KINETICS AND MECHANISM OF IODINATION
OF 1-METHYLPYRAZOLE

by

Gary L. Jewett

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I. INTRODUCTION

The kinetic studies on pyrazole (I) in this laboratory[1] suggested a study of substituted pyrazoles to determine the effect of substituents on the relative rates of iodination. The compound chosen for this study was 1-methylpyrazole (II).
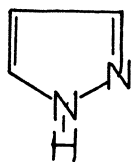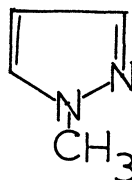
I   II

Electrophilic substitution takes place at only a single position in pyrazole which is unlike the other nitrogen heterocyclic compounds imidazole and pyrrole.

Some very interesting effects were expected due to the fact that an ionizable hydrogen atom was replaced by an unionizable methyl group.

The primary interest in this research was to determine a mechanism for an electrophilic substitution reaction on a 1-substituted pyrazole. There was also a strong interest to determine the dependence of the rate of iodination upon the hydrogen ion concentration.

Other interests lay in adding qualitative information to the relative reactivities of heterocyclic compounds.

II. HISTORICAL

A. Electrophilic Substitution Reactions
of Pyrazole and 1-Substituted Pyrazoles

Electrophilic substitutions in pyrazole, such as sulfonation, nitration, chlorination, and bromination involve the four position[2,3,4,5]. However, other positions may be attacked under more stringent conditions.

Electrophilic substitutions in one-substituted pyrazoles also involve the four position. This fact indicates that the four position is still the most reactive in one substituted pyrazoles[6].

1-Benzyl-4-bromopyrazole was obtained by treating 1-benzylpyrazole with bromine in chloroform[7].

Huttel, Schafer, and Jochum[8] obtained 1-methyl-4-iodopyrazole by treating 1-methylpyrazole in sodium acetate solution with an aqueous solution containing iodine and potassium iodide, and refluxing the solution for one-half hour. There was, however, another product obtained with the empirical formula $C_4H_5N_2I \cdot C_4H_4N_2I_2$. No structure was given for this compound, but it was thought to be a mixture of a mono- and a di-substituted pyrazole. The empirical

formula also applies to the hydrogen iodide salt of two coupled mono-substituted pyrazoles.

Halogenation of 1-phenylpyrazole introduces the halogen in position four[9,10,11].

Finar and Godfrey[12] obtained 4-chloromethyl-1-phenylpyrazole by treating 1-phenylpyrazole with paraformaldehyde, zinc chloride, and gaseous hydrogen chloride.

B. Some Kinetic Studies of Iodination of Aromatic Substrates

Lambert[1] has shown that in the iodination of pyrazole the rate law is given by the following equation

$$(1) \qquad -\frac{d(Py)}{dt} = \frac{k_1 k_2 K_2 K_3 (H_2O)(Py)(I_3^-)}{k_{-1}K_1 \ (H^+)(I^-)^2}$$

$$+ \frac{k_1 k_3 K_2 K_3 (Py)(HPO_4^=)(I_3^-)}{k_{-1}K_1 \ \ (H^+)(I^-)^2}$$

where (Py) is the concentration of pyrazole and (H^+) is the hydrogen ion concentration.

The rate law is consistent with the reaction between the pyrazolate anion and the iodinium ion.

3-Methylpyrazole[13] has been shown to have the same rate law. The rate for the iodination of 3-methylpyrazole is approximately forty-one times faster than the rate of iodination of pyrazole. The measurement of the activation energy of the two compounds shows that the rate for 3-methylpyrazole should be approximately one thousand times faster than the rate for pyrazole. However, the dissociation constant for pyrazole and 3-methylpyrazole have been estimated and it is found that the ratio of the constants is 7:1, respectively. Since the concentration of the anion of pyrazole is seven times as great as the concentration of the 3-methylpyrazolate anion, it is expected that the rate for 3-methylpyrazole would be about one seventh that expected for pyrazole. Considering both activation energy and acid dissociation, 3-methylpyrazole should iodinate about one hundred times faster than pyrazole, in line with experimental observation.

Doak and Corwin[14] used a high ratio of iodine to iodide in the study of pyrroles and found

that the major iodinating species was free iodine. The
other iodinating species was thought to be hypoiodous
acid. However, no buffer variations were done on the
system and so neither the rate determining step nor the
dependence of the reaction on hydrogen ion was
determined. Therefore, the second iodinating species
may have been the iodinium ion. This would give the
same order in the rate law with respect to iodide, but
would give no dependence on the hydrogen ion for
N-substituted pyrroles.

Berliner[15] suggested that the only possible
species in the iodination of aniline is the iodinium
ion. The rate law is given by the equation

$$(2) \qquad -\frac{dAn}{dt} = \frac{k(An)(I_3^-)}{(I^-)^2} + \frac{k'(An)(I_3^-)(B^=)}{(I^-)^2}$$

where (An) is the concentration of aniline and (B$^=$)
is the concentration of the acetate ion or the
hydrogen phosphate ion in buffered solutions.

Hypoiodous acid could have been the iodinating
agent but was discarded because of the product formed
in the reaction.

Ridd[16] studied the iodination of imidazole and found that the rate law was of the form

$$(3) \quad -\frac{dIm}{dt} = \frac{k(Im)(I_3^-)}{(H^+)(I^-)^2} + \frac{k'(Im)^2(I_3^-)}{(H^+)(I^-)^2}$$

where (Im) is the concentration of imidazole and (H^+) is the hydrogen ion concentration.

Since the square of the imidazole concentration occurs in the rate law, it was thought that 1-iodo-imidazole was formed first and that this species then iodinated another molecule of imidazole.

Soper and Smith[17] studied the iodination of phenol. Painter and Soper[18] re-examined the reaction and found that the complete rate law could be given by

$$(4) \quad -\frac{dPhOH}{dt} = \frac{k(PhOH)(I_3^-)}{(H^+)(I^-)^2} + \frac{k'(PhOH)(I_3^-)(H_2PO_4^-)}{(H^+)^2(I^-)^2}$$

where (PhOH) is the concentration of phenol and (H^+) is the concentration of hydrogen ion.

Lambert[1] has shown that the rate laws for iodination of phenol and imidazole can be explained by considering the iodinium ion as the iodinating agent.

The square of the iodide concentration in the rate law of phenol was attributed to the attack by the iodinium ion. The hydrogen ion dependence was due to the reaction of the iodinium ion with the phenolate or imidazolate anion.

The square of the imidazole concentration in the rate law for imidazole iodination was thought to be due to imidazole acting as a base. Since the reaction was run in an unbuffered solution, it was thought that imidazole was removing the hydrogen from the reaction intermediate.

