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$^-$]$_{\text{stoich}}$ 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]$_{\text{max}}$), where the values of [complex] were calculated from the appropriate K_{eq} data.[11c] The [complex]$_{\text{max}}$ corresponds to complete complexing of NaOD, the species in lower concentration. For $K_{\text{eq}} > ca.\ 10^4$, 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-S$_E$2) 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

(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).

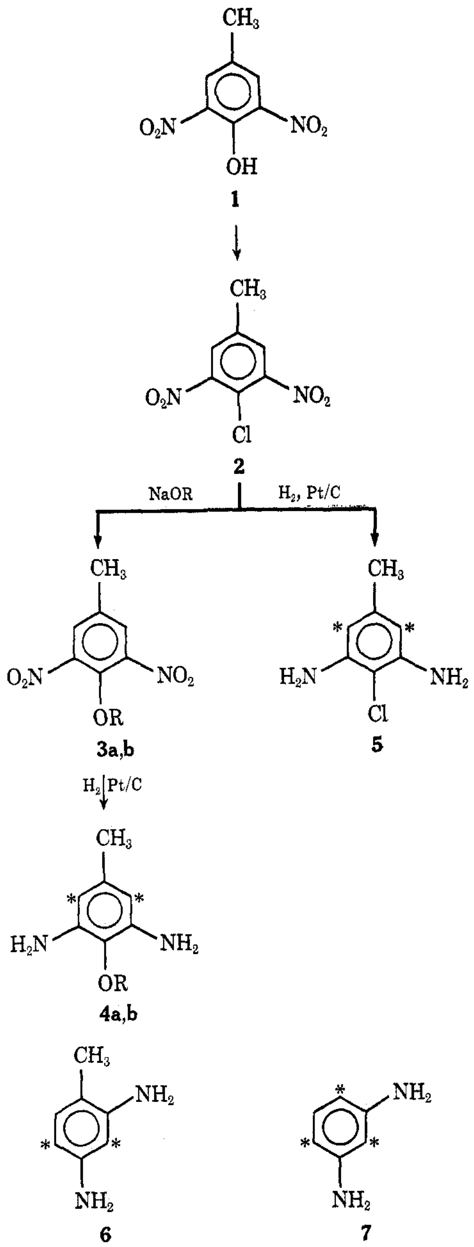
(6) W. Staedel, *Justus Liebigs Ann. Chem.*, **217**, 170 (1883).

(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°.



a, R = methyl
b, R = *n*-pentyl
* = exchangable hydrogen

within 24 hr for **4a** and **4b**, and 60 hr for **5** (Figure 1). In order to demonstrate that the two amino groups were primarily responsible for the exchange, 2,4-toluenediamine (**6**) and 1,3-phenylenediamine (**7**) were tested under the same conditions; compounds **6** and **7** behaved in a similar manner.

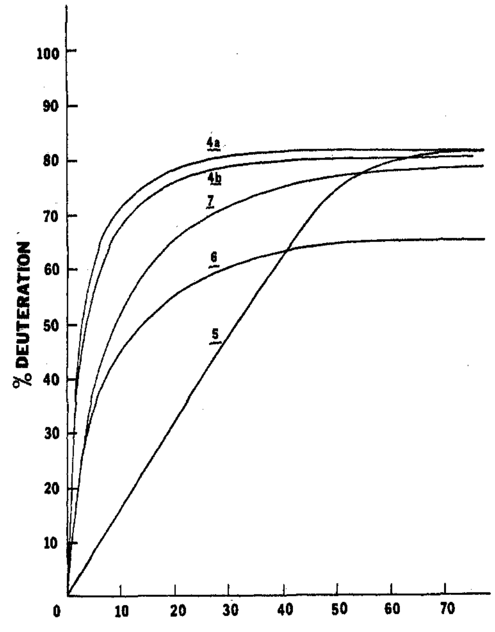


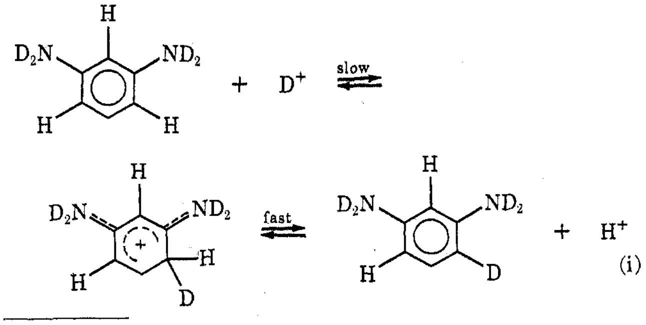
Figure 1.—Hydrogen–deuterium exchange of aromatic meta diamines **4a**, **4b**, **5**, **6**, and **7** at room temperature in the absence of catalysts (*c* 1 mmol/ml of methanol-d_4).

