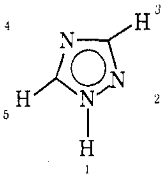
Kinetics of Deuteration of 1,2,4-Triazole

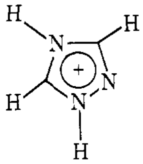
John D. Vaughan,* E. Chung Wu, and Chin Tsung Huang

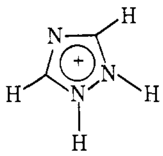
Department of Chemistry, Colorado State University, Fort Collins, Colorado 80521

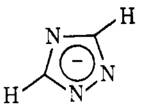
Received March 26, 1974

1,2,4-Triazole (1) can gain a proton or lose one with about equal ease to form cations 2 or 3 or an anion 4. From


1


2


3


4

literature values[1] of pK_b and pK_a for 1, the concentrations of cations and anion in a 1 *M* solution of 1 at pH 7 are calculated to be 2×10^{-5} and 5×10^{-4} *M*, respectively. In earlier work, the 4 position in pyrazole[2a] was found to undergo deuteration *via* parallel electropholic attacks of the anion and the free molecule to form σ intermediates. However, the 3(5) position in pyrazole[2a] and the 2 and 4(5) positions in imidazole[2b] were deuterated *via* proton abstraction from the cation by OD^- to form ylide intermediates; for pD > 10, deuteration of the imidazole 4(5) position involved parallel proton abstractions from both cation and molecule. Since neutral molecules, cations, and anions are all present in kinetically significant concentrations in aqueous solutions of 1,2,4-triazole, it is of interest to determine which of these forms are involved in the deuteration of the compound. In addition, it is of interest to compare the rates of deuteration of sites in 1,2,4-triazole with sites in other five-membered heterocycles.

Rates of deuteration of the 3(5) position in 1,2,4-triazole were measured as functions of pD, ammonia buffer concentration, temperature, and ionic strength. The ionic strength was held at 1.0 *M* in all runs except those in which the rate was studied as a function of ionic strength. The effect of pD upon the pseudo-first-order rate constant is shown in Figure 1. pD rate profiles qualitatively similar to this one have been observed for imidazole,[2a] substituted imidazoles,[3] and thiazole.[4] The rate constant decreases abruptly as pD decreases in the region of substrate self-buffering. When pD equals the pK_a value of the conjugate acid 2 (or 3), the rate of deuteration is halved. Thus, at pD = pK_a = 2.8, k_1^{obsd} is half that for pD values larger than 5. In ammonia buffered runs, the buffer ratio $[ND_3]/[ND_4^+]$ was fixed at 3.2 (pD 10.4). In seven such runs at 65°, in which $[ND_3]$ ranged from a low of 5×10^{-4} *M* to 1.73 *M*, k_1^{obsd} remained constant at $9.7 \times 10^{-5} \pm 0.5 \times 10^{-5}$ sec^{-1}. It is evident from this result that the deuteration reaction is not catalyzed by either the base or acid component of the buffer.

Activation parameters were determined from runs made at 55, 65, 70, and 75°; k_1^{obsd} values were 3.1×10^{-5}, 9.8×10^{-5}, 15.8×10^{-5}, and 23.7×10^{-5} sec^{-1}, respectively. The experimental activation energy was 23 ± 2 kcal and the log *A* value 13 ± 1. pD was 6.6 in these runs, while substrate concentration was 1.0 *M*.

To determine the effect of ionic strength μ upon the observed rate constant, the concentration of NaCl was varied from zero ($\mu \sim 0$) to 5 *M*. The results are shown in Table I. At low salt concentrations, no effect is discernible. The dependence of the rate constant upon μ is small even at high salt concentrations.

