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Positional Reactivities and Mechanisms of Deuteration of 1-Methylimidazole in pD and $-D_0$ Regions. Reinvestigation of the Kinetics of 2-Hydrogen Exchange in Imidazole

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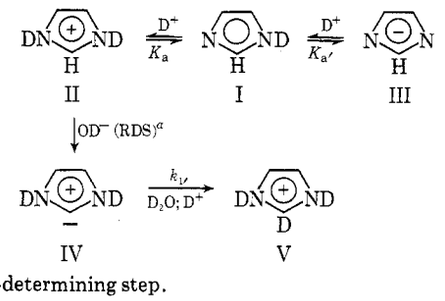
Of the rate equations 1–4 for 2-deuteration of imidazole *via* the ylide mechanism involving the OD^-, the imidazole free base, its conjugate anion, and D_2O, respectively, the experimental pD–rate profile conforms uniquely to eq 1. Rate expressions for the deuteration of the three ring sites in 1-methylimidazole by way of four independent routes are also presented (eq IIa–d). Successive exchanges of the three ring hydrogens were studied in D_2O as a function of the medium acidity. In the region of pD 0–13, the profiles for the 2-, 4-, and 5-hydrogen exchange are similar and as predicted by eq IIb. At pD > 13, eq IIa contributes significantly to the reaction at the 2 and 4 position. In strong acids, the rate of deuteration of all the ring positions increased fairly linearly with acidity as required by eq IId. Similar deuteration of 1,3-dimethylimidazolium iodide substantiates the above. These findings also allow the determination of the theoretical second-order rate constants which provide a quantitative account of the intrinsic reactivity of the 2, 4, and 5 position of 1-methylimidazole in undergoing deuteration. The relative rates are 54,500:1.6:1, respectively, *via* the ylide mechanism and 1:73:120, respectively, *via* the SEAr pathway involving the conjugate acid species.

The imidazole ring system has achieved textbook status because many substances of biological and chemical interest, both natural and synthetic, are imidazoles. Although there are many electrophilic substitution reactions of imidazoles known in the literature,[1] including, in some instances, kinetic analysis of a particular product, no quantitative data are as yet available for comparing the positional reactivities of the three potentially different carbon positions of the imidazole ring in any particular reaction. To this end 1-methylimidazole, the simplest model which possesses three unique ring positions, *viz.*, the C-5 position adjacent to a pyrrole nitrogen atom, C-4 to a pyridine nitrogen, and C-2 to both, was chosen for the present study of the reactive character of these three sites. Since typical aromatic substitutions,[1] *e.g.*, nitration, sulfonation, and halogenation, have invariably yielded a single product, they are unsuitable for a comparative study of positional reactivity. We, therefore, decided on the deuteration reaction for a comprehensive kinetic investigation. On account of what is known about the two general mechanisms of deuteration of heterocycles, *viz.*, one that proceeds *via* electrophilic aromatic substitution[2] and another *via* ionization of the carbon–hydrogen bond,[3] it is predictable that both of these pathways may be operative in the deuteration of 1-methylimidazole depending on medium acidity. This article details the kinetics and mechanisms of successive isotopic exchanges of the three ring hydrogens, and the derivation of the theoretical constants for the rate-determining steps which involve either a Wheland or an ylide intermediate. These rate constants allow the first quantitative comparison of the positional reactivities of this ring system, and may well be applicable to predicting or interpreting the orientation of other substitution reactions involving similar intermediates.

Results and Discussion

2-Deuteration of Imidazole. Consideration of General Acid and General Base Catalysis. The most general mechanism[3] of hydrogen–deuterium exchange in azoles and azolium systems involving an ylide intermediate is shown in Scheme I for the deuteration of imidazole at the

Scheme I



[a] Rate-determining step.

2 position. By analogy to the rate expression derived for thiazole exchange,[3a] the observed pseudo-first-order rate constant for imidazole 2-deuteration is given by eq 1,

$$k_{ob} = \frac{k_1 K_w'[D^+]}{K_a K_a' + K_a[D^+] + [D^+]^2} \quad (1)$$

where $K_w' = [D^+][OD^-]$ = the ion product constant for deuterium oxide, $K_a = [I][D^+]/[II]$, and $K_a' = [III][D^+]/[I]$. In the rate-determining hydrogen-abstraction step (II → IV), three general bases may participate: the imidazole free base (I), the imidazole anion (III), and deuterium oxide. By substituting the respective terms of I and III, which are both expressed as a function of the total imidazole concentration $[S]_t$, and $[D_2O]$ in place of $[OD^-]$ in the rate expression $d[V]/dt = k_1[OD^-][II]$, the following three equations for general base catalysis are obtained.

