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ABSTRACT

The addition of water to the triple bond of 3-hexyne catalyzed by sulfuric acid and mercuric sulfate was studied. The aqueous hexyne was found to undergo mercury-catalyzed autoxidation. The product of the hydration reaction, 3-hexanone, was shown by spectrophotometric methods to react with mercuric sulfate to form a stable complex. The production of 3-hexanone was followed spectrophotometrically and the rate was found to be approximately first order with respect to 3-hexyne, hydrogen ion, and mercuric sulfate.

The solubility of benzene was measured in aqueous solutions of mercuric nitrate and several other electrolytes. Only salting effects were observed. The evidence indicates that mercuric ion does not form a coordination complex with benzene in aqueous solution.

The relative nucleophilic character with respect to silver ion was determined for twenty-four polycyclic aromatic hydrocarbons. This was accomplished by measuring the solubilities of each hydrocarbon in equimolal aqueous methanol containing silver nitrate and sodium nitrate at constant ionic strength. From the variation of solubility with silver concentration the argentation or equilibrium constants for coordination of each hydrocarbon with the first and second silver ions were calculated. The argentation constants for the series of hydrocarbons were correlated with an index of relative carcinogenic potency.

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PART I

EXPLORATORY INVESTIGATION OF THE AUTOXIDATION AND HYDRATION OF 3-HEXYNE CATALYZED BY MERCURIC SULFATE AND SULFURIC ACID

INTRODUCTION

The hydration of acetylene to produce acetaldehyde, catalyzed by mercuric salts and strong acid, is an important reaction in industry, which has been the subject of much research. A great deal of information has been obtained concerning conditions, catalytic mixtures, and reaction intermediates, but only one paper has been published giving the results of an actual kinetic study of the hydration of acetylene (1). In the course of a recent investigation in these laboratories it was noticed that the compound 3-hexyne apparently reacts with atmospheric oxygen in the proportion of two moles to three in the presence of mercuric sulfate and sulfuric acid (2). These facts suggested a twofold investigation the objectives of which were first, to establish the existence or absence of the autoxidation of 3-hexyne and determine the catalysts and oxidation products, and second, to examine the kinetics of hydration of 3-hexyne catalyzed by mercuric sulfate and sulfuric acid.

LITERATURE SURVEY

It has been demonstrated that pure 1-hexyne reacts with atmospheric oxygen to produce peroxides which then react further to yield valeric acid (3). The oxidation of aqueous solutions of disubstituted acetylenes usually produces two moles of carboxylic acids (4). However, it has been shown in these laboratories that the course of permanganate oxidation and the final products are dependent upon the pH and are affected radically by the presence of silver ion. For example, the neutral permanganate oxidation of 3-hexyne in the absence of salts yields two moles of propionic acid, and with either potassium or silver nitrate present some 3,4-hexanedione is produced. Alkaline permanganate oxidation yields two moles of propionic acid in the absence of silver nitrate and equimolal amounts of propionic and acetic acids when silver nitrate is present (5).

Acetylene and some of its derivatives will add water directly when heated to 325°C. in a sealed tube (6). At room temperature acetylenic hydrocarbons in the presence of strong acids are hydrated only at a negligible rate, but traces of mercuric salts produce measurable rates of hydration. Lucas and coworkers in a kinetic study of the hydration of acetylene in 5.0 weight formal sulfuric acid have shown that the initial rate of the hydration reaction is first order with respect to acetylene concentration and second order with respect to the concentration of mercuric sulfate, and that the reaction is retarded by acetaldehyde, apparently through the reversible formation of a one-to-three complex with mercuric sulfate (1). These investigators proposed as the first step in the hydration reaction the formation of a one-to-two complex between acetylene and mercuric sulfate. Most of the common mercuric salts react with acetylenes to precipitate insoluble complex compounds which are hydrolyzed to yield ketones (7), and a complex compound has been described, having the formula $CH_3CHO \cdot HgSO_4 \cdot 2HgO$, which decomposes under the action of hydrochloric acid to give acetaldehyde (8).

Other authors have proposed mechanisms for mercury-catalyzed addition to the triple bond. Hennion and his co-workers (9) suggested a mechanism for the addition of water which involves simple addition of the mercury salt across the triple bond, according to Equations 1 to 4.

$$R\text{-}C{\equiv}C\text{-}R' + HgA_2 \rightarrow R\text{-}CA{=}CHgA\text{-}R' \tag{1}$$

$$R\text{-}CA{=}CHgA\text{-}R' + HOH \rightarrow R\text{-}COH{=}CHgA\text{-}R' + HA \tag{2}$$

$$R\text{-}COH{=}CHgA\text{-}R' + HA \rightarrow R\text{-}COH{=}CHR' + HgA_2 \tag{3}$$

$$R\text{-}COH{=}CHR' \rightarrow R\text{-}CO\text{-}CH_2\text{-}R \tag{4}$$

Mr. Henry Lemaire investigated the kinetics of addition to the triple bond catalyzed by mercuric acetate and perchloric acid in glacial acetic acid (10c). This study demonstrated that the rate of reaction of 3-hexyne is proportional to the concentration of an ion formed by the reaction of one mole each of hexyne, mercuric acetate, and perchloric acid.

MATERIALS

All inorganic chemicals were of reagent or C.P. grade. The compound 3-hexyne obtained from Farchan Research Laboratories was fractionated in a stream of nitrogen and the major part of the distillate boiling at 80.5-80.6°C.(unc.) was stored under nitrogen. This hexyne was then sealed under nitrogen in small, carefully-weighed thin-walled glass ampoules by means of a hypodermic syringe, the operation being accomplished in a nitrogen-filled dry box. The ampoules contained an average of 0.2 g. of hexyne. Eastman Kodak methyl ethyl ketone and diethyl ketone both contained impurities which reduced neutral permanganate. The methyl ethyl ketone was purified by conversion to the bisulfite compound, steam distillation, and fractionation. The diethyl ketone was purified by treatment with excess aqueous permanganate and distillation.

AUTOXIDATION OF 3-HEXYNE

<u>Absorption of Oxygen by Aqueous 3-Hexyne</u>.

A simple apparatus consisting of a 500-ml. two-necked ₮24/40 flask fitted with a mercury sealed stirrer and connected to a gas buret was checked for gas leaks at a positive pressure of 15 cm. of water. To the flask was added 250 ml. of distilled water which was then saturated with oxygen. An ampoule of hexyne was broken in the flask, the system was sealed, stirring was begun and the gas buret containing oxygen was cut in. The stirring was continued for four hours with no appreciable absorption of oxygen. Then 12 ml. of 1*N* sulfuric acid was added and stirring was continued for one hour with no sign of absorption of oxygen. After adding 0.7 g. of cupric sulfate pentahydrate dissolved in 15 ml. of water the stirring was continued for one hour without any absorption. However, when 0.8 g. of mercuric sulfate was added and shaking resumed, absorption commenced and continued for thirty-five minutes at which time absorption stopped and a total of 29.2 ml. of oxygen had been consumed. It was noted that the mercuric sulfate when added first changed to a yellow powder and then slowly dissolved. When the reaction flask was opened, the pungent, sweet odor of a higher aliphatic ketone was very noticeable. Therefore it was concluded that two reactions, autoxidation and hydration, were simultaneously being catalyzed by sulfuric acid and mercuric sulfate.

Production of Acid Accompanying Absorption of Oxygen.

Data had previously been obtained by Dr. W. S. Dorsey indicating that one mole of 3-hexyne absorbs three-halves moles by oxygen, and on the basis of this information he had proposed that the oxidation product consisted of two moles of propionic acid (2). In order to gain further evidence it was decided to determine the relation between the increase in acidity of the reaction mixture and the total equivalents of oxygen absorbed. It was necessary to consider the acid produced by hydrolysis of the mercuric sulfate as well as any organic acids produced by oxidation.

The hydrolysis of mercuric sulfate produces a yellow basic sulfate and sulfuric acid (10) according to Equation 5. In order to confirm the amount of acid produced 0.990 g.

$$3HgSO_4 + 2H_2O \longrightarrow HgSO_4 \cdot 2HgO + 2H_2SO_4 \qquad (5)$$

(3.34 millimoles) of mercuric sulfate was shaken with 50.0 ml. of distilled water until the salt was converted to a bright yellow powder and the hydrolysis appeared to be complete. Then 15.00 ml. of the clear supernatant solution was titrated with 0.1464 N sodium hydroxide solution, using a phenolphthalein endpoint. Two endpoints were recorded, the first fading slowly and the second being more stable but somewhat obscured by the precipitation of a small amount of basic salt. From the numerical results given in Table I it may be concluded that the acid produced by hydrolysis is in agreement with Equation 5.

A new measurement of oxygen absorption was now made in conjunction with measurement of the change in acidity of the

Table I

Hydrolysis of 3.34 Millimoles of Mercuric Sulfate

	Acid Produced	Deviation from Theory[a]
Theoretical	4.45 meq.	--
Found, 1st End-point	4.33	-2.7%
Found, 2nd End-point	4.55	+2.2%

[a] Equation 5.

reaction mixture. The same equipment was used as in the initial experiment. Distilled water was boiled and saturated with oxygen at atmospheric pressure, and from this water 250 ml. of solution containing 2.1 ml. of 5.67 N sulfuric acid was prepared and poured into the 500 ml. reaction flask. The system was swept with oxygen, 0.40 g. of mercuric sulfate was added, and an ampoule containing 0.2071 g. of hexyne was broken in the flask. The system was immediately sealed, the gas buret was adjusted to read zero at atmospheric pressure, and stirring was commenced. Absorption of oxygen started immediately and the buret reading was noted at intervals, the stirrer being stopped during readings. Absorption was complete in 50 minutes without further uptake in the course of an additional 30 minutes of stirring, the total consumption of oxygen being 13.0 ml. measured over water at a temperature of 24°C. and a pressure of 749 mm.

of mercury.

During the reaction the mercuric sulfate first hydrolyzed to the yellow basic salt and then slowly dissolved. Some cloudy white suspension seemed to appear but when the reaction was completed, the solution was clear and colorless. A 15.00-ml. portion of this solution was titrated with sodium hydroxide solution to a phenolphthalein end-point and was found to be 0.0578 N in acid. The end-point was sharp and there was no precipitation of mercuric salts even when the solution was made strongly basic and boiled. This indicates that the mercury is firmly bound in a complex compound, probably with the ketone, the presence of which was apparent from its odor.

Discussion of Results.

The data required to ascertain the relationship between the oxygen absorbed and the acid produced are displayed in Table II together with the calculated numerical results. The theoretical milliequivalents of propionic acid are calculated on the basis of the assumed autoxidation reaction of Equation 6. The difference between the acid increase calculated and found, 0.06 milliequivalents, amounts to 2.4% of the calculated acid increase, to 8.8% of the hypothetical propionic acid, and to 0.4% of the total acid titrated. This is satisfactory agreement between theory and experiment and

$$\text{Et-C}\equiv\text{C-Et} + 3/2\ O_2 + H_2O \longrightarrow 2\text{EtCOOH} \qquad (6)$$

provides evidence supporting the postulated oxidation of 3-hexyne to two moles of propionic acid.

Table II

Autoxidation of 3-Hexyne

Vol. oxygen over water	13.0 ml.	
Temperature	24°C.	
Atmospheric pressure	749 mm. Hg.	
Millimoles of oxygen	0.51 mml.	
Acid content, initial	11.91 meq.	
final	14.45 meq.	
Acid increase found		2.54 meq.
Acid from hydrolysis	1.80 meq.	
Propionic acid (theoretical)	0.68 meq.	
Acid increase calculated		2.48 meq.
Difference		0.06 meq.

HYDRATION OF 3-HEXYNE

Isolation and Identification of Pure 3-Hexanone.

The product of the hydration of 3-hexyne was isolated and identified by means of its boiling point, refractive index, and the melting points of two derivatives. In a small flask 25 ml. of water, 0.4 ml. of 6 N sulfuric acid, 0.2 g. of mercuric sulfate, and 1.1 g. of 3-hexyne were allowed to react for two days with about 12 hours of shaking. The reaction mixture was extracted with 25 ml. of ether, the ether solution was dried with anhydrous potassium sulfate, and the solvent was stripped off. The crude 3-hexanone was combined with that from another run and the total of 1.0 ml. of crude product was fractionated through a semi-micro fractionation column to yield 0.6 ml. of a sweet-smelling liquid boiling at 125.7-127.0°C.(unc.). Literature values for the boiling point of 3-hexanone are 123-4°C.(11a) and 122-4°C.(11b). The refractive index of the product was $n^{25}D = 1.3962$, and a literature value for the refractive index of 3-hexanone is $n^{22}D = 1.39899$. The average temperature coefficient of the index of refraction of organic liquids is $dn/dt = -4.5 \times 10^{-4}$ (11c). When the literature value at 22°C. is corrected using the above temperature coefficient the value obtained is $n^{25}D = 1.3976$. The 2,4-dinitrophenylhydrazone, recrystallized twice from ethanol, melted at 131.5-133.0°C. Dr. Henry Lemaire obtained a ketone by hydration of 3-hexyne catalyzed by boron trifluoride, which gave a 2,4-dinitrophenylhydrazone melting at 127-129°C. from ethanol-acetic acid (11d). Literature values for the melting point of the dinitrophenylhydrazone of 3-hexanone are 146.5-8.5°C. (11e) and 149-151°C. (11f). A number of dinitrophenylhydrazones of lower aliphatic ketones are isomorphous and also have more than one crystal modification, which may explain the low melting point which was found (11g). The semicarbazone melted at 110.5-111.0°C. Literature values are 111°C.(11a) and 110.5°C.(11h).

The ultraviolet absorption curve of 3-hexanone in aqueous solution III shown in Figure 1 has a maximum at 272.5 mμ. The work of F. O. Rice indicates that the maxima for the lower ketones in aqueous solution are located at 264.5 mu for acetone, 266.5 mμ for 2-butanone, 269.0 mμ for 3-pentanone, and at 272.0 mμ for 3-hexanone (12).

It may be concluded that the product of hydration of 3-hexyne has been established with reasonable certainty to be 3-hexanone.

It was found that the 3-hexanone prepared in the above manner contained small amounts of unsaturated substances which reduce neutral permanganate and manifest strong ultraviolet absorption in the region between 200 and 210 mμ. A larger quantity of 3-hexanone was prepared by hydration of 3-hexyne, and the product was purified by conversion to the semicarbazone which was recrystallized from ethanol-water and decomposed by steam distillation with excess oxalic acid. The ketone was then dried with anhydrous sodium sulfate and distilled. Hexanone purified in this manner showed much lower absorption in the far ultraviolet region between 200 and 210 mμ.

Ultraviolet Absorption of Ketones in Aqueous Solution.

Aqueous solutions of purified 3-hexanone, 3-pentanone, and 2-butanone were prepared and their ultraviolet absorption spectra taken using a Beckman Model DU spectrophotometer. Typical absorption curves are shown in Figure 1. It may be seen that the spectra are very similar, in agreement with the work of F. O. Rice (12). The fact that the sharp rise in the curve between 210 and 200 mμ occurs with each of the three ketones which were purified in different ways indicates that this is a feature of the spectra of the ketones and not of impurities, though more rigorously purified samples would be required to verify this definitely.

The Effect of Mercuric Sulfate and Sulfuric Acid upon the Absorption Spectra of Ketones.

The ultraviolet absorption spectra of several ketones dissolved in different solvent media were measured with the use of appropriate blank solutions in all cases. In 0.05 M sulfuric acid solution 3-hexanone was found to have an absorption spectrum almost identical with the spectrum in pure water. However, when mercuric sulfate was added at a concentration of 0.05 M, the absorption rapidly increased and in twenty minutes the solution became opaque in the region below 250 mμ. Figure 2 shows the ultraviolet absorption curves of various solutions of 3-hexanone. Solution IV is 0.0434 M hexanone in water and solution V contains

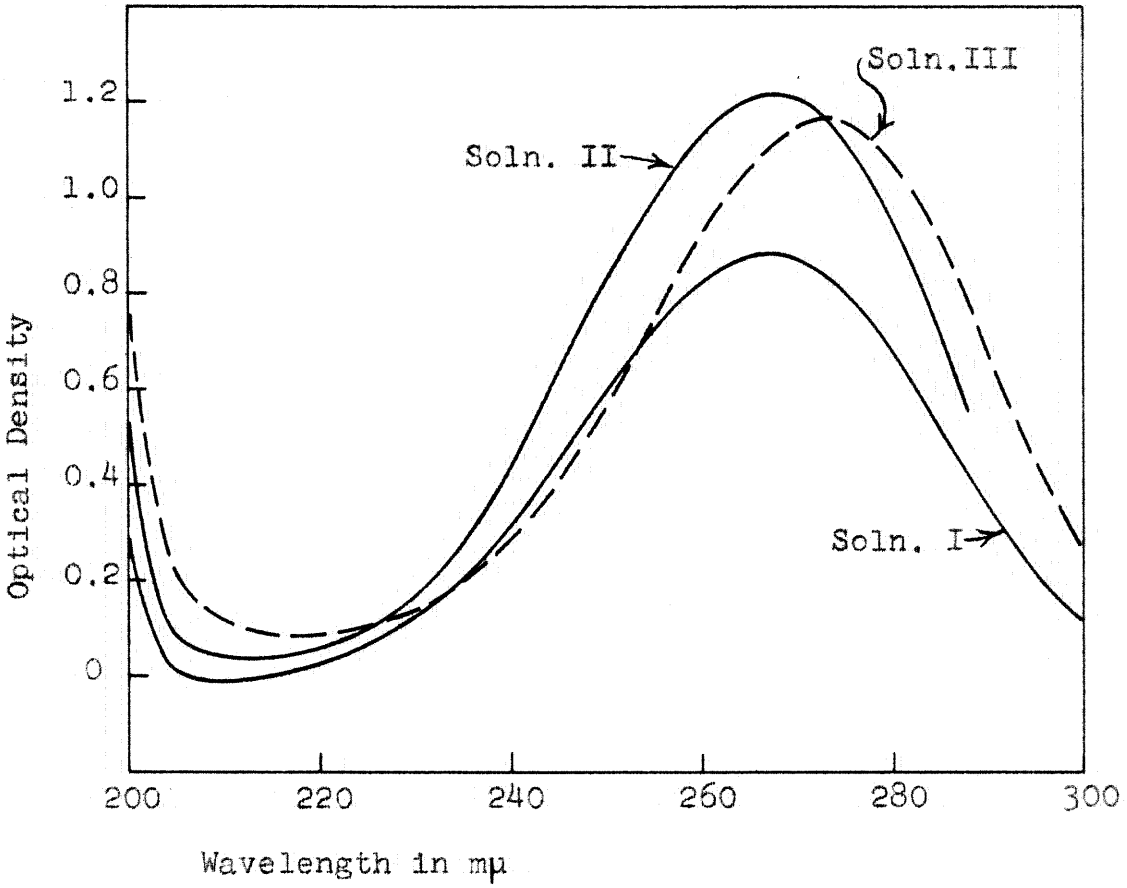

Figure 1. Ultraviolet absorption spectra of aqueous solutions of ketones: Soln. I, 0.0427 M 2-butanone; Soln. II, 0.0519 M 3-pentanone; Soln. III, 0.0425 M 3-hexanone.

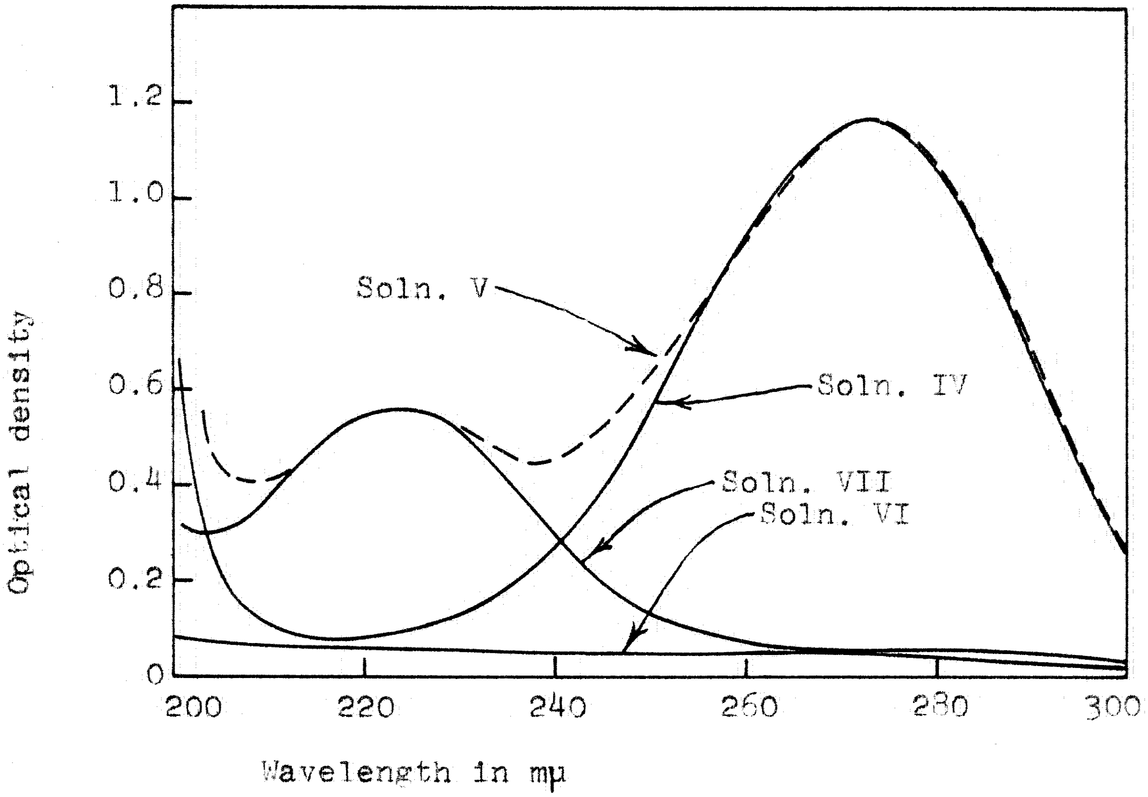

Figure 2. The influence of mercuric sulfate on the ultraviolet absorption spectrum of 3-hexanone: Soln. IV, 0.0434 M hexanone; Soln. V, about 0.0434 M hexanone, 4×10^{-5} M $HgSO_4$, and 0.04 M H_2SO_4; Soln. VI, 0.004 M hexanone; Soln. VII, about 0.004 M hexanone, 5×10^{-5} M $HgSO_4$, and 0.05 M H_2SO_4.

hexanone at about the same concentration but is 0.04 M in sulfuric acid and 4×10^{-5} M in mercuric sulfate. Solution VI is about 0.004 M hexanone in water and solution VII contains hexanone at about the same concentration but is 0.05 M in sulfuric acid and 5×10^{-5} M in mercuric sulfate. Solution VII was allowed to stand over night before its absorption was measured.

It is apparent from these absorption curves that there is an interaction between mercuric sulfate and hexanone which produces a substance with maximum absorption at 223 mμ in a concentration determined by the concentration of the mercuric sulfate. If the complex substance is assumed to contain one mole of mercury, then the molar extinction coefficient is about $1.1\text{-}1.2 \times 10^{4}$.

