

Unfortunately, our results do not shed any new light on the nature of the rearranging species. As we have indicated in Fig. 2, rearrangement may occur at various stages; the rates  $k_2$  and  $k_2'$  may apply equally well to rearrangement of propyl chloride-aluminum chloride complex,  $\pi$ -complex, or  $\sigma$ -complex without changing the interpretation of the experimental results.

We do feel that our results draw new attention to the importance of steric factors in Friedel-Crafts alkylations, and to the practical effects evidenced by the re-

orientations induced in polyalkylbenzenes to relieve steric strains.

**Acknowledgment.**—We wish to thank Dr. Jeff C. Davis, Jr., for help with the nuclear magnetic resonance spectrometric analysis. Financial assistance from the National Science Foundation and the Robert A. Welch Foundation is also gratefully acknowledged. D. S. wishes to thank the Department of State, Agency for International Development, for financial aid.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE UNIVERSITY OF HAWAII, HONOLULU, HAWAII, AND VIRGINIA POLYTECHNIC INSTITUTE, BLACKSBURG, VA.]

## Kinetics and Mechanism of Iodination of Pyrazole. Comparative Reactivities of Pyrazole and Imidazole<sup>1</sup>

BY JOHN D. VAUGHAN, DON G. LAMBERT, AND VIRGINIA L. VAUGHAN

RECEIVED FEBRUARY 24, 1964

The kinetics of iodination of pyrazole in aqueous solution has been studied. The rate was found to be separable into parallel "uncatalyzed" and buffer-catalyzed reactions. A mechanism involving attack of the conjugate base of pyrazole by iodine was given. The relative reactivities of pyrazole and imidazole in their "uncatalyzed" reactions were found to be comparable in magnitude and were discussed in mechanistic and theoretical terms.

The kinetics of iodination of aromatic nitrogen heterocycles has been reported for trisubstituted pyrroles,<sup>2</sup> imidazole,<sup>3</sup> and histidine.<sup>4</sup> The observed more rapid rate of iodination of 1-substituted pyrroles relative to pyrrole indicates that iodination probably occurs through the neutral pyrrole molecule rather than through the pyrrole anion.<sup>5</sup> In contrast, the non-reactivity of 1-substituted imidazoles suggests that the anion of imidazole undergoes iodination rather than the undissociated molecule.<sup>3a,5</sup> Similarly, the iodinations of phenol<sup>6,7</sup> and 4-nitrophenol<sup>8</sup> seem to involve attack of the anion.

Pyrazole and most substituted pyrazoles undergo iodination in the four position.<sup>9</sup> Since 1-methylpyrazole also undergoes iodination (in the four position)<sup>9</sup> De La Mare and Ridd<sup>5</sup> suggested that iodination occurs through the neutral pyrazole molecule rather than through the pyrazole anion. Brown's<sup>10</sup> molecular orbital calculations of localization energies of the pyrazole molecule and of the anion showed that the anion should be markedly more reactive to electrophilic reagents than the neutral molecule.

The purpose of the present investigation was to determine the detailed kinetics of iodination of pyrazole, and to compare the relative rates of iodination of pyrazole and imidazole under similar conditions. To provide similar conditions, it was desirable to re-examine the iodination of imidazole at higher temperatures and ionic strength than the previous study.<sup>3a</sup> This in-

vestigation revealed that pyrazole, like imidazole, appears to undergo base-catalyzed iodination through the anion, and that the relative reactivities of pyrazole and imidazole are very similar in the water-catalyzed ("uncatalyzed") reaction.

### Experimental

**Materials.**—Pyrazole (Py), obtained from Columbia Organic Chemicals Co., was recrystallized three times from cyclohexane; m.p. 68.5°. Imidazole (Im), obtained from Aldrich Chemical Co., Inc., was recrystallized three times from benzene; m.p. 88.0°. Reagent grades of KI, Na<sub>2</sub>HPO<sub>4</sub>, KH<sub>2</sub>PO<sub>4</sub>, NaNO<sub>3</sub>, and NH<sub>4</sub>NO<sub>3</sub> were dried at 110° and used without further purification. Reagent grade sublimed iodine was resublimed before use. Perchloric acid stock solution prepared from reagent grade HClO<sub>4</sub> (70%) was standardized indirectly against potassium acid phthalate.