Of the three aromatic protons of **6**, the 6-H at 6.7 ppm remained unchanged over a period of 3 days. On the other hand, the overlapping signals for 3-H (singlet at 6.08 ppm) and 5-H (doublet near 6.03 ppm) showed exchange of 60% within 48 hr (Figure 1). In the case of **7**, the overlapping signals for 2-H, 4-H, and 6-H at 6.0–6.2 ppm decreased progressively, indicating deuteration, whereas the 5-H (multiplet near 6.7–6.9 ppm) did not exchange at all. In fact, the rate of exchange could be determined by comparing the total integration of 2-H, 4-H, and 6-H with that of 5-H. In addition, the methanol impurity peak of methanol-d_4 was employed as reference with the same results. With compounds **4a**, **4b**, **5**, and **6** the integral signal of the methyl group was used to follow rates of deuteration.

Surprisingly, the aromatic hydrogens of 1,2-phenylenediamine, 1,4-phenylenediamine, their *N,N,N′,N′*-tetramethyl derivatives, and 4-toluidine showed no exchange after 3 days of standing at room temperature. In fact, no exchange was noticed when the aforementioned compounds were kept at 70° for 6 hr in ethanol-d_6. This difference in reactivity between meta-diamines on one hand, and ortho and para diamines on the other, as well as the difference in reactivity among the aromatic protons in **6** and **7**, point out conclusively that the facile exchange in the absence of catalysts requires the activation of aromatic hydrogens by at least two powerful, electron-donating amine groups.[11] One could predict that stronger activation *e.g.*, by three amine groups, would result in even faster exchange rates.

Because aromatic diamines are very weak bases, a base-catalyzed mechanism for the observed exchange should be excluded. Furthermore, if the reaction were base-catalyzed, the order of reactivity would be reversed, *i.e.*, ortho and para diamines would react

$$\mathrm{ROD} \rightleftharpoons \mathrm{RO^-} + \mathrm{D^+}$$



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[11] Stronger deuteration conditions, for example higher temperature and concentration, can bring about an extremely slow deuteration of those hydrogens in aromatic diamines which are activated by only one amino group. Such an exchange has already been noticed.

faster than meta diamines. Acid catalysis[12] is not likely either. A third, heretofore unobserved mechanism involving the direct attack of deuterium cation on the activated, electron rich carbon atoms is now postulated (i).

Evidence in support of this mechanism was provided by comparing the reactivities of **4a** and **5** under exactly the same conditions whereby the reaction rates should be related to the electron clouds at C_2 and C_6. Since **4a** and **5** differ only by the substituent at C_4, this electron density should depend mainly on the inductive effect of the methoxy and chloro groups, the σ_m values[13] of which are +0.115 and +0.373, respectively. Thus, both groups are electron withdrawing at the meta positions, the methoxy group being weaker. Consequently, the electron densities at C_2 and C_6 are higher in **4a** than in **5**, and **4a** should react faster than **5**. This is in accord with our experimental evidence, as shown in Figure 1. Finally, additional evidence in support of the mechanism was provided by observing that an increase in deuteration rate occurred when the ratio of methanol-d_4 to amine was increased.

Experimental Section

Deuterium exchange was determined with a Varian HA-100 spectrometer using tetramethylsilane as internal reference. The compounds were dissolved in methanol-d_4 at concentrations of 1 mmol/ml and allowed to stand at room temperature. The appropriate nmr peaks were integrated at time intervals until equilibrium was established. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting points were determined with a Thomas-Hoover apparatus and were not corrected.

3,5-Dinitro-4-methoxytoluene (**3a**).—A solution of 4-chloro-3,5-dinitrotoluene[9,10] (**2**, 43.2 g, 0.2 mol) and sodium methoxide (12.5 g, 0.22 mol) in methanol (500 ml) was refluxed for 12 hr and cooled. The precipitated solid was filtered off, stirred in water (300 ml), refiltered, and dried, giving pure **3a**: yield 35.2 g (83%); mp 123–124° (lit.[6,7] mp 123°); nmr ($CDCl_3$) δ 7.84 (s, 2, aromatic H), 4.02 (s, 3, OCH_3), 2.48 (s, 3, CH_3).