Mercuric sulfate was found to have a similar effect upon the absorption spectrum of 2-butanone, as is shown by the curves of Figure 3. Solution VIII is 0.0427 M butanone in water. In solutions IX and X the concentrations of butanone are 0.0416 M and 0.0376 M respectively, the concentrations of mercuric sulfate are 5×10^{-5} M and 10×10^{-5} M respectively, and the concentration of sulfuric acid is 0.05 M. It may be seen that mercuric sulfate produces a new absorption at 212 mμ, the magnitude of which is proportional to the mercury salt. Based upon the assumption that this complex substance contains one mole of mercury, the molar ex-

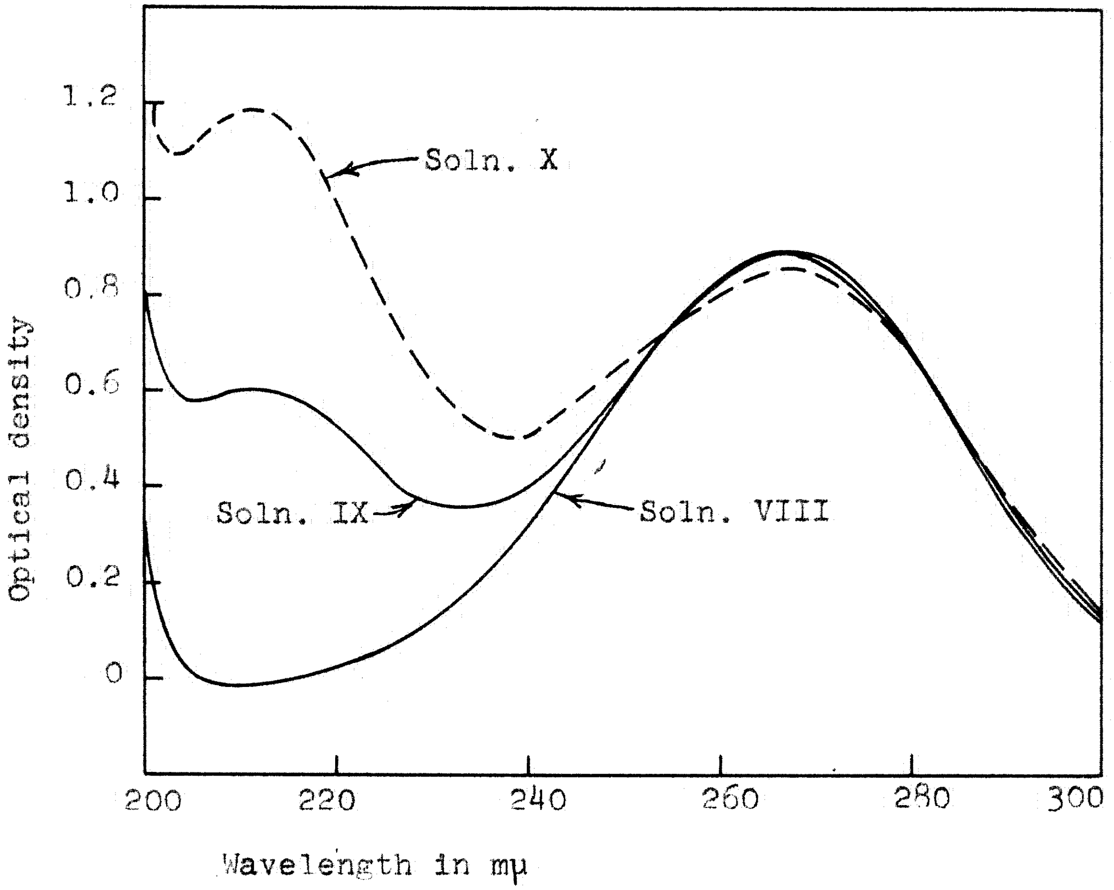

Figure 3. The influence of mercuric sulfate on the ultraviolet absorption spectrum of 2-butanone: Soln. VIII, 0.0427 M butanone; Soln. IX, 0.0416 M butanone, 5×10^{-5} M $HgSO_4$, and 0.05 M H_2SO_4; Soln. X, 0.0376 M butanone, 10×10^{-5} M $HgSO_4$, and 0.05 M H_2SO_4.

tinction coefficient is about 1.2×10^4, about the same as that produced with 3-hexanone.

The reaction of hexanone with mercuric sulfate was studied further in order to learn something about the rate and equilibrium. The initial rate of appearance of the absorption maximum at 223 mμ was measured in solutions which were 5×10^{-5} M in mercuric sulfate. This initial rate was found to vary approximately with the first power of the concentration of hexanone. The results are given in Table III.

Table III

Reaction of 3-Hexanone with 5×10^{-5} M Mercuric Sulfate

Concentration, hexanone, $M \times 10^4$	Initial rate of increase of optical density at 223 mμ, $\text{min.}^{-1} \times 10^4$
0.97	2.0
9.7	13
11.6	26

A series of solutions, 5×10^{-5} M in mercuric sulfate and 0.05 M in sulfuric acid, were prepared containing different concentrations of hexanone and the ultraviolet spectra were followed until no further change was noted. The equilibrium optical densities at 223 mμ were found to be independent of the ketone concentration and proportional to the concentration of mercuric sulfate when the molal concentration of the ketone exceeded twice that of the mercuric sulfate. On the other hand the absorption was about proportional to the ketone concentration when the ketone concentration was less than twice that of the mercuric sulfate. These data are given in Table IV, and Fig. 3.

Table IV

Dependence upon hexanone concentration of the equilibrium values of light absorption at 223 mμ in solutions 5×10^{-5} M in mercuric sulfate and 0.05 M in sulfuric acid.

Hexanone concn. M x 10^5	Equilib. optical density at 223 mμ	Days allowed for equilib.
116	0.576	1
97	.593	1
9.7	.609	4
4.85	.302	6
2.9	.245	6

Discussion of Results of Investigation of Ketone Complex.

The information which has been obtained from these studies and which is displayed in Figs. 1, 2, and 3, and in Table IV reveals the marked changes which occur in the ultraviolet absorption spectrum of ketones in the presence of mercuric sulfate and sulfuric acid. A reasonable interpretation of these data is that ketones, in particular 3-hexanone and 2-butanone, react with mercuric sulfate in dilute sulfuric acid to produce a complex substance containing two moles of ketone for each mole of mercury. The fact* that a clear reaction mixture containing hexanone and mercuric sulfate gave no precipitate of basic mercury salts when it was made strongly basic and boiled suggests that the ketone-mercury complex is very stable.

The Absorption Spectra of 3-Hexyne in the Presence of Mercuric Sulfate and Sulfuric Acid.

The ultraviolet absorption spectrum of 3-hexyne was measured in pure water and in a solution 0.05 M in sulfuric acid. The curves for solutions XI and XII reproduced in Fig. 4 show that acid has little effect upon the absorption except, perhaps, to shift absorption slightly toward the visible. The reliability of the absorption curves is not very great in the region below 210 mμ.

However, when a trace of mercuric sulfate was added to solutions containing hexyne and acid, there appeared within a few minutes a very strong absorption below 250 mμ. This absorption has a maximum near 226 mμ as shown in the curve for solution XIVa in Fig. 4, and it can be seen to be quite similar to the absorption of the ketone-mercury complex (Solution VII, Fig. 2). There also appeared a gradually increasing absorption at 272 mμ and after two days the absorption spectrum became fairly stable with the form shown for solution XIVb in Fig. 4. This final or equilibrium solution has ab-

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*Reported on page 8 of this thesis.

sorption maxima at both 226 and 272 mμ and thus appears to contain both the ketone and the ketone-mercury complex. It is evident that the absorption for solutions XIII, XIVb, and XV to XVIII inclusive all show the maxima at 226 and 272 mμ which are characteristic of the ketone-mercury complex and the free ketone, respectively. It may be concluded that hexyne has been hydrated to the ketone. This was corroborated by the detection of the sweet odor of the ketone in the equilibrium reaction mixtures.

In these equilibrium solutions the final optical density at 226 mμ is roughly proportional to the concentration of the mercuric sulfate and the optical density at 272 mμ is about proportional to the initial concentration of 3-hexyne. It may be concluded that the principal reactions which are taking place in these solutions are the mercury-catalyzed hydration of 3-hexyne and the formation of the hexanone-mercury complex demonstrated in preceding sections of this thesis.

The Rate of Hydration of 3-Hexyne Catalyzed by Sulfuric Acid and Mercuric Sulfate.

The rate of hydration of 3-hexyne was studied spectrophotometrically by following the rate of increase of the optical density at 272 mμ of aqueous solutions containing different concentrations of hexyne, mercuric sulfate, and sulfuric acid. These measurements were made at room tem-

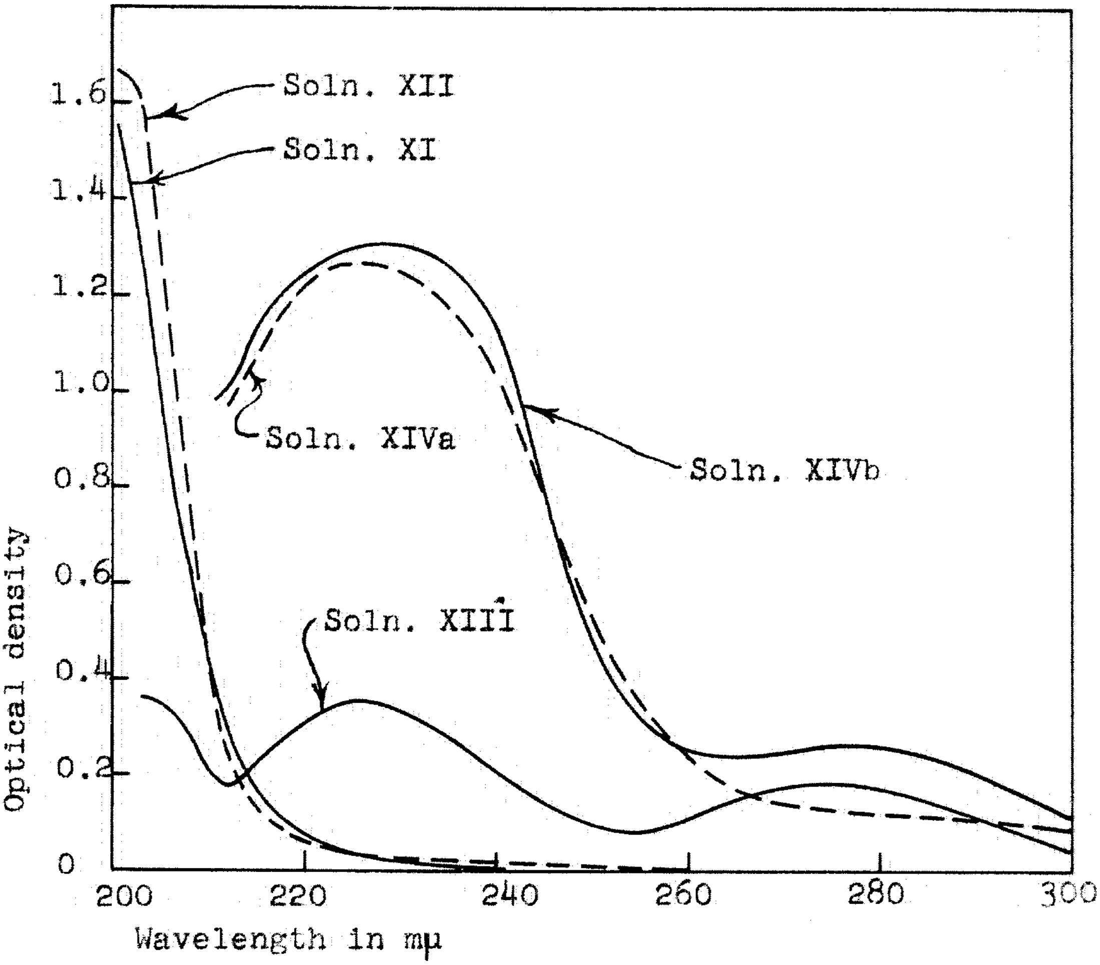

Figure 4. The absorption spectra of 3-hexyne in the presence of sulfuric acid and mercuric sulfate upon standing different lengths of time: Soln. XI, 0.0066 M hexyne; Soln. XII, 0.0077 M hexyne in 0.05 M H_2SO_4; Soln. XIII, 0.008 M hexyne, $5x10^{-5}$ M $HgSO_4$, 0.05 M H_2SO_4 after 24 hrs.; Soln. XIV, 0.011 M hexyne, $5x10^{-4}$ M $HgSO_4$, 0.05 M H_2SO_4 (a, after 20 min.; b, after 2 days). For Soln. XIV the actual optical densities were twice those shown on plot.

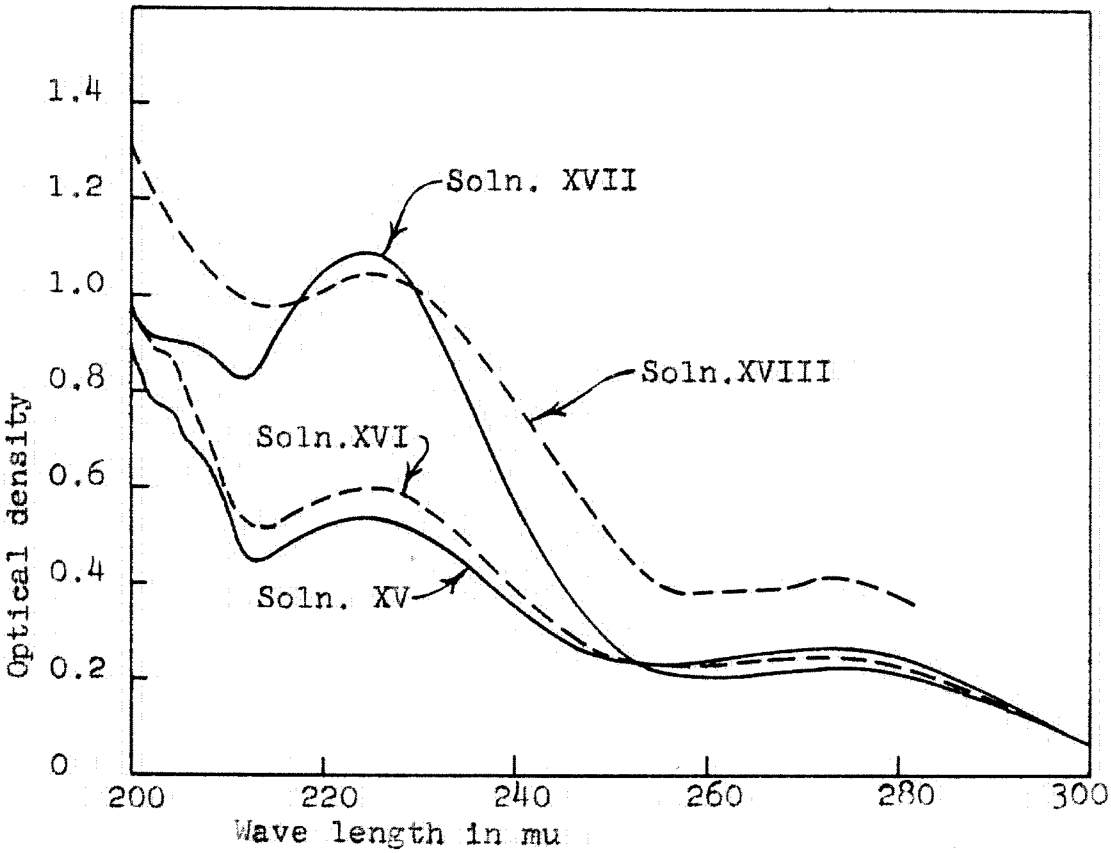

Figure 5. The absorption spectra of solutions containing 3-hexyne in the presence of sulfuric acid and mercuric sulfate after standing two days: Soln. XV, 0.009 M hexyne, 5×10^{-5} M $HgSO_4$, 0.05 M H_2SO_4; Soln. XVI, 0.0116 M hexyne, 5×10^{-5} M $HgSO_4$, 0.10 M H_2SO_4; Soln. XVII, 0.0111 M hexyne, 10×10^{-5} M $HgSO_4$, 0.05 M H_2SO_4; Soln. XVIII, 0.0134 M hexyne, 10×10^{-5} M $HgSO_4$, 0.10 M H_2SO_4.

perature without thermostatic control. Furthermore, the optical density at 272 mμ involves interference by absorbing substances other than 3-hexanone. Therefore, the data obtained are semi-quantitative in nature but they provide, nevertheless, some information about the kinetics and catalytic effects taking place in the reaction.

In carrying out a measurement of the rate of hydration there was first prepared in a 250-ml. glass-stoppered flask 200 ml. of a solution containing the desired amounts of sulfuric acid and mercuric sulfate in nitrogen-saturated water. Then an ampoule of 3-hexyne was broken in the flask, and the flask was quickly sealed and shaken violently for about five minutes until all the hexyne was dissolved. A sample from this reaction mixture was then sealed in a quartz spectrophotometer cell and the variation of optical density with time was followed at wave lengths of 272, 226 and 203 mμ, using water in the blank cell. The optical density of the ketone peak at 272 mμ showed a rapid and somewhat erratic initial increase after which the rate of increase became about constant with time and fell off after several hours. The optical density at 203 mμ, a wave length at which 3-hexyne absorbs strongly, started high and fell off to about half of the initial value toward the end of the reaction. The optical density of the complex peak at 226 mμ started high, fell off to a minimum value, and then rose to a final value which was proportional to the concentration of mercuric sulfate (See Fig. 5).

The variations of optical density at 272 mμ with time for the four kinetic runs are recorded in Table V. When the steady portion of the optical density-versus-time curve is extrapolated back to zero time, the intercept obtained is greater than zero. Since the final optical density at 272 mμ was usually somewhat greater than that corresponding to the conversion of all the hexyne to hexanone, it is assumed that the extrapolated initial optical density indicates roughly the absorption caused by interfering substances in the reaction mixtures. Thus the absorption, $\underline{D}_c$, due to hexanone can be obtained by subtracting the extrapolated initial value, $\underline{D}_o$, from the value of the optical density, $\underline{D}$, for each measurement. The optical density which would be produced by hexanone at completion of the reaction, $\underline{D}_f$, can be calculated from the initial concentration of hexyne and the molal extinction coefficient of hexanone, $E_m^{272} = 21.2$ (12). Then the fraction of hexyne unreacted is $\underline{D}_f/(\underline{D}_f-\underline{D}_c)$. If the reaction is assumed to be first order with respect to the concentration of hexyne, the relation expressed by Equation 7 should hold. Here $\underline{k}$ is the apparent first order rate constant and

$$2.303 \log \underline{D}_f/(\underline{D}_f-\underline{D}_c) = \underline{kt} \qquad (7)$$

$\underline{t}$ is the time.

The observed and calculated optical densities described

Table V

Hydration of 3-hexyne; variation of optical density of reaction mixtures at 272 mμ; results are in Table VI.

Run 1. $D_f = 0.191$

t min.	D	D_c	Log $(D_f-D_c)/D_f$
0	0.035[a]	0.0	0.0
12.5	.045	.010	.023
19	.049	.014	.033
24	.051	.016	.038
30	.047	.012	.028
37.5	.050	.015	.036
43.5	.052	.017	.041
50	.054	.019	.046
56	.057	.022	.053
62	.059	.024	.058
68	.062	.027	.066
100	.074	.039	.099
104	.074	.039	.099
194	.104	.069	.195
199	.104	.069	.195
		.191[b]	

Run 2. $D_f = 0.236$

t min.	D	D_c	Log $(D_f-D_c)/D_f$
0	0.052[a]	0.0	0.0
14	.065	.013	.024
20	.069	.017	.032
25	.068	.016	.030
30	.071	.019	.037
35	.074	.022	.042
40	.077	.025	.048
45	.079	.027	.053
50	.083	.031	.061
56	.098	.035	.070
61	.090	.038	.076
174	.147	.095	.224
180	.150	.098	.233
221	.159	.107	.262
		.236[b]	

[a] Found by extrapolation to zero time.

[b] Calculated from initial concentration of hexyne and the molal extinction coefficient of hexanone.

Table V (continued)

Run 3. $D_f = 0.246$

t min.	D	D_c	Log $(D_f-D_c)/D_f$
0	0.036[a]	0.0	0.0
12	.046	.101	.022
17	.053	.017	.031
21	.053	.018	.033
26	.057	.021	.039
31	.059	.023	.043
36	.061	.025	.046
41	.064	.028	.052
46	.068	.032	.060
51	.071	.035	.067
56	.075	.039	.075
61	.079	.043	.083
66	.082	.046	.090
73	.088	.052	.103
113	.002	.076	.160
118	.116	.080	.171
122.5	.119	.083	.179
177	.146	.110	.257
244	.177	.141	.370
250	.181	.145	.386
336	.215	.179	.565
341	.216	.180	.571
		.246[b]	

Run 4. $D_f = 0.254$[c]

t min.	D	D_c	Log $(D_f-D_c)/D_f$
0	0.0	0.0	0.0
12	.071	.030	.054
17	.073	.032	.058
21	.076	.035	.064
26	.079	.038	.070
30	.083	.042	.078
35	.087	.046	.087
41	.093	.052	.099
45	.097	.056	.108
48.5	.100	.059	.115
54	.107	.066	.131
57	.111	.070	.140
62	.117	.076	.154
66.5	.122	.081	.167
72	.129	.088	.185
125	.173	.132	.318
132	.179	.138	.340
235	.236	.195	.634
240	.239	.198 .254[b]	.657

[c] About 10% of initial hexyne did not dissolve. Initial concentration assumed to be 0.012 M.

in the preceding paragraph are tabulated in Table V and in Figures 6 and 7 the plots of log $(\underline{D}_f-\underline{D}_c)/\underline{D}_f$ versus *t* are displayed. It may be seen that the data of runs 1 and 2 fit the first order relation pretty well if the first two or three measurements taken in the intial thirty minutes of the reaction are excluded. However, the plots for runs 3 and 4, which were followed farther toward completion, exhibit definite signs of an upturn as the reaction progresses. In view of the errors involved in these measurements it is not felt that a more exact analysis of the data is warranted. The approximate first order rate constants were calculated from the slopes of the best straight lines drawn through the plots in Figures 6 and 7. The concentrations of reactants and calculated first order rate constants *k* are recorded in Table VI.

Table VI.

The first order rate constants for hydration of 3-hexyne in aqueous solutions of mercuric sulfate and sulfuric acid at approximately 25° C. Concentrations are in moles/liter.

Run No.	Concn. H_2SO_4	Concn. $HgSO_4$ x10^5	Concn. Hexyne x10^3	*k* min.$^{-1}$ x10^3	Concn. H+	Concn.^{a} Hg++ x10^6	$\frac{k}{(H^+)(Hg^{++})}$ x10^{-4}
1	0.05	5	9.0	2.2	.059	1.02	3.7
2	.05	10	11.1	2.9	.059	2.03	2.4
3	.10	5	11.6	3.4	.110	.84	3.7
4	.10	10	12.0	5.9	.110	1.68	3.2

a. Calculated using the equilibrium constants of Infeldt and Sillen (13).