**Product Analysis.**—The iodinated product of Py was prepared by the procedure of Hüttel, *et al.*,<sup>9</sup> except Na<sub>2</sub>HPO<sub>4</sub>-KH<sub>2</sub>PO<sub>4</sub> buffer was used instead of sodium acetate. Excess iodine was destroyed by NaHSO<sub>3</sub>. The product was recrystallized twice from cyclohexane (white needles, m.p. 112°). Hüttel, *et al.*,<sup>9</sup> reported that 4-iodopyrazole is pale yellow, m.p. 108.5°. Reimfinger, *et al.*,<sup>11</sup> prepared 3(5)-iodopyrazole, m.p. 72-73°. An n.m.r. spectrum of our product was that expected for 4-iodopyrazole.<sup>12</sup>

Ridd showed that the product of the iodination of Im with Im in stoichiometric excess is 2,4(5)-diiodoimidazole,<sup>3a</sup> with the initial substitution occurring in the 4-position.<sup>3b</sup>

**Kinetic Runs.**—All kinetic runs were made in aqueous solutions adjusted to a constant ionic strength of 1.00 *M*. Runs with Py substrate were buffered with either HPO<sub>4</sub><sup>2-</sup>-H<sub>2</sub>PO<sub>4</sub><sup>-</sup> or NH<sub>3</sub>-NH<sub>4</sub><sup>+</sup>, and runs with Im were self-buffered.<sup>3a</sup> The final adjustment to constant ionic strength was made by addition of aqueous NaNO<sub>3</sub>. Some of the runs with Py substrate were followed with a Beckman DU spectrophotometer, equipped with dual thermospacers. Data were taken at 400 m $\mu$ , where the absorbancy of I<sub>3</sub><sup>-</sup> is large and that of I<sub>2</sub> is small.<sup>13</sup> Other kinetic runs with Py and Im substrates were followed by titration with thiosulfate, using the procedure of Berliner.<sup>7</sup> In all runs, the

(1) Taken in part from the M.S. thesis of D. G. Lambert, V.P.I., 1962.

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

(3) (a) J. H. Ridd, *J. Chem. Soc.*, 1238 (1955); (b) A. Grimison and J. H. Ridd, *ibid.*, 3019 (1959).

(4) C. H. Li, *J. Am. Chem. Soc.*, **66**, 225 (1944).

(5) P. B. D. De La Mare and J. H. Ridd, "Aromatic Substitution: Nitration and Halogenation," Butterworths Scientific Publications, London, 1959, pp. 200-202.

(6) B. S. Painter and F. G. Soper, *J. Chem. Soc.*, 342 (1947).

(7) E. Berliner, *J. Am. Chem. Soc.*, **73**, 4307 (1951).

(8) E. Grovenstein, Jr., and N. S. Aprahamian, *ibid.*, **84**, 212 (1962).

(9) R. Hüttel, O. Schafer, and P. Jochum, *Ann.*, **593**, 200 (1955).

(10) R. D. Brown, *Australian J. Chem.*, **8**, 100 (1955).

(11) H. Reimfinger, A. van Overstraeten, and H. G. Viehe, *Chem. Ber.*, **94**, 1036 (1961).

(12) W. Goodlett, Tennessee Eastman Co., Kingston, Tenn., private communication.

(13) A. D. Autrey and R. E. Connick, *J. Am. Chem. Soc.*, **73**, 1842 (1951).

ratio of  $[I^-]$  to  $[I_3^-]$  was at least 20, and the ratio of [substrate] to  $[I_3^-]$  was also 20 or greater (to ensure pseudo-first-order kinetics).

Kinetic runs were made at 30 and 40° for both Py and Im substrates. All solutions were prepared at room temperature; since these solutions had uniform ionic strength, thermal expansions in volume were assumed uniform. Preliminary experiments indicated that small errors in solution volume led to essentially no error in the observed first-order rate constants. In spectrophotometric runs, all at 30.0°, the cell temperature was measured with a calibrated double junction copper-constantan thermocouple; the cell temperature varied less than 0.05° from the bath temperature.

### Results

**The Rate Laws.**—In Table I, the first-order dependence of the rate of iodination of pyrazole upon the concentration of pyrazole is seen.