3,5-Dinitro-4-pentoxytoluene (**3b**).—Sodium hydride (56.7% in oil, 14 g, 0.33 mol) was added portionwise with stirring to dry pentanol (400 ml). After the addition had been completed, chloride **2** (65 g, 0.3 mol) was added, and the reaction mixture was brought to 100–110° slowly (1 hr) by means of an oil bath, stirred at 100–110° for 3 hr, cooled, distilled *in vacuo* until all pentanol was removed, diluted with water (500 ml), and extracted with chloroform (three 500-ml portions). The combined chloroform extracts were clarified by gravity filtration, washed with water (two 200-ml portions), dried ($MgSO_4$), and evaporated to dryness. The crude product obtained was purified by two distillations at reduced pressure: bp 131–133° (0.15 mm); yield 44.6 g (55%); nmr ($CDCl_3$) δ 7.84 (s, 2, aromatic H), 4.12 (t, 2, $-OCH_2-$), 2.49 (s, 3, aromatic CH_3), 1.80 (m, 2, $-OCH_2CH_2-$), 1.40 (m, 4, $-OCH_2CH_2CH_2CH_2CH_3$), 0.94 (t, 3, OCH_2CH_3).

Anal. Calcd for $C_{12}H_{16}N_2O_5$: C, 53.72; H, 6.01; N, 10.44. Found: C, 53.93; H, 6.13; N, 10.37.

4-Methoxytoluene-3,5-diamine (**4a**).—3,5-Dinitro-4-methoxytoluene (**3a**, 33.4 g, 0.157 mol) in ethanol (500 ml) was hydrogenated at 25–50° (250 psi) in the presence of platinum catalyst (5% Pt/C, 1 g) in a 1-l. Parr autoclave, equipped with cooling coil and stirrer. The reaction mixture was filtered, the filtrate was evaporated to dryness, and the oily residue was distilled at reduced pressure to give an oil, bp 98–105° (0.4 mm), which solidified upon standing, mp 72–74°, yield 18.5 g (68%). The analytical sample was obtained by one recrystallization from methylene chloride–hexane: mp 73–74°; nmr ($CDCl_3$) δ 5.98 (s, 2, aromatic H), 3.72 (s, 3, OCH_3), 3.62 (s, 4, NH_2), 2.12 (s, 3, CH_3).

Anal. Calcd for $C_8H_{12}N_2O$: C, 63.1; H, 7.95; N, 18.41. Found: C, 62.98; H, 7.87; N, 18.30.

The dihydrochloride was prepared by bubbling hydrogen chloride through a solution of diamine **4a** in ethanol, mp 239–240° (lit.[7] mp 241°).

4-Pentoxytoluene-3,5-diamine (**3b** → **4b**).—This compound was prepared as described for **4a**. The crude product obtained was purified by distillation at reduced pressure: bp 134–135° (0.25 mm); yield 85%; nmr ($CDCl_3$) δ 5.97 (s, 2, aromatic H), 3.80 (t, 2, $-OCH_2-$), 3.60 (s, 4, NH_2), 2.12 (s, 3, aromatic CH_3), 1.76 (m, 2, $-OCH_2CH_2-$), 1.42 (m, 4, $-OCH_2CH_2CH_2CH_2CH_3$), 0.92 (m, 3, $-CH_2CH_3$).

Anal. Calcd for $C_{12}H_{20}N_2O$: C, 69.19; H, 9.68; N, 13.45. Found: C, 69.34; H, 9.61; N, 13.58.

The dihydrochloride was prepared as in **4a**, and purified by crystallization from ethanol, mp 279–281° subl.

Anal. Calcd for $C_{12}H_{22}Cl_2N_2O$: C, 51.25; H, 7.88; N, 9.96; Cl, 25.22. Found: C, 51.42; H, 7.75; N, 9.93; Cl, 25.45.

4-Chlorotoluene-3,5-diamine (**5**).—Hydrogenation of **2** was carried out as in **4a**. The product was purified by recrystallization from benzene: mp 115–116°; yield 88%; nmr ($CDCl_3$) δ 5.97 (s, 2, aromatic H), 3.85 (s, 4, $-NH_2$), 2.11 (s, 3, aromatic CH_3).

Anal. Calcd for $C_7H_9ClN_2$: C, 53.68; H, 5.79; Cl, 22.64; N, 17.89. Found: C, 54.59; H, 5.80; Cl, 22.49; N, 17.95.

Registry No.—**2**, 5264-65-3; **3a**, 29455-11-6; **3b**, 37780-39-5; **4a**, 37780-40-8; **4b**, 37780-41-9; **4b** 2HCl, 37780-42-0; **5**, 34207-43-7.

Acknowledgments.—The author wishes to thank Dr. R. M. Vance for a sample of 4-chlorotoluene-3,5-diamine, and Mr. Marion Yeagle for nmr spectra.

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[12] The hydrogen–deuterium exchange of the primary amine groups generates methanol, the hydroxyl protons of which conceivably may initiate an acid-catalyzed mechanism. Since methanol is a very weak acid, this possibility does not appear likely.

[13] H. H. Jaffe, *Chem. Rev.*, **53**, 191 (1953).