It appears that the majority of iodination reactions can be explained on the basis that the iodinating species is either free iodine or the iodinium ion. This may be confirmed by iodination of N-substituted pyrroles, imidazoles, and pyrazoles, which should show no dependence on the hydrogen ion concentration if iodine and/or the iodinium ion is the iodinating agent.

III. EXPERIMENTAL

A. Preparation of Reagents

1-Methylpyrazole was prepared by the method of Dedicher[19]. Twenty grams of pyrazole, eighty four grams of methyl iodide and one hundred milliliters of ether were placed in an autoclave and heated, with stirring, at 120 °C for twelve hours. The compound isolated from the reaction mixture was the methyl iodide salt of 1-methylpyrazole. The salt was thermally decomposed and the products distilled into 6 M hydrochloric acid. The acid mixture was extracted three times with ether to remove impurities. The solution was then made basic and extracted three times with ether. The second extract was then dried over magnesium sulfate and distilled. A sixty percent yield of 1-methylpyrazole was obtained. A quantitative yield based upon the weight of the methyl iodide salt was obtained.

The purity of the 1-methylpyrazole was checked on a gas chromatograph and the chromatogram showed only a single peak. The boiling point was 127 °C and

the refractive index 1.4730 at 25 °C using ordinary white light.

All solutions were prepared using doubly distilled water. The water was prepared by re-distilling distilled water from an all glass still. The center fraction of the distilled water was collected.

All Kimax glassware was used without calibration. The solutions were prepared in volumetric flasks.

Solutions of mono-basic potassium phosphate and di-basic sodium phosphate were prepared from anhydrous Fisher certified reagent grade chemicals. The salts were dried for one hour at 120 °C and kept in a desiccator. The stock solutions of mono-basic potassium phosphate and di-basic sodium phosphate were 1.0000 M and .5130 M, respectively.

Reagent grade potassium iodide was stored in a desiccator for two days before use. Fisher resublimed iodine was again resublimed from potassium iodide, placed in a capped container, wrapped with aluminum foil, and kept in the dark. Solutions of iodine-iodide were wrapped in aluminum foil and kept for no more than

two days. Some solutions were titrated with a standard solution of National Bureau of Standards arsenous oxide. Stock solutions of iodine-iodide contained about 10^{-3} molar iodine and 2×10^{-2} molar iodide.

Reagent grade sodium nitrate was recrystallized twice from distilled water, dried for two days under vacuum, dried for six hours in an oven at 120 °C, redried under vacuum for one day, and stored in a desiccator.

B. Experimental Procedure

The Beckman DU spectrophotometer was used to measure rate constants. The instrument was equipped with a Beckman dual thermospacer set. The readings were taken at either 400 or 353 millimicrons with slit widths of .2 and .3, respectively. The rate constants are not dependent on the wavelength.

A measurement of the cell temperature was made by Lambert[1] and found to vary less than 0.05 °C from the thermostat temperature.

All times were taken with an electric timer.

Initially all glassware was cleaned with cleaning solution. As this was thought to be

unnecessary, a strong detergent was used thereafter.
The equipment was rinsed several times with tap water,
several times with distilled water, and a few times
with doubly distilled water, and placed in an oven
at 120 °C to dry.

Measured amounts of di-basic sodium phosphate,
mono-basic potassium phosphate, l-methylpyrazole,
sodium nitrate, and sufficient water to bring the
volume to 95 milliliters were placed in three 200
milliliter, round-bottom flasks. The flasks were
capped with aluminum foil and placed in the constant
temperature bath. The cell holder and cells were
placed in the thermospacers.

After having come to bath temperature, a flask
was removed from the bath and five milliliters of the
iodine-iodide solution was pipeted into the flask.
The timer was started when half of the iodine-iodide
solution was in the flask. A cell was removed from
the cell holder, rinsed four times with the reaction
mixture, filled, and returned to the cell holder.
This procedure took less than three minutes. The
flasks were removed from the bath in the order from
the longest half life to the shortest half life.

The instrument was standardized with a cell containing doubly distilled water before each reading. Readings were taken until two half lives had passed on fast reactions or until one half life had passed on slow reactions. The optical density at infinite time was recorded the next day.

The reaction flasks were capped with aluminum foil and allowed to stand overnight. The next day a Beckman Model G pH meter was standardized with commercial pH 7 buffer and the pH of the reaction solutions was recorded.

The pseudo-first order rate constants were obtained by plotting the logarithm of the optical density minus optical density at infinite time versus the time. The slope of the line multiplied by 2.303 gave the rate constant.

IV. DATA AND RESULTS

A. Precision and Accuracy of Results

The first order rate constants were obtained by a graphical method (Method I). The constants that were calculated from the integrated first-order rate equation (Method II) were in very good agreement with those obtained by Method I.

Second order constants were reproducible to 5% or less, which was thought to be quite good considering the concentrations of reagents needed to produce a reaction fast enough to measure.

Because of complications, it was necessary to use selected data for the various results obtained.[*]

B. Data from a Typical Run

To show the data from a typical run, Run VIII-2 was selected. The concentrations of reagents were: 9.550×10^{-4} M iodide, 2.955×10^{-5} M iodine, and 3.525×10^{-2} 1-methylpyrazole. The rate

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* See Appendix.

constants in Table I were calculated from the integrated first-order equation

$$k_1 = \frac{2.303}{t} \log \frac{D_o - D_{oo}}{D_t - D_{oo}}$$

where D_o is the optical density at an arbitrary starting time, t_o; D_t is the optical density at time t; D_{oo} is the optical density at the completion of the reaction, and t is the time in minutes.

Table I: Rate Constants from a Typical Run

Time, min.	$D_t - D_{oo}$	$k_1 \times 10^2$ min.$^{-1}$
0.00	.135	-
7.23	.110	2.84
10.40	.099	2.88
14.00	.089	2.88
18.73	.079	2.86
22.50	.071	2.86
26.87	.062	2.90
37.40	.047	2.83
43.00	.040	2.84

The average rate constant from Table I is 2.86×10^{-2} min.$^{-1}$, while the rate constant obtained by Method I is 2.88×10^{-2} min.$^{-1}$.

C. Variation of the Rate with

1-Methylpyrazole Concentration

This study was made at a temperature of 30 °C and an ionic strength of 1.000 molar. The concentrations of the other components were constant at values of: .8022 M sodium nitrate, 1.73 x 10^{-4} M iodine, 9.345 x 10^{-4} M potassium iodide, 4.925 x 10^{-2} M di-basic sodium phosphate, and 5.000 x 10^{-2} M mono-basic potassium phosphate. Sodium nitrate was used to adjust the ionic strength to the desired value.