Table I
Effect of Ionic Strength upon the Rate Constant

μ	$k_1^{obsd} \times 10^5$, sec^{-1}
0.000	11.77
0.025	11.54
0.050	12.05
0.100	11.69
1.00	9.94[a]
2.50	9.78
5.00	8.17

[a] pD > 5, [substrate] = 1.0 *M*, average of 15 runs. In other runs, pD = 6.6, [substrate] = 0.5 *M*.

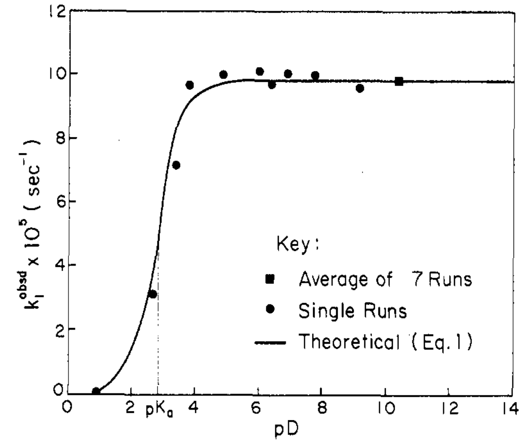
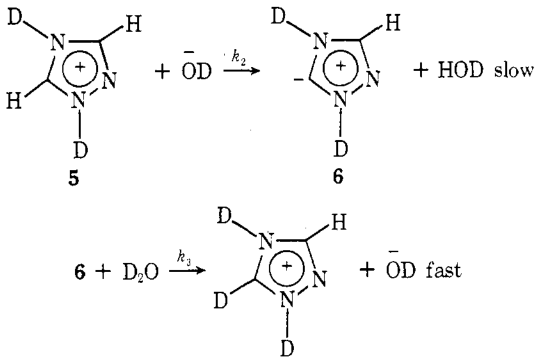
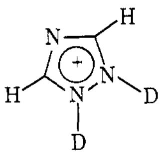


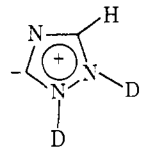
Figure 1. Dependence of the rate of deuteration of 1,2,4-triazole upon pD at 65°.

Scheme I



The pD–rate profile exhibited in Figure 1 is consistent with rate-determining ylide 6 formation (Scheme I). Alternatively, 1,2,4-triazolium-*1,2*-d_2 (7) could replace 1,2,4-triazolium-*1,4*-d_2 (5) in this scheme, leading to the corresponding ylide 8. However, ylide 8 with its adjacent lone


7


8

pairs is likely to be far less stable than ylide 6, in which the lone pairs are separated. CNDO/2 calculations carried out in this laboratory and others reported in the literature[5] suggest that 5 is slightly more stable than 7, and that 6 is markedly more stable than 8. Similarly, EHT calculations by Adam, Grimison, and Hoffmann[6] on six-membered heteroaromatic carbanions showed that carbanions with adjacent lone pairs are less stable than those with separated lone pairs. Accordingly, deuteration *via* 7 is likely to be negligible compared to deuteration *via* 5.

For deuterations conforming to Scheme I, the following equation has been derived.[2b,3b,4]

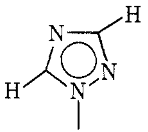
$$k_1^{\mathrm{obsd}} = k_2 K_w/(K_a + [\mathrm{D}^+]) \qquad (1)$$

Here, K_w[7] $[\mathrm{D}^+][\mathrm{OD}^-] = 2.9 \times 10^{-15}$, and $K_a = 1.6 \times 10^{-3}$ is the acid dissociation constant for cationic substrate **5** (see Experimental Section). Equation 1 provides a good fit of the data if k_2 is set equal to 8×10^7 sec^{-1} M^{-1} (solid curve in Figure 1). For $[\mathrm{D}^+] \ll K_a$, eq 1 reduces to

$$k_1^{\mathrm{obsd}} = k_2 K_w/K_a \qquad (2)$$

which is applicable for pD values larger than 5.