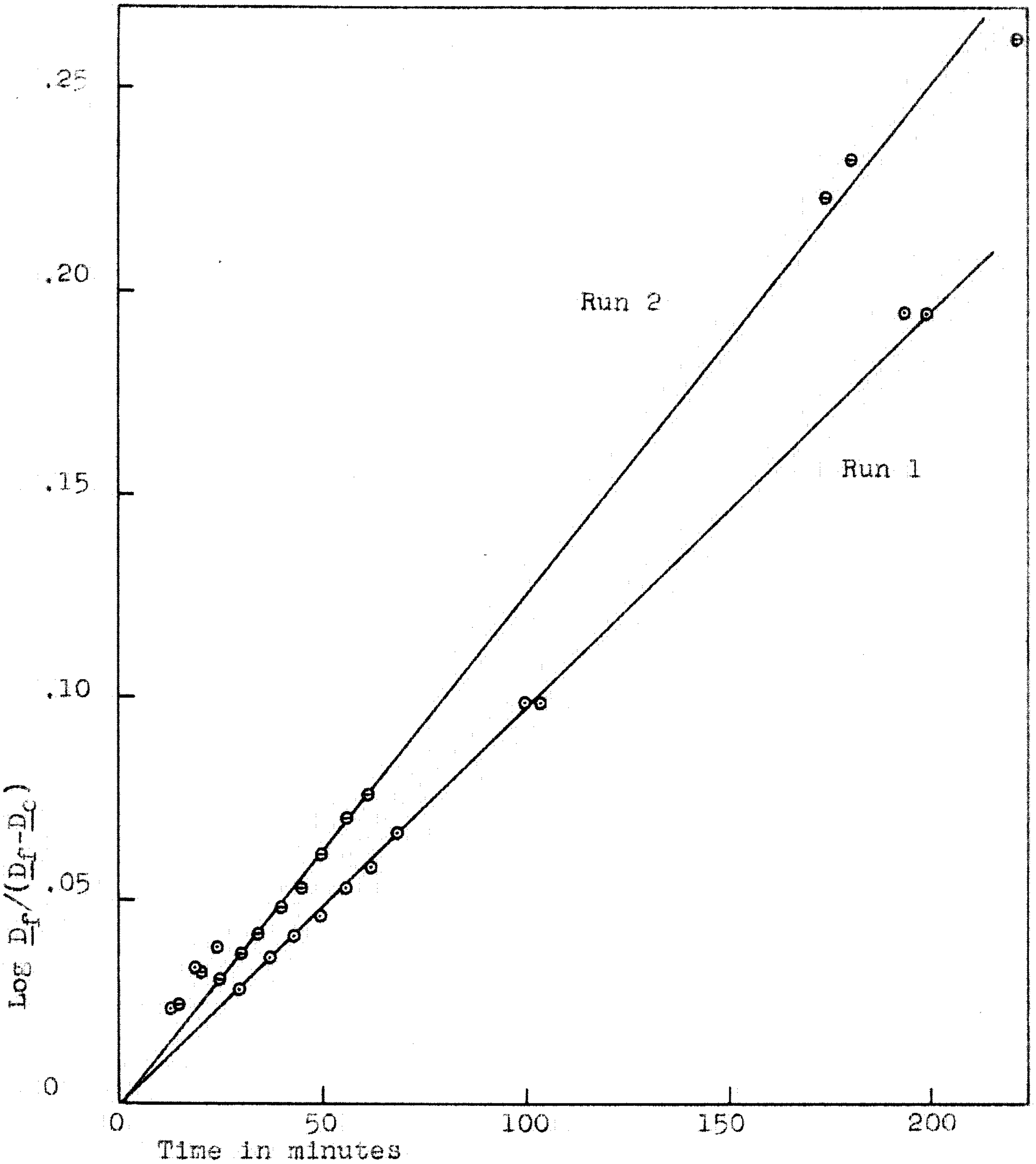

Figure 6. Plots of first-order kinetic data for Runs 1 and 2, tabulated in Table V. The results are given in Table VI.

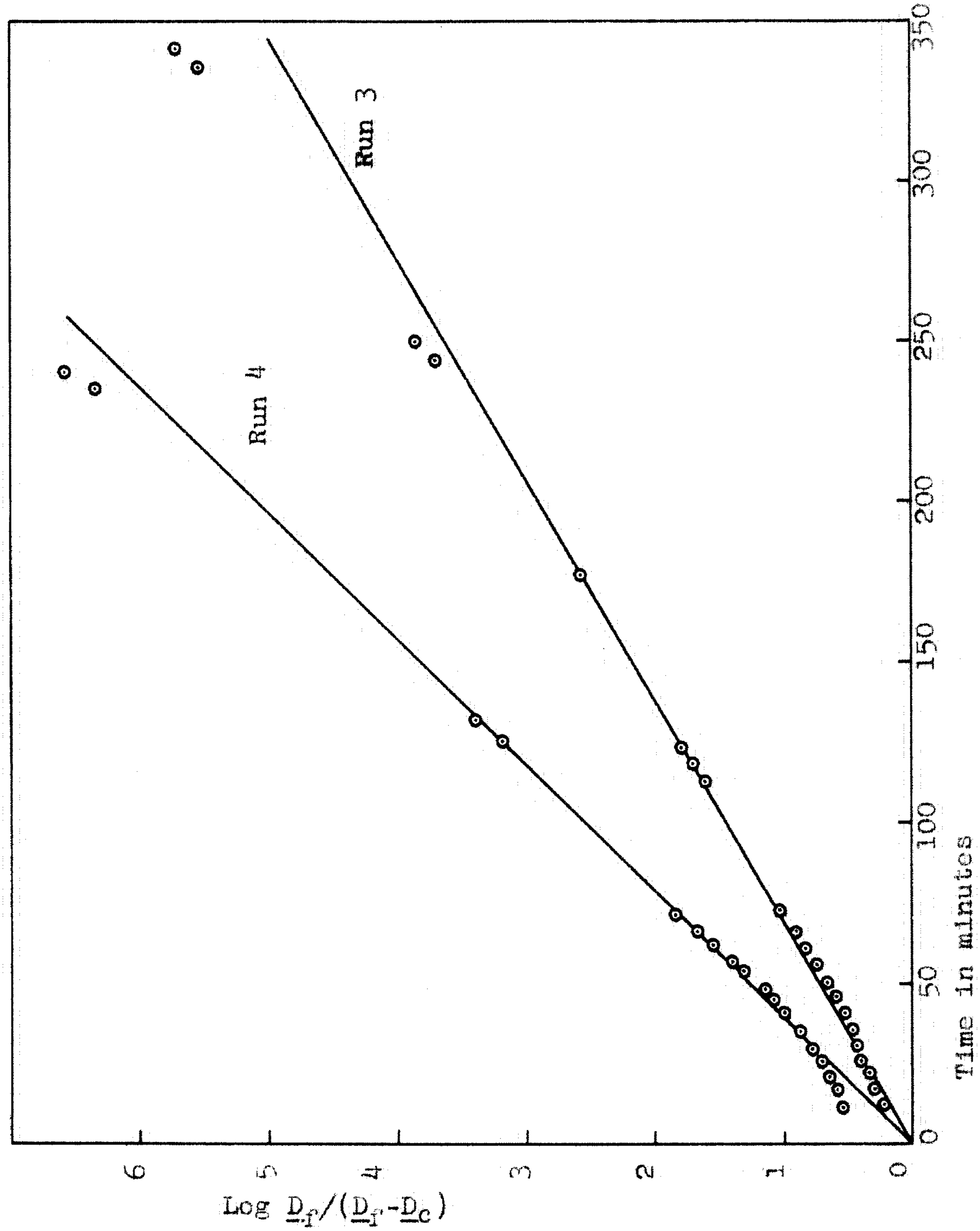

Figure 7. Plots of first-order kinetic data for Runs 3 and 4 tabulated in Table V. The results are given in Table VI.

Discussion of Results.

These results demonstrate the catalytic effect of mercuric sulfate and sulfuric acid upon the rate of hydration of 3-hexyne, but the data are not sufficiently accurate to establish unequivocably the order of the catalytic effects with respect to the concentrations of the catalysts. The effect of the hydrogen ion concentration upon the hydrolysis of mercuric ion is not thought to be important under the conditions of these measurements because at a pH of 1 only 0.2% of divalent mercury is hydrolyzed (14). On the other hand, from the results of recent work on mercuric sulfate complexes (13), it may be estimated that in 0.1 M sulfuric acid 98% of divalent mercury is in the form of the disulfate complex, $Hg(SO_4)_2^{=}$. Furthermore, as the concentration of sulfuric acid is increased from 0.05 to 0.10 M, the concentration of free mercuric ion is decreased by about 17%.

If it is assumed that the rate of hydration is proportional to the concentrations of hydrogen ion and free mercuric ion, then the quantity $k/(H^+)(Hg^{++})$ should be the third order rate constant for the hydration reaction. The last column in Table VI exhibits a fair constancy in the calculated third order rate constant. Agreement is better when the concentration of sulfuric acid is increased at constant mercuric sulfate, i.e., when runs 1 and 3 or 2 and 4 are compared. When mercuric sulfate concentration is increased at constant sulfuric acid, i.e., when runs 1 and 2 or 3 and 4 are compared, the calculated third order rate constant is seen to decrease. However, more precise values of rates measured over wider ranges of the reagent concentrations would be required to establish the kinetics of the reaction.

It is interesting to note that the first order rate constant reported for the hydration of acetylene in 5 wf sulfuric acid $5x10^{-5}$ M in mercuric sulfate has the value $4.4x10^{-3}$min.$^{-1}$ (1), which is of the same order of magnitude as the value obtained in the present investigation in 0.10 M sulfuric containing the same concentration of mercuric sulfate, viz., $3.4x10^{-3}$min.$^{-1}$. This comparison suggests that the catalytic effect of increasing the acid concentration fifty-fold is counteracted by a decrease in the catalytic effect of the mercuric ion as the result of the formation of sulfate complexes by the mercuric ion.

The situation is further complicated by the fact that as soon as the hydration reaction is initiated, the ketone produced begins to react to form the very stable complex with mercuric sulfate. Several interesting observations can be made in regard to the formation of mercury complexes in the reaction mixture. First, the initial high optical density of reaction solutions at 226 mμ which falls to a minimum and then rises to a final maximum indicates an initial rapid formation of the ketone-mercury complex, since the form of the absorption curve in this region is essentially that of the ketone-mercury complex (Solns. XIVa,b Fig. 4). However, the decrease to a minimum value at about the half-reaction point suggests that there is present from the beginning of the reaction another substance absorbing in this region, the concentration of which decreases as the hydration reaction progresses. This substance must be a complex formed between 3-hexyne and mercuric sulfate.

In this connection it was found that solid mercuric sulfate reacts with anhydrous 3-hexyne. When 0.025 mole of hexyne was mixed with 0.05 mole of solid mercuric sulfate, the mixture turned brown within one minute and at the end of an hour was black. When a similar mixture was prepared containing in addition 0.05 mole of sodium sulfate, the reaction mixture formed a cake which only became a very light grey color after one hour. These observations suggest that the mercuric sulfate reacts with the hexyne and releases concentrated sulfuric acid. In the absence of a base the sulfuric acid causes charring of the hydrocarbon. Sodium sulfate can act as a base to take up the sulfuric acid and thus prevent charring.

A second observation which may be made is that only about five minutes are required for production of a ketone concentration equal to twice that of the mercuric sulfate, although the concentration of the ketone-mercury complex does not approach its final value for several hours. It is apparent that hexyne interacts with mercuric sulfate and undergoes hydration to the ketone, at least part of which must then be released as free ketone before it forms the ketone-mercury complex.

The third observation is that during the later stages of the reaction an ever-increasing proportion of the mercury is combined with the ketone, yet there is no falling off of rate in the first order plots shown in Figs. 6 and 7. This suggests that the ketone-mercury complex also is an effective catalyst for the hydration of hexyne. The kinetic data indicate that the rate of hydration is roughly first order with respect to hexyne and is approximately proportional to the concentration of acid and free mercuric ion. Thus there appears to be some similarity to the reaction of 3-hexyne in glacial acetic acid catalyzed by mercuric acetate and perchloric acid (10d).

The preceding observations make it clear that the assumptions made in the interpretation of the rate data are almost certainly an over-simplification. It would be very difficult to separate the effects of the competing reactions for an exact kinetic study even if a more accurate method of analysis for hexanone or 3-hexyne were developed. However, on the basis of the limited data available it appears that the rate of hydration of 3-hexyne is roughly first order in hexyne, hydrogen ion, and free mercuric ion. The reactions which probably take place in the solutions, some or all of which are catalyzed by hydrogen ion, are represented by Equations 8-11.

$$C_6H_{10} + HgSO_4 \longrightarrow C_6H_{10}\cdot HgSO_4 \qquad (8)$$

$$C_6H_{10}\cdot HgSO_4 + H_2O \longrightarrow C_6H_{12}O + HgSO_4 \qquad (9)$$

$$2C_6H_{12}O + HgSO_4 \longrightarrow (C_6H_{12}O)_2HgSO_4 \qquad (10)$$

$$C_6H_{10} + H_2O \xrightarrow[(C_6H_{12}O)_2HgSO_4]{} C_6H_{12}O \qquad (11)$$

The kinetics of the mercury-catalyzed hydration of acetylene has some similarities to the situation indicated above and also some marked differences. This is to be expected, since acetylene possesses two acidic hydrogen atoms while 3-hexyne has none, and the product of hydration is an aldehyde in one case and a ketone in the other. As mentioned earlier (1), apparently acetylene forms a complex in the ratio of one mole to two with mercuric sulfate. Acetaldehyde forms a complex in the ratio of one mole to three with mercuric sulfate. The acetaldehyde complex must be much more tightly bound than that of 3-hexanone, since acetaldehyde exerts a strong inhibition upon the hydration of acetylene, whereas the hexanone complex seems to cause no inhibition of the hydration of 3-hexyne. These observations are in accord with the fact that aldehydes are considerably more reactive than are ketones.

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PART II

THE EFFECT OF MERCURIC NITRATE AND OTHER ELECTROLYTES UPON THE AQUEOUS SOLUBILITY OF BENZENE

INTRODUCTION

The coordination of olefinic compounds with silver ion in solution to produce ionic complexes is a reaction which has been well-known for over ten years. There has likewise been strong evidence adduced for the formation of even more stable ionic coordination complexes between cyclohexene and mercuric ion. More recently it has been shown that benzene and its methyl homologs and also polycyclic aromatic hydrocarbons coordinate with silver ion. These facts suggested that mercuric ion should coordinate with benzene to form a complex at least as stable as that between benzene and silver ion. The objective of this investigation was to determine whether or not mercuric ion coordinates with benzene. This was done by measuring the solubility of benzene in aqueous solutions of mercuric nitrate and other nitrates of divalent cations.

LITERATURE SURVEY

A sufficient number of olefins have been shown to react reversibly with silver nitrate or silver perchlorate with the formation of coordination complexes to establish argentation as a reaction which is characteristic of olefins (1). These olefin complexes with silver salts are of fairly low stability and the crystalline compounds have been isolated in a relatively few cases for olefins and conjugated dienes (1, b-e). Benzene and its homologs and also polycyclic aromatic hydrocarbons likewise undergo the argentation reaction and the resulting coordination compounds are generally even less stable than those formed by olefins (2, 3), though a crystalline compound of toluene and silver perchlorate has been isolated (4). Mercuric salts react with olefins to produce well-characterized addition compounds of good stability the true chemical nature of which has long been a matter of dispute (5). Mercuric salts usually form addition compounds which are hydroxymercuri-salts and which are decomposed by halogen acids to yield the free olefin. Thus there has been a question as to whether the mercury compounds are covalent addition compounds or ionic coordination compounds. A careful investigation of the reaction of cyclohexene with mercuric nitrate in dilute nitric acid provided strong evidence for the formation of two ionic complexes having the formulas $C_6H_{10} \cdot Hg^{++}$ and $C_6H_{10} \cdot HgOH^+$ (6).

The values of the equilibrium constants for the formation of some of these complex compounds are given in Table I.

Table I.

Equilibrium Constants for Coordination Reactions of Some Unsaturated Hydrocarbons.

Unsaturated compound	Inorganic salt	First Coordination constant	Ref.
Trimethylethylene	$AgNO_3$	13.3	1b
Cyclohexene	$AgNO_3$	79.3	1b
Dimethylbutadiene	$AgNO_3$	22.5	1b
Benzene	$AgNO_3$	2.4	2
Cyclohexene	$Hg(NO_3)_2$	2.2×10^4	6

In view of the preceding information it was felt that mercuric ion should form a rather stable coordination complex with benzene. The present investigation has established that mercuric nitrate does not coordinate with benzene to any measurable extent. After this investigation was completed, new work was published which dealt with the reaction of mercuric nitrate and nitric acid with cyclohexene, from which evidence was adduced against the postulated ionic coordination complexes of mercuric ion with cyclohexene (7). The evidence has recently been reviewed and judged to be in favor of the initial formation of the ionic coordination complexes (5). This question will be discussed below in the light of the results of the present investigation.

MATERIALS AND APPARATUS

All of the inorganic salts and the nitric acid used were of reagent grade. Solutions of salts were prepared by weight at concentrations accurate to within one percent, which was considered to be sufficiently exact in view of the precision of which the stripping method of analysis is capable. The benzene which was utilized in the solubility measurements was provided by Dr. Nathan Koenig and was reagent grade material purified twice by crystallization and then distilled.

The apparatus used for saturation and stripping of solutions and the special traps used to freeze out and weigh the stripped benzene were provided by Dr. Koenig and are the same as those described in his thesis (8).

MEASUREMENT OF THE AQUEOUS SOLUBILITY OF BENZENE BY THE STRIPPING METHOD

Description of the Method.

The stripping method for the measurement of aqueous solubility of volatile compounds was developed in this laboratory by Dr. Nathan Koenig (8). The procedure for benzene was as follows: A volume of the aqueous medium was saturated with benzene by stirring a two-phase system for thirty to forty minutes at constant temperature with a special stirrer which produced a moderately fine emulsion. The phases were separated by settling for five minutes and centrifuging for five minutes, and a measured volume of the saturated aqueous phase containing 0.06 to 0.14 g. of benzene was pipetted into a cylinder fitted with a fritted glass disk. Nitrogen gas was then bubbled through the solution, passed through a tube containing Drierite drying agent and then through a specially designed trap which had been weighed and submerged in a Dry Ice-acetone bath while being flushed with dry nitrogen. This stripping process was continued three hours until essentially all of the benzene had been swept out of the aqueous solution and had been frozen in the trap. Then the trap was warmed to room temperature, using a special technique, and weighed. The concentration of benzene in the saturated solution was calculated from the increase in weight of the trap.

Calibration of the Stripping Method With Benzene.

The stripping method possesses two inherent errors for which corrections must be made. These errors result from the vapor pressure of solid benzene at the temperature of the nitrogen leaving the trap and from the nitrogen displaced from the trap by benzene vapor when the cold trap is warmed to room temperature. The magnitude of the first of these errors was estimated on the basis of the vapor pressure of benzene at an assumed exit temperature for the nitrogen of -65° C. and a total volume of about 5000 ml. The magnitude of the second error was estimated on the basis of the assumption of a trap gas volume of 24 ml. saturated with benzene vapor at a temperature of 23°C. The estimated errors were 1.3 and 3.1 mg. respectively, or a total estimated correction of 4.4 mg. This is the theoretical amount which should be added to the observed weight increase of the trap to obtain the true weight of benzene in the solution which has been stripped.

This correction was determined empirically by stripping measured volumes of a series of carefully-prepared stock solutions of benzene in water. The stock solutions of aqueous benzene were prepared by weighing about 0.4 g. of benzene with Dry Ice, opening the flask and dropping it into a glass-stoppered flask containing a known volume of water, which was then shaken until the benzene dissolved. This stock solution was cooled to 10° C. for sampling in order to reduce loss of benzene vapor as the solution was pipetted. In calculating the concentration of benzene in the stock solution, corrections were made for benzene vapor in the gas spaces of the weighing flask and stock solution flask, and for the thermal contraction between the temperatures of 25° and 10° C. Table II gives the results of five calibration runs. The correction under standardized conditions was taken as +0.004 g. for all solubility measurements. This is in good agreement with the correction estimated above to be +0.0044 g.

Table II

Calibration of the stripping method for benzene.

Run No.	Vol. of Aliquote	Wt. benzene in aliquote	Trap vol.	Correction	Comment
1	50 ml.	0.0764 g	24 ml.	+.0042 g.	
2	100	.1265	24	+.0040	
3	100	.1171	27	+.0063	a
4	60	.0821	27	+.0000	b
5	50	.0695	27	+.0038	

a. Trap sealed late, benzene probably lost.
b. There is no obvious explanation for deviation.

Complexing of Mercuric Ion During Stripping.

In order to insure that no benzene would be held in the solution in complex form during the stripping process, the mercuric nitrate in the stripping bottle was converted to a stable complex by the addition of an excess of either potassium thiocyanate or potassium iodide and some phosphate buffer solution. Any nitric acid present was neutralized with sodium hydroxide solution. Several runs using the above reagents in the absence of mercuric nitrate showed that they did not interfere with the complete stripping of a saturated benzene solution.

The Effect of Stirring Time Upon the Solubility of Benzene.

Two solubility runs were made in which a longer time of stirring was used in order to see if there were any important rate effects. The results which are given in Table III indicate that complete saturation is attained with strontium nitrate in fifty minutes. In the case of the mercuric nitrate solution, however, there may be a slow rate effect.

It was noticed in a few of the two phase systems of benzene and aqueous mercuric nitrate that a small amount of a buff-colored solid was formed after standing with access to the atmosphere for several days. This substance was examined and found to be insoluble in hot or cold concentrated acids, strongly oxidizing solutions, water, or alcohol. The solids decomposed at about 300° C. with a slight puff to give a black fluffy ash which then burned to leave no residue. These characteristics suggest that the solid may contain an organic mercurial. Aqueous mercuric nitrate solution containing five percent nitric acid will react with benzene at 40° C. to yield phenylmercuric nitrate (9). However, any such reactions occurring in the saturation mixtures are very slow, and it is reasonable to assume that all salt solutions attain saturation with forty minutes of stirring.

The three-hour stripping period affords the mercuric nitrate further time to react with the dissolved benzene. But it may be seen in Figure 1 that the measured salting-out effect of the mercuric salt is less than that of the strontium or barium salts. If the salting effect of the mercuric salt is roughly equal to that of the other salts but there is a slow reaction taking place which consumes some of the dissolved benzene, then the measured salting-out effect of the mercuric salt would be expected to be greater than that of the other salts. Furthermore, the magnitude of such an effect would be expected to increase with the salt concentration. The curves in Figure 1 reveal no evidence for such influences. Therefore, it must be concluded that any slow reaction of benzene in the stripping process is very unlikely.

Table III

Effect of Stirring Time on the Solubility of Benzene in 1.0 M Salt Solutions 0.3 N in Nitric Acid.

Salt	$Hg(NO_3)_2$	$Hg(NO_3)_2$	$Sr(NO_3)_2$	$Sr(NO_3)_2$
Stirring time, min.	40	130	50	130
Sol'y bz. g./100 ml.	0.130	0.134	0.118	0.117

RESULTS OF SOLUBILITY MEASUREMENTS

The Solubility of Benzene in Aqueous Solutions of Electrolytes.

The stripping method was used to measure the solubility of benzene in aqueous solutions of several electrolytes at $25.0 \pm 0.1^\circ$ C. The electrolytes used were mercuric, strontium, barium, and potassium nitrates, and nitric acid. It was considered desirable to make the mercuric nitrate solutions acid with nitric acid in order to repress hydrolysis of the mercuric ion. Therefore, for purposes of comparison, all salt solutions were made 0.3 N in nitric acid, the effect of which upon the solubility of benzene is slight at this concentration and can be assumed with negligible error to cancel out in comparisons of the solubility effects of the salts. The results of these solubility measurements are given in Tables I, V, and VI. In Figure 1 the data are presented in a plot of the logarithm of the ratio, S/S_0, which is called the salting coefficient. S is the solubility in the given salt solution and S_0 is the solubility in 0.3 N nitric acid. It is plain from these data that mercuric nitrate and the other salts all decrease the solubility of benzene in a parallel manner.