The observed rate constant is plotted versus the 1-methylpyrazole concentration (Figure 1). The straight line passing through the origin shows that the rate is directly dependent on the 1-methylpyrazole concentration. The second order rate constants obtained by dividing the observed rate constant by the 1-methylpyrazole concentration (Table II) show that the rate is directly dependent on the 1-methylpyrazole concentration.
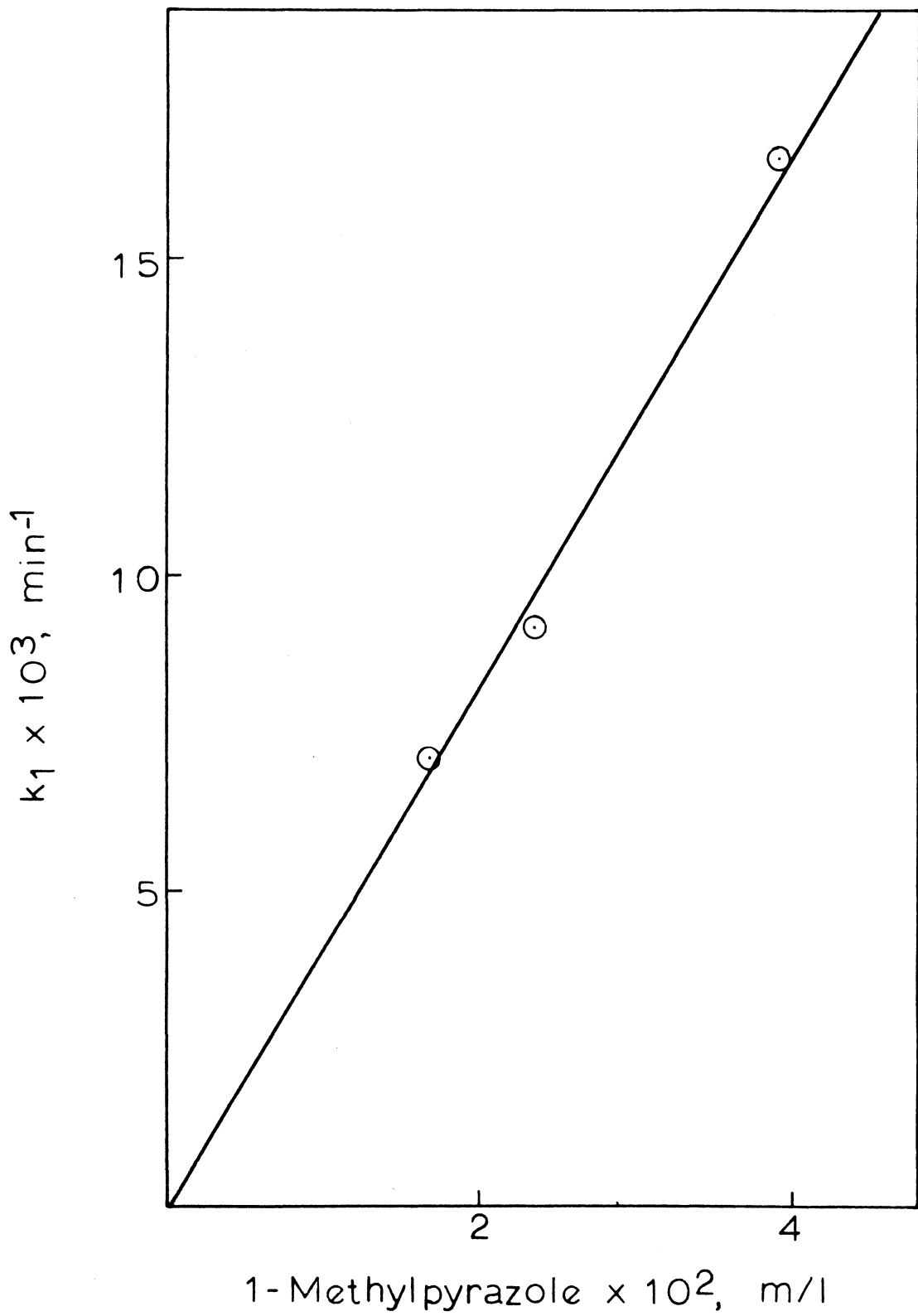
Figure 1. First Order Rate Constant Versus the
1-Methylpyrazole Concentration

Table II: Variation of the Rate with

1-Methylpyrazole Concentration

(1-MePy) x 10^2 m/l	k_1 x 10^3, sec.$^{-1}$	k_2 x 10 *
1.676	7.09	4.11
2.334	9.21	3.95
3.910	16.6	4.25

* Units of liters mole^{-1} min.$^{-1}$

D. Variation of the Rate with

Iodide Concentration

In the variation of iodide, the ionic strength
was kept constant by addition of sodium nitrate. The
concentrations of the various components in the
reaction mixtures were: 1.027 x 10^{-1} M di-basic
sodium phosphate, 5.000 x 10^{-2} M mono-basic potassium
phosphate, and .3482 M sodium nitrate.

The iodide concentration was corrected for the
initial amount combined with iodine. A value for the
equilibrium,

$$I_2 + I^- \rightleftharpoons I_3^-$$
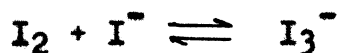
of 830[20] was used.

A plot of the logarithm of the rate constant versus the logarithm of the iodide concentration (Figure 2) shows that the order with respect to iodide is neither inversely proportional to the iodide nor inversely proportional to the square of the iodide, since the slope is 1.13. Therefore, the first order rate constant times the iodide concentration versus one over the iodide concentration was plotted (Figure 3) and found to be a straight line. Since the order is 1.13, the dependence of the rate constant on iodide concentration may be of the form

