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Reaction of 2,4-Dinitrohalobenzenes with Imidazole in Nonpolar Aprotic Solvents[1]

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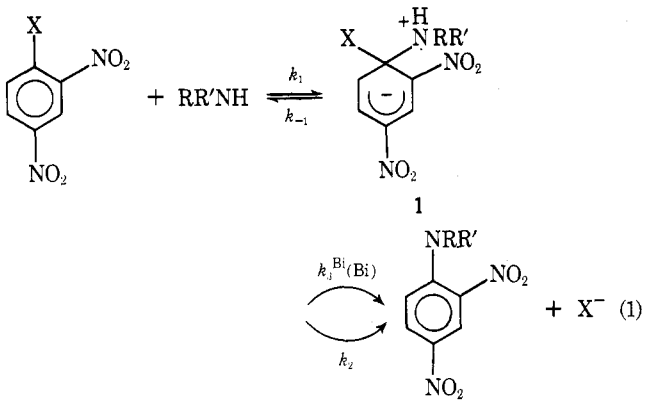
The reactions of 1-chloro-2,4-dinitrobenzene and 1-fluoro-2,4-dinitrobenzene with imidazole in benzene or chloroform were studied. It was found that the reaction of both substrates is general base catalyzed. For 1-chloro-2,4-dinitrobenzene the ratio of the catalyzed to the uncatalyzed rate coefficient (k_3^B/k_2) is 200 M^{-1} for the imidazole and 253 M^{-1} for Dabco in chloroform. The implication of base catalysis in this reaction is discussed.

The reaction of activated aromatic substrates with amines is often base catalyzed.[2] This observation has been rationalized in terms of the intermediate complex mechanism for which eq 1 is representative.



Base catalysis is experimentally observable when the product-forming steps k_2 and $k_3^{Bi}(Bi)$ are slower than the reversion of the intermediate **1** to reactants ($k_2 + \Sigma k_3^{Bi}(Bi) < k_{-1}$).

When the ratio $k_2/k_{-1} \ll 1$, base catalysis is usually observable;[2a] thus whether a given reaction is base catalyzed or not can be influenced by the factors which decrease k_2 and/or enhance k_{-1}.

With chloride as leaving group there are only a few examples where base catalysis has been unequivocally demonstrated and these are cases where the amine is weakly basic which tends to decrease the k_2/k_{-1} ratio by increasing k_{-1}. A case in point is the reaction of *p*-anisidine with 1-chloro-2,4-dinitrobenzene[3] in benzene solution.

Base catalysis in the reaction of 1-chloro-2,4-dinitrobenzene with piperidine and aniline in acetone was claimed by Hirst and Bankole,[4] but these results could not be reproduced in our hands.[5]

The reaction of imidazole with picryl chloride was shown to be catalyzed by imidazole and Dabco in chloroform.[6] Also Pietra[7] found that the reaction of 1-chloro-2,4-dinitrobenzene with imidazole is mildly accelerated by imidazole, but he did not regard this acceleration as base catalysis.

We became interested in the reaction of imidazole because we think that its behavior is important in regard to the mechanism of the k_2 step.

Base catalysis is usually recognized when a change to a better catalyst brings about stronger catalysis.[2a] Thus we investigated the reaction of 1-chloro-2,4-dinitrobenzene with imidazole in benzene and chloroform in the presence of Dabco and pyridine, in order to see whether the reactions are base catalyzed or not. We also report kinetic data on the reaction of 1-fluoro-2,4-dinitrobenzene with imidazole in chloroform catalyzed by imidazole and Dabco to compare these results with those of 1-chloro-2,4-dinitrobenzene.

Results and Discussion

1-Chloro-2,4-dinitrobenzene. In Table I the kinetic results for the reaction of the aforementioned substrate with imidazole with or without added other bases are displayed.

For the imidazole catalyzed reaction the three points at lower concentration compare well with those reported by Pietra[7] under the same experimental conditions, but the agreement is not as good at higher concentration. The ratio of the third- to the second-order rate constant is even lower in our case. The response of k_A to the base concentration is linear. For the reaction of imidazole with 1-chloro-2,4-dinitrobenzene in the presence of Dabco or pyridine the rate seems to level off at high base concentration (Table I).