TABLE I  
VARIATION OF THE RATE OF IODINATION OF PYRAZOLE WITH THE PYRAZOLE CONCENTRATION (30°)

In all runs,  $[I_2] = 5.32 \times 10^{-4} M$ ,  $[KI] = 9.648 \times 10^{-3} M$ ,  $[Na_2HPO_4] = 6.203 \times 10^{-2} M$ ,  $[NaH_2PO_4] = 5.000 \times 10^{-2} M$

$[Py] \times 10^3, M$	$k_1 \times 10^4, \text{sec.}^{-1}$	$\frac{k_1 \times 10^2}{[Py]}, \text{l. mole}^{-1} \text{sec.}^{-1}$
2.636	1.18	4.48
6.640	3.08	4.64
9.296	4.27	4.59
13.48	6.13	4.55
16.15	7.47	4.65
20.22	9.58	4.73

In Table II, the reciprocal second-order dependence of  $k_1$  of pyrazole upon  $[I^-]$  is evident for phosphate- and ammonia-buffered systems; plots of  $\log k_1$  vs.  $\log [I^-]$  gave slopes of  $-2$  for both systems. The effects of

TABLE II  
VARIATION OF THE RATE OF IODINATION OF PYRAZOLE WITH THE IODIDE CONCENTRATION (30°)

$HPO_4^{-2}, H_2PO_4^-$  buffer; in all runs,  $[Na_2HPO_4] = 6.203 \times 10^{-2} M$ ,  $[NaH_2PO_4] = 5.00 \times 10^{-2} M$ ,  $[Py] = 1.348 \times 10^{-2} M$

$[I^-] \times 10^3$	$k_1 \times 10^{1a}$	$k_1 [I^-]^2 \times 10^{3b}$
3.91	31.7	4.85
5.48	16.4	4.92
7.82	9.03	5.52
9.65	6.13	5.71
9.78	5.94	5.68
18.08	1.77	5.79
23.72	0.955	5.36

Av.  $5.40 \pm 0.44$

$NH_3, NH_4^+$  buffer; in all runs,  $[NH_3] = 9.70 \times 10^{-3} M$ ,  $[NH_4NO_3] = 9.55 \times 10^{-2} M$ ,  $[Py] = 2.00 \times 10^{-2} M$

$[I^-] \times 10^{-2}$	$k_1 \times 10^{4a}$	$k_1 [I^-]^2 \times 10^{2b}$
8.00	2.11	1.35
	2.08	1.33
	2.01	1.29
	2.02	1.29
10.00	1.26	1.26
	1.31	1.31
12.00	0.84	1.21
	0.92	1.33

Av.  $1.29 \pm 0.03$

<sup>a</sup> Sec.<sup>-1</sup>. <sup>b</sup> Sec.<sup>-1</sup> mole<sup>2</sup> l.<sup>-2</sup>.

the buffer concentration, the hydrogen ion concentration, and the temperature are observed in Table III;  $[Py]$  and  $[I^-]$  dependences were removed by multiplying  $k_1$  by  $[I^-]^2/[Py]$ . Hydrogen ion concentrations

TABLE III  
DEPENDENCE OF THE RATE OF IODINATION OF PYRAZOLE UPON THE BUFFER AND HYDROGEN ION CONCENTRATIONS

$[HPO_4^{-2}] \times 10^2$	$\frac{[HPO_4^{-2}]}{[H_2PO_4^{-}]}$	$[H^+] \times 10^7$	$k_1 [I^-]^2/[Py] \times 10^{1a}$
At 30°			
2.15	3.00	1.83	3.54
3.00			5.07
4.00			6.31
5.00			8.05
6.00			9.91
7.00			11.64
1.06	2.56	2.14	1.84
2.12			3.52
2.12			3.59
3.18			5.06
3.18			4.84
4.24			6.87
4.24			6.89
5.31			8.42
1.55	1.24	4.42	1.275
3.02			2.29
6.20			4.47
8.00			6.28
10.00			7.76
12.00			9.33
12.41			10.03
4.00	0.50	10.96	1.15
6.00			1.69
8.00			2.29
At 40°			
0.98	2.13	2.585	8.74
0.98			8.60
1.97			15.0
1.97			15.0
3.93			29.1
3.93			29.0
5.90			45.2
5.90			44.3
$[NH_3]$	$[NH_4^+]/[NH_3]$	$[H^+] \times 10^6$	$k_1 [I^-]^2/[Py] \times 10^{1a}$
At 30°			
0.485	8.85	4.68	4.87
.485			4.92
.970			6.75
.970			6.64
1.455			8.55
1.455			8.70
1.940			10.13
1.940			10.07
0.485	14.8	7.83	2.94
0.970			4.32
1.455			5.06
1.940			6.12
At 40°			
0.44	10.35	5.48	10.31
.44			10.31
.88			13.46
.88			13.50
1.33			16.00
1.33			16.50
1.77			19.26
1.77			19.40