$$k_{obs.} = \frac{K}{(I^-)} + \frac{K'}{(I^-)^2} .$$

The slope of the line in Figure 3 gives K' and the intercept is K. K' is found to be 4.11×10^{-9} min.$^{-1}$ moles^{-2} liter^{-2} and K is found to be 1.36×10^{-5} min.$^{-1}$ moles^{-1} liter^{-1}.
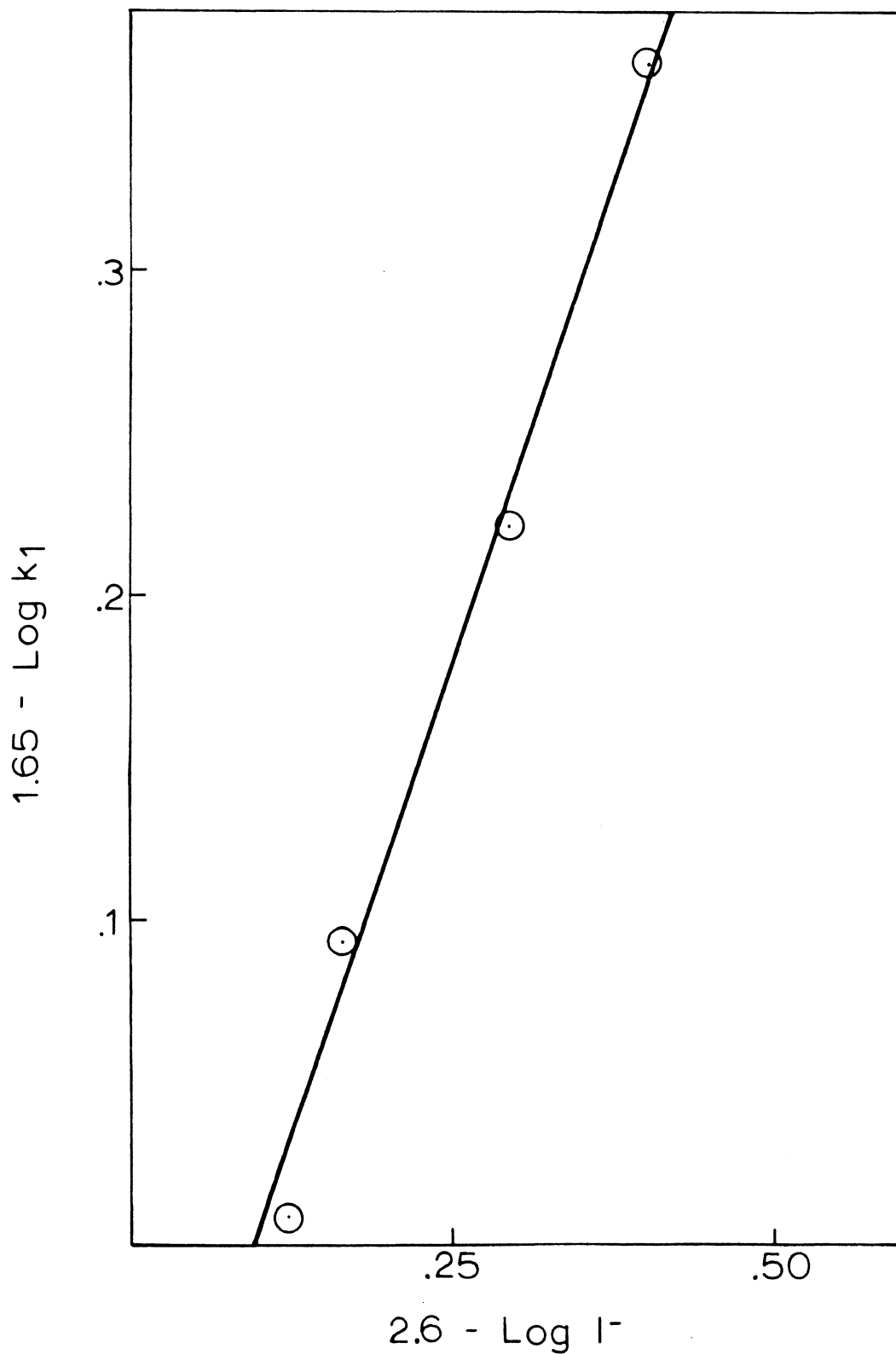
Figure 2. Logarithm of the First Order Rate Constant
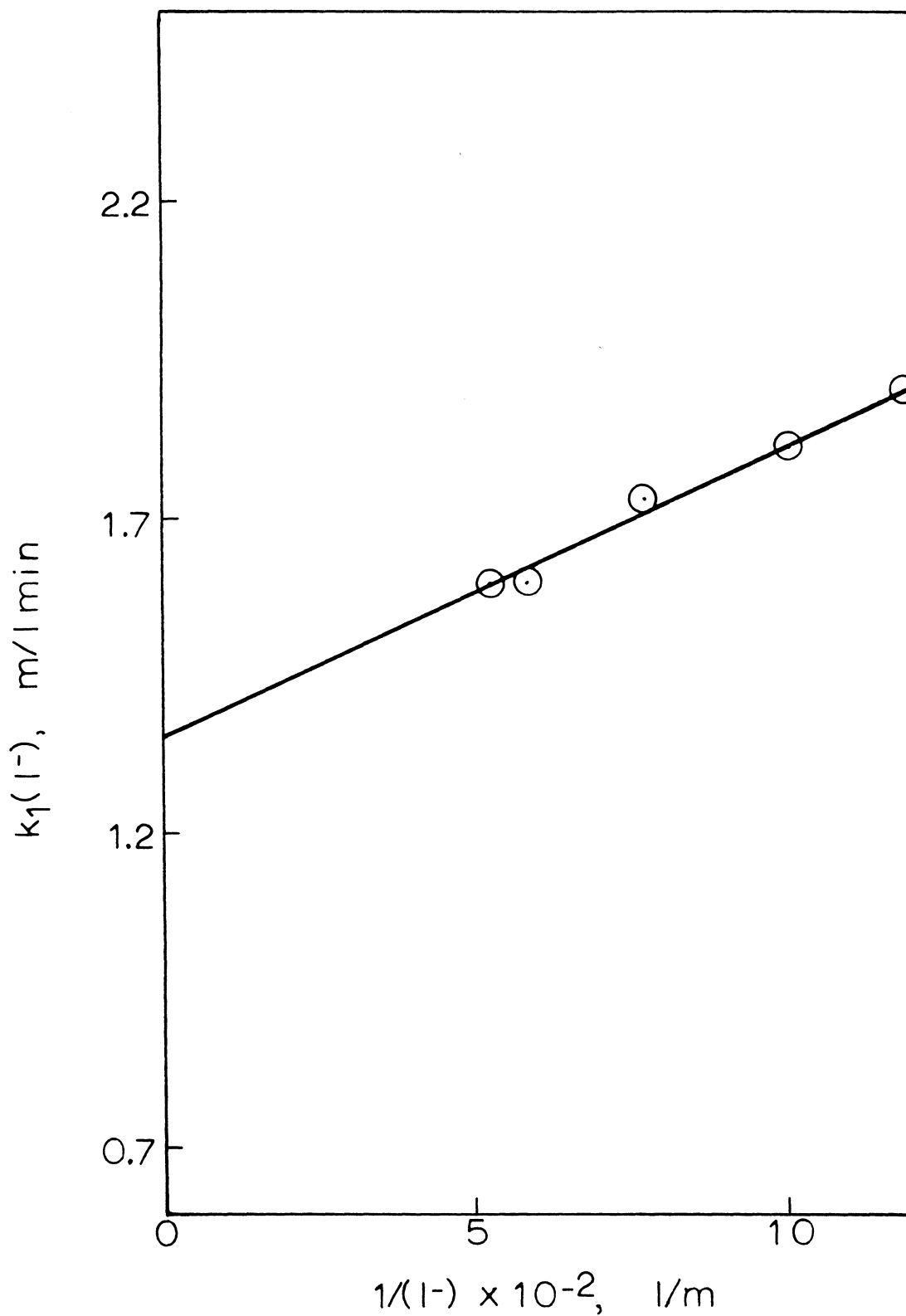Versus Logarithm of Iodide Concentration

