Hydrogen Exchange Studies. VIII.[1] Base-Catalyzed Hydrogen Exchange of 1,3,5-Trinitrobenzene in Aqueous Dimethylformamide

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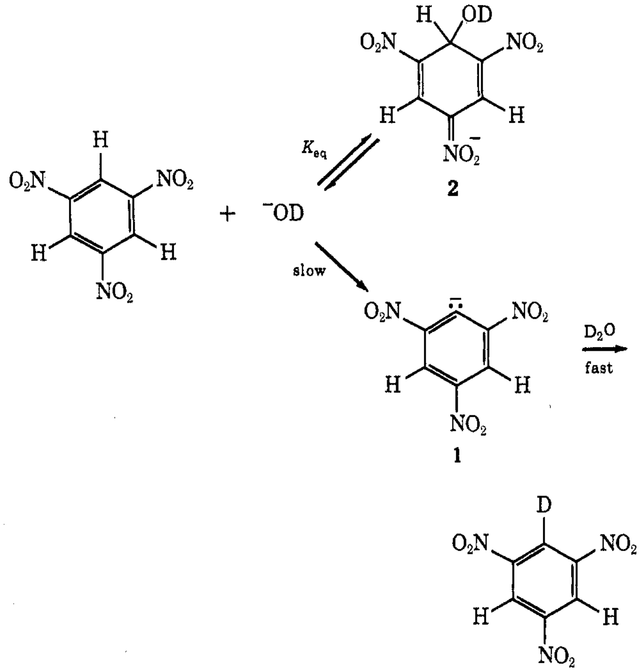
The rate of aromatic proton exchange between 1,3,5-trinitrobenzene (TNB) and dimethylformamide–D_2O containing sodium deuterioxide has been measured as a function of medium composition and reactant concentration. In contrast to the normally observed trend of base-induced exchange rates in protic–aprotic solvent mixtures, in this system the pseudo-first-order rate constants for exchange *decrease* with increasing DMF content over the range 25–80 mol % DMF, when the TNB is present in excess over the base. Also, for constant medium composition and base concentration, the rates are *halved* on doubling the TNB concentration. This unusual behavior is interpreted as arising from competition between proton exchange and Meisenheimer complex formation.

Aromatic hydrogen exchange induced by strong bases has been investigated in a variety of systems with a view to elucidating the structural and electronic factors governing the exchange process.[2] The currently accepted mechanism for proton exchange involves initial removal of the proton by base to form a carbanion in the slow step, followed by rapid neutralization of the latter by proton transfer from a solvent molecule.[3] Detailed kinetic schemes for proton transfer processes, involving also hydrogen-bonded carbanionic species, have been presented and their mechanistic implications discussed.[4]

Aromatic compounds containing two or more nitro groups are of special interest in studies of base-induced proton exchange, since with these compounds the base may take part in more than one type of interaction.[5-7] In the case of the 1,3,5-trinitrobenzene–hydroxide ion system the base can abstract a ring proton, giving the aryl carbanion 1 and leading to proton exchange with the medium, or it can add covalently to aromatic carbon to form the colored adduct 2, known as a Meisenheimer complex.[8] In the general case still other processes, involving charge-transfer complexes[9] and radical anions,[10] are also possible.

The feasibility of proton exchange for 1,3,5-trinitrobenzene in dimethylformamide–D_2O–base systems was described previously, for deuterioxide[11a] and for other Brønsted bases.[11b] We have since carried out an investigation of σ-complex formation and proton exchange in the trinitrobenzene–hydroxide ion system. The equilibrium constant data have recently been reported.[11c] Our results on hydrogen isotope exchange are now presented and the relationship with complex formation is discussed, on the basis of the following reaction scheme.



Experimental Section

Reagents.—1,3,5-Trinitrobenzene (TNB) was recrystallized from ethanol and then from chloroform, mp 122.5–123.0° (uncorrected). Dimethylformamide (DMF) was purified by the method of Ritchie and Megerle.[12] Sodium deuterioxide solutions were prepared by dissolving freshly cut sodium metal in D_2O. The DMF and NaOD–D_2O solutions were transferred under nitrogen.