The kinetic expression derived with reference to the mechanism depicted in eq 1, by means of the usual steady-state approximation, is represented in eq 2 where k_A is the observed second-order rate constant and the summation includes all the bases present in the solution including the nucleophile.

$$\frac{\text{rate}}{(\text{ArX})(\text{HNRR}')} = k_A = \frac{k_1\left[k_2 + \sum_i k_3^{Bi}(Bi)\right]}{k_{-1} + k_2 + \sum_i k_3^{Bi}(Bi)} \quad (2)$$

Linear dependence of the second-order rate constant k_A on the base concentration means that

$$k_2 + \sum_i k_3^{Bi}(Bi) \ll k_{-1}$$

which simplifies eq 2 to eq 3.

$$k_A = k_1\frac{k_2}{k_{-1}} + k_1\frac{\sum_i k_3^{Bi}(Bi)}{k_{-1}} \quad (3)$$

Table I. Reaction of 1-Chloro-2,4-dinitrobenzene with Imidazole in Benzene at (100 ± 0.2) °C[a]

A. Catalyzed by Imidazole

Imidazole, M	$k_\psi \times 10^5$, s^{-1}	$k_A \times 10^4$, $M^{-1} s^{-1}$
0.00694	0.224	3.23
0.0117	0.431	3.68
0.0135	0.518	3.84
0.0176	0.698	3.94
0.0236	1.12	4.77
0.0297	1.55	5.25

B. Catalyzed by Dabco[b]

Dabco, M	$k_\psi \times 10^5$, s^{-1}	$k_A \times 10^4$, $M^{-1} s^{-1}$
0.0214	1.27	5.80
0.0435	1.60	7.30
0.0710	1.92	8.75
0.0886	2.24	10.2 ± 0.8
0.120	2.18	10.8 ± 0.7
0.170	2.86	13.1 ± 0.6
0.201	3.31	15.1 ± 0.5
0.270[c]	3.03	13.8 ± 0.5
0.271	3.10	14.1 ± 0.6
0.101[d]	4.44	12.6 ± 0.4
0.151[d]	4.98	14.1
0.202[d]	5.67	16.1

C. Catalyzed by Pyridine[b]

Pyridine, M	$k_\psi \times 10^5$, s^{-1}	$k_A \times 10^4$, $M^{-1} s^{-1}$
0.0993	1.42	6.51 ± 0.3
0.199	1.97	8.99 ± 0.3
0.398	2.22	10.1 ± 0.7

[a] $(S_0) = 5.28–5.4 \times 10^{-4}$ M; average deviation is given when rate constants are average of two or three determinations. [b] $(\text{Imidazole})_0 = 2.19 \times 10^{-2}$. [c] $(S)_0 = 2.90 \times 10^{-4}$ M. [d] $(\text{Imidazole})_0 = 0.353 \times 10^{-1}$ M.

Curvilinear dependence of k_A vs. base concentration means that

$$k_{-1} \simeq k_2 + \sum_i k_3^{Bi}(Bi)$$

i.e. in this case k_1 is partially rate determining. The leveling off of the rate occurs when $k_A = k_1$, i.e., the plateau value (k_1) must be independent of the base catalyst. However, the data displayed in Table I part B and C seem to indicate that the rate levels off at lower value for pyridine than for Dabco, although the limited number of data concerning pyridine catalysis does not allow speculation about possible reasons.[8]

The low solubility of imidazole in benzene prevented us from doing accurate determinations at higher concentration than those reported here; thus we decided to change to chloroform, which is a better solvent for imidazole.

The reaction of imidazole with 1-chloro-2,4-dinitrobenzene in chloroform is accelerated by imidazole and Dabco (Table II). The second-order rate constant k_A is curvilinearly dependent on both bases concentration (Figures 1 and 2).