Imidazole [I] as the base

$$k_{ob} = \frac{k_2 K_a[D^+]^3[S]_t}{(K_a K_a' + K_a[D^+] + [D^+]^2)^2} \quad (2)$$

Imidazole anion [III] as the base

$$k_{ob} = \frac{k_3 K_a K_a'[D^+]^2[S]_t}{(K_a K_a' + K_a[D^+] + [D^+]^2)^2} \quad (3)$$

Deuterium oxide as the base

$$k_{ob} = \frac{k_4[D_2O][D^+]^2}{K_a K_a' + K_a[D^+] + [D^+]^2} \quad (4)$$

When general base catalysis does operate, k_{ob} may be given by any one or combination of these expressions.

The rate of deuteration at the 2 position was studied in the region of pD 0–16 at a constant concentration of 0.2 *M* of imidazole in deuterium oxide at unit ionic strength and 65°. The experimental rate profile shown in Figure 1A was obtained by plotting log k_{ob} *vs.* pD. This study was repeated at higher concentrations of imidazole, *viz.*, 0.5, 1.0, and 2.0 *M*, which yielded the same profile. For the sake of comparison, the sigmoid form rate profile reported by Vaughan, *et al.*,[4] for the same deuteration reaction is plotted in Figure 1B. On account of the shape of the profile in Figure 1A and its independence of substrate concentration, deuteration at the 2 position of imidazole must have followed the carbanion mechanism as shown in Scheme I and predicted by eq 1. The disparity between our rate plot and Vaughan's as shown in Figure 1 is most prominent in the regions of pD < 6 and pD > 14. Since their deuterium exchange of the 2 hydrogen of imidazole did not go beyond pD 13.65, the omission of the negative slope portion of the rate profile at pD > 14 is not unexpected. On the acidic side, however, the source of the discrepancy is less fathomable. The curve in their report levels off in the low pD region but ours decreases linearly with decreasing pD. The magnitude of k_{ob} differs considerably also, *viz.*, a $t_{1/2}$ (pD 2.88) of 11 hr is their result and 84 days being our observation. The abstraction of the 2 hydrogen by D_2O in the rate-determining step was proposed by them to account for the flattened profile in the acidic region. This proposal has prompted us to consider the operation of a certain general acid or general base catalysis. A general acid catalyzed mechanism can be readily dismissed, however, since the rate of the recombination step (k_1' of Scheme I) is not involved in the final rate expression. Whichever species furnishes the deuterium ion should be immaterial to the kinetic equation (1). General base catalysis by way of the imidazole free base I, the conjugate anion III, and D_2O may compete with the deuterioxide anion in the rate-determining step as expressed in terms of eq 2–4. In actuality, the inactive role of the imidazoles I and III is ascertained by the invariance of the observed pseudo-first-order rate constants in the range of

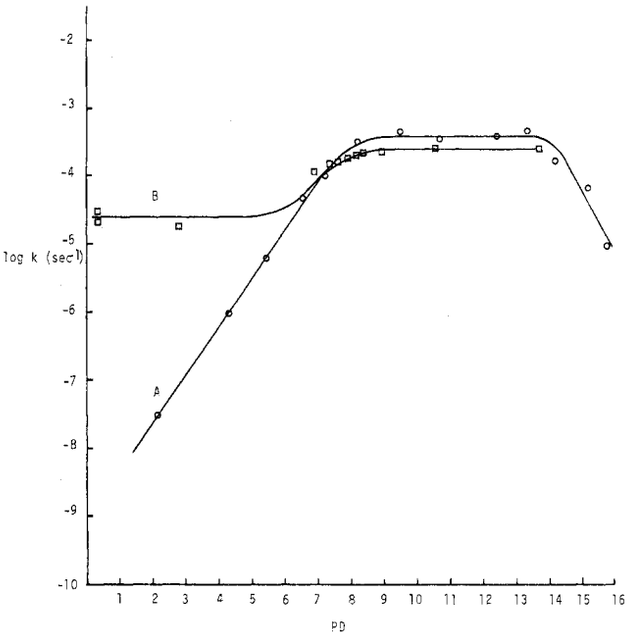
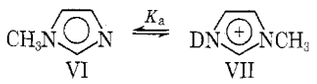


Figure 1. Experimental rate profile for 2-deuteration of imidazole at 65° and unit ionic strength: (A) this laboratory; (B) Vaughan, *et al.*, ref 6.