The Effect of Temperature Upon the Solubility of Benzene in 1.0 M Mercuric Nitrate.

In order to observe possible thermodynamic effects, the solubility of benzene was measured at $10.0 \pm 0.1^\circ$ C. in pure water and in 1.0 M mercuric nitrate solution which was 0.3 N in nitric acid. The results are given in Table VII.

Table IV

The Solubility of Benzene in Aqueous Solutions of Mercuric Nitrate 0.3 *N* in Nitric Acid at 25° C.

$Hg(NO_3)_2$ concn.	0	0	0.10	0.30	1.00
Sol'y bz. g./100 ml.	0.174[a]	0.175	0.171[b]	0.162	0.130
S/S_o [c]		1.00	.977	.926	.743
μ $Hg(NO_3)_2$	0	0	.30	.90	3.00

a. Pure water, no electrolyte present.
b. Concentration of HNO_3 is 0.15 *N*.
c. *S* is the solubility in the salt solution and S_o is the solubility in 0.3 *N* nitric acid.

Table V

The Solubility of Benzene in Aqueous Solutions of Strontium Nitrate 0.3 *N* in Nitric Acid at 25° C.

$Sr(NO_3)_2$ conc.	0	0.10	0.30	1.00
Sol'y bz. g./100 ml.	.175	.170[a]	.158	.118
S/S_o	1.00	.971	.903	.675
μ $Sr(NO_3)_2$	0	.30	.90	3.00

a. Concentration of nitric acid is 0.15 *N*.

Table VI

The Solubility of Benzene in Aqueous Solutions of Several Electrolytes at 25° C.

Electrolyte	$Hg(NO_3)_2$	$Ba(NO_3)_2$	$Sr(NO_3)_2$	KNO_3	HNO_3	HNO_3
Electrolyte con.[a]	0.30	0.30	0.30	0.90	0.30	1.00
Sol'y bz. g./100 ml.	.162	.160	.158	.141	.175	.182
$\underline{S}/\underline{S}_o$[b]	.926	.914	.903	.806	1.006	1.046
μ (salt or acid)	.90	.90	.90	.90	.30	1.00

a. The salt solutions contain nitric acid at 0.3 N
b. For $\underline{S}_o$ in the case of salts the solubility in 0.3 N HNO_3 is taken, and in the case of HNO_3 the solubility in water, 0.174 g./100 ml., is taken.

Table VII

The Solubility of Benzene in Water and in 1.0 M Mercuric Nitrate, 0.3 N in Nitric Acid, at Different Temperatures

Temperature	25° C.	10° C.
Sol'y bz. in water g./100 ml.	0.174	0.170
Sol'y bz. in 1.0 M $Hg(NO_3)_2$ g./100 ml.	.130	.118

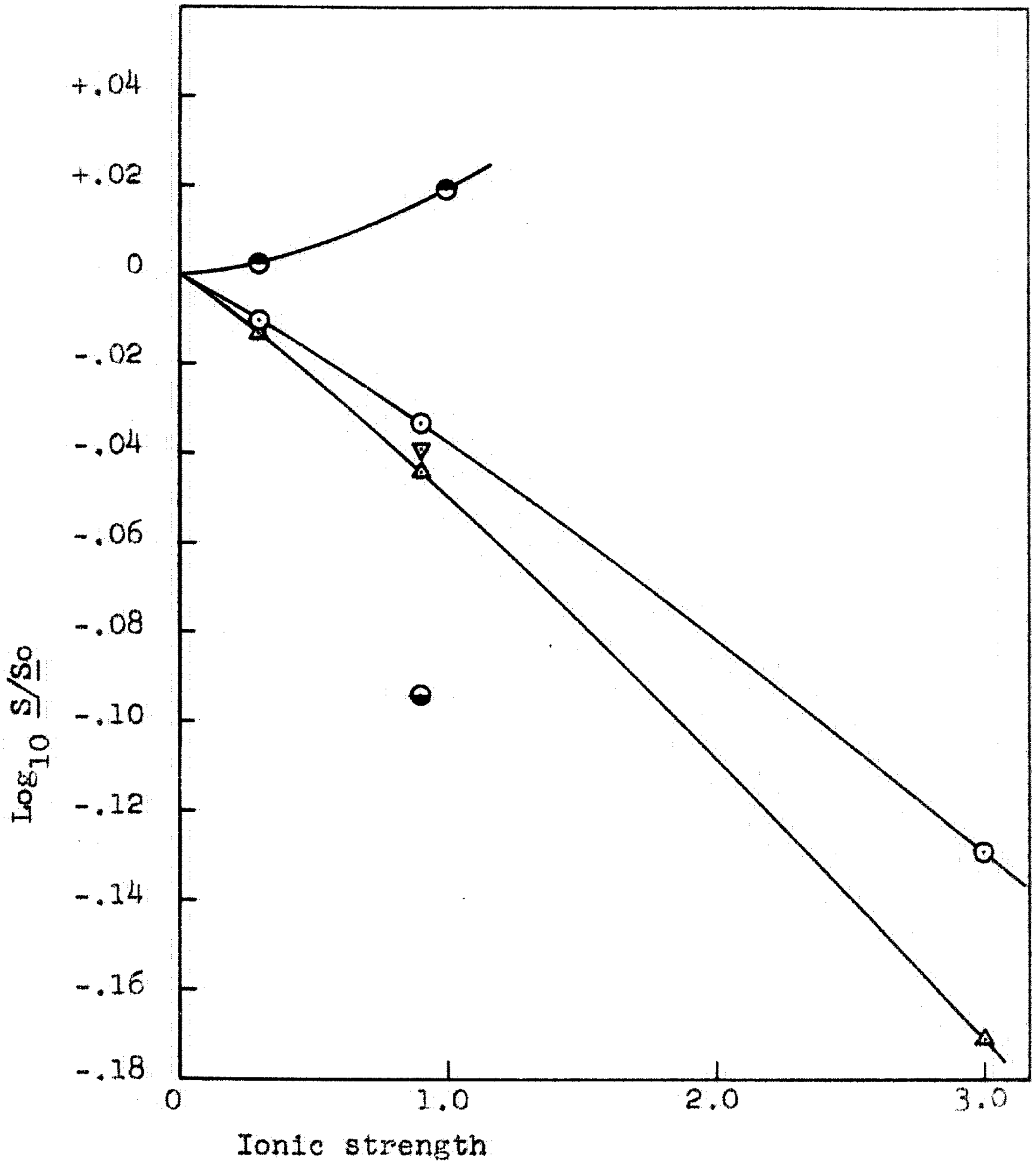

Figure 1. Plot of $\log_{10}$ of benzene salting coefficient, S/So, against ionic strength:

—◒—	Nitric acid
—⊙—	Mercuric nitrate
—▽—	Barium nitrate
—△—	Strontium nitrate
—⊖—	Potassium nitrate

DISCUSSION OF RESULTS

When the solubility data recorded in Table IV, V, and VI and in Figure 1 are examined, the most striking fact is that all of the salts investigated strongly reduce the aqueous solubility of benzene. In Figure 1 the graph of the logarithm of the salting coefficient versus the ionic strength for the salts strontium and mercuric nitrates approaches a straight line at low salt concentrations. According to the theory of Debye and McAulay pure salting action of electrolytes should produce such a linear relationship (10). It is seen that the three divalent nitrates of strontium, barium, and mercury produce the same order of salting-out effect upon benzene, although mercuric nitrate produces the least salting out. It is clear that the major effect of mercuric nitrate upon aqueous benzene is a salting out effect similar to that produced by the other inorganic salts.

Nitric acid, for which data are recorded in Table VI, is seen to increase the solubility of benzene. The work of other investigators has shown that benzene, cyclohexene, cyclohexane, and carbon tetrachloride are salted in by nitric acid and by perchloric acid (8, 11). Hydrochloric acid salts out cyclohexene but this effect reaches a maximum at an acid concentration of 1.5 N, beyond which there is an upturn in the solubility curve (8). Apparently in this case there are two competing effects, and the effect which results in increased solubility becomes determinative at higher concentrations. Now it may be noted in Figure 1 that the salting curves of strontium and mercuric nitrates show no tendency to curve upward but, rather, demonstrate a definite downward curvature. This is further evidence that both of these exert a pure salting-out effect with no competing effect to produce an increase in solubility.

The data in Table VI show the influence of temperature upon the solubility of benzene in water and in mercuric nitrate solution. As the temperature is lowered, the solubility in aqueous mercuric nitrate decreases markedly whereas the solubility in water decreases less than two percent. In other words, the salting-out effect increases strongly with decrease in temperature. If there were in these solutions an exothermic reaction occurring which tended to increase benzene solubility, then a drop in temperature would be expected to cause a decrease in the salting-out effect. Such is the case for benzene in aqueous silver nitrate (8) and for naphthalene in aqueous silver nitrate (12), since a drop in temperature markedly increases the solubility of these non-polar solutes in silver nitrate solution. The primary interaction believed to be responsible for the salting-out action of inorganic electrolytes is the hydration of the ions which makes less water available for solvation of the non-polar solute (11b, 13). Thus, ion hydration, which is probably an exothermic process in most cases, increases with decreasing temperature and, therefore, salting out would be expected to increase at lower temperatures, as has actually been found for benzene in aqueous mercuric nitrate.

The results of this investigation lead us to the conclusion that the primary influence of mercuric nitrate upon benzene in aqueous solution is a salting-out effect. Though there might possibly be a slight hidden complexing effect, there is no evidence for such an interaction, and the positive temperature coefficient of the solubility of benzene in aqueous mercuric nitrate affords evidence against such a hidden effect. Therefore, it is concluded that there is no appreciable reaction between mercuric nitrate and benzene to form an ionic coordination complex.

DISCUSSION OF THE REACTION OF MERCURIC NITRATE WITH UNSATURATED COMPOUNDS

As has been mentioned previously, olefins and aromatic compounds react with silver ion to form ionic coordination complexes of low stability, the argentation reaction proceeding to a well-defined equilibrium. A few crystalline compounds of low stability between silver salts and both olefins and aromatic compounds have been isolated. Mercuric salts, on the other hand, form addition compounds with many olefins, which are quite stable but are decomposed by halogen acids.

The equilibrium constants for the coordination reaction of mercuric nitrate with cyclohexene have been measured and found to be quite large. Finally, the present investigation has shown that mercuric nitrate does not coordinate with benzene.

The silver ion coordination complexes are almost surely π-coordination complexes in which the silver ion interacts with the π-electron cloud of the unsaturated compound. The lack of a mercuric ion interaction with benzene, however, indicates that mercuric ion is incapable of coordinating with π-electrons, at least in aqueous media. The stability of the addition compounds of mercuric salts with olefins indicates that they involve a covalent link between carbon and mercury.

In the light of these observations it appears that the complexes formed by the rapid reaction of aqueous mercuric nitrate and cyclohexene probably involve covalent bonding. It may be that there is first formed an ionic coordination complex which is unstable and goes over rapidly into a covalent compound. Possibly there is produced some sort of compound intermediate in character between true ionic coordination complexes and the stable covalent substances formed by the addition of mercuric salts to olefins. Further experimental work is required to elucidate the exact nature of these intermediate compounds, but it seems quite unlikely that mercuric ion forms with olefins stable π-complexes of just the type produced by silver ion.

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COORDINATION OF POLYCYCLIC AROMATIC HYDROCARBONS WITH SILVER ION; CORRELATION OF EQUILIBRIUM CONSTANTS WITH RELATIVE CARCINOGENIC POTENCIES.

INTRODUCTION

In the two decades since it was demonstrated that certain polycyclic aromatic hydrocarbons are, in varying degrees, carcinogenic, i.e., capable of inducing tumors in animals, much work has been done to determine relative carcinogenic potencies and attempts, only partially successful, have been made to relate these potencies to chemical reactivity, structure, and theoretical electronic properties of these molecules. Quantum mechanical calculations both by the valence bond and by the molecular orbital method indicate that in benz(a)anthracene and its homologs the so-called K-region containing the 5,6- or <u>meso</u>-bond possesses a higher electronic charge than do ordinary aromatic bonds. This bond corresponds to the reactive 9,10-bond of phenanthrene which, relative to benzene, has high reactivity toward double-bond reagents.

These facts suggested the need for an experimental method of measuring the relative nucleophilic character of polycyclic aromatic hydrocarbons. The object of this investigation was to develop a satisfactory experimental method for this purpose and to apply it to a series of carcinogenic and non-carcinogenic compounds in order to observe any possible relation between nucleophilic character and carcinogenic potency. Two experimental methods which were explored and subsequently abandoned will be described before the selected method is considered.

LITERATURE SURVEY

The history of the discovery of the carcinogenic activity of polycyclic aromatic hydrocarbons found in coal tar has been reviewed by Haddow (1), and the results of studies on hundreds of such compounds have been compiled by Hartwell (2). From these studies it has become apparent that certain structural characteristics are almost always present in carcinogenic hydrocarbons (1). Only a very few carcinogenic compounds contain less than four condensed benzene rings and virtually all the active compounds possess a *meso*-bond, i.e., a phenanthrene-9,10-bond, which is unhindered by a condensed benz-ring but may have an attached methyl group. The most active compounds contain the benz(a)-anthracene structure, illustrated in Figure 1, which is weakly active itself but becomes increasingly active when substituted with methyl groups, especially in the 7-, 8-, or 12-positions.

The chemical reactivity of carcinogenic hydrocarbons

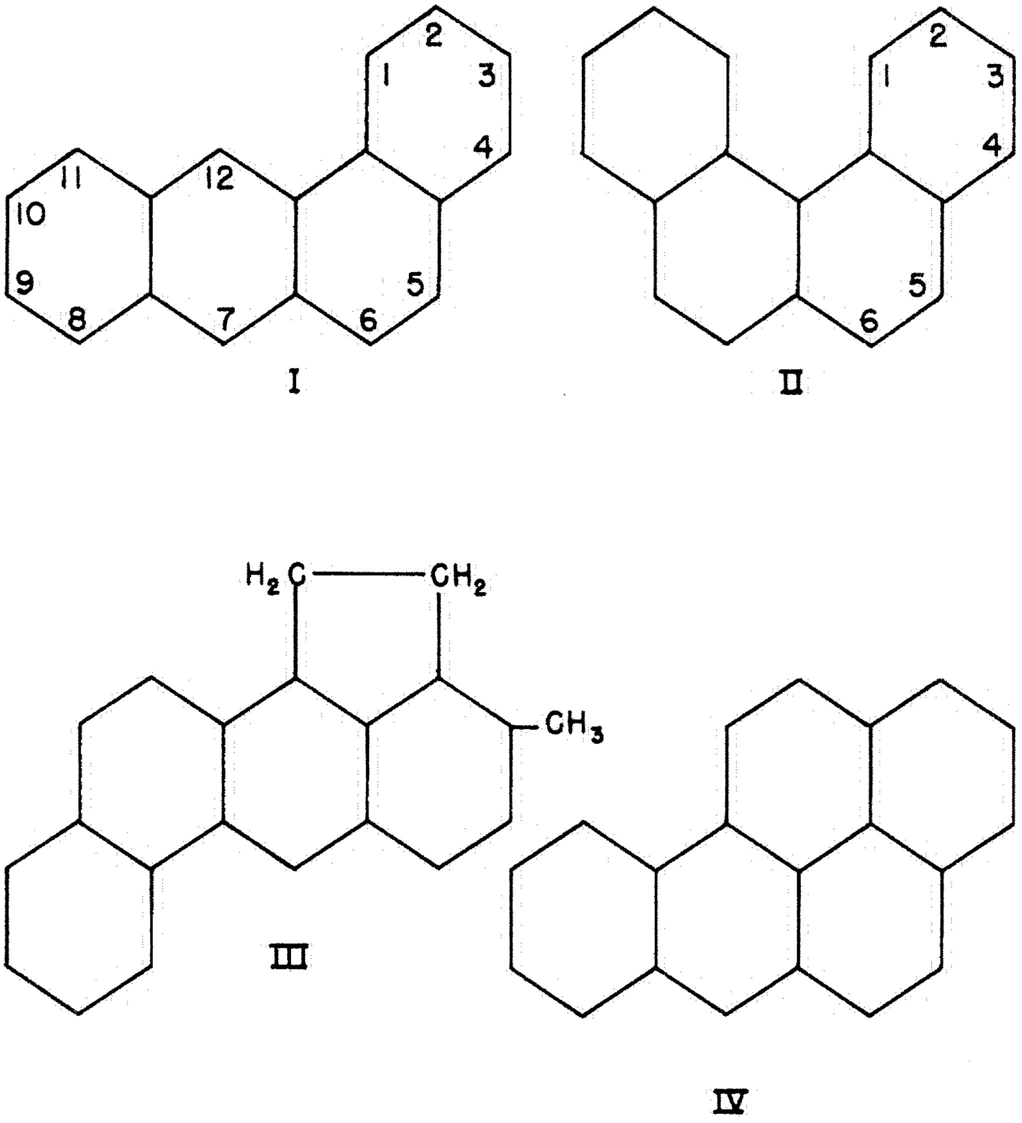

Figure. 1. Polycyclic aromatic hydrocarbons: I, benz(a)anthracene; II, benzo(c)phenanthrene; III, 3-methylcholanthrene; IV, benzo(a)pyrene.

has received considerable study and has been reviewed by Fieser (3). These hydrocarbons, though easily hydrogenated, are not very reactive toward ordinary addition reagents, but they are unusually reactive toward substitution reagents at the 7-position of the benz(a)anthracene system. The carcinogenic hydrocarbons form especially stable complexes with picric acid and trinitrofluorenone (4). A specific reaction for polycyclic aromatic hydrocarbons containing a meso-bond is the addition to this bond of the reagent osmium tetroxide to form a cyclic ester (5).

Quantum mechanics has been applied to the problem of calculating the electronic characteristics of polycyclic aromatic hydrocarbons. Both the valence bond (6) and the molecular orbital method (7) have been used, and the application of quantum mechanics to the problem of carcinogenesis has been reviewed by Coulson (8). Some degree of correlation has been found to exist between carcinogenic potency and the theoretical electronic characteristics of the meso-bond.

On the basis of the results of hundreds of studies of carcinogenesis in mice by polycyclic aromatic hydrocarbons (2) several indices of relative potency have been devised (9). The different indices vary in some details but are in general agreement. The index of relative potency which is used as a basis of comparison in this thesis is that due to Badger (9c).

EXPLORATORY INVESTIGATION OF THE INDICATOR METHOD IN GLACIAL ACETIC ACID.

Experimental Method and Theory.

The indicator method for investigating cation coordination reactions in glacial acetic acid was developed by Dr. Henry Lemaire in these laboratories and was applied by him in studies of the reaction of mercuric acetate with 3-hexyne (10). In the present study of the argentation reaction the experimental method involves the mixing of solutions in acetic acid of an unionized, moderately basic salt of the desired cation, of the hydrocarbon, of perchloric acid, and of a suitable acid-base indicator. The acidity of the various mixed solutions is then determined by measuring the optical density of the indicator, the molar extinction coefficient and acidity constant of which have been determined.

In the theoretical treatment of the data obtained the following equilibrium reactions between aromatic hydrocarbon (Ar), metal salt (MA), acid (H^+), and indicator (I) are assumed to take place:

$$I + H^+ \rightleftharpoons IH^+ \qquad (1)$$

$$MA + H^+ \rightleftharpoons M^+ + HA \qquad (2)$$

$$M^+ + Ar \rightleftharpoons ArM^+ \qquad (3)$$

The equilibrium constant for reaction 1, i.e., the indicator acidity constant, is first calculated and then is used to calculate the equilibrium constant for reaction 2, i.e, the basicity constant of the salt. Then if the hydrocarbon coordinates with the cation according to reaction 3, the equilibrium for this reaction can be calculated from the optical density of the reaction mixture and the known values of the acidity and basicity constants of indicator and salt.

Materials.

The inorganic salts used were reagent grade. Silver acetate was recrystallized from glacial acetic acid. Silver succinimide was prepared by the reaction of Eastman Kodak succinimide with silver nitrate in ethanol solution containing ammonium hydroxide (11). The indicator used was 2,4-dinitro-N,N-diethylaniline which had been prepared by Dr. Henry Lemaire. Pure glacial acetic acid was prepared by fractional distillation of Baker's 99.5% acetic acid containing one percent excess added acetic anhydride through a 90-cm. column of glass helices fitted with an electrically heated jacket and a total reflux partial take-off distilling head. One liter of pure glacial acetic acid, b.p. 116.8° C., m.p. 16.57° C., f.p. 16.57° C., temperatures uncorrected, were obtained.

Results.

Because of the low solubilities of the reagents in acetic acid, all reactants were used in concentrations of the order of 10^{-4} M. It was found that at 25° C. silver acetate and silver succinimide are both strong bases and react completely with perchloric acid. On the other hand, mercuric acetate was found not to react measurably with perchloric acid under these conditions and so is a weak base. Phenanthrene had no appreciable effect upon the acidity of these solutions. Because of these negative results, the indicator method was abandoned.

It may be added that in view of the low magnitude of the argentation constants in aqueous solvents and the low reagent concentrations required in acetic acid, it is unlikely that the argentation reaction would proceed sufficiently toward completion in acetic acid solution to produce a measurable change in acidity of the reaction mixture.

ULTRAVIOLET ABSORPTION SPECTRA OF 1,2,5,6-DIBENZANTHRACENE IN AQUEOUS METHANOL SOLUTIONS OF SALTS

Introduction.

When the indicator method in acetic acid had been rejected as inapplicable, it was decided to investigate the effect of silver salts upon the solubility of polycyclic aromatic hydrocarbons. This was done first by observing the ultraviolet absorption spectra of aqueous methanol solutions containing silver and sodium salts at constant ionic strength and saturated in 1,2,5,6-dibenzanthracene.

Materials.

Reagent grade inorganic chemicals were used. Silver perchlorate and sodium perchlorate were obtained from G. Frederick Smith Co. Baker's absolute methanol and distilled water, both saturated with nitrogen, were used to prepare solvent equimolal in methanol and water. The perchlorate salts were found to have much lower light absorption below 350 mµ than the corresponding nitrates and were, therefore, considered more desirable for this work. However, it was found impossible to render the sodium perchlorate sufficiently free of chloride so that optically clear solutions containing both the sodium and silver salts could be prepared. For this reason the nitrates were used.

Experimental Procedure.

Measurements were made using a medium equimolal in water and methanol in order to obtain satisfactory solubilities of both the inorganic salts and also of the high molecular weight hydrocarbons. Solutions of the sodium and silver salts were saturated with dibenzanthracene by rotating a 25-ml. portion of the solution with a pinch of the hydrocarbon in a paraffin-sealed 125-ml., glass-stoppered flask submerged in a thermostat at 25.0° C. for 48 hours. The absorption spectra were examined by means of a Beckman Model DU spectrophotometer using 1-cm. Corex cells with appropriate blank solutions in the blank cell. The spectrophotometer cell compartment was fitted with thermospacers and kept at 25±1° C. during measurements.

Results.