Figure 3. The Product of the First Order Rate Constant
and the Iodide Concentration Versus the
Reciprocal of the Iodide Concentration

E. Variation of Buffer Concentrations
at Constant Buffer Ratios

The concentrations of both components of the
buffer were varied, keeping the ratio $(HPO_4^=)/(H_2PO_4^-)$
constant.

In this study, the ionic strength was kept
constant and the concentrations of the other components
were: 9.550×10^{-4} M iodide, 2.955×10^{-5} M iodine,
and 3.525×10^{-2} M 1-methylpyrazole. The temperature
was kept constant at 30 °C.

A plot of the rate versus the di-basic sodium
phosphate concentration (Figure 4) at different
hydrogen ion concentrations shows that the rate is
first order with buffer concentration and independent
of the hydrogen ion concentration. Since the line
goes through the origin the uncatalyzed rate constant
is negligible.[*]

The fact that the reaction is first order with
respect to the di-basic sodium phosphate concentration
indicates that a constant should be obtained by

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* The uncatalyzed reaction refers to proton
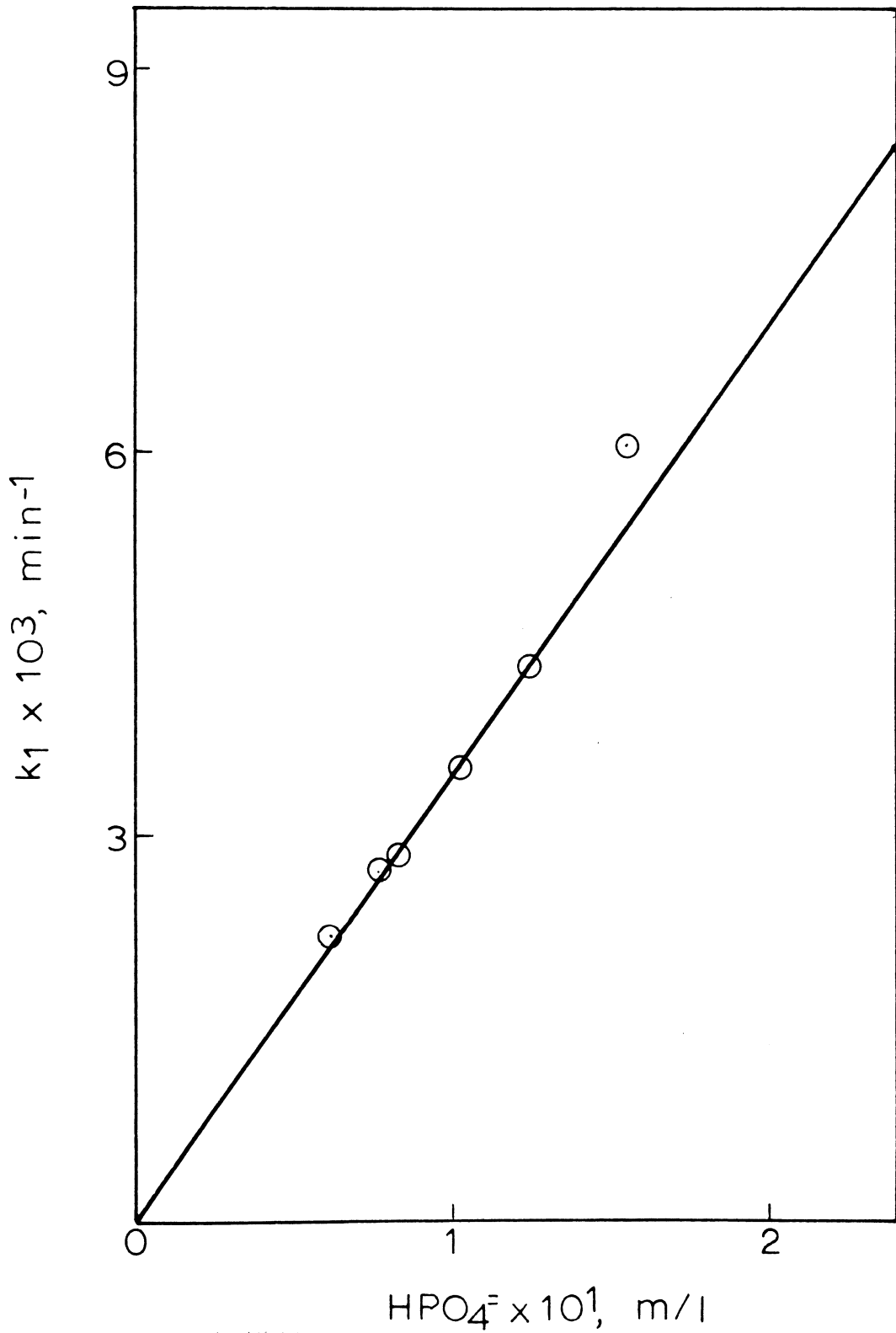removal by water molecules rather than hydrogen
phosphate ions.

Figure 4. First Order Rate Constant Versus Hydrogen
Phosphate Ion Concentration

dividing the rate constant by the buffer concentration
(Table III).

Table III: Variation of Rate with

Buffer Concentration

$(HPO_4^=)$,m/l	$k_1 \times 10^2$ min.$^{-1}$	$k_1/(HPO_4^=)$ *	Measured pH
.1540	6.08	.395	6.25
.1232	4.38	.356	6.38
.1027	3.57	.348	6.33
.08213	2.88	.351	6.33
.07700	2.79	.362	6.19
.07700	2.76	.358	6.10

* Units are liters mole^{-1} min.$^{-1}$, $k_1/(HPO_4^=) = k_2$

The average value of k_2 obtained from Table II
is .355 and the value obtained from Figure 4 is .354.
The value for the $(HPO_4^=)$ concentration of .1540 was
omitted from the average. The large deviation of the
value of k_2 for this concentration of buffer may have
been caused by replacing too large an amount of the
nitrate ions by mono-basic and di-basic phosphate ions,
which may affect the activity coefficients of the ions.
If the activity coefficients are changed by changing
the medium, the rate of the reaction may be dependent
upon the change.