0.2–2 *M* of imidazole. Both eq 2 and 3 require k_{ob} to vary with $[S]_t$. In our following studies of the exchange of the three ring hydrogens of 1-methylimidazole and its methiodide salt, we have observed the same trend of declining rate in the low pD region as that shown in Figure 1A. It is pertinent to note that such decreasing rate with lower pD was also reported for the deuteration of thiazole by Olofson, *et al.*,[3a] and the deprotonation of the pyridinium ion by Zoltewicz, *et al.*[3b]

Successive Deuteration of 1-Methylimidazole and Its Methiodide Salt. Deuteration of any carbon position in a heteroaromatic system in aqueous medium may be envisaged either as an electrophilic aromatic substitution (SE) or ionization of the carbon–hydrogen bond giving rise to a carbanion intermediate (C^-). 1-Methylimidazole exists in the neutral form VI and the conjugate acid VII. Thus,



VI VII

there are four independent routes of deuteration of the three ring sites in 1-methylimidazole. In Scheme II are

Scheme II

Mechanism	Kinetic expression	Eq
(a) C^- (VI)	$k_{ob} = \frac{k_a K_a[OD^-]}{K_a + [D^+]}$	(IIa)
(b) C^- (VII)	$k_{ob} = \frac{k_b K_w'}{K_a + [D^+]}$	(IIb)
(c) SE(VI)	$k_{ob} = \frac{k_c K_a[D^+]}{K_a + [D^+]}$	(IIc)
(d) SE(VII)	$k_{ob} = \frac{k_d[D^+]^2}{K_a + [D^+]}$	(IId)

shown these four exchange mechanisms and their corresponding kinetic expressions. Equation IIa was derived in the same manner as eq 1 for imidazole, except $[S]_t$ = VI

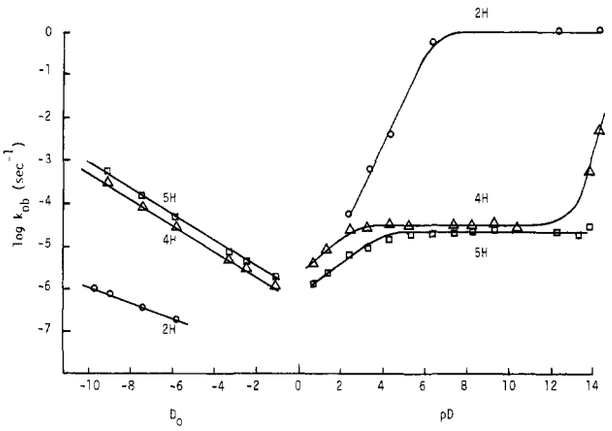


Figure 2. Experimental rate profiles for deuteration of 1-methylimidazole at 163°. Profile for the 2 position is projected from experimental values obtained at 81°.

+ VII; eq IIb from eq 1 by setting $[D^+] \gg K_a'$ and eq IIc and IId are those derived by Katritzky, *et al.*,[2] for the deuteration of heteroaromatic compounds *via* the SE route.

Deuterations at the 2, 4, and 5 position of 1-methylimidazole in a 0.2 *M* aqueous solution were studied as a function of the medium acidity. Their rate profiles are plotted in Figure 2. at the uniform temperature of 163°. All except the 2-hydrogen exchange in the pD region were conducted at this temperature. The rate constants for the latter depicted in Figure 2 were projected from the experimental values obtained at 81° using the Arrhenius equation and E_a = 20.2 kcal mol^{-1}. As a model for the deuteration of the conjugate acid species VII, 1,3-dimethylimidazolium iodide was used. The rate profiles for the deuteration at the 2 and 4(5) positions are drawn in Figure 3. The two rate equations which govern the two routes of exchange are eq 5 and 6. These equations are derivable from eq IIb and IId, respectively, by setting $[D^+] \gg K_a$.

$$k_{ob} = k_5[OD^-] \quad (5)$$

$$k_{ob} = k_6[D^+] \quad (6)$$

The rate profile for the 2-hydrogen exchange of 1-methylimidazole shown in Figure 2 is uniquely compatible with eq IIb. Thus, deuteration in this case also occurs *via* the ylide mechanism, the same as that shown for imidazole in Scheme I. The only difference in these two experimental rate profiles (*cf.* Figures 1A and 2) exists, predictably, in the high pD region where the imidazole plot becomes base dependent. The 1-methylimidazole profile continues to be level at high pD owing to the absence of the conjugate base form. The inflection point of the latter rate profile obtained at 81° at pD *ca.* 7.6 corresponds quite well to the room temperature pK_a^D of 1-methylimidazole of 7.89.[5] At 26°, the same hydrogen exchange studied by Harris, *et al.*,[6] in the acidic region is understandably sluggish. Their flattened curve of zero rate from pD 0 to 4.5 can be considered a fair representation in a preparative sense. However, it should be noted that the resulting sigmoid form of the rate plot is incompatible with eq IIb for the ylide mechanism. The profiles for the deuteration at the 4 and 5 position of 1-methylimidazole at 163° have the same general shape as that of 2-deuteration at 81° in the region of pD 0–13 (*cf.* Figure 2). This argues strongly that the same mechanism of exchange prevails in all of these cases.