Silver nitrate and perchlorate were found to increase the solubility of dibenzanthracene about 50 percent over the solubility in the corresponding sodium salts at a concentration of 0.5 M, as indicated by the optical density due to the first absorption maximum of the hydrocarbon. Figure 2 shows the absorption curves 0.5 M sodium and silver nitrates saturated in the hydrocarbon. It was noticed that the shape and position of the absorption maxima were modified slightly, being shifted slightly toward the visible. Therefore the difference in the two curves was plotted in Figure 2, and it may be seen to consist of a curve with somewhat broadened maxima shifted 3.3 mμ toward the visible from the positions of the maxima of dibenzanthracene in sodium nitrate solution. Similar curves were taken in solutions containing intermediate concentrations of silver nitrate maintained at an ionic strength of 0.5. The optical density due to hydrocarbon was seen to increase progressively

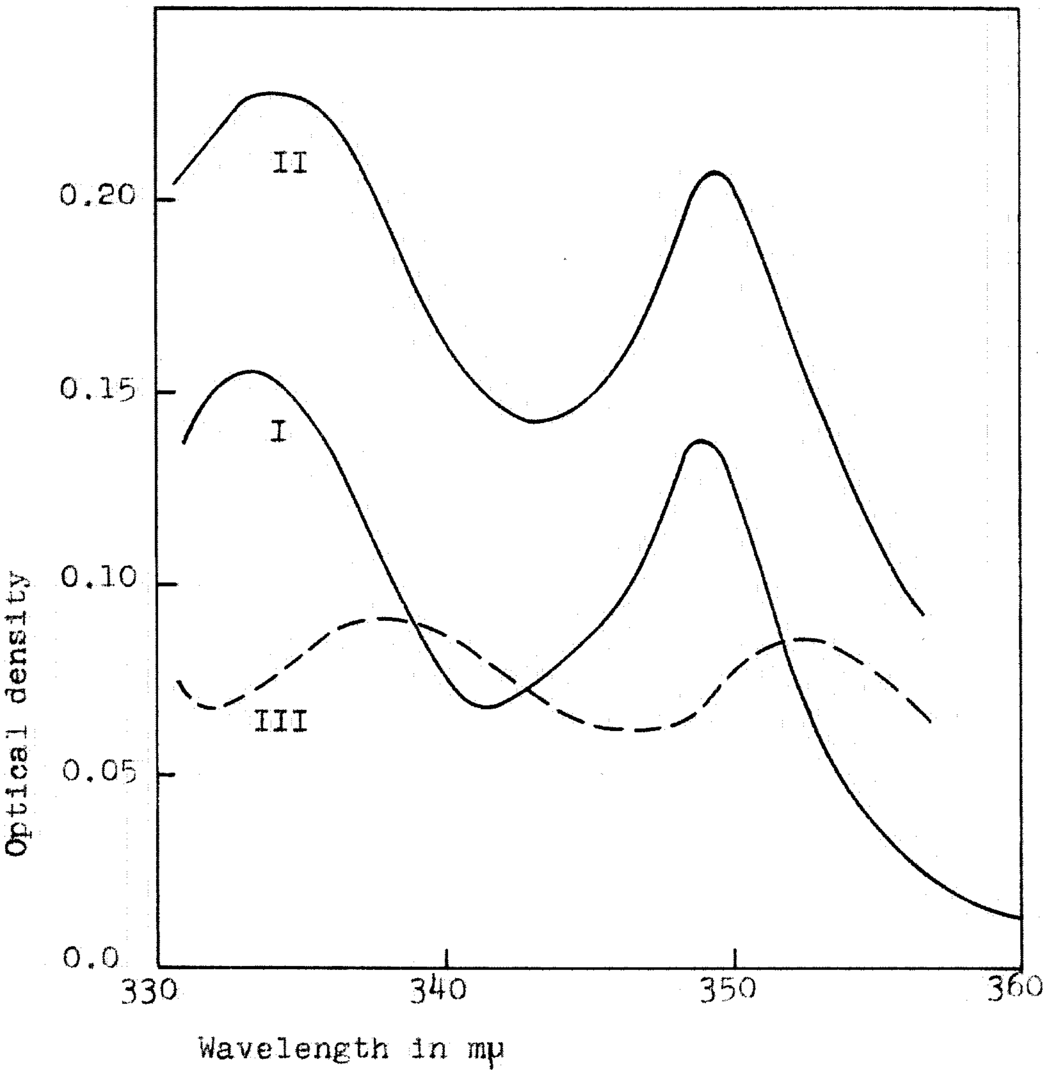

Figure 2. Ultraviolet absorption of salt solutions in equimolal aqueous methanol saturated with 1,2,5,6-dibenzanthracene: I, 0.5 N sodium nitrate; II, 0.5 N silver nitrate; III, difference between curves I and II.

with the increase in silver ion concentration.

Discussion.

It is possible that the difference curve reported above may be primarily the result of absorption by a hydrocarbon-silver coordination complex. This involves the assumption that the absorption resulting from uncomplexed hydrocarbon is the same in silver and sodium nitrate solutions at the same concentration. This assumption may be nearly true but is almost certainly not exactly valid. It was noted in later work that in the presence of 0.1 M silver nitrate the strong fluorescence of the 1,2-benzanthracenes was completely quenched. This suggests that silver ion may be able also to influence the absorption by these hydrocarbons without actually coordinating with them.

The observed shift of absorption 3.3 mμ toward the visible is in agreement with a similar shift observed by other workers in the ultraviolet absorption spectrum of the silver ion coordination complex of toluene (12).

If it be assumed that the molar extinction coefficient of the coordination complex is about equal to that of the free hydrocarbon, the data plotted in Figure 2 indicates that the argentation constant of dibenzanthracene has a value of the order of 1.0 to 1.5. Since it was apparent that thi type of data could not yield sufficiently accurate d nations of argentation constants and that the tr of the data involved assumptions of doubtful validity, this method of investigation was abandoned.

MEASUREMENT OF SOLUBILITIES BY THE EXTRACTION METHOD

Introduction.

It was finally decided that the most satisfactory means of determining the argentation constants of the polycyclic aromatic hydrocarbons would be an adaptation of the solubility-extraction method which had been used by Andrews and Keefer to determine the argentation constants of benzene and its homologs and naphthalene and phenanthrene in aqueous medium (13). Adaptation of the original method was required because the carcinogenic polycyclic aromatic hydrocarbons have such low aqueous solubility that another solvent medium was required in which to bring about the argentation reaction.

Materials.

All inorganic chemicals were of reagent grade. Baker's absolute methanol was fractionated from a small amount of sodium metal in a stream of nitrogen through 55 cm. of glass helices and pure methanol was taken over a 0.2 degree boiling range. Matheson s-tetrachloro-ethane and Eastman Kodak Spectro Grade 2,2,4-trimethylpentane (isooctane) were distilled before use.

The following hydrocarbons were obtained from Eastman Kodak: benz(a)anthracene, 7,12-dimethylbenz(a)anthracene, 1,2,5,6-dibenzanthracene, and 3-methylcholanthrene. The yellow impurity, 1,2,6,7-dibenzanthracene, was removed from 1,2,5,6-dibenzanthracene by selective oxidation with lead tetraacetate (14). Yellow oxidation impurities were removed from several of these compounds by repeatedly extracting their benzene solutions with sulfuric acid carefully adjusted in concentration so as to afford maximum extraction of oxygenated derivatives without appreciable extraction of the hydrocarbons. When the sulfuric acid concentration was made just one or two percent too high, very intense purple or red colors developed in the acid phase and a considerable amount of the hydrocarbon was lost. Satisfactory concentrations of acid for extracting the benzene solutions of several of the hydrocarbons are as follows: benz(a)anthracene, 87.5%; 3-methylchloanthrene, 82.5%; 7,12-dimethylbenz(a)-anthracene, 82.5%. The extracted benzene solutions were washed with water, dried with anhydrous potassium carbonate, filtered, and evaporated to dryness under 60 mm. Hg pressure.

Benzo(a)pyrene was obtained from Hoffman-La Roche Inc. and was used first as received and then after purification through the picrate. Phenanthrene obtained from the Matheson Company was found to contain about one percent anthracene, which was removed as the dimer by two or three exposures of the benzene solution to sunlight. The purified phenanthrene contained perhaps 0.01% of anthracene. Anthracene obtained from Eastman Kodak was purified by extraction of the benzene solution with 85% sulfuric acid (15) followed by recrystallization from benzene-ethanol.

Ten of the monomethyl benz(a)anthracenes, the 1- and 4-isomers being excepted, also benzo(c)phenanthrene and its six monomethyl homologs were donated in two-gram quantities by Dr. Melvin Newman of Ohio State University and were used as received.

Synthesis of Dihydroaromatic Compounds.

The synthesis of 7,12-dimethyl-7,12-dihydrobenz(a)benzanthracene was attempted. First 7,12-benz(a)anthraquinone was prepared, starting with naphthalene and phthalic anhydride, via Friedel-Crafts substitution and cyclization of the resulting keto acid in sulfuric acid (16). The quinone was purified by reducing it to a solution of the vat by reduction with an alkaline solution of sodium hydrosulfite and oxidizing the filtered vat solution with air (16a). The quinone was then treated with methyl magnesium bromide in ether to form 7,12-dimethyl-7,12-dihydroxy-7,12-dihydrobenz(a)anthracene which was converted to the dimethyl ether by reacting with twice the molar equivalent of potassium powder in dry benzene-ether solvent (17). The product was light lemon-yellow in color, m.p. 121.7-123.2° C. from acetone-alcohol.

Several attempts were then made to convert this aromatic hydrocarbon to the 7,12-dihydro compound by reaction with twice the molar equivalent of potassium, followed by treatment with methanol. This method has been used successfully to convert both benz(a)anthracene (18) and 12-methylbenz(a)-anthracene (19) to the corresponding 7,12-dihydro compounds. However, the only product isolated in several attempts was a very small quantity of yellow oil from which no crystals could be obtained. An attempt to go directly from the dimethyl ether to the dihydro compound using four molar equivalents of potassium produced the same results.

It was eventually concluded that either the reduction of the dimethyl compound would not take place or that the product is an oil because it consists of a mixture of four stereo-isomers. Several attempts were made to produce, 7,12-dihydrobenzanthracene from the aromatic compound, but spectrophotometric analysis indicated that the product consisted in each case of a mixture of about 45 percent of the dihydro compound with 55 percent of the unaltered aromatic hydrocarbon.

In the face of these difficulties the decision was made to prepare a quantity of a simpler dihydro compound which could be used to determine if the argentation constants of such compounds could be measured. The compound 9,10-dihydroanthracene was successfully prepared by reduction by metallic sodium of anthracene suspended in boiling n-propanol

(20). The product consisted of white, glistening needles, m.p. 109.2-110.3° C. from ethanol.

Attempted Preparation of Solid Complexes of Silver Perchlorate with Naphthalene and Phenanthrene.

The preparation of solid complexes was attempted by mixing concentrated solutions containing silver perchlorate with solutions containing naphthalene or phenanthrene, and also by dissolving the hydrocarbon with gentle heating in solutions of silver perchlorate followed by cooling. The solvents used were methanol, carbon tetrachloride, chloroform, and mixtures of these solvents. Only the hydrocarbons were recovered from the solutions. Gentle heating caused silver chloride to be precipitated from the chlorohydrocarbons.

Apparently the affinity of silver ion for all oxygenated compounds and the relatively low solubilities of the polycyclic aromatic hydrocarbons in such solvents prevent the isolation of solid complexes. The only other technique which suggests itself is the solution of solid silver perchlorate in molten naphthalene, which melts at 80° C.

Development of the Extraction Method for Measuring Solubilities.

The method used by Andrews and Keefer to determine the argentation constants of lower molecular weight aromatic hydrocarbons consisted in measuring the solubilities of the hydrocarbons in aqueous solutions of silver nitrate and sodium nitrate at ionic strength $\mu = 1$ and calculating the argentation constants from the data on the variation of hydrocarbon solubility with the concentration of silver ion. The solubilities were determined by extracting measured volumes of the saturated solutions with hexane and measuring the optical density of the hexane solutions at selected wavelengths at which the molar extinction coefficients of the hydrocarbons had been measured.

a. Selection of Reaction Solvent and Inorganic Salts.

The method described above had to be adapted for use with high-molecular weight hydrocarbons having almost immeasurably low aqueous solubilities. Equimolar aqueous methanol was chosen as the solvent because it provides satisfactory solubilities of the hydrocarbons and also sufficiently high solubility of inorganic salts to make possible the use of silver and sodium nitrates at ionic strength $\mu = 0.5$. The chief disadvantage of this mixed solvent is that methanol is rather volatile and necessitates care to prevent loss by evaporation.

Sodium nitrate was chosen instead of potassium nitrate to maintain constant ionic strength in the silver nitrate solutions because the solubility of the potassium salt is too low. The nitrate salts were chosen over the perchlorates because they are available in higher purity and are not hygroscopic.

b. Preparation of Solutions.

At first the two stock solutions 0.5 N in sodium nitrate and 0.5 N in silver nitrate were prepared by adding previously-prepared equimolar aqueous methanol to the desired salt in a volumetric flask, swirling to solution, and filling to mark. The disadvantages of this method were that there was too much opportunity for evaporation of methanol, and an excessive length of time was required for solution of the salts in the aqueous methanol.

The following procedure was used in preparing solutions for the greater part of the work reported in this thesis. Exactly 0.25 mole of the salt was weighed in a small beaker. A 500-ml. volumetric flask, filled with nitrogen, was weighed to the nearest 0.01 g. on a solution balance. The weighed salt was added to the flask by means of a funnel which was then rinsed into the flask with nitrogen-saturated redistilled water, and a total of exactly 8.4 moles by weight of water was added. The flask was stoppered and the contents were swirled to dissolve the salt. Then nitrogen-saturated methanol totaling exactly 8.4 moles was added, and the flask was stoppered and the contents swirled to obtain complete mixing. Corrections for air buoyancy were made for all weighings. The flask was then brought to a temperature of 25° C. by submerging in a thermostat, and the solution was brought to the volume mark by adding about 10 ml. of equimolar aqueous methanol. The solution was thoroughly mixed and filtered rapidly through coarse filter paper into a 500-ml. glass-stoppered, paper-covered storage bottle. These stock solutions were used within one to two weeks of the time of preparation.

The solutions containing sodium and silver nitrates at ionic strength $\mu = 0.5$ were prepared by pipetting appropriate volumes totaling 25 ml. of the two stock solutions into the saturation tubes containing 0.3 g. samples of the hydrocarbon the solubility of which was to be measured.

c. Attainment of Equilibrium.

Since the reaction mixture is a two-phase system and solubilities of the hydrocarbons are exceedingly low, the attainment of equilibrium, i.e., the saturation of the salt solutions with the solid hydrocarbons was an important problem. Only two-gram samples were available of most of the hydrocarbons tested. It was decided that for each hydrocarbon a series of six solubility measurements would be made, using six salt solutions containing silver nitrate at concentrations of 0.0, 0.1, 0.2, 0.3, 0.4, and 0.5 $\underline{M}$ respectively. This would make possible the use of about 0.3 g. of hydrocarbon in each reaction mixture, and 25-ml.

samples of solution were considered to be a volume commensurate with a reasonable time for equilibration. Even so, saturation was attained only slowly.

The saturation procedure finally adopted consisted of shaking at about 30° C. on a mechanical shaker for twenty-four hours, followed by rotation in a thermostat at $25.00 \pm 0.03^{\circ}$ C. for forty-eight hours. The equilibration was accomplished in specially manufactured 35-ml. centrifuge tubes fitted with ₸ 19/38 glass stoppers which were sealed on with paraffin wax melted one-fourth inch into the ground glass joint.

d. Sampling of Saturated Solutions.

There was some difficulty in freeing the saturated solutions from suspended solid hydrocarbons. The procedure which proved satisfactory was the following: Three of the six saturation tubes were removed from the thermostat and placed in a holder so that they were partially submerged in a water bath at $25 \pm 1^{\circ}$ C. and rotation of the remaining three tubes was resumed. The glass stoppers were removed and replaced by foil-wrapped corks, and the tubes were centrifuged for five minutes at moderate speed. Then plugs of Pyrex wool were placed in the tubes and centrifuging was resumed for three minutes so that the plugs were forced tightly on top of the solid hydrocarbon. The samples of clear supernatant solutions to be extracted were drawn into pipets tipped with small pads of Pyrex wool held in place by fine copper wire.

e. Extraction Procedure.

The characteristics required for the extraction solvent are the following: transparency to ultraviolet light, low aqueous solubility, reasonably low volatility, and good solvent power for hydrocarbons. The initial work was performed using as the extraction solvent s-tetrachloroethane, b.p. 146° C., aqueous solubility about 0.3 percent. Investigation revealed, however, that in the extraction process the concentration of hydrocarbon in the tetrachloroethane was increased by two to four percent as a result of the aqueous solubility of the chloro-hydrocarbon.

The extraction solvent chosen for the final work was Eastman Kodak 2,2,4-trimethylpentane (isooctane), b.p. 99° C., aqueous solubility negligible. When isooctane was used, the increase in hydrocarbon concentration in the extraction process was found to be less than one percent, which is probably the result of evaporation. Furthermore, isooctane smells better. A second extraction with isooctane of an aqueous solution containing methylcholanthrene was found to remove no additional hydrocarbon. Therefore extraction is effectively complete with only one extraction with isooctane.

The following extraction procedure was finally developed.

The 5-to-20-ml. portion of solution to be extracted was pipetted into a 140-ml. glass-stoppered bottle containing a pipetted volume of isooctane of 10 to 25 ml. Then approximately 100 ml. of nitrogen-saturated water was metered into the bottle, it was stoppered, and shaken on a reciprocal shaker for fifty minutes. The bottle was allowed to stand for several minutes and then the contents were poured into a 125-ml. separatory funnel, the aqueous phase drawn off, and the isooctane phase run into a 25-ml. glass-stoppered mixing cylinder from which portions were pipetted into cells for analysis by means of a spectrophotometer. Neither rinsing the isooctane portions with a volume of water nor drying with sodium sulfate were found to alter the ultraviolet absorption and so these measures were not adopted.

f. Spectrophotometric Analysis for Polycyclic Aromatic Hydrocarbons.

The isooctane extraction solutions were analyzed for their content of aromatic hydrocarbon in 1-cm. quartz absorption cells using a Beckmann DU Spectrophotometer. The optical density of the solutions was measured at several selected wave lengths corresponding to absorption maxima for which the molar extinction coefficients had been determined, from the absorption of a standard solution of the hydrocarbon. The standard solutions were made by dissolving in 50 or 100 ml. of isooctane generally about two to three milligrams of the solid, weighed on a semi-micro balance which was capable of a precision of about one percent in this range. The cell compartment of the spectrophotometer was kept at a temperature of 24±1° C. while absorption measurements were made. The extraction ratios were selected as much as possible so that the optical densities measured were between the values 0.2 and 0.9. Work by other investigators has shown that naphthalene and phenanthrene obey Beer's law in hexane solution.

g. Modifications in the Straight Aqueous System.

For the solubility measurements for naphthalene and phenanthrene which were made in aqueous solvent, silver and potassium nitrate were utilized at ionic strength $\mu = 1.0$ in order to make possible comparison with the work of Andrews and Keefer. It was found that saturation could be attained by rotation at temperature for twenty-four hours only. However, the hydrocarbons could not be centrifuged to the bottom of the dense aqueous solutions. The solutions were sampled by forcing into pipets with air pressure through medium grade sintered glass filter sticks. This method would probably have been excellent for all of the solubility work but, unfortunately, it was discovered only at the close of the prolonged investigation.

Experimental Problems.

a. Formation of Yellow Contaminants During Extraction.

It was noticed that in the case of about one-third of the hydrocarbons of the benzanthracene series and about two-thirds of those of the benzophenanthrene series the isooctane extraction solutions from the higher silver mixtures developed very slight to quite appreciable yellow colors. The yellow contaminants were found to have an absorption maximum at about 430 mμ. The original silver nitrate solutions saturated with hydrocarbon could be examined in the pipet when samples were drawn from the saturation bottles. No yellow color was ever noticed in these solutions. The yellow color thus appeared in some later step of the analysis procedure.

Air-free water and methanol were used to make up all solutions for saturation with hydrocarbon. Initially, the saturation tubes were swept with nitrogen before sealing, and also nitrogen-saturated water was used in the dilution of the extraction mixture. However, the use or neglect of these latter precautions seemed to have no relation to the appearance or absence of yellow contaminants. Sweeping of saturation tubes with nitrogen before sealing was abandoned because it promoted evaporation of the solvent.

The ultraviolet spectra of the extraction solutions were examined to determine whether the contaminants interfere with analysis for the content of aromatic hydrocarbons. This was done by examining the ratio of the optical densities for the first two absorption maxima of the hydrocarbons in the isooctane extraction solutions. In practically all cases the analysis for the hydrocarbon was made using the second absorption maximum which was usually in the region between 350 and 370 mμ. The second maximum generally is about 10 to 20 mμ toward the visible. Thus if a contaminant absorbs appreciably in this region it would probably alter the ratio of the hydrocarbon peaks. Some of the pertinent data are given in Table I for the hydrocarbons 2-methyl- and 6-methylbenzo(c)phenanthrene.

The value of the ratio R of the second to the first absorption maximum is 1.251 for the pure 2-methyl benzo(c)-phenanthrene and 1.626 for the pure 6-methyl compounds. Thus it can be seen from Table I that for the 2-methyl compound for which all of the solutions are colorless and exhibit no appreciable absorption at 430 mμ, the ratio R varies within a range of one percent of the value for the pure hydrocarbon, which is within experimental accuracy for spectrophotometric work. On the other hand, for the 6-methyl compound the solutions corresponding to higher silver concentrations are noticeably yellow, have a measurable absorption at 430 mμ, and exhibit an increasingly lower value of the ratio R. This

Table I

Interference By Yellow Contaminant With the U. V. Absorption Spectra of 2-methyl- and 6-methylbenzo(c)phenanthrene In Isooctane Extraction Solution.

$(AgNO_3)$ M	0.0	0.1	0.2	0.3	0.4	0.5
2-MeBPh. R	1.249	1.251	1.244	1.253	1.251	1.257
D at 430 mμ	0.002	0.001	0.002	0.002	0.005	0.003
Color	c	c	c	c	c	c
6-MeBPh. R	1.620	1.616	1.596	1.587	1.592	1.546
D at 430 mμ	0.001	0.004	0.019	0.022	0.031	0.067
Color	c	c	Yel(1)	Yel(1)	Yel(2)	Yel(3)
xs D max.1	0.0	0.001	0.005	0.007	0.006	0.020
xs D as %	0.0	0.4	1.9	2.3	1.8	5.3

"R" is the ratio of second to first absorption maximum.
"D" at 430 mμ" refers to optical density at 430 mμ.
"Color" refers to relative visual color intensity.
"c" means colorless.
"Yel(1,2, or 3)" indicates relative intensity of yellow color.
"xs D max.1" refers to the calculated excess optical density at first maximum due to contaminant.
"xs D as %" refers to the preceding item expressed as percent of absorption due to first maximum of hydrocarbon.

latter fact means that the contaminant creates greater interference in the region of the first absorption peak of the hydrocarbon than at the second peak, which is farther removed from the absorption maximum of the contaminant at 430 mμ.

The above observations led to the use of the second absorption maximum in the quantitative analysis for the aromatic hydrocarbons. If it is assumed that there is no interference at the second absorption maximum, simple calculations yield the data in the last two rows of Table I. The calculated excess optical density at the first peak is seen to be roughly proportional to the absorption due to the contaminant alone at 430 mμ. When this is expressed as percentage of the optical density due to the hydrocarbon at its first absorption peak, it is found that the maximum interference at the first peak is about five percent. It seems, therefore, in such cases of appreciable discoloration, that the maximum interference at the second peak is of the order of one percent.

