrogen exchange. The equation relating the total specific activity to time becomes

$$\begin{aligned} \text{Overall specific} \\ \text{radioactivity} \end{aligned} = \frac{[\text{TA}]}{[\text{HA}]} \cdot \frac{k_o}{k_o'} \left[14 - 2e^{-\alpha k_B' [\text{HA}] t} \right. \\ \left. - 2e^{-\beta k_B' [\text{HA}] t} - e^{-\gamma k_B' [\text{HA}] t} - 9e^{-k_c' [\text{HA}] t} \right] \quad [8]$$

The data were fitted to Equation [8] by the trial-and-error method.

Analysis of Data for Exchange in Benzene

If the amount of each reactant used in a run is known and if no isotopic fractionation occurs, a theoretical value for the specific radioactivity of benzene at equilibrium can be calculated. Such calculations were made, and after 3000 hours, the benzene radioactivity had reached a value only about one-third that of the calculated value. From a plot of the specific radioactivity of benzene versus time the increase in the amount of tritium in benzene seemed to be leveling off too rapidly for the calculated equilibrium value ever to be reached. Nevertheless, an equilibrium constant for benzene drastically different from that for an alkylbenzene was hard to rationalize. In 3000 hours the exchange of aromatic hydrogen in an alkylbenzene has essentially reached equilibrium, and an experimental value can be calculated for

the equilibrium constant for the reaction. Despite arguments which could be made for the opposite choice, the equilibrium distribution of tritium between benzene and the solvent was assumed to be the same as that for alkylbenzene and the solvent.

Equation [6] in Chapter III can be mathematically manipulated to leave only the exponential term on one side, and the resulting equation can be solved for k_B' by taking the logarithm of both sides of the equation. The ratio of forward to reverse rate constants, k_B/k_B' , is defined as K_e , $[B_T]/[B]$ as SB, and $[TA]/[HA]$ as SA. This relationship is expressed in Equation [9]. With the data from the first competitive

$$k_B' = - \frac{\log_e \left[1 - \frac{SB}{6K_e \cdot SA} \right]}{[HA]t} \quad [9]$$

exchange involving benzene and toluene, Equation [9] was used to calculate the reaction rate constant for exchange in benzene. For each datum time a decrease in the calculated value of the rate constant from that for the previous time was observed. The nature of Equation [9] is such that smaller values for K_e , other variables remaining constant, increase the value of the rate constant. Values of the equilibrium constant different from the experimentally determined value were also tried to see if more consistent values could be obtained. The results of the various calculations are shown in Table XXV. Clearly there is a large variation in the calculated value for the rate constant from the beginning of an experiment to the end. Since the rate constant should not vary, a definite possibility, even probability, exists that the data were being fitted to the wrong model. All derivations and

calculations were rechecked several times but no errors could be found.

TABLE XXV

CALCULATED VALUES FOR THE BENZENE RATE CONSTANT USING
VARIOUS VALUES FOR THE EQUILIBRIUM CONSTANT

Time, hrs.	$10^5 k'_B$, liter mole ⁻¹ hr. ⁻¹							
	Equilibrium Constant							
	0.3	0.4	0.5	0.7	0.8	0.9	1.0	2.0
96	16.7	12.2	9.6	6.7	5.9	5.2	4.7	2.3
337	11.3	7.9	6.1	4.2	3.6	3.2	2.9	1.4
672	8.6	5.9	4.4	3.0	2.7	2.3	2.0	0.96
3245	8.9	3.3	2.2	1.4	1.1	0.99	0.87	0.40

The equations in Chapter III were all derived under the assumption that the change in the specific radioactivity of tritium in the acid solvent was constant. From the beginning of this study this assumption was known not to be strictly correct but the experiments were all designed to minimize the decrease as much as was practical. This change in the specific radioactivity of the acid, though only about 6 per cent, possibly was sufficient to cause this regular decrease in the rate constant. From Equation [9], one would predict that if the activity of the acid (SA) were smaller than its initial value at some time $t_i \neq t_o$, then the quantity in brackets would be less than before and the logarithm of the quantity would be more negative. Qualitatively this change is in the direction needed to make the values in Table XXV more consistent. A quantitative prediction of the amount of the change would be difficult to make.

Some correction for the change in the specific radioactivity of the

acid solvent had to be made. An immediate problem was that of how to account for the change. The rate equation was derived for the decrease in the activity of the acid in a competitive run involving benzene and an alkylbenzene. However, the rate constants for hydrogen exchange in the hydrocarbons also entered in and solution of the differential equation was impossible.

The specific activity of the acid could be calculated at each point where samples were analyzed. The amount of tritium remaining in the acid was calculated by subtracting from the initial amount of tritium present in the acid the total amounts of tritium which had been incorporated into benzene and the alkylbenzene at each point a sample was taken. The specific activity of the acid was calculated by dividing the total amount of tritium remaining in the acid by the total number of moles of labile hydrogen in the acid components. Rapid re-equilibration of the tritium in the acid must occur for these calculations to be valid. The decrease in the activity of the acid was not linear but resembled more an exponential decay curve over a narrow range. This behavior might have been predicted since three of the five positions in the alkylbenzene are highly activated toward electrophilic substitution relative to benzene. The remaining two positions, though still more active than benzene, react slower than the first three. A rapid decrease in the specific activity of the acid results during the first hours of the exchange, but after about 300 hours, the decrease becomes almost linear.

Several attempts were made to approximate the effective value for the specific activity of the acid during the reaction. Some of the methods involved numerical averages of the activity of the acid.

Suppose that Equation [9] was being used to calculate the rate constant at each time t a sample was taken. One of these approximation methods involved averaging the specific activities initially and after t hours of reaction. Another approximating method was that of weighted averages. None of these averaging methods gave an effective value for the specific activity of the acid which led to a calculated rate constant varying by less than a factor of two from the beginning to the end of an experiment.

The change in the specific activity of the acid is less in going from t_1 to t_2 than from t_0 to t_2 (refer to Figure 2). Therefore, the value for SA can more properly be considered constant in each of the intervals of time, and in the interval t_0 to t_1 , SB_1 is proportional to SA_0 . The rate constant in this interval can be calculated from Equation [9].