F. Variation of the Reaction Rate
with Temperature

The activation energy was determined at different temperatures keeping the ionic strength at 1.000 M. The buffer concentration was kept constant at each temperature, but varied at different temperatures. The pyrazole concentration was varied at each temperature.

Table IV shows the variation of the second order rate constants with temperature.

Table IV: Variation of the Rate with Temperature

T, °C	k_2 *
30.00	.421
35.00	.814
40.00	1.65

* $k_2 = k_1/(1\text{-MePy})$; units are liters mole^{-1} min.$^{-1}$

The activation energy was found from a plot of the logarithm of the second order rate constant versus the reciprocal of the absolute temperature (Figure 5). The value is 25.8 Kcal/mole.
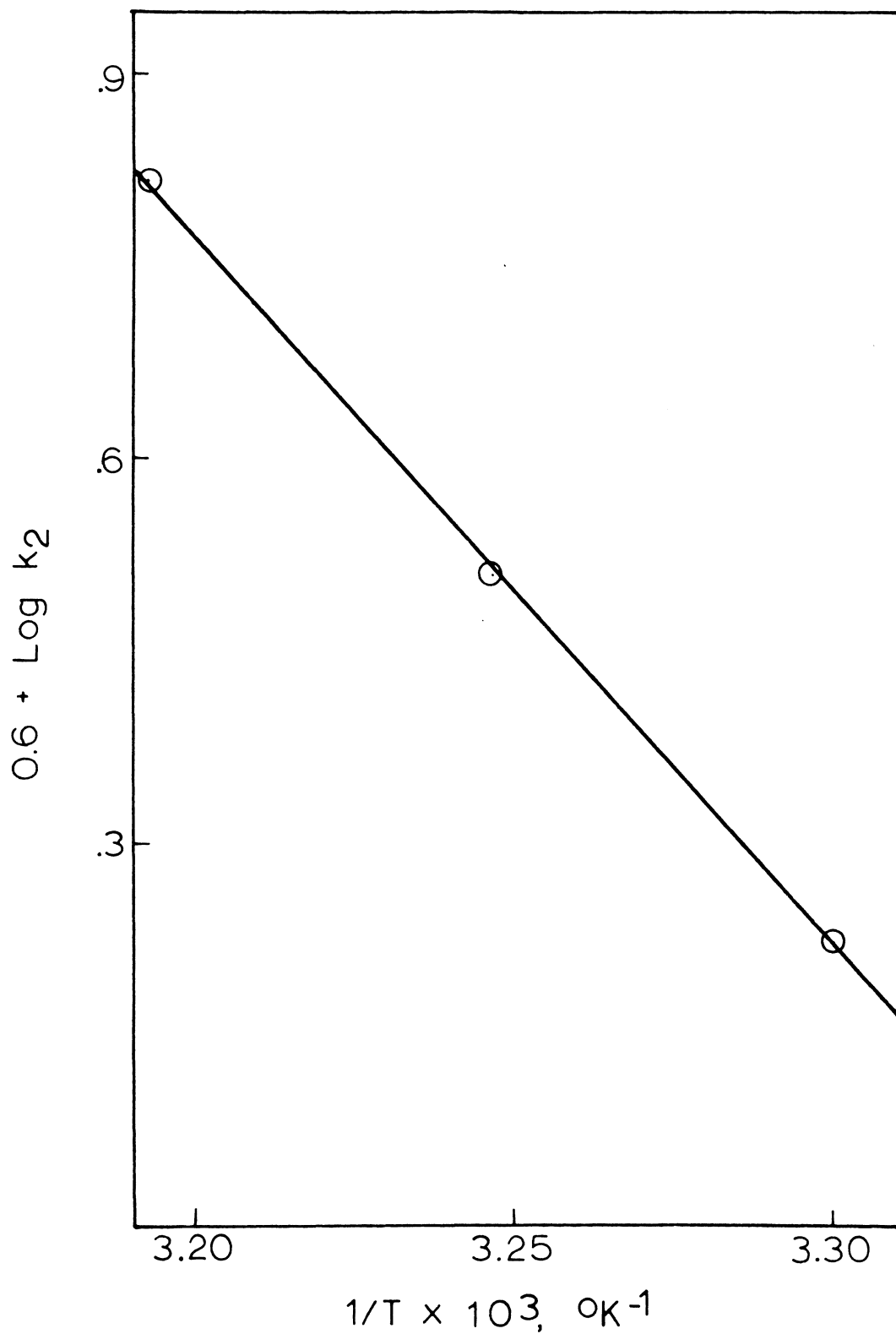
Figure 5. Logarithm of the First Order Rate Constant
Versus the Reciprocal of the Absolute
Temperature.

V. DISCUSSION

A. The Rate Law

The data presented show that the rate of disappearance of 1-methylpyrazole is independent of the hydrogen ion concentration, proportional to the tri-iodide concentration, proportional to the 1-methylpyrazole concentration, proportional to the buffer concentration, and inversely proportional to a mixed order of the iodide concentration. Therefore, the rate law may be expressed as

$$(5) \quad -\frac{d(1\text{-MePy})}{dt} = k_{cat} \frac{(1\text{-MePy})(I_3^-)(HPO_4^=)}{k'(I^-)^2 + k(I^-)}$$

where (1-MePy) is the concentration of 1-methylpyrazole, and k_{cat} is the rate constant for the catalyzed reaction. There was no uncatalyzed reaction observed.

B. Mechanism of Iodination of 1-Methylpyrazole

The observed rate law may be obtained by postulating an attack on the 1-methylpyrazole nucleus by both iodine and the iodinium ion. In a subsequent

step, the hydrogen phosphate ion then removes the
proton from the positively charged intermediate. The
mechanism is presented in Figure 6.

The concentrations of the reacting species are
found from the equilibria

(6) $K_1 = \dfrac{(I_2)(I^-)}{(I_3^-)}$,   and

(7) $K_2 = \dfrac{(I^+)(I^-)}{(I_2)}$.

Solving the two equations for (I^+) and (I_2)
gives,

(8) $(I^+) = \dfrac{K_1 K_2 (I_3^-)}{(I^-)^2}$,   and

(9) $(I_2) = \dfrac{K_1 (I_3^-)}{(I^-)}$.