The effect of ionic strength upon k_1^{obsd} can be predicted by first applying the Brønsted–Bjerrum equation[8] to the slow bimolecular formation of **6**, then replacing the concentration of **5** in the differential rate equation by the concentration of 1,2,4-triazole-*1-d*$_1$ (**9**). Thus, we find



9

$$\text{rate} = -\frac{\mathrm{d}}{\mathrm{d}t}[\mathbf{9}] = k_2^{\circ}(\gamma^{(4)}\gamma_{\mathrm{O\bar{D}}}/\gamma^{\ddagger})[\mathbf{4}][\mathrm{O\bar{D}}]$$

$$[\mathbf{4}] = \frac{1}{K_a^{\circ}}(\gamma_{\mathrm{D^+}}\gamma^{(9)}/\gamma^{(4)})[\mathbf{9}][\mathrm{D}^+]$$

Here the superscript ° indicates infinite dilution and γ the activity coefficient. Substituting the second equation into the first,

$$\text{rate} = \frac{k^{\circ(2)}}{K_a^{\circ}} K_w^{\circ} \frac{\gamma^{(9)}}{\gamma^{\ddagger}}[\mathbf{9}] = k_1^{\mathrm{obsd}}[\mathbf{9}]$$

$$k_1^{\mathrm{obsd}} = \frac{k_2^{\circ}}{K_a^{\circ}} K_w^{\circ} \frac{\gamma^{(9)}}{\gamma^{\ddagger}} \qquad (3)$$

where $K_w^{\circ} = \gamma_{\mathrm{D}^+}\gamma_{\mathrm{OD}^-}[\mathrm{D}^+][\mathrm{OD}^-]$. Since both **9** and the transition state leading to the ylide intermediate (**6**) have zero charge, $\gamma^{(9)}$ and $\gamma^{\ddagger}$ are each unity for low salt concentrations (Debye–Hückel region). Therefore, eq 3 predicts the observed independence of k_1^{obsd} upon ionic strength for low ionic strength. This agreement at low ionic strength provides additional support for Scheme I. Outside the Debye–Hückel region, eq 3 cannot predict the dependence of k_1^{obsd} upon ionic strength, because estimates of the magnitudes of activity coefficients of uncharged solutes in media of high ionic strength cannot be reliably made.[9]

Most of the rate data on hydrogen exchange in five-membered heterocyclic cations reported in the literature[4,10-12] were taken at 31 and 33°. The k_2 value for 1,2,4-triazolium cation calculated for 33° using the Arrhenius equation is 1.5×10^6 sec^{-1} M^{-1}. Carrying out similar reductions of k_2 from higher temperatures to 33° for positions in imidazolium and pyrazolium cations, the following comparison with literature values was obtained.

1,4-diethyltetrazolium (5 position)[10]	$\sim 10^{9.5}$
3,4-dimethyloxazolium (2)[12]	$\sim 10^{5}$
1,2,4-triazolium (5), thiazolium (2)[4]	$\sim 10^{3.5}$
3,4-dimethylthiazolium (2)[12]	
imidazolium (2)[2b]	$\sim 10^{0}$
1,3-dimethylimidazolium (2)[10]	
1,3,4-trimethylimidazolium (2)[12]	
imidazolium [4(5)][2b]	$\sim 10^{-5}$
pyrazolium [3(5)][2a]	$\sim 10^{-5}$–10^{-7}
1,2-dimethylpyrazolium (3,5)	

No distinction was made in this reactivity order between unsubstituted and *N*- or *C*-alkyl substituted cations, since these substituents have relatively small effect upon the exchange reactivity.[2b] As expected, the exchange reactivity of 1,2,4-triazolium lies between the reactivities of imidazolium and tetrazolium cations.