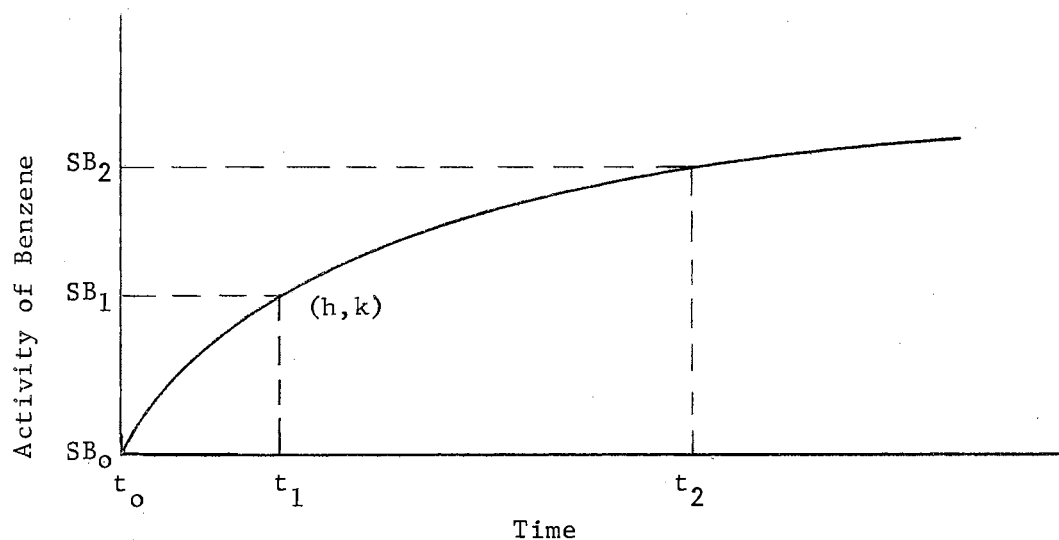


Figure 2. Variation of the Activity of Benzene with Time

In an attempt to minimize the error due to the change in the specific activity of the acid from t_0 to t_2 , the origin in the original case was translated to a new point (h,k) for the calculation of the rate constant in the interval t_1 to t_2 . After the coordinate axes are translated, Equation [9] becomes [10]

$$SB_2 - k = 6 SA_1 \cdot K_e \left[1 - e^{-k_B [HA](t_2 - h)} \right] \quad [10]$$

The value of SA_1 was assumed to be constant over the interval t_1 to t_2 , and a value for the rate constant was calculated in that interval. Experimental data from the first competitive run involving benzene and toluene were analyzed with this change in the equation. Values for the rate constant only slightly less variable than before were obtained. Further use of the equation was not attempted.

After all other known possible points which might cause this variation in the rate constant with time had been checked, it appeared that only the change in the specific activity of the acid could be causing the discrepancy. Furthermore, it appeared that the change in the activity must be very closely approximated to obtain a constant value for the rate constant. To account exactly for the change mathematically, the specific activity of the acid must be related to time by a known function. This functional relationship could then be incorporated into Equation [2], Chapter III, and the differential equation could be solved if the functional relationship did not make integration impossible.

Attempts were made to fit several exponential curves to the specific-activity-versus-time data. No models were found which fit the data well for more than three points. In the region where the specific

activity of the acid was changing most rapidly, the hydrocarbons were assayed at shorter time intervals, and the decrease in the specific activity of the acid between two consecutive sampling times could closely be approximated as linear. Then in Figure 3, the specific activity (SA) of the acid in the time interval t_2 to t_3 is

$$SA = SA_2 + m_{2,3} (t - t_2)$$

where $m_{2,3}$ is the slope of the line joining P_2 and P_3 .

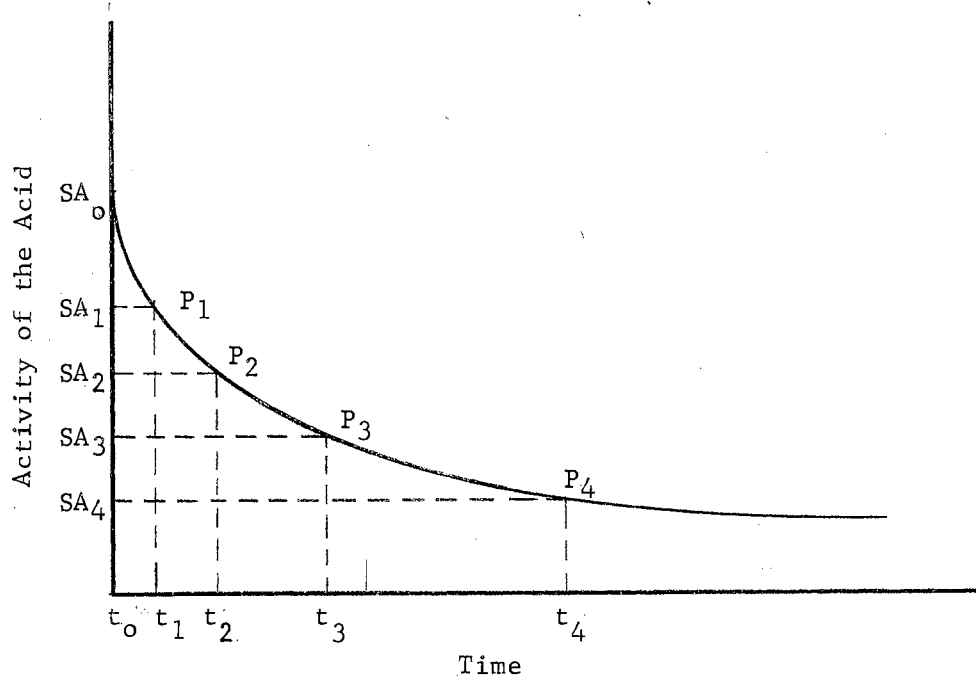


Figure 3. Variation in the Activity of the Acid Solvent with Time.

In general, the specific activity in the time interval t_i to t_{i+1} is

$$SA = SA_i + m_{i,i+1} (t - t_i) \quad [11]$$

where $m_{i,i+1}$ is the slope of the line from SA_i to SA_{i+1} .

Equation [11] was incorporated into the rate expression (Equation [2] in Chapter III) and the rate expression became Equation [12].

$$\frac{1}{[HA]} \left\{ \frac{d[B^*]}{dt} + k'_B [HA][B^*] \right\} = 6k_B [B] \left[SA_i + m_{i,i+1} (t-t_i) \right] \quad [12]$$

In solving this linear differential equation, the equation was treated just as was done in Chapter III. Equation [12] was integrated between the limits of t_i and t_{i+1} and the corresponding $[B_i^*]$ and $[B_{i+1}^*]$. After straight-forward but rather tedious algebraic manipulations, the integrated form of Equation [12] became Equation [13].

$$SB_{i+1} = \left\{ SB_i - 6 \frac{k_B}{k'_B} \left[SA_i - \frac{m_{i,i+1}}{k'_B [HA]} \right] \right\} e^{k'_B [HA] (t_i - t_{i+1})} + 6 \frac{k_B}{k'_B} \left[SA_i + m_{i,i+1} \left(t_{i+1} - t_i - \frac{1}{k'_B [HA]} \right) \right] \quad [13]$$

An attempt was made to fit the experimental data previously used to this model. The calculations were first done by hand on a desk calculator to see if the method would work before a program was written to do the calculations on the computer. In Equation [13] there are two parameters, the rate constant and the equilibrium constant. The equilibrium constant for the alkylbenzene-hydrogen exchange in these data was about 0.75 so this value was used in the calculations. Several different values for the rate constant were used and the value for the benzene specific activity was calculated. This value was compared with the observed value. Some results from these calculations are shown in Table XXVI.