At pD 13 and above the rate of 4-deuteration shows direct dependence on base concentration. This fits the equation $k_{ob} = k_a[OD^-]$ which can be derived from eq IIa

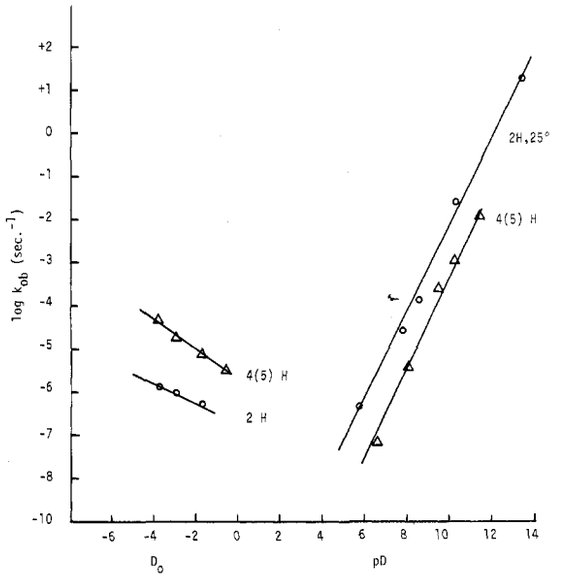


Figure 3. Experimental rate profiles for deuteration of 1,3-dimethylimidazolium iodide at 163°, except for 2 hydrogen at 25° in pD region.

when $K_a \gg [D^+]$. It appears that in this alkaline region a base-catalyzed reaction also occurred on the free base form VI, in the same way as the deuterium exchange of pyridine in NaOD–D_2O mixtures at 198° reported by Zoltewicz, *et al.*[3b] Although the rate enhancement in the high pD region was not found for 2-deuteration at 81°, a strong case of such involvement can be projected for this exchange at 163°, at which point the rate of 2-deuteration was too rapid to measure by the pmr technique. It is known that metalation of 1-methylimidazole with *n*-butyllithium occurs solely at the 2 position.[7] Thiazole 2-H exchange was shown[3a] to exhibit this rapid rate increase at higher base concentration, denoting ionization of the free base form. Since inductive stabilization of the carbanion intermediate is expected to be greatest at the 2 position of VI which is adjacent to both heteroatoms, the dual mechanism represented by eq IIa and IIb that was operative in 4-deuteration must also have prevailed in the 2-hydrogen exchange under the same conditions. The 5 position of the free base form VI, being next to a pyrrole nitrogen, showed much less tendency to follow eq IIa, and the entire profile for 5-deuteration is consistent with the ylide mechanism defined by eq IIb.

In strong acids in the $-D_0$ region and at 163°, the rate of exchange of all the ring hydrogens increased fairly linearly with acidity as depicted in Figure 2. This behavior is compatible with eq IId for an electrophilic substitution occurring on the conjugate acid VII. At $[D^+] \gg K_a$, eq IId becomes $k_{ob} = k_d[D^+]$. The strongly acidic conditions used necessitate the use of the acidity function D_x^+, and $D_x^+ = -\log [d_x^+]$. Thus, eq IId′ predicts that a plot of log

$$k_{ob} = k_d[d_x^+]$$

$$\log k_{ob} = \log k_d - D_x^+ \quad (IId')$$

k_{ob} *vs.* D_x^+ should increase with acidity and have a slope of −1. Since D_x^+ values are undetermined for the acidic conditions used, log k_{ob} is plotted as a function of D_0. D_0 is assumed[8] to be equal to H_0.[9] As the acids used deviate from ideal behavior, the slope of −1 no longer holds. The slope of the 4- and 2-hydrogen curves in Figure 2 are −0.50 and −0.25, respectively. A slope of −0.45 was observed by Katritzky, *et al.*,[2c] in the deuteration of 2,4,6-trimethylpyridine at 219° under these strong acid conditions.

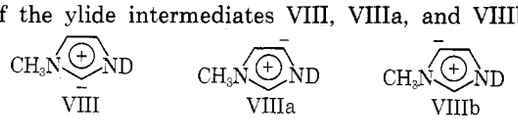
Table I
Calculated Second-Order Rate Constants of Deuteration at 163° for All Ring Sites[a]