We have treated our data as follows.[9] In the absence of Dabco or pyridine and assuming that $k_{-1} \gg k_2$ (justified later), which permits one to neglect k_2, eq 2 can be inverted to give eq 4.

$$\frac{1}{k_A} = \frac{1}{k_1} + \frac{k_{-1}}{k_1 k_3^{Im}(Im)} \quad (4)$$

Table II. Reaction of Imidazole with 1-Chloro-2,4-dinitrobenzene in Chloroform at (69 ± 0.1) °C[a]

A. Catalyzed by Imidazole

Imidazole, M	$k_\psi \times 10^5$, s^{-1}	$k_A \times 10^4$, $M^{-1} s^{-1}$
0.0201	0.120	0.596 ± 0.03
0.0398	0.415	1.04 ± 0.08
0.0602	0.818	1.36 ± 0.08
0.0699	1.02	1.48 ± 0.03
0.0803	1.28	1.59 ± 0.06
0.0941	1.49	1.58 ± 0.05
0.110	1.89	1.72 ± 0.06
0.130	2.38	1.83 ± 0.05
0.140	2.71	1.94 ± 0.04
0.152	3.16	2.07 ± 0.04

B. Catalyzed by Dabco[b]

Dabco, M	$k_\psi \times 10^5$, s^{-1}	$k_A \times 10^4$, $M^{-1} s^{-1}$
0.0126	0.873	1.46
0.0220	0.977	1.63
0.0300	0.956	1.60
0.0518	1.07	1.79
0.0681	1.12	1.87
0.100	1.27	2.13
0.130	1.26	2.12
0.150	1.42	2.34
0.180	1.43	2.40
0.200	1.41	2.36
0.240	1.47	2.46

[a] $(\text{Substrate})_0 = 5.03 \times 10^{-4}$ M; average deviation is given when rate constants are average of two or three determinations. [b] $(\text{Imidazole})_0 = 0.0598$ M.

A plot ("inversion plot") of k_A^{-1} vs. $(Im)^{-1}$ (not shown) yields a straight line from which $k_1 = 3.03 \times 10^{-4}$ $M^{-1} s^{-1}$ and $k_3^{Im}/k_{-1} = 12.3$ M^{-1} were determined.

An alternative form of eq 2, again in absence of Dabco or pyridine but without neglecting k_2, is eq 5.

$$\frac{k_A}{k_1 - k_A} = \frac{k_2}{k_{-1}} + \frac{k_3^{Im}}{k_{-1}}(Im) \quad (5)$$

Plotting the left-hand side of eq 5 vs. (Im) yields $k_2/k_{-1} = 0.06$, and $k_3^{Im}/k_{-1} = 12.0$ M^{-1}. This latter value is in excellent agreement with k_3^{Im}/k_{-1} determined from eq 4. This and the low value of k_2/k_{-1} (0.06) justifies the assumption $k_2 \ll k_{-1}$ which underlies eq 4. In fact, the curve of k_A vs. (Im) calculated on the basis of the obtained k_1, k_2/k_{-1}, and k_3^{Im}/k_{-1} values describes the experimental data very well.

To calculate k_3^D/k_{-1} for Dabco catalysis we use again eq 5 including now the term $k_3^{Im}(Im)/k_{-1}$ in the intercept since the experiments (Table IIB) were carried out at constant imidazole concentration.

It is not possible in this case to draw a similar "inversion plot" as for the imidazole-catalyzed reactions because there were no experimental conditions accessible where $k_3^{Im}(Im) + k_2 \ll k_{-1}$.

From the slope of the plot of $k_A/(k_1 - k_A)$ vs. Dabco concentration, k_3^D/k_{-1} is reckoned as 15.2 M^{-1}. Dabco is only a slightly better catalyst than imidazole. The ratio k_3^B/k_2 is 200 M^{-1} for imidazole and 253 M^{-1} for Dabco; these values are well above the limit proposed by Bunnett[10] in order to decide whether an acceleration should be considered as genuine base catalysis.