No effective means were found to eliminate the occasional appearance of the yellow contamination. However, the error introduced is probably not serious in comparison with other experimental errors. The yellow contaminant may be formed during the extraction procedure by autoxidation of the hydrocarbon catalyzed by silver ion.

b. The Destruction of Dihydroanthracene During Extraction.

As was described in an earlier section, 9,10-dihydroanthracene was synthesized in order to determine whether the argentation constants of such dihydro-compounds can be measured by the methods of this investigation. The data from a determination of the solubility of this compound in the aqueous methanol system are given in Table II. The isooctane extraction solutions were increasingly yellow for the higher concentrations of silver nitrate.

Table II

Optical Densities of Extraction Solutions in Solubility Determination for Dihydroanthracene

$(AgNO_3)$ <u>M</u>	<u>D</u> at 258 mμ.
0.0	1.020
.1	1.199
.2	1.356
.3	1.049
.4	.982
.5	.947

From the above information it is apparent that silver nitrate not only causes the formation of a yellow contaminant, but it also brings about the destruction of a considerable fraction of the dihydroanthracene, thus making the measurement of the argentation constant impossible. This interfering reaction was investigated in some detail in order to establish its nature and discover a way of eliminating it. The most important observations and conclusions of this study will now be given.

The yellow color was never observed in the silver nitrate solutions but only in the isooctane extraction solutions. There was never any evidence of reduced silver. Oxygen bubbled for hours through a solution of silver nitrate and dihydroanthracene in methanol produced no yellow color. Therefore the yellow contaminant must be produced by a silver-ion-catalyzed reaction during the extraction process. A series of analyses were carried out to determine if the yellow color developed at a measurable rate and if precipitation of the silver as an insoluble salt would prevent the formation of the color.

The color was found to be formed quite rapidly and there was some evidence that less color was produced when nitrogen-saturated water was used in the extraction process. Precipitation of the silver as the chloride prevented the appearance of the yellow color, but a large fraction of the hydrocarbon, approximately the amount present as silver complexes in the saturated solution, was firmly adsorbed by the precipitate. Anthracene also was adsorbed by a silver chloride precipitate as noted in the footnote to Table III. Both potassium cyanide and sodium thiosulfate when used to remove silver ion from solution introduced strong background absorption into the isooctane solutions, and potassium thiocyanate produced a stable emulsion with the isooctane.

On the basis of these and other experiments it was finally concluded that it would be very difficult to prevent the destruction of dihydroanthracene since probably a completely air-free system for both the saturation and extraction processes would be required. Therefore this study was dropped.

The reaction responsible for the destruction of the dihydroanthracene is probably an autoxidation primarily of the complexed hydrocarbon, catalyzed by silver ion, which takes place rapidly when the clear silver nitrate solution saturated with hydrocarbon is pipetted into the extraction bottle and diluted with water in the presence of small amounts of dissolved oxygen.

c. Solubilities of Dihydroanthracene in the Aqueous System: Appearance of Anthracene in the Isooctane Extraction Solutions.

When the solubilities of dihydroanthracene in the aqueous system were measured, it was found that anthracene appeared in the isooctane extraction solutions at concentrations equal roughly to ten percent of the molar concentration of the dihydro-compound as determined by the ultraviolet absorption. No influence by the concentration of silver nitrate upon this concentration ratio was noticed. The anthracene either was produced in the solutions by some oxidation reaction or else there was a small amount of anthracene present in the original dihydroanthracene. The latter possibility seems more likely since the dihydro-compound was prepared by hydrogenation of anthracene.

An examination of the U.V. absorption spectrum which was taken of the freshly-prepared dihydroanthracene and comparison with literature data (21) indicates that the content of anthracene is 0.01% or less. However, the spectrum taken of the same material eight months later indicates an anthracene content of about 0.03%. This increase in the content of anthracene suggests that some oxidation of the dihydroanthracene occurred during the storage period. This oxidation would be expected to take place near the surface of the solid and thus the oxidation product would be preferentially dissolved in the solubility determination. These facts were not discovered until the investigation was terminated. However, the solubilities and the argentation constants obtained for dihydroanthracene in the aqueous system are approximately correct, since anthracene does not interfere with the absorption maximum of the dihydro-compound at 270.5 mμ.

Solubility Data.

The solubilities of each hydrocarbon in the series of six solutions containing different concentrations of silver nitrate were calculated from the optical densities of the isooctane extraction solutions and the values of the extraction volume ratio. The solubility data for twenty-four hydrocarbons are recorded in Table III. The data for the compound anthracene are presented graphically in Figure 3. The solubility data are given in Table IV for phenanthrene and for naphthalene at three different temperatures in the aqueous system.

Precision in Solubility Data.

An examination of the solubility data shows that the precision of individual solubility measurements is such that in

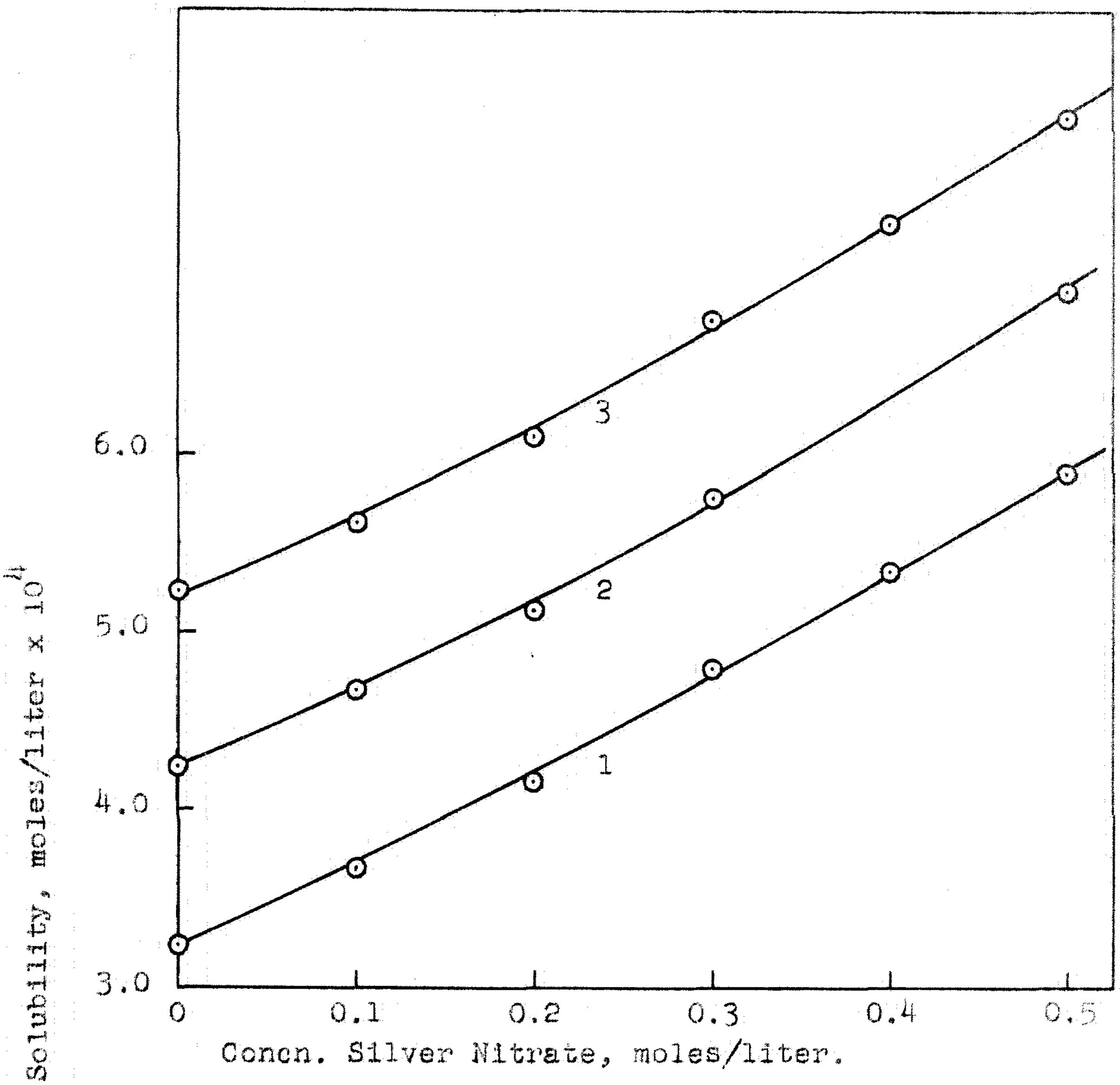

Figure 3. Solubility of anthracene in equimolal aqueous methanol containing sodium nitrate and silver nitrate at ionic strength 0.50. Scales for runs 2 and 3 have been raised one and two units, respectively.

Table III

Solubilities of Polycyclic Aromatic Hydrocarbons in Equimolar Aqueous Methanol Containing Sodium and Silver Nitrates at Ionic Strength 0.500 at 25° C.
(In each group of six values the concentrations of silver nitrate from top to bottom were 0.0, 0.1, 0.2, 0.3, 0.4, 0.5 $\underline{M}$, respectively.)

Benz(a)anthracenes. $\underline{M} \times 10^4$

Parent cpd.	2-Me	2-Me	3-Me	3-Me	5-Me	5-Me	6-Me
3.33	1.63	1.69	2.03	2.06	1.31	1.22[a]	2.81
3.74	1.84	1.90	2.29	2.20[a]	1.45	1.45	3.20
4.27	2.11	2.12	2.66	2.67	1.65	1.66	3.61
4.88	2.30	2.44	2.99	3.04	1.88	1.88	4.14
5.49	2.64	2.70	3.40	3.42	2.12	2.10	4.66
6.12	2.94	3.00	3.78	3.85	2.33	2.34	5.09

6-Me	7-Me	7-Me	8-Me	8-Me	9-Me	9-Me	10-Me
2.79	2.08	2.12	1.96	1.98	1.35	1.33	.604
3.16	2.48	2.58	2.22	2.24	1.51	1.49	.666
3.57	2.91	2.97	2.53	2.54	1.72	1.72	.775
4.15	3.38	3.48	2.94	2.94	1.96	1.97	.876
4.56	3.84	4.13	3.32	3.32	2.19	2.18	.972
5.04	4.51	4.74	3.73	3.68	2.45	2.43	1.101

10-Me	11-Me	11-Me	12-Me	12-Me	7,12-DM	7,12-DM	7,12-DM
.604	3.12	3.03	1.39	1.11	2.02	1.98	2.19
.670	3.61	3.44	1.65	1.28	2.39	2.38	2.59
.769	4.00	3.88	1.92	1.48	2.85	2.79	3.08
.880	4.64	4.44	2.21	1.72	3.36	3.28	3.54
.975	5.20	5.04	2.55	1.97	3.90	3.78	4.20
1.10	5.67	5.61	2.89	2.22	4.46	4.33	4.70

Benzo(c)phenanthrenes. $\underline{M} \times 10^3$

Parent cpd.	Parent cpd.	1-Me	1-Me	2-Me	2-Me	3-Me	3-Me
2.85	2.75	.337	.328	1.24	1.22	1.61	1.66
3.19	3.20	.393	.379	1.43	1.36	1.90	1.89
3.60	3.57	.439	.419	1.59	1.51	2.12	2.10
4.09	3.99	.501	.481	1.83	1.70	2.44	2.40
4.48	4.52	.575	.531	1.98	1.91	2.69	2.66
5.03	5.00	.646	.591	2.23	2.09	3.02	2.95

Table III. (continued)

4-Me	4-Me	5-Me	5-Me	6-Me	6-Me
1.33	1.35	1.08	1.03	.996	.979
1.57	1.53	1.23	1.17	1.14	1.12
1.77	1.73	1.40	1.32	1.28	1.26
2.00	1.99	1.56	1.48	1.45	1.43
2.26	2.24	1.75	1.66	1.67	1.59
2.48	2.54	1.95	1.85	1.85	1.81

3-Methylcholanthrene $\underline{M} \times 10^5$		Dibenznthracene $\underline{M} \times 10^5$	Benzo(a)pyrene $\underline{M} \times 10^4$		
2.57	2.72	.786	1.11	1.15	1.16
3.59	3.70	.930	1.33	1.34	1.43
4.40	4.37	1.07	1.47	1.52	1.60
5.40	5.30	1.22	1.72	1.69	1.89
6.24	6.13	1.38	1.94	1.93	2.09
7.10	7.09	1.55	2.14	2.19	2.38

Anthracene $\underline{M} \times 10^4$			Phenanthrene $\underline{M} \times 10^3$	
3.26	3.26	3.23	7.12	7.35
3.68	3.68	3.62	7.88	8.12
4.16	4.13	4.11	8.79	8.87
4.80	4.76	4.77	9.85	10.05
5.35	5.55[b]	5.31	10.87	11.00
5.91	5.93	5.90	12.00	12.12

a. Discard

b. Silver was precipitated from the extraction mixture with NaCl. Apparently the complexed anthracene is adsorbed by the silver chloride precipitate. Discard this value.

Table IV

Solubility Data in Aqueous Solutions Containing Potassium and Silver Nitrates at Ionic Strength 1.00.
(In each group of six values the concentrations of silver nitrate from top to bottom were 0.0, 0.2, 0.4, 0.6, 0.8, and 1.0 $\underline{M}$ respectively.)

Phenanthrene at 25° C.

$\underline{M} \times 10^6$

5.35	5.80[a]	5.41
9.90	11.84[a]	10.02
16.58	16.42	16.85
25.45	25.40	25.43
37.38	36.82	37.30
52.21	51.67	52.21

Napthalene at 25° C.

$\underline{M} \times 10^4$

2.18
3.74
5.74
8.18
11.10
14.54

Naphthalene at 20° C.

$\underline{M} \times 10^4$

1.78	1.75
3.17	3.16
4.96	4.94
7.15	7.20
9.80	9.86
13.00	13.02

Naphthalene at 30° C.

$\underline{M} \times 10^4$

2.66	2.64	----	----	----
4.37	4.37	----	----	----
6.60	6.60	----	----	----
9.28	9.24	----	----	----
13.03[a]	12.48	12.40	12.44	12.50
17.31[a]	16.58[a]	16.22	16.14	16.14

9,10-Dihydroanthracene
25° C. $\underline{M} \times 10^5$

	(Content of anthracene)
3.44	0.33
4.32	.40
4.69	.47
7.02	.77
8.49	.91
10.38	1.12

Benzo(c)phenanthrene

at 25° C. $\underline{M} \times 10^6$

1.03
1.89
1.47
2.94
4.18
5.17

a. Discard.

the aqueous methanol system the mean deviation is of the order of one to two percent, in cases for which an appreciable systematic error is not involved. In the aqueous system the mean deviation of solubility values is about 0.3%. The values of molar extinction coefficients used to calculate solubilities were reproducible generally to within about one percent.

CALCULATION OF EQUILIBRIUM CONSTANTS FROM SOLUBILITY DATA.

Theoretical Interpretation of Solubility Data.

The interpretation of the solubility data in the aqueous methanol system, following the work of Andrews and Keefer (12), is based upon two assumed reversible coordination reactions which may be represented by the following equations:

$$\mathrm{Ar} + \mathrm{Ag}^{+} \rightleftharpoons \mathrm{ArAg}^{+} \qquad \underline{K}_1 = (\mathrm{ArAg}^{+})/(\mathrm{Ar})(\mathrm{Ag}^{+}) \qquad (4)$$

$$\mathrm{ArAg}^{+} + \mathrm{Ag} \rightleftharpoons \mathrm{ArAg}_2^{++} \qquad \underline{K}_2 = (\mathrm{ArAg}_2^{++})/(\mathrm{ArAg}^{+})(\mathrm{Ag}^{+}) \qquad (5)$$

In order to calculate the values of the equilibrium constants, three assumptions were made concerning activities of the chemical species taking part in the reactions: 1) the activity of the hydrocarbon is the same in all solutions, 2) the activity coefficient of the dissolved hydrocarbon is constant for constant ionic strength, and 3) the activity coefficients of the Ag^{+} and ArAg^{+} ions are equal at constant ionic strength. It follows from these assumptions that the total concentration of hydrocarbon in the solutions should be a second degree function of the concentration of silver ion only:

$$(Ar)_t = (Ar)_o[1 + \underline{K}_1(Ag^+) + \underline{K}_1\underline{K}_2(Ag^+)^2] \qquad (6)$$

In this equation $(Ar)_o$ signifies the concentration of hydrocarbon in 0.5 $\underline{M}$ sodium nitrate solution saturated with the hydrocarbon.

The silver involved in complexes was appreciable relative to the total silver concentration only in the case of phenanthrene. For this compound the required correction, determined by a method of approximation, produced a change of only one percent in the calculated equilibrium constants. For all other compounds tested the total concentration of hydrocarbon is a second degree function of the total silver concentration, and the best values of $(Ar)_o$ and of $\underline{K}_1$ and $\underline{K}_2$, which have been termed argentation constants, may be found by fitting a second degree curve to the data.

Method of Calculation.

Since measurements in the aqueous methanol system yield solubility values with a mean deviation of one to several percent, it seemed that the only satisfactory way to treat the data so as to avoid bias was by the method of least squares (22). The standard least squares method is based upon the assumption of constant probable absolute error in each measurement, whereas there are in the solubility data obtained in this investigation some errors with constant probable relative magnitude. However, there appears to be some tendency for the errors with constant probable absolute magnitude to predominate, and in any case, the standard least squares treatment is the only practicable one. Therefore, a second degree curve was fitted to the data from each solubility run comprising six solubility measurements, by the least squares method, and the equilibrium constants were calculated from the three constants of the second degree equation thus obtained.

Calculated Equilibrium Constants.

In Table V are compiled the wave length of the ultraviolet absorption maximum used in analysis for each hydrocarbon, the corresponding molal extinction coefficient, and the solubility of each hydrocarbon in equimolal aqueous methanol 0.5 N in sodium nitrate. In table VI are presented the equilibrium constants calculated from the solubility data in the aqueous methanol system given in Table III. Table VII displays the equilibrium constants calculated from the solubility data in the aqueous system given in Table IV. Each table contains other pertinent information about each hydrocarbon.

Precision.

The precision indices attached to the constants given in Tables VI and VII are the probable errors calculated in

Table V

Some Information About Polycyclic Aromatic Hydrocarbons.

Compound[a]	Wave Length mμ	Molal Extinct. Coefficient in Isooctane	Solubility in 0.5 M $NaNO_3$ in H_2O-MeOH, M x 10^4
3-Mechol.	359.5	8440	.266
7-12-DMBA.	363	8860	2.09
Benz-pyr.	403.5	4080	1.15
DBA.	348.5	16400	.0792
Anthracene	370	3890	3.23
Phenanthrene	346	219.4	72.2
BA.	358.5	5260	3.31
2-MBA.	359	5760	1.65
3-	360.5	5170	2.04
5-	357	5400	1.30
6-	385.5	1354	2.78
7-	370	6520	2.11
8-	361	5970	1.96
9-	360	4570	1.33
10-	349	5170	5.99
11-	365	3940	3.07
12-	350	7290	1.20
BP.	371	164.2	28.0
1-MBP.	321	9390	3.34
2-	375	380	12.3

Table V. (continued)

Compound	Wave Length mμ	Molal Extinct. Coefficient in Isooctane	Solubility in 0.5 M $NaNO_3$ in H_2O-MeOH $M \times 10^4$
3-	355.5	3.3	16.4
4-MBP.	357	294.5	13.4
5-	356	364	10.6
6-	358.5	341.3	9.9

a. The abbreviations are as follows: mechol., methylcholanthrene; DMBA., dimethylbenz(a)anthracene; benz-pyr., benzo(a)pyrene; DBA., 1,2,5,6-dibenzanthracene; BA., benz(a)anthracene; MBA., methylbenz(a)anthracene; BP., benzo(c)phenanthrene; MBP., methylbenzo(c)phenanthrene.

Table VI

Argentation Constants of Polycyclic Aromatic Hydrocarbons in Equimolal Aqueous Methanol at μ = 0.5 and 25° C.

Compound	Calculated Argentation Constants		Weighted Mean Argentation Constants	
	$\underline{K_1}$	$\underline{K_2}$	$\underline{K_1}$	$\underline{K_2}$
3-Mechol.	3.437	0	3.31±.12	0
	3.179	0		
7,12-DMBA	1.888±.028	.598±.038	1.87±.01	0.55
	1.870±.015	.534±.021		
	1.855±.076	.521±.106		
Benz-pyr.	1.676±.041	.210±.057	1.69±.05	.36
	1.302±.029	.697±.039		
	1.871±.048	.179±.066		
DBA.	1.652±.006	.314±.008	1.65±.01	.31
Anthracene	1.400±.077	.387±.108	1.35±.04	.48
	1.299±.069	.577±.096		
	1.369±.089	.489±.12		
Phenanth.	1.108±.062	.531±.086	1.09±.06	.58
	1.011±.14	.626±.20		
BA.	1.327±.051	.577±.07	1.33±.05	.58
2-MBA	1.200±.046	.665±.064	1.23±.03	.62
	1.251±.036	.518±.049		
3-	1.421±.036	.473±.05	1.34±.02	.55
	1.333±.011	.619±.015		
5-	1.268±.034	.554±.046	1.25±.02	.58
	1.239±.024	.599±.032		
6-	1.465±.071	.280±.098	1.35±.04	.38
	1.317±.034	.482±.047		
7-	1.575±.095	.835±.131	1.66±.05	.86
	1.692±.063	.883±.087		
8-	1.370±.039	.689±.053	1.41±.02	.47
	1.442±.031	.440±.042		

Table VI. (continued)

Compound	Calculated Argentation Constants		Weighted Mean Argentation Constants	
	K_1	K_2	K_1	K_2
9-	1.270±.019	.608±.026	1.32±.05	.48
	1.446±.032	.347±.044		
10-MBA.	1.250±.162	.675±.223	1.25±.10	.67
	1.256±.138	.662±.19		
11-	1.502±.103	.222±.142	1.34±.08	.56
	1.301±.046	.654±.063		
12-	1.716±.020	.508±.027	1.64±.06	.57
	1.549±.017	.626±.024		
BP.	1.229±.055	.496±.076	1.30±.04	.44
	1.359±.053	.375±.074		
1-MBP.	1.321±.071	.757±.098	1.34±.05	.55
	1.360±.071	.339±.098		
2-	1.384±.040	.269±.055	1.19±.07	.42
	1.132±.022	.571±.031		
3-	1.517±.037	.261±.051	1.37±.07	.34
	1.291±.027	.417±.037		
4-	1.629±.023	.115±.032	1.39±.13	.49
	1.242±.018	.856±.024		
5-	1.332±.009	.409±.012	1.30±.03	.46
	1.268±.003	.506±.005		
6-	1.253±.023	.741±.032	1.24±.01	.72
	1.229±.017	.709±.024		

Table VII

Argentation Constants in Aqueous Solutions of Potassium and Silver Nitrates at Ionic Strength 1.00.