TABLE XXVI

CALCULATED AND OBSERVED SPECIFIC ACTIVITIES OF BENZENE
FOR SOME REACTION RATE CONSTANTS AND AN
EQUILIBRIUM CONSTANT OF 0.75

$$A: k_B' = 10 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$$

$$B: k_B' = 8 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$$

$$C: k_B' = 5 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$$

Time, hrs.	Specific Activity of Benzene, $\mu\text{c./mmole}$			
	Observed	Calculated		
		A	B	C
96	9.59	14.35	11.50	7.32
337	20.13	43.04	35.70	23.33
672	27.36	70.71	60.76	42.23
3245	52.41	120.9	118.20	106.6

The data in Table XXVI were plotted to see if any trends could be detected. The calculated values are graphically compared with the observed values in Figure 4. Clearly all three values give fair fits to the observed values in the early part of the reaction but all show large divergence from the observed values in the middle and latter parts of the reaction. For all points a value for k_B' of 1×10^{-4} liter mole⁻¹ hr.⁻¹ gave a calculated specific activity of benzene greater than the observed. The same was true for a value of 8×10^{-5} liter mole⁻¹ hr.⁻¹, but the divergence was not so great. At 96 hours, a k_B' value of 5×10^{-5} liter mole⁻¹ hr.⁻¹ gave a calculated value for the specific activity which was less than the observed but by 337 hours, the situation had just reversed. These results seemed to indicate that the reaction was fairly rapid but possibly did not go very far until

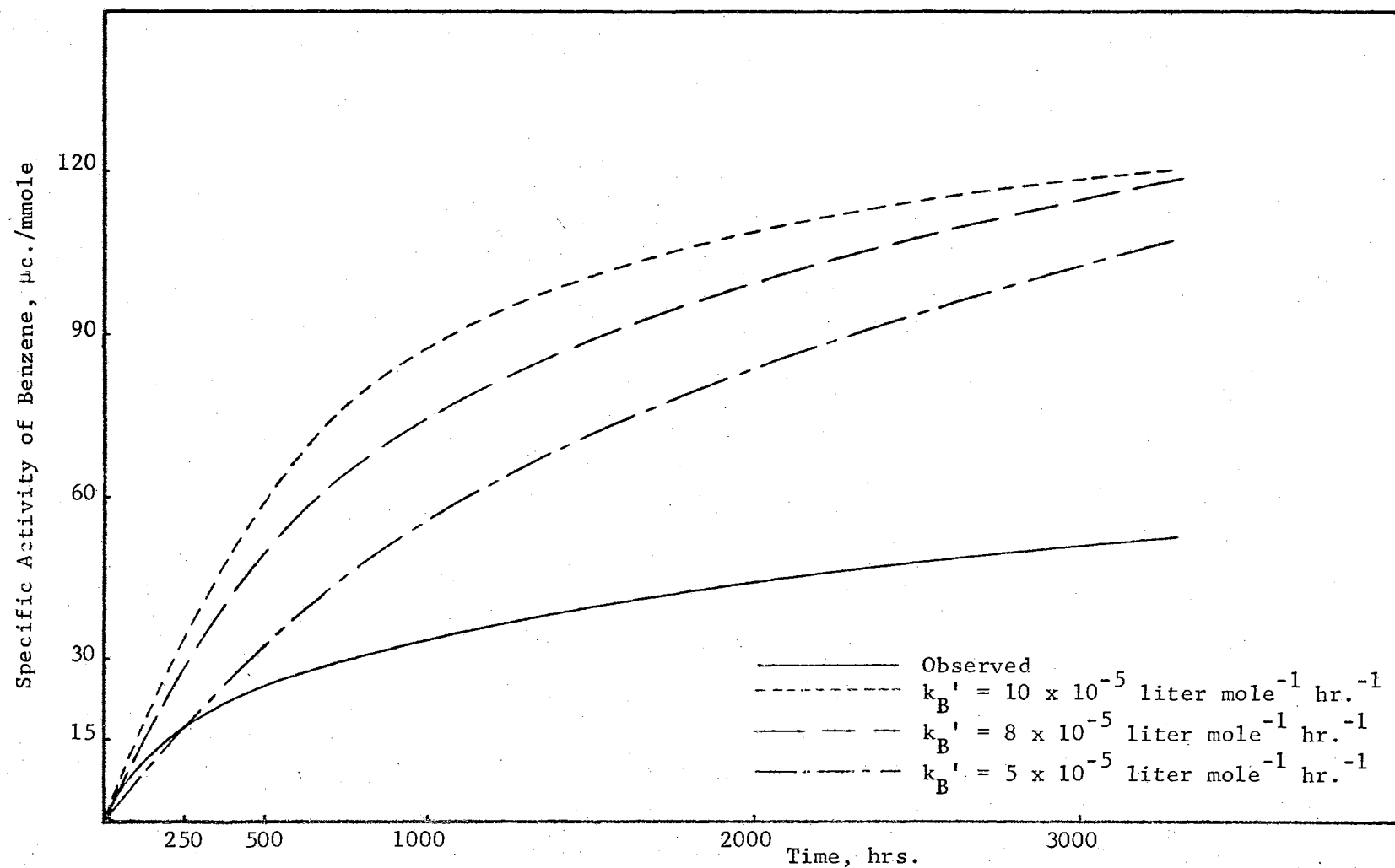


Figure 4. Calculated Activities of Benzene for Several Values for the Rate Constant and an Equilibrium Constant of 0.75

equilibrium was established. Certainly the rate constant must lie between 5×10^{-5} and 1×10^{-4} liter mole⁻¹ hr.⁻¹.

Although the value for the equilibrium constant for exchange in benzene was at first assumed to be the same as that for the alkylbenzene, the value of the equilibrium constant was varied for the same values of the rate constant. These calculations were not difficult once those reported in Table XXVI had been done. A comparison is made in Table XXVII of the divergence of the calculated values from the observed values for the specific activity of benzene when several different values were used for the equilibrium constant. For purposes of comparison part of Table XXVI is repeated in Table XXVII.

The data from Table XXVII were plotted and are shown in Figures 5, 6, and 7. From a comparison of Figure 4 with Figures 5, 6, and 7, a decrease in the value of the equilibrium constant from 0.75 to 0.35 makes the agreement between the calculated and observed values much better. A rate-constant value of 1×10^{-4} liter mole⁻¹ hr.⁻¹ also appears to give a much better fit than does 5×10^{-5} liter mole⁻¹ hr.⁻¹. These plots show that a relatively fast reaction is needed but one in which equilibrium does not lie very far to the right.

This method of analyzing the benzene exchange data was programmed for the digital computer once the discrepancy in the original model was found and corrected. The program was written so that a range of values could be searched for both the equilibrium constant and the rate constant. For each combination of constants, the specific activity of benzene was calculated at each time a sample was taken, and the calculated values were compared with the observed values. A least-squares treatment on the differences in the observed and the calculated values

was used as a criterion for the goodness of the fit.