<sup>a</sup> Sec.<sup>-1</sup> mole l.<sup>-1</sup>.

were calculated from the appropriate buffer equilibrium expression

$$K_a = [HPO_4^{-2}][H^+]/[H_2PO_4^{-}] = 5.48 \times 10^{-7}$$

or

$$K_b = [\text{NH}_4^+]/10^{-14}/[\text{NH}_3][\text{H}^+] = 1.89 \times 10^{-5}$$

where  $K_a$  was computed from the measured pH value of 6.67 for the buffer ratio  $[\text{HPO}_4^{2-}]/[\text{H}_2\text{PO}_4^-] = 2.56$ , and  $K_b$  from the pH value of 8.33 and the buffer ratio  $[\text{NH}_4^+]/[\text{NH}_3] = 8.85$ .  $K_a$  and  $K_b$  so computed are not correct thermodynamic dissociation constants for these buffers at an ionic strength of 1.000 *M*, but permit accurate calculations of relative values of  $[\text{H}^+]$  corresponding to different buffer ratios at this fixed ionic strength.<sup>3a</sup>

In the ammonia-buffered system, the reciprocal first-order dependence of  $k_1$  on  $[\text{H}^+]$  is shown in Fig. 1, where  $k_1[\text{I}^-]^2[\text{H}^+]/[\text{Py}]$  vs.  $[\text{NH}_3]$  for runs at 30° is seen to be linear. The slopes and intercepts shown in Fig. 1 for runs at 30 and 40° reveal "uncatalyzed" and base-catalyzed reactions, respectively. Figure 2 indicates the similar behavior of the phosphate-buffered system. The intercepts were less clearly defined by the points of Fig. 2 than those of Fig. 1; we therefore based the intercepts shown in Fig. 2 upon those obtained in Fig. 1.

Figure 3 indicates the buffer dependence of the rate of iodination of imidazole (Im) at 30 and 40° at pH 7.10. Here Im serves the dual role of substrate and buffer.<sup>14</sup> Following Ridd,<sup>3a</sup> the buffer ratio was controlled by measured addition of perchloric acid.

The experimental rate law found for the iodination of pyrazole and applicable also for the iodination of imidazole<sup>3a</sup> is given by

$$-d[\text{I}_3^-]/dt = k_2[\text{I}_3^-][\text{S}]$$

where

$$k_2 = \{k_0 + k_{\text{cat}}[\text{B}]\} \frac{1}{[\text{I}^-]^2[\text{H}^+]}$$

Here  $k_0$  is the rate constant for the "uncatalyzed" iodination of substrate (S), and  $k_{\text{cat}}$  is the rate constant for the base (B) catalyzed iodination of S. For pyrazole substrate, B =  $\text{HPO}_4^{2-}$  or  $\text{NH}_3$ , and for imidazole substrate B = Im.

$k_0$  and  $k_{\text{cat}}$  values for Py and Im obtained from the slopes and intercepts of Fig. 1 and 2 and Fig. 3, respectively, are given in Table IV.

TABLE IV  
RATE CONSTANTS FOR THE UNCATALYZED AND CATALYZED IODINATIONS OF PYRAZOLE AND IMIDAZOLE

<i>t</i> , °C.	$k_0 \times 10^{13a}$	$k_{\text{cat}} \times 10^{11b}$
Pyrazole		
30	"Uncat." 1.5 ± 0.2 <sup>c</sup>	1.7 ± 0.2
40		
30	NH <sub>3</sub> 4.0 ± 0.2	3.7 ± .3
40		
30	HPO <sub>4</sub> <sup>2-</sup> 1.7 ± 0.2	2.9 ± .3
40		
Pyrazole		
30	"Uncat." 3.8 ± 0.5	2.9 ± 0.3
40		
30	Im 10.5 ± 0.7	8.7 ± 0.5
40		

<sup>a</sup> 1.2 mole<sup>-2</sup> sec.<sup>-1</sup>. <sup>b</sup> 1. mole<sup>-1</sup> sec.<sup>-1</sup>. <sup>c</sup> Uncertainties estimated graphically.