For discussing relative reactivities of cationic substrates undergoing hydrogen exchange according to Scheme I, the ylide intermediate is probably a reasonable model for the transition state.[2-5,10-12] Factors that stabilize the intermediate would tend to stabilize the transition state. If a β C–H group in imidazolium cation is replaced by a pyridine-type nitrogen atom, yielding 1,2,4-triazolium ion, the rate constant for hydrogen exchange is enhanced by a factor of $10^{3.5}$; this enhancement is the same as that observed by Olofson, *et al.*,[11] when an extra β nitrogen was added to the thiazole molecule yielding 1,3,4-thiadiazole. A second pyridine-type nitrogen atom added to imidazolium, yielding tetrazolium, produces an additional increase in rate constant of 10^6. It is evident that the second nitrogen heteroatom provides significantly greater stabilization in the ylide intermediate than does the first one. Further, a vicinal pair of nitrogen heteroatoms, as in 1,2,4-triazolium cation, stabilizes the five-membered ylide to about the same extent as a single sulfur heteroatom, as in thiazolium.

Experimental Section

Materials. 1,2,4-Triazole from Aldrich Chemical Co. was recrystallized three times from a benzene–ethanol solution (4:1 by volume), mp 120°. The nmr spectrum of 1,2,4-triazole exhibited two singlets (δ 4.8 and 8.5 relative to TMS) attributed to hydroxyl protons and protons in equivalent 3 and 5 positions, respectively. It is clear that nitrogen protons exchange rapidly with deuterons in heavy aqueous solution.

Kinetic Runs. The details of the kinetic procedures are given elsewhere.[2] The ionic strength of solutions was adjusted by measured addition of heavy aqueous NaCl. All deuterations were carried out in 100-ml round-bottom flasks held at constant temperature in a water bath. Aliquots of 2 ml each were removed periodically, then thermally quenched (0°). Proton peak areas for substrate exchange sites were determined for each aliquot using the Varian A-60A spectrometer.[2] Pseudo-first-order rate constants ($k_1^{\mathrm{obsd}} = k_2[\mathrm{D_2O}]$) were obtained from [−slope of ln (peak area)] *vs.* time plots.

pD values were measured at room temperature with the Beckman Zeromatic pH meter, corrected by the formula of Glaskoe and Long (pD = meter reading + 0.4).[13] The pK_a value for 1,2,4-triazolium cation was determined in heavy water solutions at ionic strength of 1.0 M and at buffer ratios [triazole]/[triazolium] of 1:1 and 1:3. The value pK_a = 2.8 ± 0.1 is the average of two measurements.

Temperatures were reproducible to within ±0.1° and rate constants to within ±10%. Uncertainties in concentrations arising from thermal changes in volume are discussed elsewhere.[2]

Registry No.—1,2,4-Triazole, 288-88-0.

References and Notes

(1) A. Albert, "Heterocyclic Chemistry," 2nd ed, The Athlone Press, University of London, 1968, p 441.

(2) (a) E. C. Wu and J. D. Vaughan, *J. Org. Chem.*, **35**, 1146 (1970); (b) J. D. Vaughan, Z. Mughrabi, and E. C. Wu, *ibid.*, **35**, 1141 (1970).

(3) (a) T. M. Harris and J. C. Randall, *Chem. Ind.* (*London*), 1728 (1965); (b) J. H. Bradbury, B. E. Chapman, and E. A. Pellegrino, *J. Amer. Chem. Soc.*, **95**, 6139 (1973).

(4) R. A. Coburn, J. M. Landesberg, D. S. Kemp, and R. A. Olofson, *Tetrahedron*, **26**, 685 (1970).

(5) M. A. Schroeder and R. C. Makino, *Tetrahedron*, **29**, 3469 (1973).

(6) W. Adam, A. Grimison, and R. Hoffmann, *J. Amer. Chem. Soc.*, **91**, 2590 (1969).

(7) A. K. Covington, R. A. Robinson, and R. G. Bates, *J. Phys. Chem.*, **70**, 3820 (1966).

(8) S. Glasstone, "Textbook of Physical Chemistry," 2nd ed, Van Nostrand, Princeton, N. J., 1946, p 1114.