Notably, the ratios k_3^B/k_2 are much higher than those re-

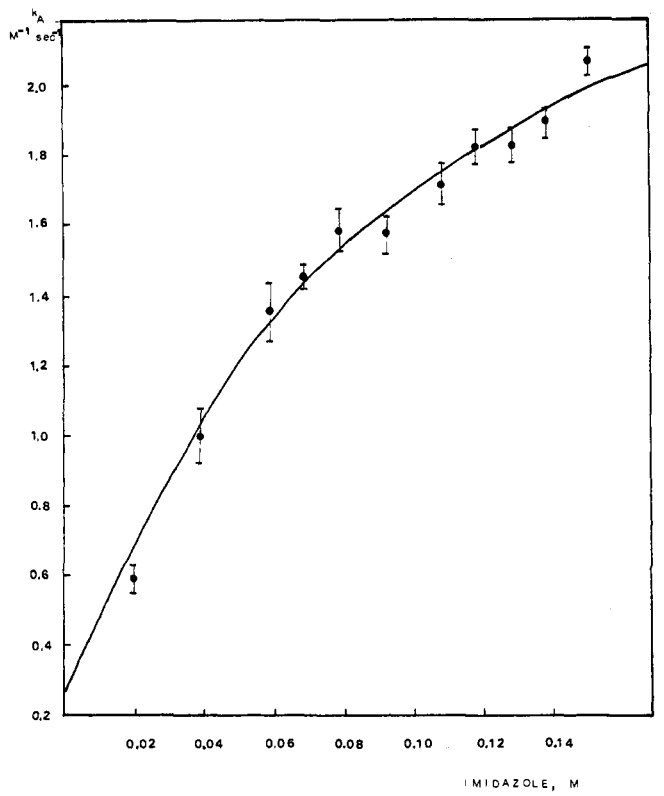


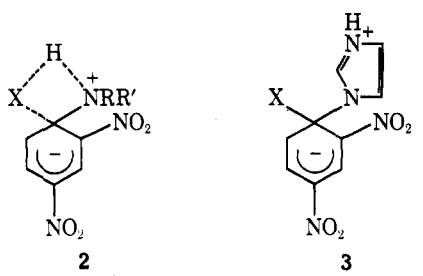
Figure 1. Second-order rate constant for the reaction of 1-chloro-2,4-dinitrobenzene with imidazole in chloroform as a function of imidazole concentration. Data from Table IIA. The solid line is calculated from eq 2 with $k_1 = 3.03 \times 10^{-4}$ M^{-1} s^{-1}, $k_2/k_{-1} = 0.06$, and $k_3^{Im}/k_{-1} = 12$ M^{-1}.

ported for other reactions of several amines with 1-chloro-2,4-dinitrobenzene in chloroform (between 0.2 and 4.6).[11] The small acceleration in these latter reactions is probably not due to genuine base catalysis[2a] and in those reactions k_2/k_{-1} is probably $\gg 1$.

The fact that for the imidazole reaction base catalysis is observed but not for most other reactions of 1-chloro-2,4-dinitrobenzene with amines is a consecuence of an unusually small k_2/k_{-1} ratio.

The factors affecting k_{-1} have been discussed recently.[12] It appears to us that steric effects in the intermediate together with a relatively low basicity of imidazole ($pK_a = 7$) certainly play a role in increasing k_{-1} but it may not be the only factor affecting the ratio k_2/k_{-1}. It has been suggested that the transition state for the k_2 step may be represented as in **2**[2a,12] where the proton is transferred to the leaving group in concert with leaving group departure.

When imidazole is the nucleophile the intermediate may probably be represented as **3** where the proton is not at a



2 **3**

bonding distance to the leaving group as in **2**. If **3** is the intermediate, the proton is not available for intramolecular assistance to the leaving group departure; k_2 is thus decreased.