(14) Pyrazole may not serve as its own buffer in a similar manner to that of imidazole, because its basicity is about 10<sup>-4</sup> that of imidazole.

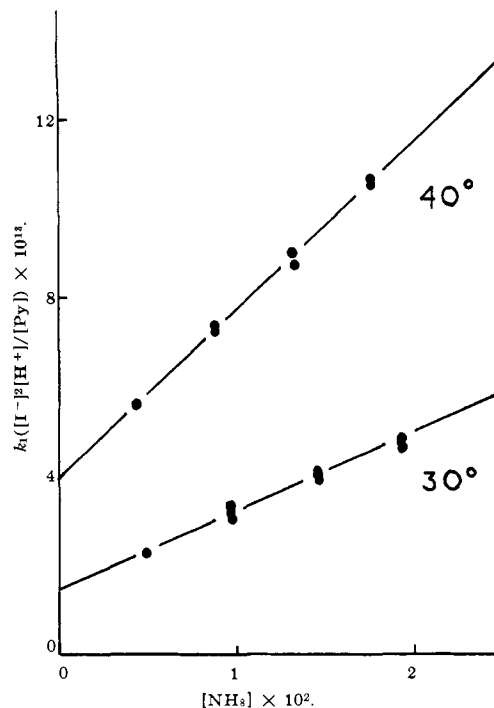


Fig. 1.—Dependence of the rate of iodination of pyrazole upon the buffer concentration.

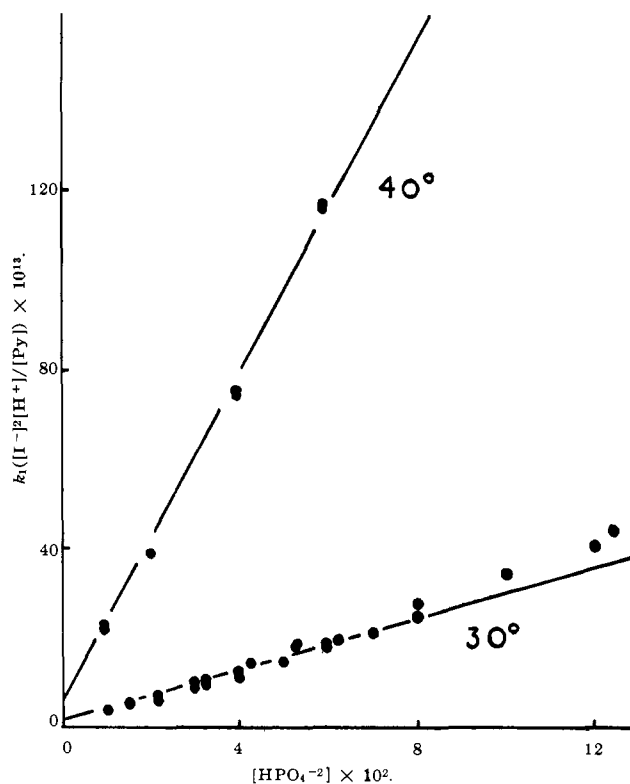


Fig. 2.—Dependence of the rate of iodination of pyrazole upon the buffer concentration.

Experimental activation energies and experimental frequency factors calculated from the results in Table IV are given in Table V.

### Discussion

**Mechanism.**—Several mechanisms are possible for these base-catalyzed reactions. A recent study of the iodination of 4-nitrophenol by Grovenstein and Arahamian<sup>8</sup> showed that iodination by  $\text{I}^+$  could not account for the observed kinetics, but that iodination