Kinetic Method.—The kinetic data were obtained by the sealed tube method, as follows. To a weighed quantity of TNB

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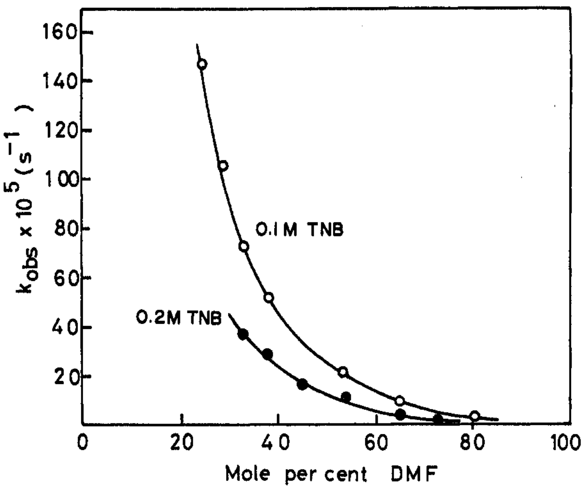

Figure 1.—Plots of k_{obsd} (50°) for hydrogen exchange in TNB in DMF–D_2O containing NaOD (0.02 *M*) as a function of medium composition: open circles, 0.1 *M* TNB; shaded circles, 0.2 *M* TNB.

TABLE I

PSEUDO-FIRST-ORDER RATE CONSTANTS FOR PROTON EXCHANGE IN TRINITROBENZENE AS A FUNCTION OF TNB CONCENTRATION AND MEDIUM COMPOSITION (DMF–D_2O)

	Mol % DMF	10^5k_{obsd}, sec^{-1} 25°	50°
0.100 *M* TNB	24.8		147
0.020 *M* NaOD	28.8	4.20	105
	33.1		72.5
	38.2	1.85	51.5
		1.83	
	53.6	0.603	21.8
			19.3
	65.1	0.272	8.35
		0.253	
	80.5	0.054	2.03
0.200 *M* TNB	33.1		36.0
0.020 *M* NaOD			38.5
	38.2		30.7
			26.3
	45.0		16.6
			15.0
	53.6		10.7
			9.8
	65.1		3.65
			3.93
	72.9		1.67
	80.5		0.75

TABLE II

PSEUDO-FIRST-ORDER RATE CONSTANTS FOR PROTON EXCHANGE IN TRINITROBENZENE (0.200 *M*) AS FUNCTION OF DEUTERIOXIDE ION CONCENTRATION IN DMF–D_2O AT 50°

[NaOD]	10^5k_{obsd}, sec^{-1} 38.2 mol % DMF	53.6 mol % DMF
0.0040	4.60	1.48
	5.17	1.51
0.0075	10.5	3.80
	10.7	
0.010	15.1	4.92
	14.4	4.82
0.0150	21.0	7.77
	22.2	
0.020	30.7	10.7
	26.3	9.8

(*ca.* 1 g) in a 50-ml volumetric flask were added DMF and D_2O in the requisite amounts, and the solution temperature was brought to 25°. Just prior to starting the run the NaOD–D_2O was added, resulting in instantaneous appearance of red color, and then DMF was added to the mark. The flask was cooled by means of a Dry Ice–acetone bath and transferred to a nitrogen-flushed drybox for filling of the Pyrex reaction tubes, which were then sealed and placed in unison in the constant-temperature bath. The tubes were withdrawn individually over a period corresponding to 1–2 half-lives for exchange and cooled, and the contents (*ca.* 6.5 ml) were added to *ca.* 30 ml of dilute sulfuric acid. The red color of the reaction solutions disappeared instantly on acidification, but in some cases a dark brown coloration remained, indicative of decomposition. (For solutions of high DMF content neutralization gave on occasion a transitory green color which was readily bleached in light.) The precipitated TNB was filtered, washed with distilled water, and dried. The yield of TNB was generally about 75% of theoretical and selected samples had mp 121–123°, indicating a satisfactory purity for isotopic analysis by infrared spectrometry. The extent of deuteration was determined by measuring the CH and CD[13] peak heights at 3100 and 2305 cm^{-1} for 1 *M* solutions in acetonitrile, using 0.1 mm calcium fluoride cells and a standard calibration curve. The instrument employed, a Perkin-Elmer Model 21, gave an estimated precision of 2–4%. Pseudo-first-order rate constants (k_{obsd}) were obtained from least squares calculations for linear plots of log (100 − % exchange at time *t*) *vs.* time; the estimated error is ±5%. The values of k_{obsd} refer to exchange of all three hydrogens in the TNB molecule.