Ring position	1-Methylimidazole k, M^{-1} sec^{-1}	1-Methylimidazole Rel rate	1,3-Dimethylimidazolium iodide k, M^{-1} sec^{-1}	1,3-Dimethylimidazolium iodide Rel rate
		A. pD 0–13		
2	1.11×10^{2} (25°)[b]		2.70×10^{2} (25°)[c]	
	9.00×10^{6} [b]	54,500		
4	2.60×10^{2}	1.56	3.42×10^{2}	
5	1.65×10^{2}	1.00	3.42×10^{2}	
		B. D_0 − 10–0		
2	8.32×10^{-7}	1.00	1.62×10^{-5}	1.0
4	6.03×10^{-5}	73	6.39×10^{-4}	39
5	9.78×10^{-5}	120	6.39×10^{-4}	

[a] Calculations are based on k_{ob} (163°) at pD 7.4 and D_0 − 2.84 for 1-methylimidazole and k_{ob} (163°) at pD 11.4 and D_0 − 2.84 for the imidazolium salt. [b] Calculated from k_{ob} (25°) and k_{ob} (163°) which are extrapolated from the experimental value of k_{ob} (81°) by the use of the Arrhenius equation and E_a = 20.2 kcal mol^{-1}, the latter being determined in the temperature range of 30–81°. [c] Calculated from the experimental value of k_{ob} (25°).

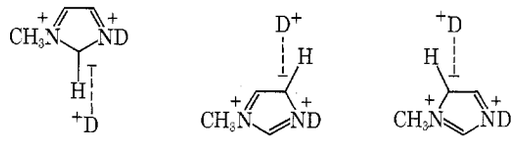
These mechanistic postulates for the deuterations of 1-methylimidazole in the pD and $-D_0$ regions are further reinforced by the kinetic behavior of the deuteration of 1,3-dimethylimidazolium iodide under similar conditions. With reference to Figure 3, the profiles observed in the pD region for deuteration at the 2 position at 25° and the 4(5) position at 163° increase linearly with basicity and have slopes of 1.0 and 1.2, respectively. This is ideally suited to eq 5 denoting the carbanion mechanism. In strong acids, the rates of 2- and 4(5)-hydrogen exchanges increase linearly with acidity as predicted by eq 6, and in the same manner as shown by the exchanges of the 1-methylimidazole hydrogens. This again corroborates the electrophilic substitution mechanism proposed for the latter heterocycle. Further revelation of the consistency of these deuteration mechanisms for the two compounds can be seen in the quantitative comparison of the calculated second-order rate constants shown in Table I and the discussion which follows.

Positional Reactivities of 1-Methylimidazole. The kinetics of deuteration of the three ring positions of 1-methylimidazole are defined by eq IIb in the region of pD 0–13 and by eq IId in the $-D_0$ region. Given the observed pseudo-first-order rate constants at 163°, the second-order rate constants k_b and k_d can be obtained from the above equations for each ring position. These constants k_b and k_d, uncluttered by parameters such as the substrate concentration, solution pD, as well as pK_a^D and pK_w', have provided a quantitative account of the intrinsic reactivity of the 2, 4, and 5 positions in undergoing deuteration. In Table I are shown the theoretical constants for a specific deuteration site in 1-methylimidazole and its methiodide salt. These values are approximate solutions of eq IIb and IId, since pK_a^D,[5] pK_w',[10] and [D$^+$], which were measured at room temperature, are used in conjunction with k_{ob} at 163° uncorrected for the temperature difference. However, the accuracy of rate comparison is not compromised. The relative rates of deuteration at the 2, 4, and 5 positions at pD 0.13 are 54,500:1.6:1. These reflect the inherent stability of the ylide intermediates VIII, VIIIa, and VIIIb, respectively. The 2 hydrogen is expected to exchange fastest, since the carbanion is uniquely flanked by two nitrogens. The large inductive effect of nuclear nitrogen atoms in promoting deprotonation of some azoles was shown by Olofson, *et al.*[11] Similar inductive reasoning allows that the reaction at the 5 position should be depressed relative to that at the 4 position because of the proximity of the N_1-methyl group. By the same token the relationship of $k_2 > k_4 > k_5$ should also hold at pD > 13, although no meaningful numerical data are available to make the comparison.



VIII VIIIa VIIIb

The relative rates of deuteration in strong acids in the 2, 4, and 5 position of 1-methylimidazole are 1:73:120, respectively. In comparing the transition states, the electrophile D$^+$ would encounter less charge repulsion in transition states VIIb and VIIc than in VIIa. The two positive



VIIa VIIb VIIc

nitrogens are cross conjugated in VIIb and VIIc but fully conjugated in VIIa; the latter, therefore, is destabilized more. Thus, the greater reactivity of the 4 and 5 position can be rationalized on the basis of the proposed SEAr mechanism involving the conjugate acid VII. The faster rate of 5- over 4-deuteration is attributable to the electron-donating effect of the N_1-methyl group.