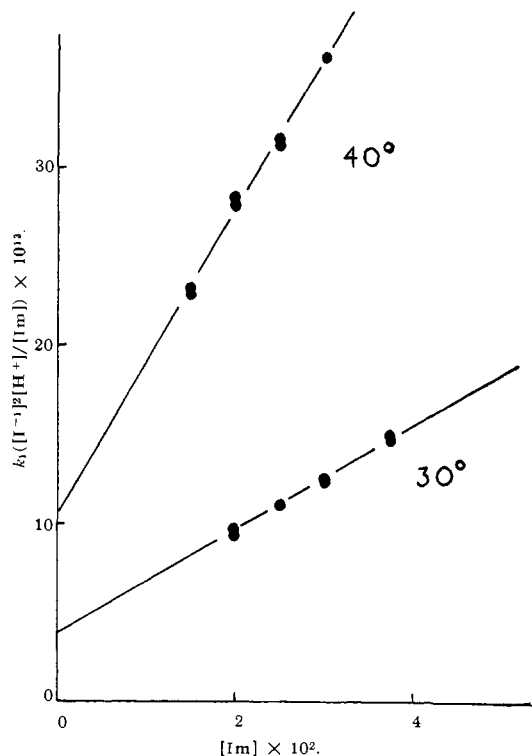


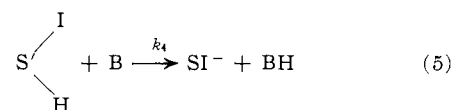
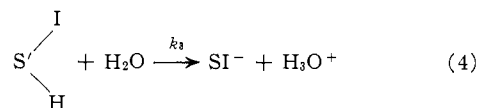
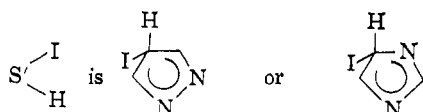
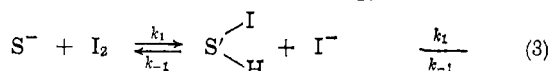
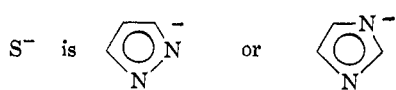
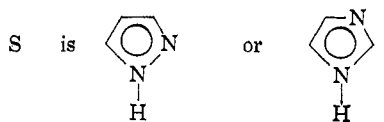
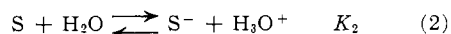
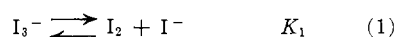
Fig. 3.—Dependence of the rate of iodination of imidazole upon the buffer concentration.

TABLE V  
EXPERIMENTAL ACTIVATION ENERGIES AND EXPERIMENTAL  
LOG FREQUENCY FACTORS

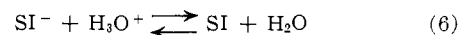
	$\log A^{\text{exp}}$	$E_a^{\text{exp}}$ , kcal./mole <sup>b</sup>
Pyrazole		
"Uncatalyzed"	0.51	18.5
Catalyzed (NH <sub>3</sub> )	-0.31	14.7
Catalyzed (HPO <sub>4</sub> <sup>-2</sup> )	14.33	34.5
Imidazole		
Uncatalyzed	1.42 (1.12) <sup>a</sup>	19.2
Catalyzed (Im)	4.90 (4.60) <sup>a</sup>	20.7

<sup>a</sup> Values in parentheses correspond to monoiodination, given by  $\log A^{\text{exp}} - \log 2$ . <sup>b</sup>  $\pm \sim 2$  kcal./mole.

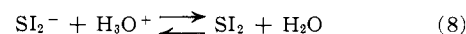
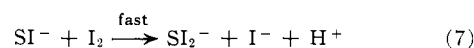
by I<sub>2</sub> could do so. Accordingly, we assume that I<sub>2</sub> is the iodinating reagent for pyrazole and imidazole. The mechanism of Grovenstein and Aprahamian adapted to these substrates follows



where B is NH<sub>3</sub> or HPO<sub>4</sub> when S is Py, or B is Im when S is Im. For Py



For Im



If we assume that (4) and (5) are rate determining, and assume that

$$k_3 \ll k_{-1} \gg k_4$$

the steady state approximation gives

$$k_2 = \left\{ (k_3[H_2O] + k_4[B]) \frac{k_1}{k_{-1}} K_1 K_2 \right\} \frac{1}{[H^+][I^-]}$$