Once the variation in the specific activity of the acid solvent had been accounted for and the benzene data were shown to give consistent values for the rate constant, a similar change was made in the equations for exchange in the alkylbenzenes.

TABLE XXVII

CALCULATED AND OBSERVED SPECIFIC ACTIVITIES OF BENZENE FOR
DIFFERENT VALUES FOR THE REACTION RATE AND
EQUILIBRIUM CONSTANTS

$$A: K_e = 0.75$$

$$B: K_e = 0.50$$

$$C: K_e = 0.40$$

$$D: K_e = 0.35$$

Specific Activity of Benzene, $\mu\text{c./mmole}$					
Time, hrs.	Observed	Calculated			
		A	B	C	D
$k_B' = 10 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$					
96	9.59	14.35	9.58	7.65	6.70
337	20.13	43.04	28.6	23.0	20.0
672	27.36	70.71	47.2	37.7	33.0
3245	52.41	120.9	80.6	64.4	56.5
$k_B' = 8 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$					
96	9.59	11.5	7.66	6.14	5.37
337	20.13	35.7	23.8	19.0	16.6
672	27.36	60.8	40.5	32.4	28.4
3245	52.41	118.2	78.8	63.0	55.2
$k_B' = 5 \times 10^{-5} \text{ liter mole}^{-1} \text{ hr.}^{-1}$					
96	9.59	7.32	4.88	3.90	3.42
337	20.13	23.3	15.6	12.4	10.9
672	27.36	42.2	28.2	22.5	19.7
3245	52.41	106.6	71.0	57.7	49.7

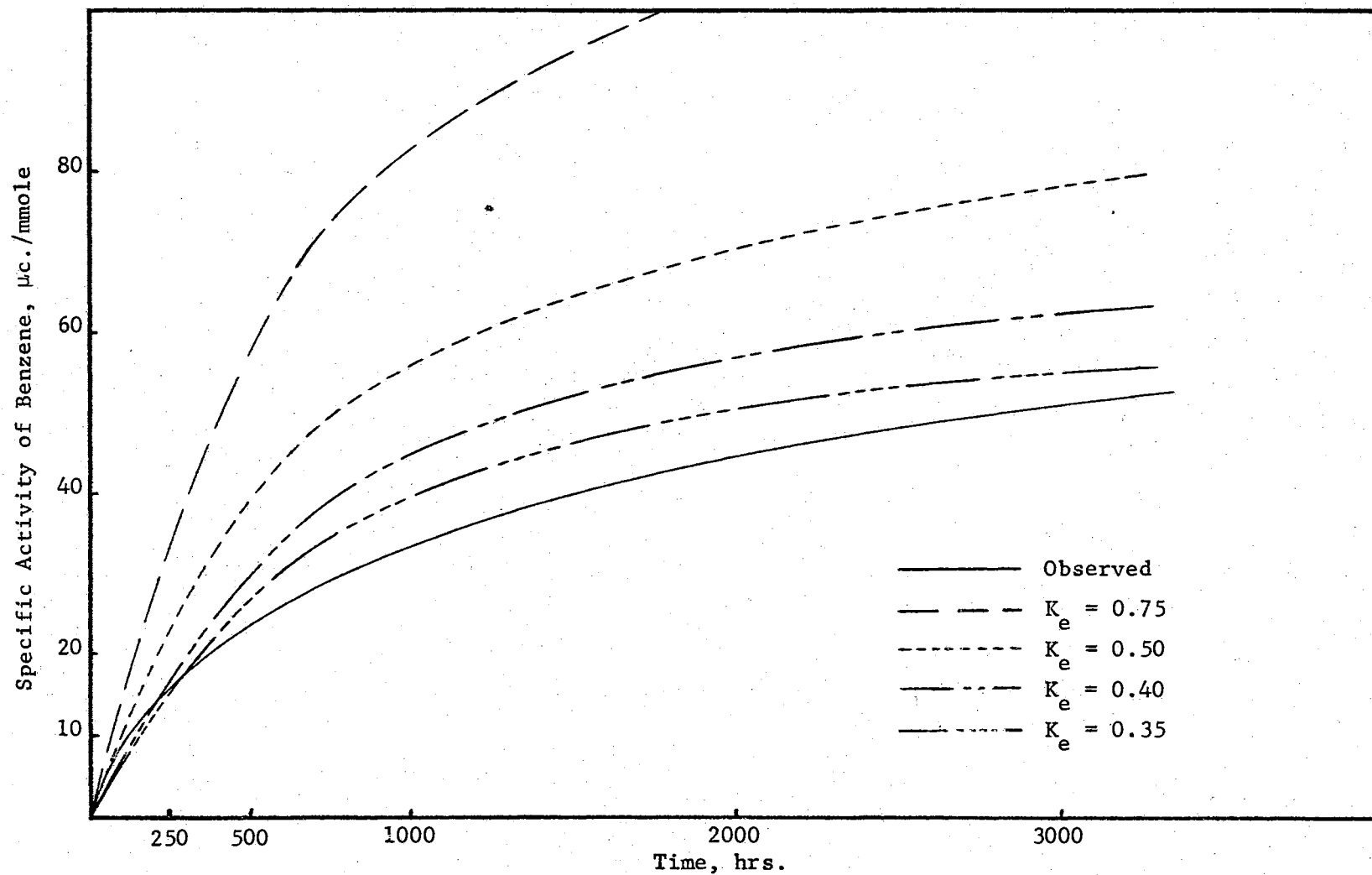


Figure 5. Calculated Activities of Benzene for Several Values for the Equilibrium Constant:
 $k'_B = 1 \times 10^{-4}$ liter mole⁻¹ hr.