Compound	Temp. °C.	Solubility 1 M KNO_3 M x 10^4	K_1	K_2	K_3
Naphthalene	20	1.78	3.212±.058	0.966±.024	
	25	2.19	2.937±.040	.909±.017	0±.04
	30	2.66	2.726±.054	.866±.022	
Phenanthrene	25	.0537	3.55	.99	.47

the process of least squares treatment utilizing the principles given by David Brunt (23). The average values of the constants K_1 are the weighted mean values. The data from three solubility runs with anthracene displayed graphically in Figure 3 reveal a systematic error. This error causes the consecutive points in the first group of three measurements and also in the second group of three measurements in a run to fall increasingly lower with respect to the least squares curve. Careful check was made of the pipet calibrations used in the preparation of the solutions and in the sampling for analysis, and it was concluded that the systematic error in question could not be the result of errors in the calibration of volumetric glassware. Therefore this error must be the result of a slow loss of hydrocarbon due to unknown causes during some step in the sampling or analysis of each group of three saturated solutions. This error in the solubility data probably introduces an error of about one or two percent into some of the calculated equilibrium constants.

GENERAL DISCUSSION OF THE ARGENTATION REACTION

Evidence for Formation of Aryl-Silver Ion Complexes.

As was noted in Part II of this thesis, the argentation reaction has been demonstrated to be a reaction characteristic of olefins and aromatic hydrocarbons, the most direct evidence being the measurement of equilibrium constants for the argentation reaction and the isolation of crystalline coordination compounds of both olefins and aromatic hydrocarbons (24). Further evidence for the argentation reaction is provided by a study of the ultraviolet absorption spectrum of toluene in aqueous solutions containing sodium and silver perchlorates (12). This work showed that in the presence of silver ion new absorption developed and the first absorption maximum, enhanced and shifted slightly toward the visible, was attributed to the mono-silver-toluene complex. Similar information concerning 1,2,5,6-dibenzanthracene was reported in an earlier section of this thesis.* Rather conclusive evidence for a strong interaction is found in the Raman spectrum of benzene in aqueous silver perchlorate which shows a marked shift of spectral lines corresponding

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* Reported on page 64 of this thesis.

to C-C bond stretching frequencies (25).

Evidence for Higher Argentation Complexes.

a. Argentation of Toluene and Naphthalene.

There is considerable evidence for the formation of complex ions containing more than one silver ion. In the work mentioned above on the ultraviolet spectrum of toluene in aqueous silver perchlorate good evidence was found for ultraviolet absorption by two complex ions in addition to uncomplexed toluene (12). In the present investigation, the work in the aqueous system provides strong support for the formation of higher complexes. In the section above on the theoretical interpretation of solubility data it was shown that, on the basis of a few simple assumptions concerning activity coefficients at constant ionic strength, the solubility of the hydrocarbons should be a second degree function of the silver ion concentration. The solubility data for naphthalene given in Table IV for temperatures of 20°, 25°, and 30° C. were fitted to a second degree function of the silver ion concentration with root mean square deviations of 0.020, 0.014, and 0.021, respectively, which corresponds roughly to an average deviation of experimental solubilities from the least squares curve of 0.3 percent. From the values of the calculated equilibrium constants the estimated concentrations of mono- and di-silver complexes of naphthalene are 44 and 40 percent, respectively, of the total dissolved hydrocarbon in 1.00 M aqueous silver nitrate. This is larger than any activity effect to be expected as a result of the replacement of potassium by silver ion. Therefore the existence of di-silver complexes of aromatic hydrocarbons is believed to be well-established.

b. Argentation of Phenanthrene.

The solubility data for phenanthrene in the aqueous system given in Table IV when fitted to a second degree function of the silver ion concentration yielded for the argentation constants the values $K_1 = 2.56$ and $K_2 = 2.22$, with an r.m.s. deviation of 0.23 or about 0.8 percent from the least squares curve. The calculated constants for naphthalene at 25° C. are $K_1 = 2.94$ and $K_2 = 0.91$ with r.m.s. deviation of 0.014 or about 0.25 percent. Thus the two constants given above for phenanthrene are nearly equal, in contrast to those for naphthalene and also of the other benzene homologs investigated by other workers, for all of which the second constant is much smaller than the first.

On the other hand, when the data for phenanthrene are fitted to a third degree function of silver ion concentration, the constants obtained are $K_1 = 3.55$, $K_2 = 0.99$, and $K_3 = 0.47$, with r.m.s. deviation of 0.035 or about 0.12 percent from the least squares curve. Thus the fit of the third degree function is better and the relative values of the constants are in better agreement with those for other compounds. If the assumptions regarding activity coefficients are applicable in the case of the higher silver complexes, these calculated constants are evidence for the formation of a tri-silver complex of phenanthrene. The available evidence, therefore, seems to establish definitely that di-silver complexes and very probably higher complexes are formed in the reaction of aromatic hydrocarbons with silver nitrate.

The Effects Upon the Argentation Reaction of Solvent and Ionic Strength: Validity of Assumptions Concerning Activity Coefficients.

The measurements with naphthalene and phenanthrene in aqueous medium were made in order to establish a relationship between the studies in mixed solvent and those of the lower aromatic hydrocarbons in aqueous medium investigated by Andrews and Keefer. The first argentation constant for phenanthrene in the aqueous system at unit ionic strength is about 3.3 times as large as that in equimolar aqueous methanol at 0.5 ionic strength. The effects both of the solvent and of ionic strength enter into this difference.

Work on the solubility of toluene in aqueous solutions of silver perchlorate and sodium perchlorate shows that the first argentation constant of toluene varies from a value of 2.63 at unit ionic strength to a value of 5.8 at ionic strength 5.0 (12). Thus the argentation constant is strongly affected by ionic strength. From this information, assuming a more or less parallel variation for phenanthrene, it may be roughly estimated that the argentation constant for phenanthrene in water at ionic strength 0.5 is about 3.3. Thus at ionic strength 0.5 the first argentation constant of phenanthrene in water is probably three times as great as its value of 1.1 in equimolal aqueous methanol. Therefore, the medium also strongly affects the argentation constant owing to changes in the dielectric constant and solvation powers of the medium which produce changes in the activity coefficients of the reacting species.

The assumptions, utilized in this thesis, that the activity coefficient of the hydrocarbon is constant and that the activity coefficients of silver ion and the complex ions are constant and equal at constant ionic strength, have been questioned (26). Potassium nitrate has about a 6 percent stronger salting out effect than has silver nitrate upon such solutes as carbon tetrachloride and cyclohexane (27). This corresponds to a difference in activity coefficients of about 6 percent for the organic solutes in 1.0 M KNO_3 and $AgNO_3$. Furthermore, on theoretical grounds it seems reasonable that the activity coefficient of the mono-silver complex ion is greater than that of the silver ion, though their ratio may be fairly constant at constant ionic strength (28). Thus, the argentation constants calculated on the basis of the assumptions listed above are not true thermodynamic equilibrium constants. Nevertheless, the assumptions are approximately valid, provide a simple and consistent interpretation of the solubility data, and almost surely give a satisfactory basis for the comparison of the affinity for silver ion of the different hydrocarbons.

Relation of Calculated Argentation Constants to Thermodynamic Equilibrium Constants.

A more careful analysis of the conditions existing in the solutions will now be given to show the relation between the calculated argentation constant, $\underline{K}_1$, and a true thermodynamic equilibrium constant for the first argentation reaction and to demonstrate the basis for comparing the argentation constants of different hydrocarbons. First, let the standard state of each of the reacting species, Ar, Ag^+, and $ArAg^+$, be chosen so that the ratio $\underline{a}/\underline{m} \rightarrow 1$ as $\underline{m} \rightarrow 0$, where $\underline{a}$ and $\underline{m}$ are the activity and the molar concentration of a reactant in pure solvent, respectively. The standard state of each reactant is then an hypothetical state at unit activity in pure solvent, activity being measured in the same units, moles/liter.

The argentation reaction was studied not in pure solvent, but in salt solutions at constant ionic strength. The calculated value of the first argentation constant is given in Equation 7.

$$\underline{K}_1 = \frac{(ArAg^+)}{(Ag^+)(Ar)} \qquad (7)$$

Here (Ar) is the solubility of the hydrocarbon at zero silver ion concentration and $(ArAg^+)/(Ag^+)$ is the slope at zero silver concentration of the plot of total hydrocarbon concentration versus total silver concentration, molar concentrations being used. However, the true thermodynamic equilibrium constant must be expressed in terms of activities or of concentrations and activity coefficients, γ.

$$\underline{K}_1{}^{o} = \frac{\underline{a}_{ArAg^+}}{\underline{a}_{Ag^+}\cdot\underline{a}_{Ar}} = \frac{\underline{m}_{ArAg^+}}{\underline{m}_{Ag^+}\cdot\underline{m}_{Ar}} \frac{\gamma_{ArAg^+}}{\gamma_{Ag^+}.\gamma_{Ar}} \qquad (8)$$

The activity coefficient of the hydrocarbon, γ_{Ar}, since the solubilities of the hydrocarbons are very small, is just the ratio of the solubility in pure solvent to the solubility in the salt solution at zero silver concentration. This ratio and, therefore, the activity coefficient, should be very nearly the same for a series of hydrocarbons of similar molecular size and shape. Of course, the activity coefficient of silver ion, γ_{Ag^+}, is virtually independent of the hydrocarbon which is involved.

As was mentioned above, the substitution of sodium or potassium ion by silver ion probably produces an appreciable though small effect upon the activity coefficients of the reacting species. However, the calculated equilibrium constant, $\underline{K}_1$, is calculated from the solubility of the hydrocarbon and the slope of the total-hydrocarbon-versus-silver-ion plot, both measured at zero silver ion concentration. The influence of varying silver ion upon the initial slope of the least squares curve is certainly only a second order effect.

It follows from the preceding considerations that the calculated first argentation constants for a series of similar hydrocarbons differ from the true thermodynamic equilibrium constants to a good approximation only by a constant factor. Thus, following from Equation 8 we have Equation 9.

$$\underline{K}_1^o = \frac{(ArAg^+)}{(Ar)(Ag^+)} \cdot \frac{\gamma_{ArAg^+}}{\gamma_{Ar}\gamma_{Ag^+}} = \underline{K}_1 \cdot \underline{R} \qquad (9)$$

Consequently, the free energies of reaction calculated from the argentation constants for such a series of hydrocarbons will differ from the standard free energies by a constant amount.

$$\Delta \underline{F}_1^o = -RT \ln \underline{K}_1^o = -RT \ln \underline{K}. - RT \ln \underline{R} = \Delta \underline{F}_1 + C \qquad (10)$$

A similar statement cannot be made at present for the calculated second argentation constants, since their calculation involves the curvature of the solubility curve at large silver concentrations for which the influence of silver ion upon the various activity coefficients has not been determined quantitatively.

It may be concluded that the calculated equilibrium constants, $\underline{K}_1$, for the first argentation reaction provide a dependable relative measure of the free energy of argentation [illegible] the series of polycyclic aromatic hydrocarbons used in this investigation

The Interactions Involved in the Argentation Reaction and the Structure of the Complexes.

a. Ionic Character.

The essential ionic character of the argentation complexes is evidenced by the influence upon the equilibrium constant of the medium which was reported above. The equilibrium constant increases in a medium of higher ionic strength, which is to be expected if the product is ionic in character. Further support for the ionic character is given by the fact that though silver perchlorate will dissolve in anhydrous benzene, in a two-phase system the complex is distributed virtually entirely in the aqueous phase.

b. Nature and Site of Bonding.

The interaction of a silver ion with an aromatic or olefinic molecule is probably with the π-electrons of the hydrocarbons. An electronic structure has been proposed for the olefin-silver ion complex involving resonance between a predominant no-bond and two-bonded structures in which the bonding electron pair is provided by the π-electrons of the olefinic bond (29). A similar description might be applied to the aromatic argentation complexes. A more recent theory postulates a "charge-transfer" resonance to account for complexes between aromatic compounds with both halogens and silver ion (31). By this theory it has been deduced from the electronic symmetry of the benzene-silver complex that the most likely position for the silver ion is above the plane of the benzene and between two carbon atoms. With reference to the structure of the benzene-silver perchlorate complex, Raman spectra indicate that the silver is located on the six-fold axis of symmetry of the benzene (25). On the other hand preliminary interpretation of data from X-ray diffraction photographs of the crystalline benzene-silver perchlorate complex indicate that the position of the silver ions is about in the position suggested by the "charge-transfer" theory with a silver-carbon distance of about 2.6 Å (31). Of course, it is quite possible that the silver ions have a somewhat different location in the dissolved and crystalline complexes. Furthermore, it should be noted that the reported X-ray crystal structure determination (31) is only the preliminary interpretation, and a detailed structure has not been published.

In the next section on correlations it is shown that there is a small degree of correlation between the magnitude of the argentation constants for polycyclic aromatic hydrocarbons and the theoretical electronic characteristics at the _meso_-bond calculated by quantum mechanics. From this fact and the evidence adduced above the most likely position for the first coordinated silver ion is above the plane of the aromatic molecule and between the carbon atoms of the *meso*-bond, which has the highest theoretical π-electron density in these molecules.

c. Relative Magnitudes of the First and Second Argentation Constants: Influence of the Electric Field Effect.

A consideration of the relative magnitudes of the successive argentation constants is of interest at this point. Since the mono-silver complex is charged, the coordination of a second silver ion will involve electrostatic energy of repulsion between two silver ions. The theory of Bjerrum (32) dealing with the relative magnitudes of the first and second dissociation constants of symmetrical dicarboxylic acids, as refined by Kirkwood and Westheimer (33) may be adapted for the calculation of the distance between the two silver ions in di-silver complexes of aromatic molecules. In the treatment of short-chain symmetrical dicarboxylic acids by the Kirkwood theory it is assumed that the only interaction between the two carboxyls is the energy of electrostatic repulsion between two protons. It is found that the two ionization constants should obey Equation 7.

$$\log_{10}\underline{K}_1/\sigma\underline{K}_2 = \underline{e}^2/2.303\underline{rk}TD_e \qquad (7)$$

In this equation $\underline{e}$ is the electronic charge, $\underline{r}$ is the distance between the protons, $\underline{k}$ is the Boltzman constant, T is the absolute temperature, and D_e is the effective dielectric constant (a function of the internal dielectric constant of the molecule, the assumed spherical shape of the molecule, and the position of the charges within the molecule.) The quantity σ is a statistical factor or symmetry number, the value of which for the symmetrical dibasic acids is 4.

The argentation of aromatic hydrocarbons to form first a mono-silver and then a di-silver complex is similar in some respects to the ionization of a dibasic acid. In the argentation of benzene, for example, the two silver ions probably occupy equivalent positions on opposite sides of the benzene molecule. The silver ions are large enough compared to the benzene ring that even if their position is not on the six-fold axis, there are still in effect just two coordination sites on the benzene. Each of the two faces of the benzene ring provides one coordination site. Furthermore, the approach of the second silver ion is opposed by the electrostatic repulsion between two mono-positive ions. Thus, if it is assumed that the only interaction between the silver ions is electrostatic, the Kirkwood theory can be adapted to the treatment of the argentation constants of benzene, with the use of the same statistical factor, 4. Then Equation 7 may be used to calculate a value for the distance between the two silver ions in the di-silver complex.

If the theory is applied to the polycyclic hydrocarbons, the parallel with the dibasic acids is not as complete. The two silver ions do not necessarily have equivalent positions, and the value of the statistical factor is not so unequivocal. In the case of naphthalene, if it is assumed that coordination at each face of a ring is independent of the other faces, then the statistical number is $\frac{4}{1}x\frac{2}{3} = 2.67$, since the first silver can attach itself at any of four faces and leave from one position, while the second silver can attach at any of three faces and leave from either of two positions. Applying these principles and using the Kirkwood theory which assumes the molecule to be spherical with the charged atoms at the ends of a diameter (this corresponds to a value of 127 for D_e), the distances between the silver ions in a number of di-silver complexes were calculated. The results are given in Table VIII.

As mentioned earlier, the X-ray crystal structure determination of the benzene-silver perchlorate complex indicates that the silver ions are located above the plane of the benzene and between two carbon atoms with a carbon-silver distance of 2.6 Å. If it is assumed that in solution the two silver ions coordinate on opposite faces of the benzene about 2.5 Å from the plane of symmetry as indicated by the X-ray data and on opposite sides of the six-fold axis, then the distance between these atoms will be 5.2 Å. For naphthalene the silver ions would be separated by a minimum distance of 5.2 Å if they were on opposite sides of the same benz-ring

Table VIII

Calculated Silver-silver Distances in Di-silver Complexes of Aromatic-silver Nitrate Complexes

Aromatic compound	$\underline{K}_1$	$\underline{K}_2$	Stat. factor	$\underline{K}_1/\underline{K}_2$	Calc'd Dist. $\underline{r}$ cm. x 10^8		Estd. Dist.
					d	e	f
Benzene[a]	2.41	0.212	4	11.4	4.22		5.2
Toluene[b]	2.63	.23	4	11.4	4.22		5.2
o-Xylene[a]	2.89	.315	4	9.18	5.32		5.2
m-Xylene[a]	3.03	.320	4	9.47	5.12		5.2
p-Xylene[a]	2.63	.331	4	7.95	6.44		5.2
Naphthalene[c]	2.94	.909	2.67	3.23	23.1	9.2	5.2-6.5
Biphenyl[a]	3.94	1.01	2.67	3.90	11.7	6.6	5.2-7.8
Diphenyl-methane[a]	3.46	1.04	2.67	3.33	19.8	8.7	
Phenanthrene[c]	3.55	.99	2.40	3.59	11.0	7.6	5.2-7.5

a. Argentation constants from reference 13.
b. Argentation constants from reference 12.
c. Argentation constants from this thesis.
d. Distances calculated using the theory of Kirkwood (33) with statistical factors given in column 4.
e. As in note (d) but using statistical factor 2.0.
f. Minimum and maximum distances estimated on the basis of approximate X-ray crystal structure data (31).

and by a maximum distance of 6.5 Å if they were on opposite sides of the molecule and attached to different benz-rings. Similarly minimum and maximum distances may be estimated for other polycyclic compounds and these are tabulated in the last column of Table VIII. Comparison of these estimated distances with those calculated from the ratio $\underline{K}_1/\underline{K}_2$ reveals in the case of benzene and its methyl homologs fairly good agreement, in view of the approximations involved in applying the Kirkwood theory to aromatic hydrocarbons. However, the agreement is poor in the case of the polycyclic hydrocarbons. The magnitudes of the second argentation constants for these compounds are considerably greater than would be expected on the basis of the approximate statistical factors and the electrostatic repulsion energy.

The deviations from the Kirkwood theory by the polycyclic aromatic hydrocarbons may be the result of one or more of several factors. First, the approximations made here in applying the theory to these compounds are not very accurate. For example, these compounds do not have spherical molecules and also the two coordination sites are not necessarily equivalent. However, since there is fairly good agreement in the case of the benzenes, the large deviation from theory in the case of naphthalene must also involve other factors.

A second possible factor in deviations from the Kirkwood theory by the polycyclic compounds is error in the statistical factors recorded in Table VII. These statistical factors were computed on the basis of the very approximate assumption that each free face of a benzene ring has equal potentiality as a site for coordination, independent of the situation at other ring faces. If it is assumed instead that the first silver ion can coordinate on either side of a planar aromatic molecule and that the second silver must coordinate on the other side at a non-equivalent position, the statistical factor might conceivably have the value 2. If the value 2 is used for the four polycyclic compounds listed in Table VIII, the four calculated distances recorded in column 7 of Table VIII are obtained. Most of these values fall in the correct range, but it is not clear that the symmetry number 2 should be used for these compounds.

A third factor in the deviation from the Kirkwood theory may be resonance interaction between two silver ions coordinated to the same aromatic molecule. If the valence bond electronic resonance structures are counted for the mono- and di-silver complexes of benzene and naphthalene, neglecting structures involving positive charges on adjacent carbon atoms, the resulting totals are: for benzene, 8 and 18; and for naphthalene, 15 and 50 resonance structures, respectively, for the mono- and di-silver complexes. Thus the greater resonance stabilization would be expected for the di-silver relative to the mono-silver complex in the case of naphthalene than in the case of benzene. This would cause the second argentation constant to be larger relative to the first than it would be in the absence of resonance. Therefore, the effect of resonance upon silver-ion binding energies for the polycyclic compounds would result in the calculation of large values for silver-silver distances by use of the Kirkwood theory, which Table VIII shows to be the case.

The deviation of the ratios of the first to the second argentation constant for polycyclic compounds from the values predicted on the basis of electrostatic repulsion energy probably results from the influence of several factors. It is not possible with present knowledge to mediate between these effects, but resonance interaction in the di-silver complexes is probably important.

d. Relative Values of the Argentation Constants for Anthracene and Phenanthrene.

The relative magnitudes of the first argentation constants of anthracene and phenanthrene pose an interesting problem. The values obtained for $\underline{K}_1$ in the aqueous methanol system are for anthracene, 1.35, and for phenanthrene, 1.09. The 9,10-bond of phenanthrene is generally considered to have greater double-bond character than the 1,2-bond of anthracene, since it exhibits greater reactivity toward double-bond reagents, such as bromine. Furthermore, simple valence bond calculations assign a double-bond character of 3/4 to the anthracene bond and 4/5 to the phenanthrene bond (34). Therefore phenanthrene would be expected to have the greater affinity for the electrophilic silver ion.

The explanation for this apparent anomaly may lie in an entropy factor in the free energy for the argentation reaction of anthracene. Since anthracene possesses four ring faces which contain a 1,2-bond whereas phenanthrene has only two ring faces which have the 9,10-bond, it is reasonable then that anthracene should have a larger argentation constant relative to phenanthrene than would be predicted from consideration of bond energy alone. Evidence concerning this hypothesis could be obtained by measuring the temperature coefficient of the argentation constants of the two compounds, from which the heat and entropy of the argentation reactions could be calculated. This could be done in the aqueous system for phenanthrene, but, as was noted elsewhere, attempted solubility measurements with anthracene in the aqueous system were exceedingly erratic. On the other hand, with the present techniques, the values of argentation constants for the aqueous methanol system are not considered to be sufficiently accurate to make possible a dependable measurement of the temperature coefficient.

e. Estimation of Bond Strengths for the Argentation Complexes.

The determination of the argentation constants of naphthalene at three different temperatures in the aqueous system as reported in Table IV makes possible the calculation of the entropy and heat of the argentation reaction. The relation which is used is the familiar van't Hoff equation, expressed in the form:

$$d(\ln \underline{K})/d(1/T) = -\Delta \underline{H}/\underline{R} \qquad (8)$$

This equation indicates that over a temperature range for which $\Delta \underline{H}$ is constant a plot of the logarithm of $\underline{K}$ versus $1/T$ should be a straight line with the slope equal to $-\Delta \underline{H}/\underline{R}$. The plot in Figure 4 shows that the first and second argentation constants of naphthalene obey this relationship well within the limits of probable error of the calculated values of the constants. The resulting thermodynamic information for naphthalene at 25° C. in the aqueous system are given in Table IX.