Referring to the experimental rate law, we see that

$$k_0 = (k_1/k_{-1})k_3K_1K_2[H_2O] \quad (9)$$

and

$$k_{\text{cat}} = (k_1/k_{-1})k_4K_1K_2$$

Since we have made the usual assumption that water serves as base catalyst for the "uncatalyzed" reaction for Py and Im,<sup>3a,15</sup> we expect the efficiencies of the various catalysts to depend upon their relative basicities. This relation clearly exists for the uncharged bases; *i.e.*, water and ammonia for pyrazole substrate and water and imidazole for imidazole substrate. In the case of HPO<sub>4</sub><sup>-2</sup> and NH<sub>3</sub> catalysts, we note that  $k_{\text{cat}}^{\text{NH}_3} < k_{\text{cat}}^{\text{HPO}_4^{-2}}$  despite  $K_B^{\text{NH}_3} > K_B^{\text{HPO}_4^{-2}}$  at 30 and 40°. This latter result suggests that the role of HPO<sub>4</sub><sup>-2</sup> in base catalysis is significantly different from that of NH<sub>3</sub>. In addition, the markedly higher experimental activation energy and experimental frequency factor for HPO<sub>4</sub><sup>-2</sup> catalysis compared with H<sub>2</sub>O and NH<sub>3</sub> catalysis (and Im catalysis) also points to a different role; the nature of this difference is not clear from the kinetic data. Base catalysis of the iodination of Py by a number of charged and uncharged bases is presently being studied and will be presented in a later paper.

**Reactivities of Pyrazole and Imidazole.**—To compare the reactivities of these substrates in iodination reactions, one must compare the "uncatalyzed" (water-catalyzed) reactions, rather than the base-catalyzed reactions, since the same buffer was not used for the two substrates. From eq. 9, we may write

$$\frac{1/2 k_0^{\text{Im}}}{k_0^{\text{Py}}} = \frac{(k_1/k_{-1})^{\text{Im}} K_2^{\text{Im}} k_3^{\text{Im}}}{(k_1/k_{-1})^{\text{Py}} K_2^{\text{Py}} k_3^{\text{Py}}}$$

where the factor 1/2 corrects the rate constant for the diiodination of imidazole to monoiodination<sup>3a</sup>; this ratio is  $\sim 1.3$  at 30 and 40° (Table IV), to indicate

the very similar reactivities of the two substrates. The acid ionization constants ( $K_2$ ) are reported to be  $10^{-14}$  and  $10^{-14.6}$  for Py and Im, respectively,<sup>16</sup> indicating that the equilibrium concentrations of anions available for iodination is of the same order of magnitude for Py and Im in solutions of the same stoichiometric concentration. The other two factors,  $k_1/k_{-1}$  and  $k_3$ , cannot be separated. However, we note that the ratio  $k_1/k_{-1}$  will determine the steady-state concentra-

tion of the Wheland intermediate  $\left( \begin{array}{c} \text{H} \\ \diagdown \text{S}' \\ \diagup \text{I} \end{array} \right)$ ; the forma-

tion of this intermediate involves localization of two electrons to form a  $\sigma$ -bond between C and I. Therefore, the atom localization energy at the 4-position of Py and Im should provide at least a semiquantitative comparison of the relative values of  $k_1/k_{-1}$  for the two substrates.

Brown<sup>10</sup> calculated atom localization energies for the 4-positions of Py and Im by the simple molecular orbital method (neglecting overlap) and made no distinction between the pyridine-type nitrogen ( $>\text{N}$ ) and the pyrrole-type nitrogen ( $\text{N}-\text{H}$ ); that is, he assigned a common inductive parameter  $h$  for the coulomb integral  $\alpha_{\text{N}} = \alpha_{\text{C}} + h\beta$  for the two N atoms. Here  $\alpha_{\text{N}}$  is the coulomb integral for nitrogen,  $\alpha_{\text{C}}$  that for carbon, and  $\beta$  is the resonance integral. Brown gave localization energies for values of  $h$  ranging from  $-1$

(16) A. Albert, "Heterocyclic Chemistry," Essential Books, Fair Lawn, N. J., 1959, p. 143.