Results and Discussion

Kinetic Results and Concentration Dependence of Proton Exchange.—The kinetic data for proton exchange in trinitrobenzene obtained by the method described above are given in Tables I and II. Pseudo-first-order rate constants measured as a function of medium composition at 25 and 50° for two values of TNB concentration, with constant NaOD concentration, are contained in Table I. The effect of varying the NaOD concentration is shown in Table II for two values of the medium composition.

It is apparent from the data of Table I (see also Figure 1) that for a given medium composition and NaOD concentration the rate of proton exchange is greater for the *lesser* of the two concentrations of TNB. This result, which may not have been expected, is tied intimately to the interdependence of the proton exchange process and Meisenheimer complex formation. It was shown previously[11c] that the equilibrium constant (K_{eq}) for formation of adduct 2 from TNB and hydroxide ion increases sharply with increasing DMF content of the medium, from its value of 3.0 l. mol^{-1} in purely aqueous medium to *ca.* 2 × 10^4 l. mol^{-1} in 34 mol % DMF. Thus for a given $[NaOD]_{stoich}$, the concentration of *free* deuterioxide ion is an inverse function of $[TNB]_{stoich}$. For example, for 33.1 mol % DMF, where K_{eq} is estimated as *ca.* 2 × 10^4, one calculates that for $[NaOD]_{stoich} = 0.02$ *M* and $[TNB]_{stoich} = 0.2$ *M*, $[OD^-]_{free} \cong 6 \times 10^{-6}$ *M;* on the other hand, for $[NaOD]_{stoich} = 0.02$ *M* and $[TNB]_{stoich} = 0.1$ *M*, $[OD^-]_{free} \cong 13 \times 10^{-6}$ *M*. This calculated increase of *ca.* 2 in $[OD^-]_{free}$ on decreasing [TNB] from 0.2 to 0.1 *M* compares favorably with an observed increase of 2.0 in the pseudo-first-order rate constant for exchange at this solvent composition at 50° (Table I). Although the K_{eq} data were measured in DMF–H_2O at 25° but applied to DMF–D_2O at 50° (*i.e.*, both temperature and solvent isotope effects were not

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(13) H. F. Shurvell, J. A. Faniran, E. A. Symons, and E. Buncel, *Can. J. Chem.*, **45**, 117 (1967).

taken into account), moderate changes in the value of K_{eq} are not expected to have a significant effect on this result.

The data of Table II show that the rate of proton exchange is directly proportional, within experimental error, to $[NaOD]_{stoich}$ for both medium compositions. Because of the relatively large magnitude of K_{eq} for complex formation in these media and the use of excess TNB, the $[NaOD]_{free}$ which determines the proton abstraction process is proportional to $[NaOD]_{stoich}$ within experimental error, though of course $[NaOD]_{free} \ll [NaOD]_{stoich}$.