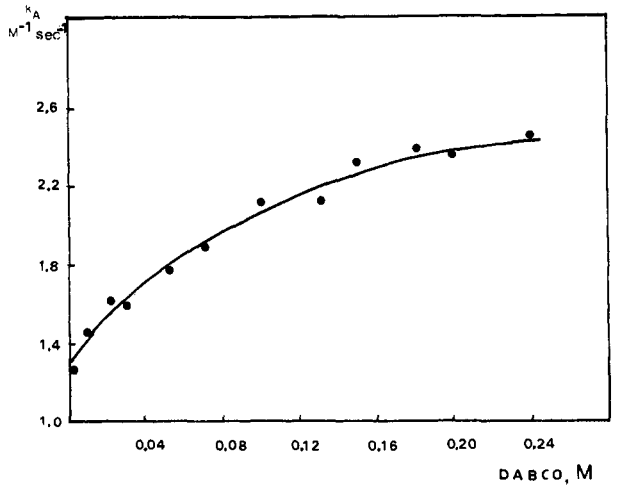


Figure 2. Second-order rate constant for the reaction of 1-chloro-2,4-dinitrobenzene with imidazole in chloroform as a function of Dabco concentration. Data from Table IIB. The solid line is calculated from eq 2 with $k_1 = 3.03 \times 10^{-4}$ M^{-1} s^{-1}, $k_2/k_{-1} = 0.06$, $k_3^{Im}/k_{-1} = 12$ M^{-1}, and $k_3^{D}/k_{-1} = 15.2$ M^{-1}.

Table III. Reaction of 1-Fluoro-2,4-dinitrobenzene with Imidazole in Chloroform at (52.5 ± 0.1) °C[a]

A. Catalyzed by Imidazole[a]

Imidazole, M	$k_\psi \times 10^4$, s^{-1}	$k_A \times 10^2$, M^{-1} s^{-1}
0.0025	0.335	1.34
0.0050	0.737	1.47
0.0200	9.06	4.53
0.0402	28.2	7.01
0.0600	50.7	8.45 ± 0.1
0.0798	82.0	10.3 ± 0.6
0.100	124	12.4 ± 0.5
0.120	151	12.6 ± 0.4
0.140	190	13.6 ± 0.5

B. Catalyzed by Dabco[a,b]

Dabco, M	$k_\psi \times 10^4$, s^{-1}	$k_A \times 10^2$, M^{-1s-1}
0.040	17.4	8.70
0.060	19.7	9.87
0.080	23.5	11.8
0.100	26.3	13.2
0.120	29.7	14.9
0.140	34.0	17.0
0.160	32.8	16.4
0.180	36.0	18.0
0.200	38.0	19.0

[a] $(S)_0 = 5 \times 10^{-6}$; average deviation is given when rate constant are average of two or three determinations. [b] (Imidazole) = 0.02 M.

Since it is known that k_2/k_{-1} decreases with decreasing polarity of the solvent, it is expected that this ratio in benzene be at least as low as in chloroform; thus the rate acceleration observed in benzene may be interpreted as base catalysis, although there seems to be a complicating effect which prevents further analysis of the data.

1-Fluoro-2,4-dinitrobenzene. The reaction of 1-fluoro-2,4-dinitrobenzene with imidazole is catalyzed by imidazole (Table IIIA) and Dabco (Table IIIB); k_1 and the ratios k_2/k_{-1}, k_3^{Im}/k_{-1}, and k_3^{D}/k_{-1} were reckoned as 0.25, 0.039, 9.45 M^{-1}, and 11 M^{-1}, respectively, from eq 4 and 5. However, the rate

constants determined at high imidazole concentration are not very accurate because the rate of reaction is too fast at this high concentration and difficult to measure with our experimental technique; thus we regard the value of k_1 as only approximate and so of course the other parameters which are calculated from it.

Experimental Section

Materials. Benzene (Erba) was shaken repeatedly with sulfuric acid to remove thiophene[13] and distilled before use from Na wire. Chloroform (Erba) was obtained free of ethanol by washing it several times with water; it was dried with $CaCl_2$ and stored in the refrigerator under N_2 in the dark. We noted that when this care was not taken the solutions of 1-chloro-2,4-dinitrobenzene or imidazole in this solvent turned yellow. The purified chloroform was used at most over 10 days. 1-Fluoro-2,4-dinitrobenzene (Merck) was distilled under vacuum. 1-Chloro-2,4-dinitrobenzene (Merck) was twice recrystallized from absolute ethanol. Dabco was sublimed at 40 °C (10 Torr). Pyridine was left over potassium hydroxide for 2 days and distilled under N_2 from KOH before use. Imidazole was recrystallized several times from benzene and then sublimed under vacuum. *N*-2,4-Dinitrophenylimidazole was prepared from 5 mmol (340 mg) of imidazole dissolved in 2 ml of dry benzene and 1-chloro-2,4-dinitrobenzene (2.5 mmol). The solution was boiled for 30 min and the benzene was evaporated. This yellow residue was recrystallized several times from methanol, yield 60%, mp 141–142.5 °C (lit.[14] 146–148 °C). During the synthesis and workup, the product was protected from light.