to  $+1$ . Hamano and Hameka<sup>17</sup> calculated accurate dipole moments for Py and Im by a simple molecular orbital method, using  $h = 2.70$  for the pyrrole-type N and  $h = 0.38$  for the pyridine-type N. In the anion, both nitrogen atoms are pyridine types; hence a common  $h$ -value is applicable. Because of the accuracy of the Hamano and Hameka calculations for the molecules of Py and Im, we assume  $h = 0.38$  for the two pyridine-type atoms of the anion. Brown's atom localization energies for  $h = 0.38$  are  $2.1$  ( $-\beta$ ) for imidazole and  $2.13$  ( $-\beta$ ) for pyrazole. If we assume that the entropies of formation of the Wheland intermediate for imidazole and pyrazole are comparable in magnitude, then these nearly identical atom localization energies suggest that the free energy of formation of the intermediates of Py and Im will likewise be comparable, and therefore that  $k_1/k_{-1}$  of the two substrates will have nearly the same value. We may conclude therefore that the rate-determining rate constants ( $k_3$ ) of Py and Im must also have nearly the same value. The comparable values of the experimental activation energies of the "uncatalyzed" reactions of Py and Im support this argument, since any significant difference in the energy barriers of the rate-determining reactions would be reflected by a difference in the experimental activation energies.<sup>18</sup>

**Acknowledgment.**—We wish to thank Dr. D. E. Boswell of Socony-Mobile Oil Co., Inc., for helpful suggestions.

(17) H. Hamano and H. F. Hameka, *Tetrahedron*, **18**, 985 (1962).

(18) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 209 ff.

[JOINT CONTRIBUTION FROM THE ELECTROCHEMICALS DEPARTMENT AND THE CENTRAL RESEARCH DEPARTMENT, E. I. DU PONT DE NEMOURS AND CO., INC., WILMINGTON 98, DEL.]

## Hydroxy-1,2,5-thiadiazoles. I. A Novel Route from Potassium Cyanide and Sulfur Dioxide

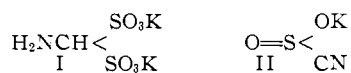
By JOHN M. ROSS<sup>1</sup> AND WILLIAM C. SMITH<sup>2</sup>

RECEIVED OCTOBER 7, 1963

3-Cyano-4-hydroxy-1,2,5-thiadiazole has been obtained from the reaction of potassium cyanide and sulfur dioxide at  $25-85^\circ$  in the absence of hydroxylic solvents. The structure was elucidated by degradation to diethylaminoacetamide and to N-sulfamoyloxamic acid dipotassium salt, and by independent synthesis from isonitrosocyanacetamide and sulfur dichloride. Various 3-hydroxy-1,2,5-thiadiazole derivatives were prepared including several potassium acid salts involving symmetrical hydrogen bonding of the acidic 3-hydroxyl proton.

The reaction of potassium cyanide and sulfur dioxide in aqueous solution has been known since Etard<sup>3</sup> obtained a crystalline product by passing sulfur dioxide through 40% aqueous potassium cyanide. The identity of this product as dipotassium aminomethanesulfonate (I) was more clearly elucidated by von Pechmann and Manck.<sup>4</sup>

Reactions under other conditions have received only cursory examination. The formation of potassium cyanosulfinate (II) was postulated by Jander and co-



(1) Organic Chemicals Department, Jackson Laboratory, E. I. du Pont de Nemours and Co., Wilmington 99, Del.

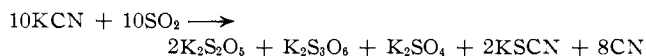
(2) Fabrics and Finishes Department, Experimental Station, E. I. du Pont de Nemours and Co., Wilmington 98, Del.

(3) A. Etard, *Compt. rend.*, **88**, 649 (1879).

(4) H. von Pechmann and Ph. Manck, *Ber.*, **28**, 2374 (1895).

workers<sup>5</sup> to account for the break in the potentiometric titration of potassium cyanide with sulfur dioxide dissolved in liquid hydrogen cyanide, but no reaction product was characterized.

More recently Seel and Müller<sup>6</sup> reinvestigated the work of Jander and co-workers and showed that the precipitate formed by addition of sulfur dioxide to a solution of potassium cyanide in liquid hydrogen cyanide was potassium pyrosulfite. They further studied the product obtained by prolonged exposure of potassium cyanide to liquid sulfur dioxide at room temperature and concluded that the over-all reaction could be described by the equation



(5) G. Jander, B. Grüttner, and G. Scholz, *ibid.*, **80**, 279 (1947).

(6) F. Seel and E. Müller, *ibid.*, **88**, 1747 (1955).