The second-order rate constants for 1,3-dimethylimidazolium iodide undergoing the ylide deuteration route are very comparable to those for 1-methylimidazole. In strong acids where an electrophilic substitution mechanism prevails, the additional methyl group in the methiodide salt exerts further stabilization of the transition state. This results in higher rate constants than their counterparts in the deuteration of 1-methylimidazole.

Experimental Section

Materials. Imidazole and 1-methylimidazole were purchased from Aldrich Chemical Co.; the former was sublimed at 50° (2 mm) and recrystallized from benzene, mp 90°, and the latter was redistilled before use. 1,3-Dimethylimidazolium iodide was prepared according to Overberger.[12]

Sample Preparations. In the pD region, 1 ml of a 0.2 *M* solution of the imidazole in D_2O was prepared. To it was added 0.05 ml of a 0.2 *M* solution of 3-(trimethylsilyl)propanesulfonic acid sodium salt in D_2O as the internal pmr standard. Desirable acidities of pD 0–13 were obtained by adding micro amounts of 6 *N* NaOD or 38% DCl, and the pD values were calculated by adding 0.4 to the observed pH-meter values.[13] Strongly alkaline solutions with pD > 13 were prepared from concentrated NaOD solutions which were standardized by titration with standard 0.1 *N* acid, and the pD values were calculated from the equation pD + pOD = 14.86.[10] Generally, the initial and the final pD values measured at the end of the deuteration experiments agreed to within 0.1 pD unit. In a few instances additional runs were made using phosphate buffers. We found no real difference in rate when they were

Table II
Rate of Exchange of Imidazole at 65°

pD	k_{ob}, sec^{-1}
15.7	8.70×10^{-6}
15.3	6.55×10^{-5}
14.2	1.56×10^{-4}
13.3	4.22×10^{-4}
12.4	3.84×10^{-4}
10.7	3.24×10^{-4}
9.5	4.03×10^{-4}
8.2	3.06×10^{-4}
7.2	9.16×10^{-5}
6.5	4.34×10^{-5}
5.4	6.06×10^{-6}
4.3	8.83×10^{-7}
2.1	2.89×10^{-8}

compared to the unbuffered ones. For the exchange of the 2 hydrogen in imidazole, the ionic strength of the imidazole solutions was adjusted to 1.0 M with sodium chloride solution. This was done to reproduce precisely the reaction conditions described by Vaughan, *et al.*[4] This adjustment was not made in other exchange experiments, since 2-deuteration of 1-methylimidazole at pD 10.9 and 81° and ionic strength varying between 0.02 and 1.1 showed that the rate dependence on ionic strength is negligible and within experimental error. For experiments to be carried out at less than 100°, the sample was heated in the nmr tube. At >100°, samples were heated in a sealed glass ampoule or in a stainless steel bomb for strongly alkaline solutions (pD > 13). In the concentrated acid region, the deuteration of 1-methylimidazole was done in D_2SO_4–D_2O mixtures. Commerical 98% D_2SO_4 was standardized against sodium hydroxide solution of known molarity. Solutions of specific D_0 values were prepared by dilution with D_2O and it was assumed[8] that D_0 was numerically equal to the reported[9] values of H_0. Mixtures of DCl–D_2O of varying D_0 values[9] were used as media for the deuteration of 1,3-dimethylimidazolium iodide, since this salt was found to react with sulfuric acid at raised temperatures.

Kinetic Measurements. The kinetics of deuteration were followed by pmr technique using a Varian A-60A spectrometer. At various intervals until 1 half-life had elapsed, the pmr spectra of the sample were recorded and integrated at two or more spectrum amplitudes for four times each. The fraction of hydrogen left at a given time for an exchanging proton was calculated by reference to a nonexchanging proton or group. The N-methyl group was used as reference peak for 1-methylimidazole and the dimethyl salt. For imidazole, the trimethylsilyl peak of the internal standard 3-(trimethylsilyl)propanesulfonic acid sodium salt was integrated and used as reference. A plot of the natural logarithm of the fraction of hydrogen left *vs.* time gave a linear plot. This indicates a first-order or a pseudo-first-order reaction. The slope of the plot is the negative of the observed rate constant. The pseudo-first-order rate constants were calculated using a standard linear least-squares routine.[14] These were run on the IBM 360-40 computer. Statistical analysis produced correlation coefficients of greater than 98%. Specific conditions for the exchange study of the three different imidazoles are described below.

Imidazole. δ (D_2O, pD 12.4) H-2 7.80, H-4(5) 7.17. Exchange of the 2 hydrogen was done in a nmr sample tube at 65 ± 0.1° in a thermostatically controlled constant-temperature bath. The sample was quenched by cooling before pmr analysis. Rate data are summarized in Table II.