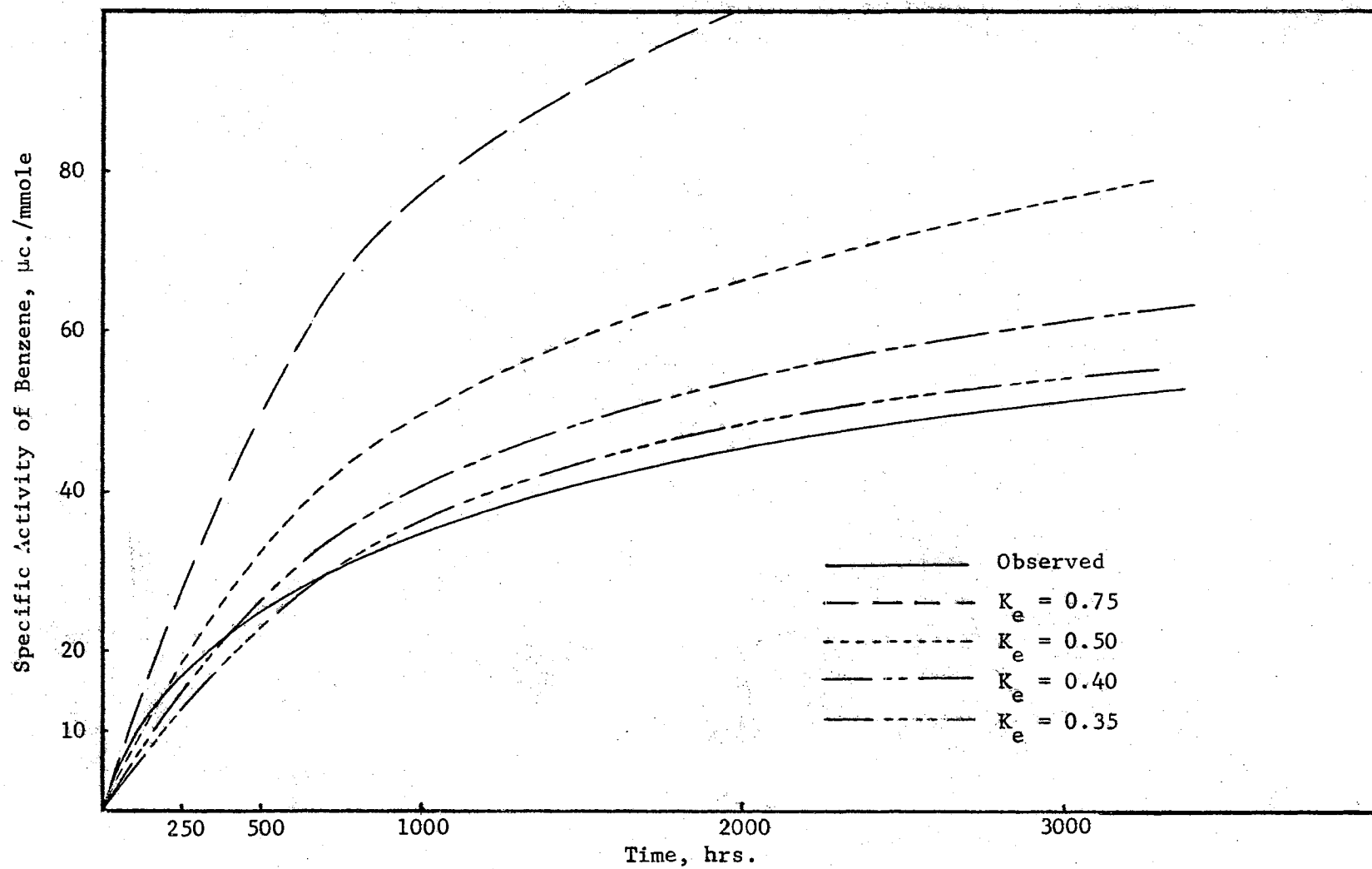


Figure 6. Calculated Activities of Benzene for Several Values for the Equilibrium Constant:
 $k_B' = 8 \times 10^{-5}$ liter mole⁻¹ hr.⁻¹

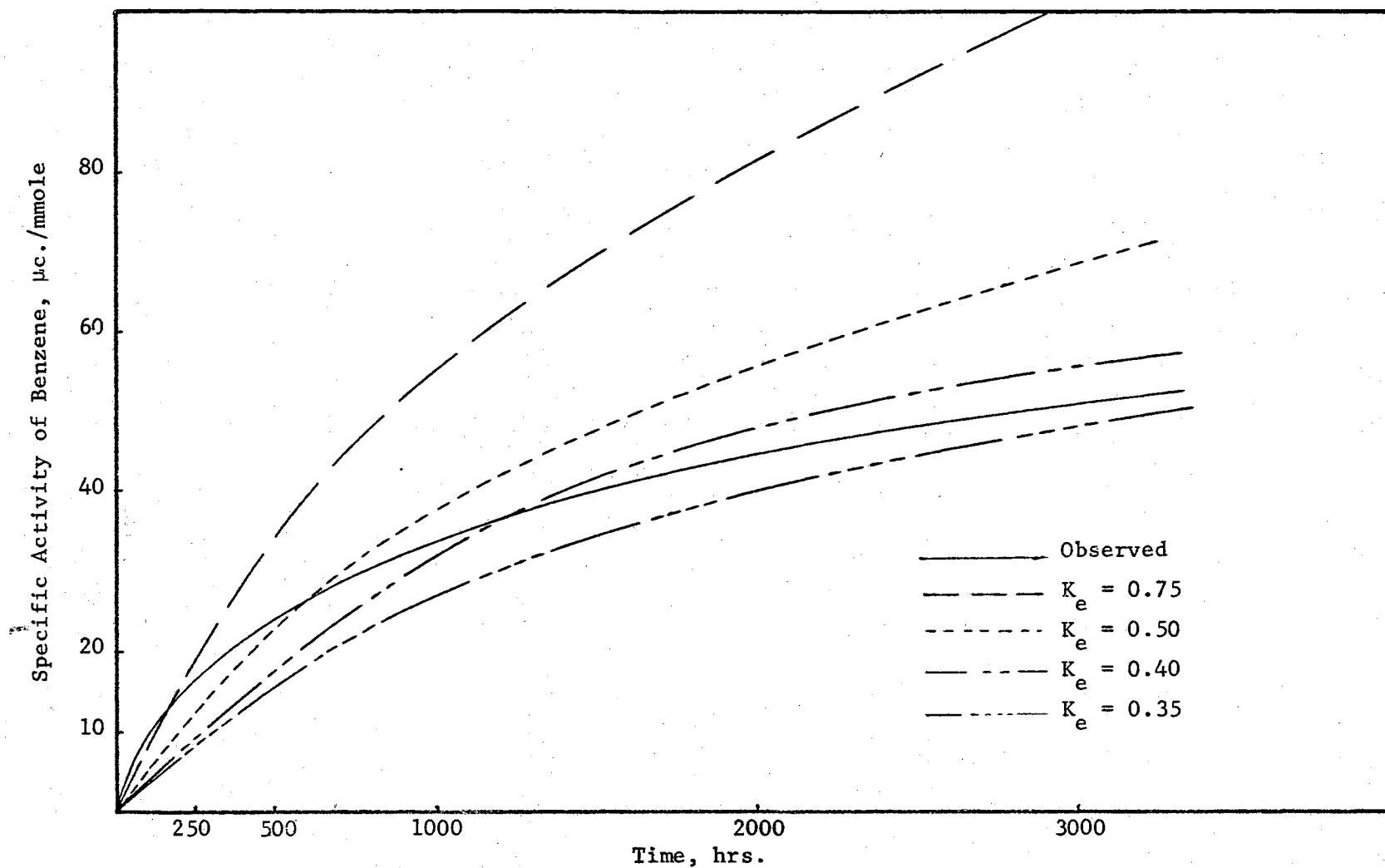


Figure 7. Calculated Activities of Benzene for Several Values for the Equilibrium Constant:
 $k_B' = 5 \times 10^{-5}$ liter mole $^{-1}$ hr. $^{-1}$

CHAPTER VII

RESULTS

Benzene Reaction Rate Constant

The data for the exchange of hydrogen in benzene were analyzed by the method in the preceding chapter. For the equilibrium constant, the range 0.25 to 0.45 was searched and for the reaction rate constant, the range was 7×10^{-5} to 14×10^{-5} liter mole⁻¹ hr.⁻¹. The results of the three best combinations from each run are shown in Table XXVIII. It is obvious from the table that the data are not too sensitive to changes in the combination of the parameters. An error of 3-5 per cent is inherent in the assay method and this error surely contributes to this insensitivity.