The extensive complexing of deuterioxide ion in these TNB–OD^-–DMF systems effectively eliminates the possible problem of limited solubility of NaOH in media rich in DMF.[14] This complexing also bears directly on the question of whether reaction of hydroxide ion with DMF (hydrolysis to formate ion and dimethylamine) interferes significantly with the proton exchange process. From previous work[14] one can estimate that for 38.2 mol % DMF, 0.02 *M* NaOH, 25°, the half-life for reaction of DMF with hydroxide ion is *ca.* 6.3 min. From the data of Table I, for 38.2 mol % DMF the half-life for the deuterioxide ion catalyzed proton exchange of TNB (0.1 *M*) at 25° is 630 min. A similar disparity in rates occurs at the other solvent compositions. However, the following consideration indicates that the DMF–OD^- reaction[15] does not interfere appreciably with the proton exchange process under the experimental conditions $[TNB] > [NaOD]$. For 38.2 mol % DMF and $[TNB]_{stoich} = 0.1\ M$, $[NaOD]_{stoich} = 0.02\ M$, one estimates[11c] from the K_{eq} data for complex formation that $[NaOD]_{free} \cong 6 \times 10^{-6}\ M$. On the assumption that one-half of the *free* base is consumed by reaction with DMF for each hydrolysis half-life, and that this loss can be linearly extrapolated to an exchange half-life, then the net loss in base during the exchange half-life is *ca.* 2% of $[NaOD]_{stoich}$. The maximum calculated loss in OD^- over the solvent composition range studied is 5% per exchange half-life. Since σ-complex formation and breakdown is effectively instantaneous, the deuterioxide ion consumed in DMF hydrolysis is replaced from this reservoir, so that the free base concentration will remain essentially constant during the exchange run. It is important, however, to point to the necessity in the proton exchange studies to prepare reaction solutions in such a sequence that the TNB be present in the aqueous DMF solution *prior* to the addition of base; the reverse procedure would lead to premature loss of some base *via* hydrolysis.

Medium Dependence of Proton Exchange.—The effect of changing solvent composition on the rate of proton exchange of TNB is given by the data of Table I and is seen more clearly in Figure 1 (kinetic data at 25° yield a curve which is closely similar to that given in Figure 1 for the 50° data). It is apparent that the rate as given by the pseudo-first-order constants *decreases* sharply as the DMF content of the medium increases. This behavior is in contrast to the well-documented[17] general increase in rate of reactions of anionic nucleophiles with various substrates in mixtures of protic and dipolar aprotic solvents. By analogy with other proton transfer processes in DMSO–water or DMSO–methanol systems, to which most of the available literature data apply,[18] one might have expected a rate increase of *ca.* 10^4 in the present system on increasing the DMF content from 25 to 80 mol %.

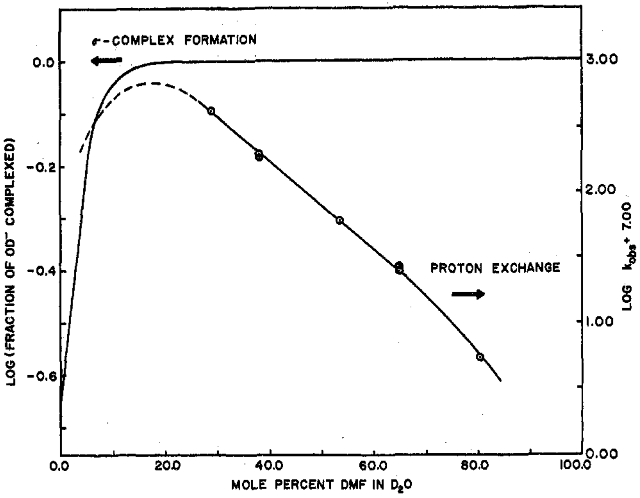

Figure 2.—Plots showing correlation between rate of proton exchange (25°) in TNB and the degree of σ-complex formation as a function of medium composition (0.1 *M* TNB, 0.02 *M* NaOD).