The rate law is written for the disappearance
of 1-methylpyrazole in terms of the concentration of
the intermediate. The steady state approximation is
used to obtain the concentration of the intermediate.
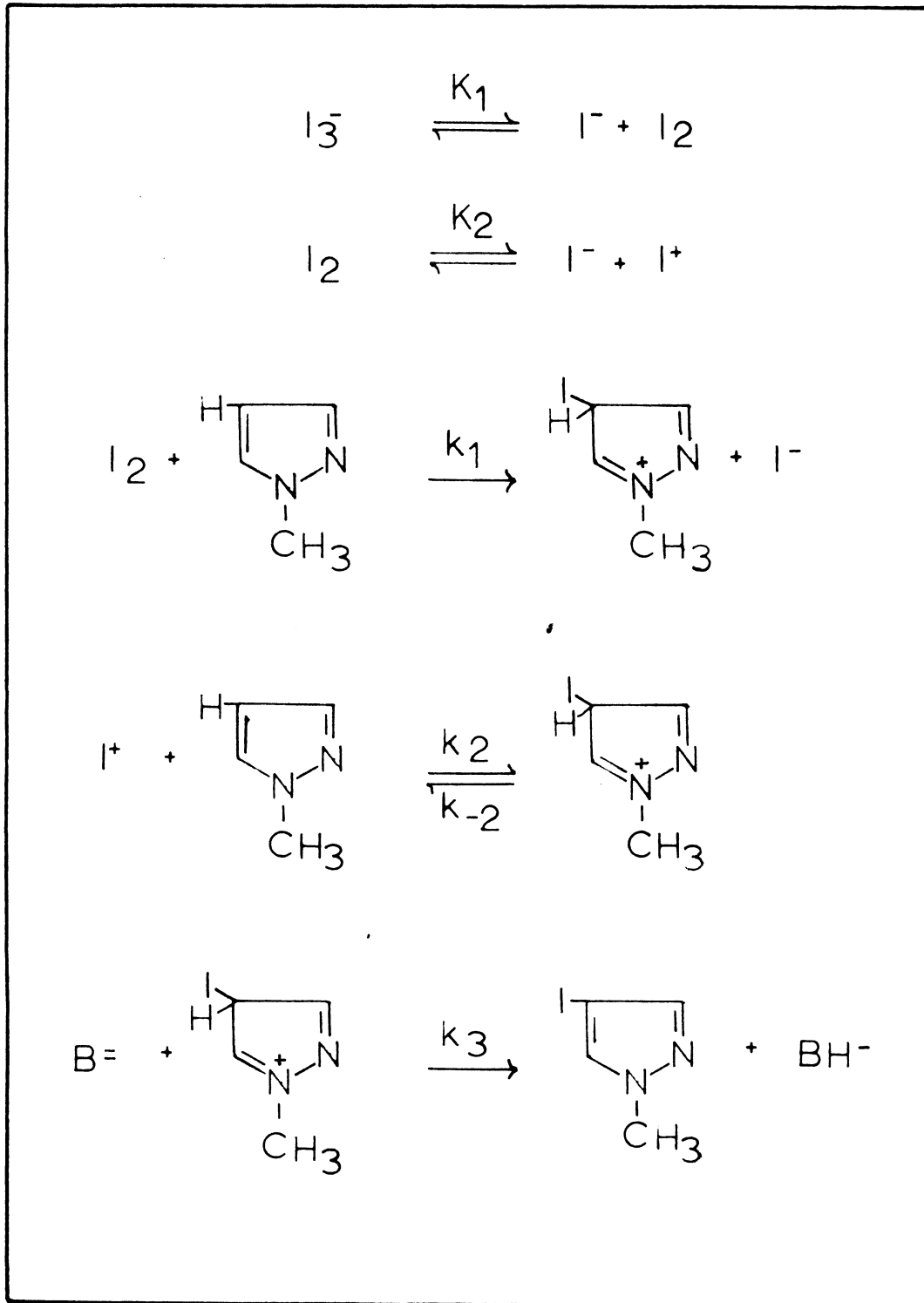
Figure 6. Proposed Mechanism for the Iodination
of 1-Methylpyrazole.

Denoting the intermediate III by (MePyI$^+$),

III
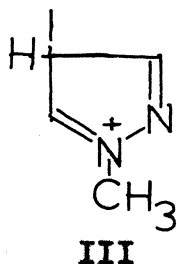
the rate of disappearance of l-methylpyrazole with time may be written

$$(10) \qquad - \frac{d(MePy)}{dt} = k_3(MePyI^+)(HPO_4^=) \ .$$

The rate of formation of the intermediate III is

$$(11) \qquad \frac{d(MePyI^+)}{dt} = k_1(MePy)(I_2) + k_2(MePy)(I^+)$$

$$- k_{-2}(MePyI^+) - k_3(MePyI^+)(HPO_4^=) \ .$$

The steady state approximation is used by setting Equation 11 equal to zero and solving for (MePyI$^+$).

$$(12) \qquad (MePyI^+) = \frac{k_1(MePy)(I_2) + k_2(MePy)(I^+)}{k_{-2} + k_3(HPO_4^=)} \ .$$

Substituting Equation 12 into Equation 10 and making the assumption that k_{-2} is much larger than $k_3(HPO_4^=)$, we find

$$(13) \qquad -\frac{d(MePy)}{dt} = \frac{k_3k_1(MePy)(I_2)(HPO_4^=)}{k_{-2}}$$
$$+ \frac{k_3k_2(MePy)(I^+)(HPO_4^=)}{k_{-2}} \, .$$

The final form of the rate law is obtained by substituting Equation 8 and Equation 9 into Equation 13 for the iodinium ion and the iodine, respectively, to obtain

$$(14) \qquad -\frac{d(MePy)}{dt} = \frac{K_1k_1k_3(MePy)(I_3^-)(HPO_4^=)}{k_{-2}(I^-)}$$
$$+ \frac{K_1K_2k_2k_3(MePy)(I_3^-)(HPO_4^=)}{k_{-2}(I^-)^2} \, .$$

This is the experimentally observed rate law.

C. Evidence for the Mechanism

Since it requires a combination of iodinating
species and independence of the hydrogen ion
concentration to give the experimentally observed
rate law, it is not difficult to eliminate possible
iodinating species. Hypoiodous acid can be eliminated
because it would show hydrogen ion dependence. An
acid catalyzed reaction of hypoiodous acid with
1-methylpyrazole would show no hydrogen ion dependence,
but a plot of the observed rate constant versus buffer
concentration would have an intercept other than zero
and no such intercept was found.

Other iodinating species have been eliminated
on chemical grounds[15].

Since it has been shown that the iodination
of phenol, imidazole, pyrazole, and aniline[1,15]
possibly have the same iodinating species, support is
given to the postulate that iodine and the iodinium
ion are the iodinating species in the iodination of
1-methylpyrazole.