Partial Rate Factors for the Alkylbenzenes

The data from the exchange of hydrogen in the alkylbenzenes were analyzed by the trial-and-error method discussed in the previous chapter. After the analysis of the experimental data for exchange in benzene showed that several values for the equilibrium constant gave essentially equivalent fits, it was decided that a range of values for the equilibrium constant should be searched in analyzing the data for exchange in the alkylbenzenes. The range was selected after an experimental value for the equilibrium constant had been calculated. A range was also

TABLE XXVIII

REACTION RATE CONSTANT AND EQUILIBRIUM CONSTANT FOR HYDROGEN
EXCHANGE IN BENZENE

Competitive Reaction With	Run Number	K_e	$10^4 k_B$, liter mole ⁻¹ hr. ⁻¹	Overall Least-Squares Fit
Toluene	1	0.32	1.0	24.00
		0.33	0.9	24.85
		0.33	1.0	27.05
Toluene	2	0.31	1.1	10.58
		0.32	1.0	11.70
		0.31	1.0	12.21
Ethylbenzene	1	0.28	1.0	22.38
		0.27	1.0	23.05
		0.27	1.1	23.16
Ethylbenzene	2	0.28	0.9	20.14
		0.27	1.0	21.51
		0.29	0.9	21.85
Cumene	1	0.26	0.9	26.10
		0.27	0.8	27.20
		0.25	1.0	29.13
Cumene	2 ^a	0.25	0.9	16.86
		0.26	0.9	17.67
		0.27	0.8	19.36
<u>tert</u> -Butylbenzene	1	0.38	1.0	11.90
		0.38	1.1	12.54
		0.39	1.0	13.23
<u>tert</u> -Butylbenzene	2	0.39	1.0	7.53
		0.38	1.0	9.12
		0.38	1.1	10.69

^aThe data for 3679 hours were not used since this point showed a large deviation from the calculated value. The remaining four points which were used very closely paralleled the corresponding points in the first run.

established for each of the partial rate factors. With a given value for the equilibrium constant, the range for each partial rate factor was systematically searched and the sum of the squares of the differences in the observed and calculated values for the specific activity at each datum time was calculated over all of the data. For a particular value for the equilibrium constant, the combination of partial rate factors giving the lowest value for this sum was assumed to be the best set. A partial tabulation of the results of such calculations for the second run involving benzene and toluene is shown in Table XXIX. An equilibrium-constant value of 0.82 was used.

When experimental error is considered, all of the sets of partial rate factors in Table XXIX give equally good fits but there is obviously a large difference in the ortho/para ratio obtained, and the least-squares method over all data points did not prove to be satisfactory. There was a definite possibility that some of the combinations of partial rate factors were giving a fit at each individual point better than were other sets, but that both sets gave nearly equivalent overall fits.

Separation of the ortho and para partial rate factors from one another would not be a simple task; however, the meta partial rate factor could be separated from the other two in the latter part of the reaction. For a benzene rate constant of 1×10^{-4} liter mole⁻¹ hr.⁻¹, an acid concentration of about 12 moles liter⁻¹, and a partial rate factor of 300, the ortho and para reactions are 99.5 per cent equilibrated after 15 hours. The significant ortho and para contributions to the total specific activity are made only during the first few hours of the exchange and any additional contribution made later on will be due to the meta position.

TABLE XXIX

INADEQUACY OF THE OVERALL LEAST-SQUARES METHOD IN DETERMINING
PARTIAL RATE FACTORS AND THE ORTHO/PARA RATIO

Assumed Set of Partial Rate Factors			Overall Least-Squares Fit	Ortho/Para Ratio
<u>ortho</u>	<u>meta</u>	<u>para</u>		
500	4.5	400	96.23	1.25
600	4.5	400	96.24	1.50
450	6.0	700	96.32	0.64
400	5.5	850	96.50	0.47
400	6.0	700	96.78	0.57
500	6.0	600	96.89	0.83
550	5.0	550	96.96	1.00
500	5.5	650	97.00	0.77
600	6.0	400	97.04	1.50
550	6.0	500	97.11	1.10
600	5.5	450	97.15	1.33
550	5.5	550	98.39	1.00
400	4.5	700	98.52	0.57
400	4.5	750	99.07	0.53
450	5.0	800	99.69	0.56
400	4.5	650	99.74	0.62
400	5.0	900	99.75	0.44

The trial-and-error computer program previously used for the data analysis was expanded in an attempt to separate the ortho and para reactions from the meta reaction. The square of the residuals was summed separately over about the first 15-25 hours and over the next 600-800 hours. In this way the sum of the residuals squared for the data in the latter part of the reaction gave a measure of the fit of the meta partial rate factor to the observed data. The same data which were used to get the results reported in Table XXIX were analyzed by this modified method. The results are shown in Table XXX. It is evident from Table XXX that the best overall fit can occur for a set of partial rate factors which does not give the best fit in the meta region of the curve. Since the meta partial rate factor was well separated from the other two, it was felt that the meta partial rate factor could be determined most accurately from the experimental data. In Table XXX, the fit in the meta region is best for a value for the meta partial rate factor of 5.0. This value was then taken as the best for the meta partial rate factor, and the combination of ortho and para partial rate factors which gave the best overall fit for a value for the meta partial rate factor of 5.0 was 550 and 550, respectively, although the combinations 500 and 400, 400 and 850, and 450 and 700 gave a better overall fit.

The computer output from each run and for every assumed value of the equilibrium constant was tabulated in much the same way as the data in Table XXX. The range for the meta partial rate factor was changed until the fit first reached a minimum in the time interval where only the meta position was reacting. When the best value for the meta partial rate factor had been established, the range for the ortho and para positions was then decided. For each run and for each value of the

TABLE XXX

DETERMINATION OF THE META PARTIAL RATE FACTOR

A: For the first four data points

B: For the last four data points

C: For all data points

Assumed Set of Partial Rate Factors			Least-Squares Fit		
<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>A</u>	<u>B</u>	<u>C</u>
500	4.5	400	36.15	60.08	96.23
600	4.5	400	36.10	60.14	96.24
400	4.5	700	38.43	60.09	98.52
400	4.5	750	38.97	60.09	99.07
400	4.5	650	39.65	60.08	99.74
550	5.0	550	42.76	54.19	96.96
450	5.0	800	45.50	54.18	99.69
400	5.0	900	45.59	54.16	99.75
400	5.5	850	40.44	56.06	96.50
500	5.5	650	40.91	56.08	97.00
600	5.5	450	41.06	56.08	97.15
550	5.5	550	42.30	56.09	98.39
450	6.0	700	32.34	63.98	96.32
400	6.0	700	32.81	63.97	96.78
500	6.0	600	32.90	63.98	96.89
600	6.0	400	33.05	63.98	97.04
550	6.0	500	33.13	63.98	97.11

equilibrium constant, the two sets of partial rate factors which seemed to fit the data best were tabulated and are shown in Tables XXXI through XXXIV.