The reversed medium effect measured in this system can be explained by considering the medium effect on the two concurrent processes, proton exchange and complex formation. Directly relevant to our discussion is the study by Crampton and Gold[5] dealing with proton exchange and complex formation for 1,3-dinitrobenzene (DNB) in DMSO–methanol–sodium methoxide. Proton exchange in DNB was followed by measuring the tritium uptake from methanol-*t*, with NaOMe (0.25 *M*) in excess over DNB (0.17 *M*), over the range of medium composition 10–88 mol % DMSO. The rate of exchange was found to *increase* over the range 10–60 mol % DMSO and thereafter level off, remaining approximately constant. Parallel spectrophotometric measurement of apparent extinctions showed increasing complex formation up to *ca.* 70 mol % DMSO and then a levelling off, indicating virtually complete complexing of the DNB. The levelling off in rate of proton exchange was accounted for on the basis that the colored species (Meisenheimer complex formation by addition of MeO^- at C-4) represented an unreactive form of the substrate and that exchange occurred *via* a very small concentration of carbanion.

For the trinitrobenzene–deuterioxide ion system, the relationship between isotopic exchange and σ-complex formation is shown in Figure 2, in the form of plots of log k_{obsd} (exchange) and log (fraction of

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[14] E. Buncel and E. A. Symons, *Chem. Commun.*, 164 (1970); E. Buncel, S. Kesmarky, and E. A. Symons, *ibid.*, 120 (1971).

[15] No account is taken here of the solvent isotope effect[16] on the DMF hydrolysis reaction.

[16] P. M. Laughton and R. E. Robertson, "Solute–Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 7.

[17] (a) A. J. Parker, *Chem. Rev.*, **69**, 1 (1969); (b) C. D. Ritchie, "Solute–Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 4.

[18] (a) R. Stewart and J. R. Jones, *J. Amer. Chem. Soc.*, **89**, 5069 (1967); (b) A. F. Cockerill and W. H. Saunders, Jr., *ibid.*, **89**, 4985 (1967); (c) R. Stewart, J. P. O'Donnell, D. J. Cram, and B. Rickborn, *Tetrahedron*, **18**, 917 (1962).

stoichiometric OD$^-$ complexed)[19] *vs.* mol % DMF. The latter function shows that, for TNB, 99% of the base has already been complexed by 15–20 mol % DMF. In contrast, in the DNB–OMe$^-$ system[5] the 99% complexing stage (of the component present in deficit which in this case was DNB) does not occur until *ca.* 88 mol % DMSO. In the DNB–OMe$^-$ system there is less than 0.1% complexing in the medium of 20 mol % DMSO.

Crampton and Gold predicted[5] that in the DNB–OMe$^-$ system the log (rate) *vs.* H_- (or solvent composition) profile should pass through a maximum and then decrease as the extent of complexing continued to increase. However, data were not available to demonstrate this point experimentally. In the present work we have been able to verify their prediction by employing the TNB–OD$^-$ system, in which the degree of complexing is more extensive than for DNB under identical solvent conditions. In Figure 2 a maximum is sketched in for the TNB plot in the solvent composition region where the fraction of [OD$^-$]$_{stoich}$ removed by complex formation becomes significant.[20,21] Thus Crampton and Gold's study with DNB[5] and our own with TNB are complementary in their attempt to demonstrate and explain the competition which occurs between proton exchange and σ-complex formation for nitroaromatic substrate–base systems in solution. These results are also consistent with the recently reported[22] hydrogen exchange of DNB in MeONa–MeOD, in which system the degree of complexing is expected to be negligible.

Registry No.—1,3,5-Trinitrobenzene, 99-35-4; dimethylformamide, 68-12-2.

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[19] This function was determined as log([complex]/[complex]$_{max}$), where the values of [complex] were calculated from the appropriate K_{eq} data.[11c] The [complex]$_{max}$ corresponds to complete complexing of NaOD, the species in lower concentration. For $K_{eq} > ca.\ 10^4$, the limit of experimental data (34 mol % DMF), this function takes the value 0.00.

[20] A maximum in the rate–medium composition profile will be predicted if the degree of complexing of OD$^-$ increases more rapidly with increasing content of the dipolar aprotic component than does the effectiveness of OD$^-$ for catalysis of proton exchange.

[21] Proton exchange measurements were not made for the low-DMF region because of increasingly limited solubility of TNB in these media.

[22] I. R. Bellobono and G. Sala, *J. Chem. Soc., Perkin Trans. 2*, 169 (1972).