(9) K. J. Laidler, "Chemical Kinetics," 2nd ed, McGraw-Hill, New York, N. Y., 1965, p 229.

(10) R. A. Olofson, W. R. Thompson, and J. S. Michelman, *J. Amer. Chem. Soc.*, **86**, 1866 (1964).

(11) R. A. Olofson, J. M. Landesberg, K. N. Houk, and J. S. Michelman, *J. Amer. Chem. Soc.*, **88**, 4265 (1966).
(12) P. Haake, L. P. Bauscher, and W. B. Miller, *J. Amer. Chem. Soc.*, **91**, 1113 (1969).
(13) P. K. Glaskoe and F. A. Long, *J. Phys. Chem.*, **64**, 188 (1960).

Electrogenerated Chemiluminescence. XIX. Preparation and Chemiluminescence of 5,12-Dibromo-5,12-dihydro-5,6,11,12-tetraphenylnaphthacene[1]

Csaba P. Keszthelyi and Allen J. Bard*

Department of Chemistry, The University of Texas at Austin, Austin, Texas 78712

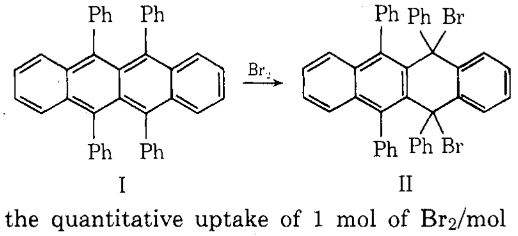
Received February 27, 1974

In recent years considerable interest has been centered on reactions that convert chemical energy directly to light, with the discovery of new chemiluminescor compounds comprising an important segment of the work. Two general types of electrogenerated chemiluminescence (ecl) have been investigated. The most widely studied is ecl occurring when reduced (A^-) and oxidized (D^+) species (frequently radical ions) generated at an electrode undergo an electron transfer reaction producing an electronically excited state (eq 1).[2] A second form of ecl involves the reduction of certain halogenated hydrocarbons [*e.g.*, 9,10-dichloro-9,10-dihydro-9,10-diphenylanthracene ($DPACl_2$)] at an electrode without the electrogeneration of an oxidant;[3,4] chemical reduction of these same compounds, *e.g.*, $DPACl_2$, by naphthalene or 9,10-diphenylanthracene (DPA) radical anions was shown to produce light in earlier studies.[5] The ecl studies of Siegel and Mark[3,4] demonstrated that the electrode potential must be such that reduction of the $DPACl_2$ and the generation of a radical anion occurs for emission to be observed. Thus reduction of $DPACl_2$ and 5,6,11,12-tetraphenylnaphthacene (rubrene) (I) produces emission characteristic of rubrene fluorescence[3,4] while reduction of $DPACl_2$ and $\alpha,\beta,\gamma,\delta$-tetraphenylporphin (TPP) produces emission from excited TPP.[6] We report here the preparation of 5,12-dibromo-5,12-dihydro-5,6,11,12-tetraphenylnaphthacene (RBr_2) (II) and the luminescence produced on its electroreduction. The preparation and chemiluminescent properties of this molecule have not previously been reported.

$$A^- + D^+ \longrightarrow D + A^*(\longrightarrow A + h\nu) \qquad (1)$$

Results

When rubrene in dry dichloromethane solution is treated with bromine at room temperature, RBr_2 is produced (eq 2)



I II

(2)

with the quantitative uptake of 1 mol of Br_2/mol of rubrene, without further bromination even in the presence of excess bromine. The solid RBr_2 decomposes at atmospheric pressure at temperatures above 120° to produce rubrene (identified by its fluorescent spectrum) and bromine; thermogravimetric studies of RBr_2 confirm the liberation of 1 mol of Br_2/mol of RBr_2 with the production of pure rubrene.[7] Uv irradiation of solutions of RBr_2 also causes decomposition with the production of rubrene. RBr_2 itself shows weak fluorescence emission (λ_{max} 402 nm) and an excitation maximum at 320 nm; these results are consistent with absorption and emission from a molecule containing a conjugated diphenylnaphthalene chromophore.