1-Methylimidazole. δ (D_2O, pD 12.4) H-2 7.63, H-4 7.13, H-5 7.03, NCH_3 3.27. Deuteration at the 2 position in the pD region at 81° was carried out as above. Other exchanges in the pD and $-D_0$ regions were done in a sealed tube at 163 ± 2.0° using refluxing bis(2-methoxyethyl) ether as the constant-temperature heating medium. The 2 hydrogen was measured directly by pmr technique. In acidic solutions of pD < pK_a, the 4 and 5 protons of 1-methylimidazole merge into a single peak. Therefore, a slightly different procedure was necessary in order to observe the exchange of these protons individually. In the region of pD 0–6, 3-ml samples were used in the exchange experiments. Aliquots of 0.5 ml were withdrawn at invervals of heating and cooled, and concentrated NaOD was added to bring the pD of the solution to *ca.* 8 so that the 4 and 5 protons were distinct. For the exchange studies in the $-D_0$ region, this treatment led to a large amount of sodium salt in the sample, which lowered the quality of the spectrum. Hence the 1-methylimidazole was extracted into carbon tetrachloride for spectral measurements. No decomposition was observed in any of these samples studied. The rate data are shown in Table III.

Table III
Rate of Exchange of 1-Methylimidazole

pD (D_0)	k_{ob}, sec^{-1} 2-H (81°) (163°)*	4-H (163°)	5-H (163°)
14.2	3.00×10^{-3}	3.64×10^{-3}	
13.9		4.86×10^{-4}	2.42×10^{-5}
13.4		1.07×10^{-4}	1.85×10^{-5}
12.4	2.94×10^{-3}	3.08×10^{-5}	1.72×10^{-5}
10.4		2.20×10^{-5}	
9.4		3.48×10^{-5}	2.66×10^{-5}
8.4		2.86×10^{-5}	2.25×10^{-5}
7.4		2.78×10^{-5}	1.84×10^{-5}
6.4	2.06×10^{-3}	3.50×10^{-5}	1.75×10^{-5}
5.4		2.78×10^{-5}	1.63×10^{-5}
4.4	1.49×10^{-5}	3.25×10^{-5}	1.23×10^{-5}
3.4	2.29×10^{-6}	2.92×10^{-5}	8.91×10^{-6}
2.4	2.20×10^{-7}	2.62×10^{-5}	6.22×10^{-6}
1.4		9.20×10^{-6}	1.97×10^{-6}
0.8		4.06×10^{-6}	1.37×10^{-6}
−1.06		1.37×10^{-6}	2.18×10^{-6}
−2.42		3.25×10^{-6}	4.50×10^{-6}
−3.30		5.67×10^{-6}	1.01×10^{-5}
−5.82	2.35×10^{-7} *	3.00×10^{-5}	4.08×10^{-5}
−7.46	3.92×10^{-7} *	9.66×10^{-5}	1.37×10^{-4}
−9.01	8.22×10^{-7} *	3.89×10^{-5}	5.28×10^{-4}
−9.98	1.03×10^{-6} *		

Table IV
Rate of Exchange of 1,3-Dimethylimidazolium Iodide

pD (D_0)	k_{ob}, sec^{-1} 2-H (25°) (163°)*	4(5)-H (163°)
13.4	1.81×10^{1}	
11.4		1.24×10^{-2}
10.3	2.52×10^{-2}	1.04×10^{-3}
9.5		2.44×10^{-4}
8.5	1.22×10^{-4}	
8.0		3.20×10^{-6}
7.8	2.35×10^{-5}	
6.6		5.95×10^{-8}
5.7	4.17×10^{-7}	
−0.615		3.17×10^{-6}
−1.73	4.72×10^{-7} *	6.65×10^{-6}
−2.84	8.56×10^{-7} *	1.84×10^{-5}
−3.80	1.12×10^{-6} *	4.42×10^{-5}

1,3-Dimethylimidazolium Iodide. δ (D_2O, pD 12.4) H-2 8.65, H-4(5) 7.43, NCH_3 3.98. The 2-hydrogen exchange was studied at 25° in the pD region and all other deuterations at 163° by methods as shown above. The pmr measurements of the 4(5) hydrogens, however, require a comment. Since the 4 and 5 protons of this salt are indistinguishable, initial exchange may occur at either position. This represents an example of two consecutive first-order reactions

$$A \xrightarrow{k_1} B \xrightarrow{k_2} C$$

where A = undeuterated salt, B = monodeuterated salt, and C = dideuterated salt, and $k_2 = k_1/2$ since the 4 and 5 protons are indistinguishable. During an exchange reaction the area of the pmr signal of the 4(5) protons is proportional to the concentration of A plus half the concentration of B at the given time. It follows directly from the usual kinetic treatment of consecutive first order reactions that when $k_2 = k_1/2$

$$A + B/2 = A_0 e^{-k_1 t/2}$$

so that

$$\ln \frac{A + B/2}{A_0} = -k_1 t/2$$

Since $(A + B/2)/A_0$ is measured directly by pmr, a plot of these ln values *vs.* time gives a straight line which has a slope of $-k_1/2$. Since $k_2 = k_1/2$, a pmr experiment gives k_2 directly. Therefore, the rate constant directly measured by nmr represents the rate of exchange of only one of the indistinguishable protons.