A Facile Exchange of Aromatic Hydrogen with Deuterium in the Absence of Catalysts. Meta Aromatic Diamines

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m-Phenylenediamines exchange ring hydrogen with deuterium at room temperature in the absence of catalysts. At concentrations of 1 mmol of amine per 1 ml of methanol-d_4 equilibrium at 60–80% deuteration is established within 24–60 hr. Under the same conditions *o*- and *p*-phenylenediamines completely fail to react. Only hydrogens at ortho and/or para positions to *both* amine groups exchange. A third mechanism, involving the direct attack of a deuterium cation on the electron-rich carbon atom in the rate-determining step, is postulated.

Acid-catalyzed hydrogen exchange on aromatic nucleus is a reversible electrophilic substitution reaction (A-SE2) in which the rate-controlling step is the slow transfer of a proton to the substrate.[1] Several examples of base-catalyzed isotopic exchange of aromatic hydrogen support a rate-limiting proton abstraction,[2,3] but this mechanism has not yet been elucidated fully. On the other hand, in the absence of acidic or basic catalysts isotope exchange either does not occur or proceeds at extremely slow rates. For example, the extent of exchange between dimethylaniline and tritiated water in the absence of acids is negligible[4] after 24 hr at 80°. We have now found that a facile exchange does take place at room temperature in the absence of catalysts, provided that the aromatic hydrogens are activated by at least two amino groups.

The exchange was first observed with certain *m*-toluenediamines (**4**, **5**) prepared in connection with other studies as shown in the reaction scheme.

3,5-Dinitro-4-methoxytoluene (**3a**) can be obtained by the action[5] of diazomethane on **1**, the methylation of the silver or sodium salt of **1** by methyl iodide[6] or dimethyl sulfate,[7] and the nitration[8] of 4-methoxytoluene. In this work, **3a** and **3b** were prepared from 3,5-dinitro-4-chlorotoluene[9,10] (mp 115°) by displacing chloride with alkoxide ion (**2** → **3**). Hydrogenation of **3a** and **3b** in the presence of platinum catalyst proceeded smoothly to give diamines **4a** and **4b**, of which only the dihydrochloride of **4a** has been reported. Hydrogenation of **2** also afforded **5** in excellent yield.[10]

When diamines **4a**, **4b**, and **5** were dissolved in methanol-d_4 at concentrations of 1 mmol/ml, a nearly instantaneous, quantitative exchange of the four amine protons occurred. This was followed by the slow deuteration of both aromatic protons until equilibrium was established at *ca.* 78–81% deuterium exchange

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[1] R. O. C. Norman and R. Taylor, "Reaction Mechanisms in Organic Chemistry," Monograph 3, C. Earbon, Ed., Elsevier, New York, N. Y., 1965, p 203.

[2] R. D. Guthrie and D. P. Wesley, *J. Amer. Chem. Soc.*, **92**, 4057 (1970).

[3] J. A. Zoltewicz and L. S. Helmick, *ibid.*, **92**, 7547 (1970).

[4] B. B. P. Tice, I. Lee, and F. H. Kendall, *ibid.*, **85**, 329 (1963).

[5] W. Borsche and E. Faske, *Chem. Ber.*, **59**, 687 (1926).

[6] W. Staedel, *Justus Liebigs Ann. Chem.*, **217**, 170 (1883).

[7] G. Schieman and M. Seyhan, *Chem. Ber.*, **70B**, 2396 (1937).

[8] W. E. Chamberlain, *Amer. Chem. J.*, **19**, 534 (1897).

[9] R. M. Vance, U. S. Patent 3,221,065 (Nov 30, 1965); *Chem. Abstr.*, **64**, 8082 (1966).

[10] An early publication [M. Hönig, *Chem. Ber.*, **20**, 2419 (1887)] describes the isolation of **2**, mp 48°, by nitrating 4-chlorotoluene. That nitration gave probably a mixture of isomers, which should account for the low melting point reported. Reduction of this mixture gave **5**, mp 111°.