D.   Comments on the Activation Energies

of Pyrazole, 1-Methylpyrazole,

and 3-Methylpyrazole

The activation energy given for pyrazole[1] is

29.3 Kcal/mole, for 3-methylpyrazole[13] 25.4 Kcal/mole,

and for 1-methylpyrazole 25.8 Kcal/mole.

By comparing activation energies, one might

expect that 1-methylpyrazole would iodinate much faster

than pyrazole but slightly slower than 3-methylpyrazole.

However, for given concentrations of iodide, buffer

solutions, and pyrazoles, 3-methylpyrazole has the

fastest rate, followed by pyrazole and then

1-methylpyrazole.

A partial explanation would be that the

postulated intermediate for the iodination of

1-methylpyrazole has a positive charge while that

for pyrazole does not. Since the rate determining

step is the removal of the proton by the divalent

buffer, this removal would be facilitated by the

positive charge on the intermediate, hence lowering

the activation energy. However, the rate also depends

upon the steady state concentration of intermediate III.

It is likely that this factor is the major one on the

overall rate which makes 1-methylpyrazole iodinate at a much slower rate than pyrazole.

The activation energies for pyrazole and 3-methylpyrazole indicate that 3-methylpyrazole should iodinate from 500 to 1000 times faster than pyrazole. However, the actual rate is only about forty one times faster. This fact is explained[13] by considering the ionization constants for the two compounds. The estimated values of the ionization constants for pyrazole and 3-methylpyrazole[1,13] are 7×10^{-14} and 1×10^{-14}, respectively. Since the concentration of the pyrazolate anion is seven times the concentration of the 3-methylpyrazolate anion, the rate of iodination of pyrazole would be much larger compared to the iodination of 3-methylpyrazole than that expected from consideration of the activation energies. The fact that 1-methylpyrazole cannot form an anion suggests a much slower rate of formation of intermediate III. This factor would then account for the low steady state concentration of intermediate III.

VI. SUMMARY

A spectrophotometric method was used to determine the rate law in buffered aqueous iodine-iodide solutions. Three iodinating agents other than iodine were considered: direct attack by hypoiodous acid, acid catalyzed attack by hypoiodous acid, and the iodinium ion. The first two were discarded because of the observed dependence of the rate on the buffer concentration and the observed independence of the rate on the hydrogen ion concentration.

The postulated mechanism is in agreement with the mechanisms for aniline and pyrazole. The rate determining step is the removal of the proton from the intermediate by the buffer. However, it was found that iodine was the major iodinating species and that the iodinium ion had a much smaller effect.

A qualitative discussion of the reactivities of pyrazole, 3-methylpyrazole, and 1-methylpyrazole was made. An attempt was made to show possible reasons for the observed results.

VII. SUGGESTIONS FOR FURTHER WORK

The fact that the rate of iodination of 1-methylpyrazole was found to be independent of the hydrogen ion concentration suggests that a study should be made on 1-substituted imidazoles and pyrroles. The results of these studies would be very helpful in the determination of iodinating species.

Other 1-substituted pyrazoles such as 1-isopropylpyrazole should also be studied to give more information to the mechanism of iodination of aromatic substrates.

VIII. BIBLIOGRAPHY

1. Don G. Lambert, M. S. Thesis (V. P. I.), "The Kinetics and Mechanism of Iodination of Pyrazole," August, 1962.

2. E. Buechner, Ann., 273, 214 (1893).

3. R. Huttel and F. Buchele, Chem. Ber., 88, 1586, (1955).

4. R. Huttel and G. Welzel, Ann., 598, 186 (1956).

5. C. Musante, Gazz. chim. ital., 78, 178 (1948).

6. T. L. Jacobs, "Pyrazole and Related Compounds" in Heterocyclic Compounds, Vol. 5, R. C. Elderfield, Ed., John Wiley and Sons, New York, 1957, p. 99.

7. R. G. Jones, J. Am. Chem. Soc., 71, 3994 (1949).

8. R. Huttel, O. Schafer, and P. Jochum, Ann., 593, 200 (1955).

9. v. Auwers and Heimke, Ann., 458, 186 (1927).

10. Michaelis, Ann., 385, 1 (1911).

11. Michaelis and Kading, Ann., 373, 202 (1910).

12. I. L. Finar and K. E. Godfrey, J. Chem. Soc., 2293 (1954).

13. J. H. Alexander, B. S. Thesis (V. P. I.), "Reactivity of 3-Methylpyrazole," August, 1962.

14. K. W. Doak and A. H. Corwin, J. Am. Chem. Soc., 71, 159 (1949).

15. E. Berliner, J. Am. Chem. Soc., 72, 4003 (1950).

16. J. H. Ridd, J. Chem. Soc., 1955, 1238.

17. F. G. Soper and G. F. Smith, J. Chem. Soc., 1927, 2757.

18. B. S. Painter and F. G. Soper, J. Chem. Soc., 1947, 342.

19. T. Dedicher, Chem. Ber., 38, 1831 (1906).

20. M. Eigen and K. Kustin, J. Am. Chem. Soc., 84, 1355 (1962).

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X. APPENDIX

The discovery that iodine was evaporating from the reaction cells required that only those runs in which no loss was observed be used for the variations of the buffer and the iodide. The loss of iodine was shown by adding a solution of iodine-iodide of concentration equal to that of a typical run to a cell and observing the decrease in optical density with time. Placing a piece of tissue paper soaked in starch solution over the top of the flask, and placing the flask in a constant temperature bath showed a blue color indicating the loss of iodine by evaporation.

If the loss of iodine were constant, the observed rate constant would be too high due to the added rate of loss of iodine. However, since the rate of substitution is proportional to the 1-methylpyrazole concentration, the effect of a constant rate of loss of iodine would be only to shift the position of the plotted line. The line would still have the same slope, i.e., the second order rate constant would not be affected.

ABSTRACT

The rate of iodination of 1-methylpyrazole has been studied and the rate law and a possible mechanism for this reaction has been determined. The experimentally determined rate law shows independence of the hydrogen ion concentration, direct dependence on the buffer concentration, direct dependence on the 1-methylpyrazole concentration, direct dependence on the tri-iodide concentration, and inverse dependence to a mixed order of the iodide concentration.

The proposed mechanism, which agrees with the experimentally observed rate law, includes both free iodine and the iodinium ion as iodinating agents. The rate-determining step being the removal of the hydrogen ion by the buffer from the reaction intermediate.

From the most current data and reviews on the iodination of aromatic substrates, it appears that most of the iodination reactions can be explained by considering either free iodine or the iodinium ion or both as iodinating species.