This quantity is comparable to the data for one-proton exchange determined for other imidazoles. The rate data are summarized in Table IV.

Registry No.—1-Methylimidazole, 616-47-7; 1,3-dimethylimidazolium iodide, 4333-62-4.

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Transfer-Hydrogenation and Transfer-Hydrogenolysis. IV. Catalytic Dehydrogenation by a Quinone

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The dehydrogenation of 2-propanol by chloranil was found to occur in the presence of several transition metal complexes to give acetone and tetrachlorohydroquinone. Some of these reactions seem to be explained by a mechanism that requires both the donor and the acceptor to coordinate simultaneously on the central metal of the catalyst, and hydrogen atoms to be transferred directly from the former to the latter without forming hydride complexes. The dehydrogenation of tetralin and 2,5-dihydrofuran, which are unsaturated compounds, was not influenced by the addition of the metal complexes.

The dehydrogenation of unsaturated compounds by quinones is well known and has been considered to proceed *via* a two-stage ionic process involving a charge transfer complex.[1] The reaction usually requires double bonds or aromatic rings in the hydrogen donors, so that dehydrogenation of saturated heterocompounds by quinones is unusual.[1]

We have found that catalytic hydrogen transfer from 2-propanol[2] or dioxane[3] to olefins proceeds *via* hydride complexes. Moreover, direct hydrogen transfer involving no hydride complex seems not to have been reported in the hydrogenation of olefins[4] or quinones[1,4] catalyzed by transition metal complexes. This study was undertaken to examine the possibility that direct hydrogen transfer can take place from a hydrogen donor to a quinone, without involving a hydride complex, when the reactants do not form a charge transfer complex but are simultaneously coordinated to a transition metal complex.

Results

Hydrogen Donors. As hydrogen acceptor, chloranil was mainly used because of its relatively high thermal stability and hydrogen accepting power. Duroquinone also was used in some cases.

The desirable hydrogen donors for the purpose of this study are those which do not form charge transfer complexes with quinones but do coordinate to transition metals. From this viewpoint, various saturated heteroatom compounds were examined as hydrogen donors.

A hydrogen donor and chloranil (0.25 mol each) and 0.025 mol of $NiBr_2(PBu^n{}_3)_2$ were heated in *o*-dichlorobenzene at 170° for 2 hr. 2-Propanol gave a considerable amount of acetone along with 2-chloropropane. Cyclohexanol and cyclohexyl chloride gave phenol and chlorobenzene, respectively, but the yields were less than 5%. In the reaction of *N*-methylpyrrolidine as a hydrogen donor, neither the expected product, *N*-methylpyrrole, nor unreacted *N*-methylpyrrolidine was detected after the reaction. The same result was obtained in the reaction of the amine at 140°. This observation may be explained by the assumption that the tertiary amine reacted with chloranil.[5] In the reaction of the amine with duroquinone in the presence of $NiBr_2(PBu^n{}_3)_2$, *N*-methylpyrrolidine survived, but *N*-methylpyrrole was not detected.

The reaction in which 2-propanol was used as a hydrogen donor was examined in detail, because the alcohol donated hydrogen catalytically in spite of the formation of 2-chloropropane in a side reaction. For comparison, the reactions of tetralin and 2,5-dihydrofuran, which are unsaturated compounds, were also investigated.

Solvents. To find a suitable solvent, equimolar amounts of 2-propanol and chloranil were heated in several solvents in the presence of $NiBr_2(PBu^n{}_3)_2$ and the reaction mixtures were submitted to gas–liquid chromatographic analysis. The results are summarized in Table I. The solvents of moderate coordinating ability were found to be suitable. Because of the convenience of the analysis, the experiments hereafter were carried out in chlorobenzene.

Dehydrogenation of 2-Propanol. 2-Propanol and chloranil gave acetone, tetrachlorohydroquinone, and 2-chloropropane in the presence of catalysts. The formation of tetrachlorohydroquinone was confirmed by isolation of it as crystals from the reaction mixture and by comparison with an authentic sample. Though the yield of acetone based on the amount of charged chloranil was much higher when 2-propanol was used as hydrogen donor and solvent, the solubility of catalysts in the alcohol was small. The reactions were therefore carried out in chlorobenzene at 170° for 2 hr. The results are summarized in Table II.