TABLE XXXI

PARTIAL RATE FACTORS FOR HYDROGEN EXCHANGE IN TOLUENE

A: For the first four data points

B: First Run, for the last five data points

Second Run, for the last four data points

C: For all data points

Equilibrium Constant	Partial Rate Factor			Least-Squares Fit		
	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>A</u>	<u>B</u>	<u>C</u>
	<u>First Run</u>					
0.76	600	10.0	600	50.29	49.72	100.02
0.76	550	10.0	750	50.47	49.72	100.19
0.78	550	8.0	600	38.40	53.31	91.71
0.78	500	8.0	750	38.43	53.30	91.74
0.80	550	6.5	500	26.98	71.38	98.37
0.80	500	6.5	600	26.93	71.38	98.32
0.82	500	5.0	500	20.46	94.15	114.62
0.82	450	5.0	650	19.71	94.15	113.87
	<u>Second Run</u>					
0.76	550	10.0	600	70.29	25.82	96.12
0.76	500	10.0	650	74.08	25.82	99.90
0.78	550	8.0	550	53.14	36.15	89.30
0.78	500	8.0	600	54.18	36.14	90.33
0.80	500	6.5	550	37.56	47.38	84.94
0.80	450	6.5	650	41.92	47.37	89.30
0.82	500	5.0	500	26.22	54.16	80.38
0.82	450	5.0	600	28.24	54.16	82.40

TABLE XXXII

PARTIAL RATE FACTORS FOR HYDROGEN EXCHANGE IN ETHYLBENZENE

A: For the first four data points

B: For the last five data points

C: For all data points

Equilibrium Constant	Partial Rate Factor			Least-Squares Fit		
	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>A</u>	<u>B</u>	<u>C</u>
<u>First Run</u>						
0.76	550	12.0	750	93.96	74.32	168.28
0.76	600	12.0	650	92.72	74.33	167.05
0.78	550	11.0	650	58.59	49.18	107.77
0.78	500	11.0	750	60.08	49.18	109.26
0.80	550	9.0	550	43.84	54.50	98.35
0.80	500	9.0	600	44.58	54.50	99.08
0.82	500	8.0	550	24.39	81.20	105.59
0.82	450	8.0	650	25.16	81.20	106.37
<u>Second Run</u>						
0.76	500	10.0	550	29.13	162.89	192.03
0.76	450	10.0	650	32.86	162.87	195.73
0.78	500	9.5	500	14.62	151.29	165.92
0.78	450	9.5	550	15.52	151.26	166.79
0.80	450	7.5	500	8.23	166.43	174.66
0.80	400	7.5	650	11.88	166.42	178.30
0.82	450	5.5	450	4.22	183.43	187.65
0.82	400	5.5	550	5.87	183.41	189.29

TABLE XXXIII

PARTIAL RATE FACTORS FOR HYDROGEN EXCHANGE IN CUMENE

A: For the first four data points

B: For the last three data points

C: For all data points

Equilibrium Constant	Partial Rate Factor			Least-Squares Fit		
	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>A</u>	<u>B</u>	<u>C</u>
<u>First Run</u>						
0.76	400	7	350	155.38	21.86	177.25
0.76	300	7	500	151.36	21.86	173.22
0.78	400	6	400	192.31	30.10	222.41
0.78	400	6	500	206.60	30.07	236.68
0.80	300	5	350	226.00	40.83	266.83
0.80	400	5	400	237.86	40.75	278.62
0.82	300	4.5	350	252.40	56.03	308.43
0.82	400	4.5	400	300.39	55.90	356.30
<u>Second Run</u>						
0.76	300	9	350	72.56	120.58	193.14
0.76	400	9	400	118.27	120.70	238.98
0.78	300	9	350	96.15	105.11	201.27
0.78	200	9	350	151.92	103.65	255.57
0.80	300	8.5	350	127.31	113.87	241.18
0.80	200	8.5	350	142.62	112.20	254.83
0.82	300	7	350	156.67	127.79	284.46
0.82	200	7	350	138.06	125.96	264.03

TABLE XXXIV

PARTIAL RATE FACTORS FOR HYDROGEN EXCHANGE IN TERT-BUTYLBENZENE
 k' for Side Chain Exchange = 1.0×10^{-4} liter mole⁻¹ hr.⁻¹

A: For the first four data points

B: For the last four data points

C: For all data points

Equilibrium Constant	Partial Rate Factor			Least-Squares Fit		
	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>A</u>	<u>B</u>	<u>C</u>
<u>First Run</u>						
0.78	400	10	400	92.96	345.13	438.09
0.78	400	10	500	93.09	345.36	438.46
0.80	400	10	400	60.86	226.74	287.60
0.80	400	10	500	72.40	226.91	299.31
0.82	400	10	400	43.57	182.59	226.17
0.82	400	10	500	67.08	182.70	249.79
0.84	300	10	500	27.48	212.60	240.08
0.84	400	10	400	41.10	212.66	253.76
0.86	300	10	400	13.96	317.04	331.01
0.86	400	10	400	53.44	316.95	370.39
<u>Second Run</u>						
0.78	400	10	400	59.39	267.52	326.91
0.78	300	10	500	83.87	267.15	351.02
0.80	400	10	400	44.68	153.97	198.65
0.80	300	10	500	48.07	153.71	201.78
0.82	300	10	500	25.97	114.41	140.38
0.82	400	10	400	44.75	114.54	159.30
0.84	400	10	400	59.62	149.25	208.88
0.84	300	10	400	10.53	149.22	159.75
0.86	400	10	400	89.28	258.10	347.39
0.86	300	8	400	6.51	244.54	251.06

CHAPTER VIII

DISCUSSION OF RESULTS

The calculated values of the reaction rate constant for benzene in Table XXVIII are in good agreement from one run to another. The value for the equilibrium constant for the exchange was found to be considerably less than that for the alkylbenzenes, but this difference is greater than would arise from experimental error in the assays. There is no explanation for the fact that the equilibrium constant varied from the competitive experiments with one alkylbenzene to those with another alkylbenzene. As mentioned earlier, the experimental data are not sensitive to changes in the combination of the rate constant and the equilibrium constant. While this error is not particularly significant for benzene, it makes the determination of the partial rate factors for the alkylbenzenes subject to an increased error of about 15 per cent.