The value of the heat of the first argentation reaction, 2.9 kcal., is of the same order of magnitude as that reported for the argentation of cyclohexene in the aqueous system, 6.0 kcal. (29), and that reported for the heat of formation of the benzene complex with silver perchlorate in an anhydrous system, 8.1 kcal. (35). The energy of hydration of silver ion is about 111 kcal. (36). If the coordination number of silver ion with water molecules is four (37), then coordination of hydrated silver ion with a naphthalene molecule must involve the displacement of at least

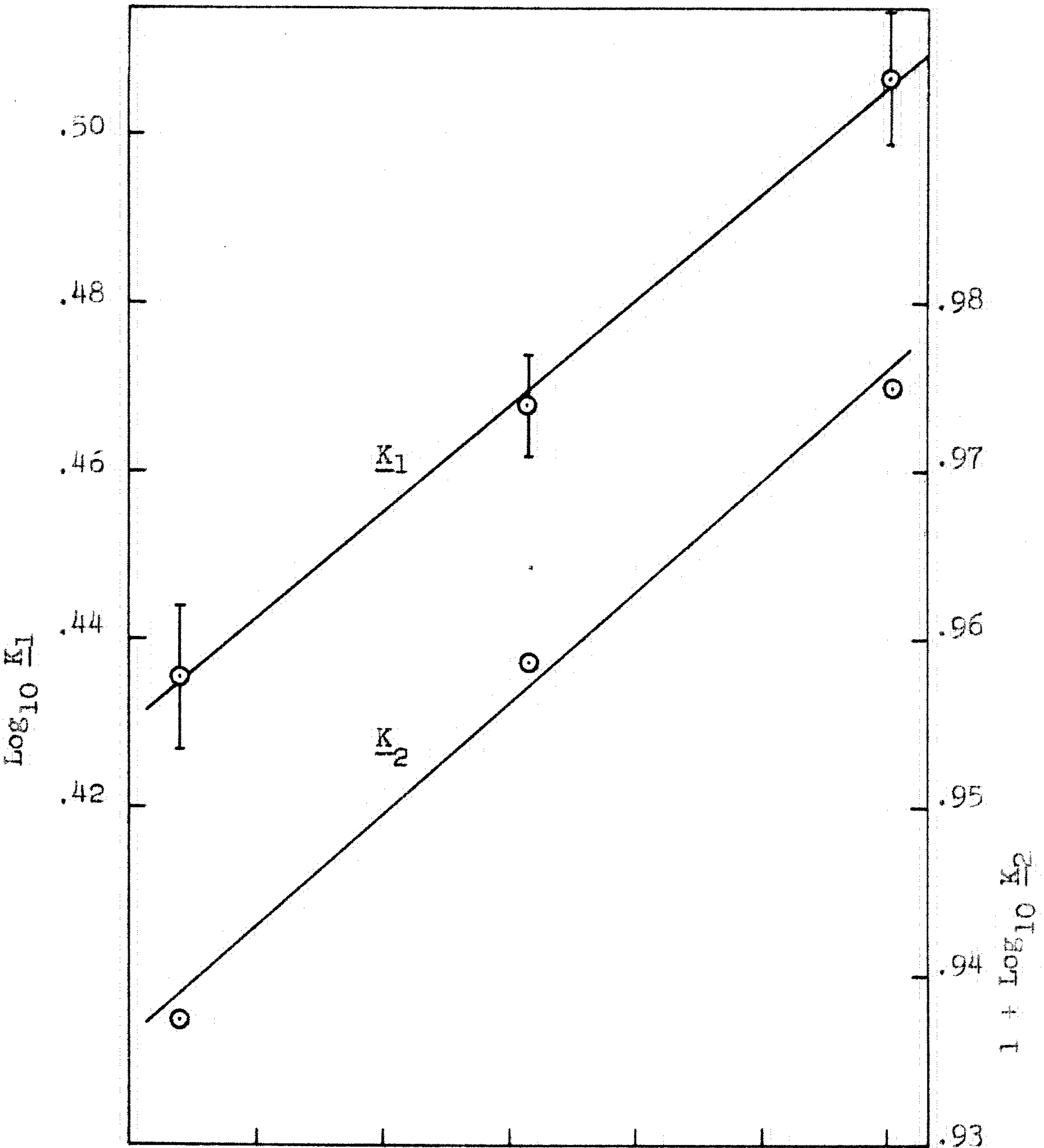

Figure 4. Argentation of naphthalene in aqueous medium: variation of first and second argentation constants with temperature. The vertical bars represent the estimated limits of probable error of the calculated constants. The calculated thermodynamic information is given in Table IX.

Table IX

Thermodynamic Data for the Argentation of Naphthalene in the Aqueous System at 25° C.

	$\Delta \underline{F}$ Cal./mole	$\Delta \underline{H}$ Cal./mole	$\Delta \underline{S}$ Cal./mole.deg.
First argentation reaction	-638 ± 8	-2900 ± 200	-7.5 ± 1.3
Second argentation reaction	+56.4	-1520	-5.3

one water molecule which would require an energy expenditure of about 25 kcal. Since the argentation of naphthalene by aqueous silver nitrate is just slightly exothermic, the bonding energy between silver ion and naphthalene must be of the same order of magnitude, about 25 kcal. The data available for the cyclohexene complex and the benzene-silver perchlorate complex also indicate a bonding energy of about 25 kcal. for the silver ion π-complex, assuming a silver ion-hydration number of four (35).

The preceding considerations indicate that the silver-ion π-bond is a bond of moderate strength. It can be seen, furthermore, that as a result of the affinity of silver ion for water and other oxygenated solvents, the extent of the argentation reaction may be expected to be much more limited in water than in anhydrous hydrocarbon solvents. This conclusion is in agreement with observation.

CORRELATIONS OF EXPERIMENTAL AND THEORETICAL CHEMICAL DATA WITH BIOLOGICAL ACTIVITY

Previous Work.

Only two investigations are reported in the literature in which the chemical reactivities of the members of a series of carcinogenic and non-carcinogenic hydrocarbons toward a particular reagent were determined quantitatively. The rates of addition of osmium tetroxide to the members of a series of polycyclic aromatic compounds in chloroform solution were measured by Badger (5). The reagent adds to the *meso*-bond of the hydrocarbon molecule to form a cyclic ester which can be hydrolyzed to the corresponding dihydrodiol. There is a significant correlation between the rate of this addition reaction and the relative potencies of the compounds investigated, as may be seen from the data in Table X.

A different type of reaction was investigated by Newman and his co-workers, who measured the dissociation constants in chloroform solution of the trinitrofluorenone complexes of the complete series of monomethylbenz(a)anthracenes and benzo(c)phenanthrenes (4). The results of this investigation, also included in Table IX, exhibit no satisfactory correlation with carcinogenic potency. If there were correlation, the most potent carcinogens would be expected to have the smallest dissociation constants. Another reaction of polycyclic aromatic hydrocarbons, investigated semi-quantitatively by Fieser, is the coupling reaction with p-nitrobenzene-diazonium chloride (36). The rate of this reaction is greatest with several of the most powerful carcinogens, but it is equally high with several non-carcinogenic ace-compounds and shows a strong degree of specificity for ace-compounds. Therefore, the overall correlation of this coupling reaction with carcinogenicity is rather poor.

Table of Correlations.

The hydrocarbons studied in the present investigation are listed in Table X in order of decreasing order of magnitude of their first argentation constants, and there are tabulated the values of the argentation constants, the rate of addition of osmium tetroxide, the values of the dissociation constants of the trinitrofluorenone complexes, the relative carcinogenic potencies, and the two quantum mechanical indices of electronic properties at the *meso*-bond. In the first group are compounds which contain the benz(a)anthracene structure, in the second group are two common tri-cyclic hydrocarbons, and in the third group are the benzo(c)phenanthrenes. This separation is made for two reasons. First factors of general molecular shape and size are undoubtedly important, in addition to electronic characteristics, in determining carcinogenic potency. Second, the benzo(c)-phenanthrenes have not been studied as thoroughly with re-

Table X

Comparison of Chemical, Biological, and Theoretical Data

Compound	K_1 (a)	Rate OsO_4 (b) x 10^3	TNF(c) Dissoctn. x 10^2	Carc. Skin	Pot.(d) Subcutaneous	P.E.(3)	Q(f)
3-Mechol.	3.31	1.1		++++	++++		1.330
7-12-DBA	1.87	2.7		+++	++++		1.319
Benz-pyr.	1.69	.94		++++	++++		
7-MBA.	1.66	.91	2.28	+++	++++	3.3006	1.306
DBA.	1.65	.64		++	++		
12-MBA.	1.64		1.89	++	+++	3.3146	1.296
8-	1.41		4.50	++	++	3.3213	1.296
6-	1.35		1.23	+	++		1.298
11-	1.35		2.31	+	0	3.3248	1.292
3-	1.34		2.86	0		3.3265	
BA.	1.33	.48	3.34	0	0(g)	3.3282	1.283
9-MBA.	1.32	.64	1.89	+		3.3248	1.294
5-	1.25		2.60	+	++		1.298
10-	1.25		1.92	+	+	3.3213	1.294
2-	1.23		4.38	0		3.3146	
Anthrac.	1.35			0	0		
Phenanth.	1.09	($\ll$ .48)		0	0		
4-MBP.	1.39		4.29	+	0		1.305
3-	1.37		8.63	+	0		1.304
1-	1.34		17.1				
5-	1.30		5.8	+++	+		1.312

Table X. (continued)

Compound	K (a)	Rate OsO_4(b) x 10^3	TNF(c) Dissoctn. x 10^2	Carc. Skin	Pot.(d) Subcutaneous	P.E.(e)	Q(f)
BP.	1.30		9.83	+	0		1.293
6-MBP.	1.29		5.24	++	0		1.310
2-	1.19		4.96	+	+		1.312

(a) Equilibrium constant for coordination reaction of hydrocarbons with silver ion at 25° C. in equimolal aqueous methanol containing $NaNO_3$ and $AgNO_3$ at ionic strength 0.5.
(b) Rate of addition to hydrocarbons of OsO_4 in $CHCl_3$ as determined by Badger (5).
(c) Dissociation constants of hydrocarbon complexes with 2,4,-7-trinitrofluorenone in $CHCl_3$ at 25° C. as determined by Takemura and co-workers (4).
(d) Relative carcinogenic potencies in mice, compiled by Badger (9c).
(e) Polarization energy of the meso-bond carbon atoms involving hyperconjugation with methyl groups, calculated by Pullman and co-workers using a molecular orbital method (7b).
(f) Total charge at meso-bond, calculated by Pullman using a valence bond method (6).
(g) Benz(a)anthracene has been shown recently to possess a low carcinogenic potency when applied in relatively large subcutaneous injections in mice (39).

spect to carcinogenic potency as have most members of the benz(a)anthracene series. It is reported that carefully standardized studies of the carcinogenic potencies of the benzanthracenes and benzophenanthrenes are now being carried out at two institutions (4).

Discussion of Correlations.

The information in Table X reveals a definite correlation between the argentation constants and the relative carcinogenic potencies in the benzanthracene series. The most noticeable discrepencies in this agreement are for the compounds 1,2,5,6-dibenzanthracene, 5-methylbenz(a)anthracene, and anthracene. In the case of dibenzanthracene experimental difficulties were encountered, including formation of yellow contaminants and erratic results, so the argentation constant reported is the result of just one experimental determination which seemed to give the most consistent data. However, it is interesting that a statistical factor may explain the high argentation constant of dibenzanthracene just as has been suggested previously for anthracene, since both of these molecules possess two equivalent benz rings having theoretically high π-electron concentrations. On the other hand the 5-methyl compound has a methyl group attached to one of the meso-bond carbon atoms which may hinder the approach of a silver ion and thereby decrease the value of the argentation constant.

From the preceding considerations it appears possible that the heats of the argentation reactions might exhibit a more complete correlation with carcinogenic potencies than do the argentation constants, which are a measure of the free energy of reaction.

A fair correlation is evident in Table IX between the argentation constants and the rate of addition of osmium tetroxide. In contrast, there is no significant agreement between the argentation constants and the TNF-complex dissociation constants. The reason for this relationship must lie not in the solvent, but rather in the site and character of the chemical interaction. The argentation reaction and the addition of osmium tetroxide are both believed to take place at the <u>meso</u>-bond. The complex compounds which aromatic hydrocarbons form with picric acid and trinitrofluorene are considered to involve interaction between many points on the molecules with their planes oriented parallel and in close contact (40). Although the electronic characteristics are important for such interaction, steric factors may and undoubtedly do become dominant (40). Thus the correlation between argentation constants and rates of addition of osmium tetroxide provides additional support for the hypothesis that the first argentation reaction takes place at the <u>meso</u>-bond of polycyclic aromatic hydrocarbons.

Finally, it may be observed that there is a significant correlation between carcinogenic potencies and the quantum mechanically calculated electronic characteristics at the meso-bond. Coulson has discussed the quantum mechanical calculations made for polycyclic aromatic hydrocarbons and has pointed out the approximations involved and the partial agreements of results calculated by different methods (8). If an adequate theory is devised for these molecules, it will almost certainly be semi-empirical in its practical application.

At this point the validity of the relative carcinogenic potencies used in Table X should be considered. The indices used were set up by G. M. Badger (9c) and are considered by the writer to be the most prudent and sensible attempt to reduce the maze of available experimental data to a scale of relative potencies. In over-all relationships this scale agrees with the two other scales which have been proposed (9a,b), but it differs from them in that it divides carcinogenic compounds into only four classes or magnitudes of potency instead of using ten magnitudes or a continuous index. This degree of definition is commensurate with the accuracy and reproducibility in the results of bio-assay methods using mice. Further factors which limit the dependability of potency indices are the fact that in devising such an index both the latent time for tumor initiation and also the total yield of tumors must be considered, and the fact that different tissues show different orders of potency as can be seen from the two scales given in Table X.

In view of the probable errors in the argentation constants reported in this thesis and the degree of reproducibility and validity of the indices of carcinogenic potency, this writer believes that the correlation shown in Table X is as complete as can be expected. In fact, even if a much more accurate method is found for measuring the relative nucleophilic character of the hydrocarbons, because of the uncertainties in the biological data, it is doubtful whether a more complete correlation can be obtained, assuming that nucleophilic character and carcinogenic potency are directly related.

Relation of the Magnitude of Argentation Constants to the Mode of Action of Carcinogens.

It is not the province of this thesis to make an extended discussion of the biochemical mechanism of carcinogenesis by hydrocarbons. However, a brief presentation of some of the more recent evidences and theories bearing on the carcinogenic mechanism will help to suggest the possible significance of the findings of this thesis.

To recapitulate, it was concluded in the preceding section that there is a definite correlation between the magnitude of the argentation constants and the biological potencies of the carcinogenic hydrocarbons. Furthermore, it was noted that there appears to be a significant degree of correlation between the argentation constants and the rates of irreversible addition of osmium tetroxide (5).

There is good evidence also for the reversible formation by these hydrocarbons of complexes with substances found in living cells. Weil-Malherbe measured quantitatively the solubilization of a number of polycyclic hydrocarbons in dilute aqueous solutions of a large number of purines and pyrimidines and also isolated some solid complexes (41). The data from that investigation indicates the formation by the hydrocarbons of both mono- and di-purine complexes. When the data of Weil-Malherbe is combined with the estimated aqueous solubilities from the information in Tables III and IV of this thesis, it is possible to calculate approximate values of equilibrium constants for the formation of di-caffeine complexes by the hydrocarbons phenanthrene, anthracene, benz(a)-anthracene, benzo(a)pyrene, 7,12-dimethylbenz(a)anthracene, and 3-methylcholanthrene. The values of the constants obtained, in units of liters^2 moles^{-2} are 3.9×10^4, 7.2×10^5, 7.5×10^5, 2.8×10^6, 3.4×10^4, and 7.5×10^4, respectively. Thus the formation of purine complexes is well established, but it can be seen there is no satisfactory correlation of the equilibrium constants with the carcinogenic potencies of these hydrocarbons.

E. Boyland in a recent review dealing with the possible modes of action of carcinogens mentioned the results of an investigation which showed that in vitreo aqueous solutions of nucleic acid also dissolve polycyclic hydrocarbons and aromatic amines (42). Actual experiments in vivo were carried out in mice by E. C. Miller and J. A. Miller who demonstrated the formation of a tightly-bound complex of benzo(a)-pyrene with proteins and nucleoproteins in mouse skin (43), and also by 4-dimethylaminoazobenzene and related compounds with proteins in mouse liver (44). A more conclusive investigation was performed by Wiest and Heidelberger who demonstrated the formation in vivo of tightly-bound complexes by dibenzanthracene-9,10-C^{14} with proteins and nucleoproteins but not with nucleic acids (45).

Another type of information which is significant concerns the mutual inhibition and summation effects of some of the carcinogenic hydrocarbons (46, 39). The administration to mice of a mixture of two strong carcinogens or of two weak carcinogens produces an effect which is equal to a partial summation of the effects of the two substances administered separately. On the other hand, the administration of a mixture of a strong and a weak carcinogen produces an effect which is a great deal less than that of the strong carcinogen administered alone.

A number of mechanisms which postulate the initial formation of complexes have been proposed for carcinogenesis by hydrocarbons. These theories are still largely speculative, but from the information recorded above it may be concluded that there is now good experimental evidence to suggest that the initial action of carcinogenic hydrocarbons is the formation of some type of complex compound with a cell component. R. Daudel postulated the formation of a complex with a substrate which controls cell division (47). L. A. Pinck postulated the formation in vivo by the hydrocarbon of a very reactive double bond which can react with a cell constituent by a reaction which he compares with a Michael condensation (48). Boyland proposes that the hydrocarbons induce mutations by forming a loose complex with and thus bringing about an alteration of chromosomal desoxyribose nucleic acid (42). The most recent theory is that proposed by Wiest, Heidelberger, and Miller who suggest that the hydrocarbon enters the cell where it is first metabolized to a derivative which unites with certain cell proteins and eventually gives rise to cells which lack some proteins and are not subject to bodily growth controls (43, 44, 45).

The findings of the present investigation which show a correlation between the argentation constants and carcinogenic activity provide evidence that the characteristic property required for the initial step in carcinogenesis is a region having a high π-electron density. Such a region would enable the hydrocarbon to react reversibly to form a complex with an electrophilic cell component. Subsequent irreversible reactions might then lead to the metabolizing of the hydrocarbon or the direct formation of a more stable complex with a cell component.

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PROPOSITIONS

1. The compound benzyltrimethylammonium iodide undergoes rapid rearrangement in liquid ammonia in the presence of sodamide to produce dimethyl-o-xylylamine (1). This rearrangement has been shown to take place by means of attack upon the ortho position by an N-methide carbanion via a cyclic transition state. It is proposed that the reaction of o-chlorobenzyltrimethylammonium iodide in the same medium be examined for possible formation of the stable compound N,N-dimethyldihydroisoindolinium iodide (2). Nucleophilic displacement of aromatic halogen by carbanions in liquid ammonia occurs easily (3).

2. Nucleophilic displacement of aliphatic halogen atoms by N-methide carbanions which takes place in ether (4) should be investigated in the ammonia system. The compound o-chloromethylbenzyltrimethylammonium iodide may undergo such an intramolecular displacement reaction to produce N,N-dimethyltetrahydroisoquinolinium iodide. Interesting questions concerning relative rates of competing reactions would be involved in this system.

3. In recent years a number of studies have been made of physical and chemical properties of cis- and trans-diiodoethylenes (5). The high-melting trans isomer has been obtained pure, but as yet the pure cis isomer is not available, since fractional crystallization yields the eutectic mixture

containing about eighty percent of the *cis* compound (5b). Andrews and Keefer determined the argentation constants of the *trans* isomer and of the eutectic mixture to be 5.5 and 17.8, respectively (5a). It is proposed that extraction of the eutectic mixture with aqueous methanolic silver nitrate, coupled with fractional crystallization be used to obtain pure *cis*-diiodoethylene.

4. Cristol, *et al*., have suggested that *trans* elimination reactions proceed by a one-step concerted mechanism, and that *cis* elimination involves the formation of an intermediate carbanion (6). Miller and Noyes have studied the basic elimination reactions of *cis*- and *trans*-diiodoethylene in methanolic sodium methoxide and have obtained results consistent with this view (7), and they cite one additional item of supporting evidence from the literature (8). It is proposed that a study of deuterium-hydrogen exchange in the basic elimination reaction of the *cis* and *trans* isomers of dideuterodiiodoethylene would provide evidence concerning the formation of an intermediate carbanion.

5. Recently the compound diazocyclopentadiene has been prepared by the reaction of *p*-toluenesulfonylazide with cyclopentadienyllithium (9). It should be possible to prepare 3-diazo-1,4-pentadiene by the analogous reaction of 1,4-pentadienyllithium (10).

6. The hydration of 3-hexyne catalyzed by mercuric sulfate

and sulfuric acid requires further investigation. The catalytic effect of the hexanone-mercuric sulfate complex (11) could be established by adding 3-hexyne to a solution of the complex and observing any hydration which takes place. A possible analytical method for following the hydration reaction is extraction of portions of the reaction mixture with an organic solvent in which the ketone concentration could be measured spectrophotometrically.

7. The compound trifluoromethylacetylene undergoes hydration catalyzed by mercuric sulfate and sulfuric acid to form the ketone and the aldehyde, ketone being the predominant product (12). The compound hexafluoro-2-butyne reacts with sodium acetate in acetic anhydride to form the acetal which hydrolyzes to the ketone (13). With sodium ethoxide the acetal is produced which hydrolyzes to form the ketone (14). The hydration of hexafluoro-2-butyne catalyzed by mercuric sulfate and sulfuric acid should be investigated.

8. By measuring the argentation constant of naphthalene at ionic strengths approaching zero as has been done at unit ionic strength (15) it would be possible to determine the variation with ionic strength of the activity coefficient of the mono-silver complex.

9. Simple valence bond theory (16) gives the following values of double bond character: naphthalene(1-2 bond) 2/3, anthracene(1-2 bond) 3/4, phenanthrene(9-10 bond) 4/5. How-

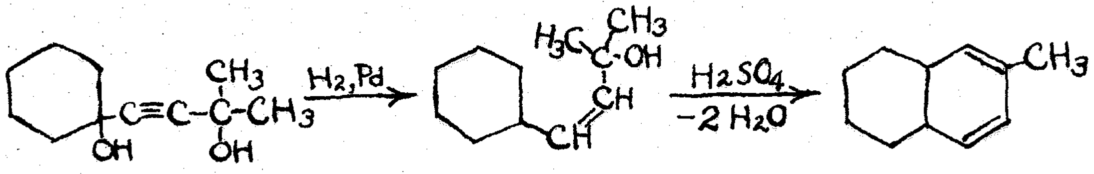
ever, the values of the first argentation constants in the aqueous system at unit ionic strength are 2.94, 4.35, and 3.55, respectively (17). It is proposed that this discrepancy is the result of a statistical factor which would become apparent in the entropy of argentation determined by measurement of the temperature coefficients of the argentation reactions.

10. The vic diiodo alkanes are somewhat unstable compounds which slowly decompose on standing to yield free iodine and olefin (18). It is proposed that addition of iodine to a rigid cyclic olefin such as 1,4,4a,5,6,7,8,8a-octahydronaphthalene would yield a trans diiodide which would be more stable than acyclic vic diiodides (19).

11. The reaction of chlorobenzene-1-C^{14} with potassium amide in liquid ammonia results in the formation of nearly equal amounts of aniline-1-C^{14} and aniline-2-C^{14} (20). The displacement of chloride ion from chlorobenzene by carbanions in the same system (3) should be investigated using chlorobenzene-1-C^{14} to see if a similar rearrangement occurs.

12. It is proposed that certain substituted bicyclic and tricyclic dienes may be synthesized by the dehydration and cyclization with sulfuric acid of substituted 1,4-dihydroxy-2-butenes which are available by catalytic hydrogenation (21) of the corresponding butynediols obtained by the condensation of acetylene with ketones (22). An example would be

the preparation of 5,6,7,8,8a,4a-hexahydro-2-methylnaphthalene by the following reactions:



13. It would be desirable for undergraduate organic chemistry laboratory courses to give the student practical experience with a greater range of reactions and compounds than has hitherto been possible. This might be accomplished with economy in both time and materials by the use of simplified semimicro procedures for the preparation of 100- to 500-milligram quantities such as are currently used in qualitative analysis (23).

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