Kinetics. The product *N*-2,4-dinitrophenylimidazole has no absorption maximum in the spectral region available for examination in benzene or chloroform. Moreover, at the wavelength useful for examination (where the difference in the extinction coefficient of starting material and product is higher) the extinction coefficient of the *N*-2,4-dinitrophenylimidazole is quite low (ca. 2500 M^{-1} cm^{-1}); thus the total change in optical density over the reaction is also low. Thus we decided to monitor the concentration of 1-chloro-2,4-dinitrobenzene making use of its fast reaction with piperidine. In all the reactions in benzene or chloroform with imidazole with or without other bases added, the sealed ampule technique was utilized. The reactions at low base concentration were followed over ca. 10% conversion; after the desired time the ampule was cooled to room temperature and 1.0 ml of its contents was added to about 8 ml of benzene or chloroform contained in a 10-ml volumetric flask. Then 0.2 ml of piperidine was added and the flask diluted to the mark. After about 10 min all the 1-chloro-2,4-dinitrobenzene has reacted and the optical density of the product, *N*-2,4-dinitrophenylpiperidine, formed was measured at its maximum (380 nm). *N*-2,4-Dinitrophenylimidazole does not react with piperidine under these conditions during about 1 h. The rate constant was reckoned as 2.3 times the slope of the plot of log *A* vs. time. All the reactions were carried out under pseudo-first-order conditions. The reactions of 1-fluoro-2,4-dinitrobenzene with imidazole were carried out in the thermostated cell of the spectrophotometer.[15]

Acknowledgment. We thank Professor Claude F. Bernasconi for criticism of the manuscript.

Registry No.—Imidazole, 288-32-4; 1-chloro-2,4-dinitrobenzene, 97-00-7; 1-fluoro-2,4-dinitrobenzene, 70-34-8.

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The Acid-Catalyzed Nitramine Rearrangement. 8. Solvent Viscosity Effects[1,2]

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The rearrangement of *N*-nitro-*N*-methylaniline in methanol–glycerol mixtures of various compositions and viscosities was studied. In the presence of hydroquinone (which eliminates the intermolecular portion of the rearrangement), the yields of nitroanilines and the ortho to para isomer ratio increased with viscosity. The enhanced yield is explained by the lessened tendency of the intermediate solvent caged particles to dissociate in the higher viscosity solvents. The greater ortho to para isomer ratio must be caused by solvent interference to the migration of the nitro group within the solvent cage to the more distant para position. This hindrance increases with solvent viscosity. Rearrangement in the absence of hydroquinone scavenger yields similar results although more nitrated product is formed. The data can be quantitatively accounted for in terms of the mechanism shown in Chart II. This mechanism postulates a solvent viscosity effect within the solvent cage.

The outcome of the nitramine rearrangement frequently appears to be affected by the nature of the solvent. For example, the isomerization of *N*,2,4-trinitro-*N*-methylaniline proceeded normally in 80 or 96% sulfuric acid to yield 2,4,6-trinitro-*N*-methylaniline.[3] However, only the denitrated product, 2,4-dinitro-*N*-methylaniline, was formed from the same nitramine in 1:1 sulfuric acid–acetic acid mixture or in hot dilute hydrochloric acid. Rearrangement of 2,4,6-tribromo-*N*-nitroaniline in aqueous acids produced the expected mixture of isomeric nitrodibromoanilines.[4] Different products, 2,4,6-tribromobenzenediazonium ion and a quinoneanil, were formed when the medium was changed to acetic acid–sulfuric acid. Rearrangement of *N*-nitroaniline is also affected by the solvent.[5] Decreasing the molarity of the acid catalyst lowered the yield of nitrated products from 95% to 60% and changed the ortho–para ratio from 19.0 to 3.5. Similar behavior was noted in the rearrangements of *N*-nitro-1-naphthylamine and *N*-nitro-*N*-methyl-1-naphthylamine.[6]