From Tables XXXI through XXXIV it can be seen that no very consistent values for the partial rate factors were obtained. Less consistency was found for the ortho/para ratio. It was impossible to distinguish between an ortho/para ratio of about 0.6 and 1.0. The insensitivity of the experimental data to changes in the combination of partial rate factors did not permit an unbiased determination of the partial rate factors. If one were to choose some criterion for deciding between sets of partial rate factors, the results would still be consistent. The results from the data analyses were all parallel and there

was no evidence for any greater steric effect at the ortho position in tert-butylbenzene than in toluene. These partial rate factors are considerably greater than those reported by Gold (12) and Melander and Olsson (23-27) for exchange in toluene. However, these results closely parallel in magnitude those of several other research groups (7,21,22).

The value for the equilibrium constant for exchange in the alkylbenzenes which could be calculated from experimental data always gave a poorer least-squares fit to the data than did smaller values. It was necessary to search a range of values for the equilibrium constant. The necessity of having to search a range of values for the equilibrium constant greatly added to the time requirement for the data analysis. In general, for each value of the equilibrium constant, the least-squares fit for 1500-2000 combinations of the partial rate factors was calculated and the results were recorded. Although these calculations were done on an electronic computer and required only approximately one-third second per combination, the hours of computer time which were used is obvious. Furthermore, the amount of output data which must be scanned by hand is almost staggering.

For tert-butylbenzene, the equilibrium constant for exchange of the methyl hydrogen atoms was assumed to be the same as that for aromatic hydrogen. This assumption was not verified and might have been responsible for some of the error in those data analyses.

The assumption that the equilibrium constant for exchange at each of the positions on the ring was equal was never investigated. The insensitivity of the data to changes in the ortho/para ratio would not permit such a study by the trial-and-error method for analyzing the data.

The trial-and-error approach for handling equations which have no analytical solution is not new in the field of chemistry. The method certainly has merit and its use should be encouraged when no other method can be found. In the age of the electronic computer such methods are not the chore that they once were. However, use of the method should be limited to cases where no more than three parameters are to be fitted to the data, and much better results will be obtained for cases involving less than three parameters.

The closeness in the fits of sets of partial rate factors having different ortho/para ratios might be due to experimental error in the tritium assays, and more accurate data would be very helpful in deciding the value for the ortho/para ratio. In subsequent studies in this area more accurate data might be obtained in several ways. The hydrocarbons could be more accurately assayed for tritium with the static ionization chamber for the vibrating-reed electrometer than with the flow ionization chamber. A method must be found to separate the hydrocarbon mixture and purify each component. An alternate approach would be to follow the reaction with deuterium. The hydrocarbons could be analyzed for their deuterium content by mass spectrometry, and for cumene and tert-butylbenzene, the deuterium in the side chain could be measured. These deuterium analyses would be more accurate than those for tritium.

The ortho and para partial rate factors for the alkylbenzenes are subject to a large error due to the relative reactivity at those two positions. It is difficult to do much sampling of the reaction mixture before reaction at those two positions is complete. To change the reaction conditions such that the specific reaction rate constants were no more than one-tenth of their magnitude in these experiments would be

desirable. However, a competitive experiment with benzene would then be almost impossible within a reasonable length of time. In addition to being able to collect more data while the ortho and para positions were reacting, a slower reaction would be helpful in analyzing the data. The regression method described in Chapter VI could be used for the data analysis.

CHAPTER IX

CONCLUSIONS

In the alkylbenzenes studied--toluene, ethylbenzene, cumene, and tert-butylbenzene--hydrogen exchange was found to occur readily. In the compounds containing straight-chain aliphatic groups, exchange occurred at only the nuclear positions. In cumene and tert-butylbenzene, exchange also occurred in the side chain of the molecule. No evidence could be found for rearrangement during exchange of the side chain in cumene and tert-butylbenzene. If the tert-butyl group did isomerize during the reaction, the experimental conditions again caused rearrangement to the more stable tert-butyl group before the nuclear magnetic resonance spectra were taken.

The common mathematical method to handle non-linear regression problems was found not to work for parameter values of the order of magnitude of those in this study. The data were analyzed by a trial-and-error method which proved to be only partially successful.

The equilibrium distribution of tritium in the hydrocarbon, i.e., the equilibrium constant for the reaction, was found to be considerably less than the one. Furthermore, the equilibrium constant for exchange in benzene was much less than that for the alkylbenzenes.

Due to experimental error in the tritium assay method and to the trial-and-error method of data analysis, no consistent values were obtained for the partial rate factors. Ortho and para partial rate

factor combinations of 300-600 and 600-600 gave equally good fits to the data, and within experimental error, one set could not be chosen over the other.

The ortho/para ratio for the alkylbenzenes could be taken as either about 0.6 or 1.0. Due to the approximate nature of the trial-and-error method, no distinction would be made between the two. The data analyses were very closely parallel for each run for all of the alkylbenzenes. No evidence was found for any greater steric effect at the ortho position in tert-butylbenzene than in toluene.

CHAPTER X

SUMMARY

The exchange of protium in benzene, toluene, ethylbenzene, cumene, and tert-butylbenzene for tritium in the solvent was studied. A mixed solvent of trifluoroacetic acid, sulfuric acid, and tritiated water was used and all reactions were done at $40.00 \pm 0.02^\circ$. Exchange of hydrogen in the alkylbenzenes was made competitive with benzene. Aliquots of the reaction mixture were removed from a constant-temperature bath at predetermined times, and the reaction was stopped by neutralizing the acid.

The hydrocarbon mixture was separated into its components by vapor-phase chromatography. The hydrocarbons were assayed for their total tritium content with a flow ionization chamber hooked to a vibrating-reed electrometer. No distinction could be made in tritium at the ortho, meta, and para positions of the ring.

The solution of the rate equations for incorporation of tritium into the hydrocarbon gave a functional relationship between the overall specific radioactivity of the hydrocarbon and time. The equation so derived was non-linear. An attempt was made to determine the partial rate factors for the alkylbenzenes by a non-linear regression technique. The method failed for parameters of the order of those in this study. The data were analyzed by a trial-and-error method; the least-squares method was used as a criterion for the goodness of the fit.

The change of the tritium content in the acid solvent was about five per cent but was assumed to be constant. Analysis of the benzene exchange data led to inconsistent results. The variation in the specific activity of the acid was shown to cause the discrepancy. The change in the specific activity of the acid was calculated at each datum time and the decrease in the activity was approximated as linear. This relationship was incorporated into the specific activity-versus-time relationships.

Experimental error in the tritium assays and the relatively large rates for the reaction led to a wide variation in the ortho/para ratio for a given alkylbenzene. Ortho-para combinations of about 300-600 and 600-600 gave equally good fits to the experimental data. No unbiased choice could be made in the values for the partial rate factors or for the ortho/para ratio for the alkylbenzenes. No evidence was seen of any greater steric effect at the ortho position in tert-butylbenzene than in toluene.

Hydrogen exchange was observed in the side chain of cumene and tert-butylbenzene, but no evidence was found for isomerization of the alkyl group during the exchange.

The equilibrium constant for the hydrogen exchange reactions was less than one for all of the compounds studied. The equilibrium constant for benzene was less than that for the alkylbenzenes.

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