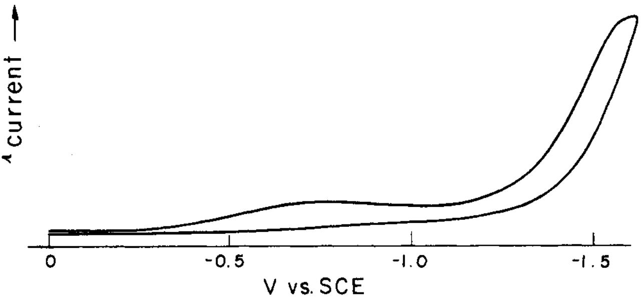


Figure 1. Cyclic voltammogram of a dichloromethane solution containing 1 m*M* RBr_2 and 0.1 *M* TBAP at a platinum electrode; the solvent background reduction occurs shortly beyond the span shown.

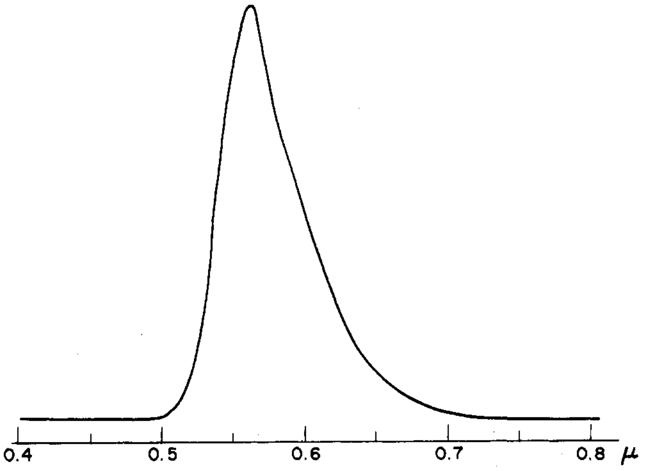


Figure 2. Electrogenerated chemiluminescence observed in the solution of Figure 1 upon application of a steady potential corresponding to the reduction peak.

A cyclic voltammogram for the reduction of RBr_2 in dichloromethane containing 0.1 *M* tetra-*n*-butylammonium perchlorate (TBAP) at a platinum electrode, shown in Figure 1, shows an irreversible reduction wave at about −1.5 V *vs.* sce. Since the reduction of rubrene (R) to its radical anion ($R\cdot^-$) occurs with an $E_{1/2}$ value of −1.39 V *vs.* sce, any rubrene produced in the reduction of RBr_2 is immediately reduced further. The electroreduction is accompanied by the emission of radiation characteristic of rubrene fluorescence (λ_{max} 560 nm) (Figure 2). Although a detailed mechanistic study of the mechanism of electroreduction of RBr_2 has not been carried out, the reaction probably follows a sequence of electron transfers and loss of bromide ions (an ecec reaction) leading to rubrene, as observed in the electrochemistry of other organic halides.[8] The overall electrode reaction is thus

$$RBr_2 + 3e \longrightarrow R^{\cdot-} + 2Br^- \qquad (3)$$

By analogy with previous systems of this type,[3-5] the production of excited state rubrene probably results from reaction of a strong oxidant intermediate (formed by reduction of the RBr_2 diffusing toward the electrode by $R\cdot^-$ diffusing away from it) with another molecule of $R\cdot^-$, for example

$$RBr_2 + R^{\cdot-} \longrightarrow RBr\cdot + Br^- + R \qquad (4)$$

$$RBr\cdot + R^{\cdot-} \longrightarrow R + Br^- + R^* \qquad (5)$$