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SELF-CATALYSIS AND MOLECULAR COMPLEXES IN AROMATIC NUCLEOPHILIC SUBSTITUTION REACTIONS: REACTION BETWEEN 1,3,5-TRINITROBENZENE AND 1,8-DIAZABICYCLO[5.4.0]UNDEC-7-ENE IN TOLUENE

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ABSTRACT

The formation of a σ-like complex by reaction between 1,3,5-trinitrobenzene and 1,8-diazabicyclo[5.4.0]-undec-7-ene was investigated in toluene at various temperatures. The kinetic data showed autocatalytic behaviour. Inspection of the reaction mixtures at zero reaction time indicated the presence of an equilibrium preceding the attack of the nucleophile, affording a molecular complex (substrate–nucleophile) which is responsible for the observed kinetic features. The present and the previous data led to the conclusion that the catalytic behaviours usually observed in S_NAr reactions (in apolar solvents with amines as nucleophiles) are better explained by the presence of substrate–catalyst interactions than by catalysis on departure of the proton and leaving group from the zwitterionic intermediate.

INTRODUCTION

Our interest lies in aromatic nucleophilic substitution reactions in very poorly polar solvents using neutral nucleophiles (amines).[1] For these systems the kinetic constant values (in s^{-1} mol^{-1}) are increased by raising the initial concentrations of the nucleophiles. This kinetic feature is generally explained[2] in terms of departure of the leaving group and the proton from the zwitterionic intermediate, in a step catalysed by the reacting nucleophile itself or by another added catalyst.

Against this interpretation, we proposed previously[3,4] that the experimental reaction order in amine (which is higher than 1) may be explained by considering the interaction between the substrate and nucleophile (or catalyst) in a rapidly established equilibrium preceding the substitution process.

In solvents of low polarity, the substrate–catalyst molecular complex is assumed to be more reactive than the 'free' substrate (complexed or solvated by the solvent). Consequently, the second experimental order in amine arises from the presence of a pre-equilibrium, setting a further molecule of the amine (or of the catalyst) in the transition state. The pre-equilibrium may be considered to involve several interactions (such as charge transfer or hydrogen bonding)

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which are well known, but have not been fully investigated in systems reacting by an S_NAr mechanism.[5,6]

Recently, the presence of a particular charge-transfer complex has been indicated to be active in the S_NAr reaction pathway by MNDO calculations.[7] Our previous findings agree well with the presence of molecular complexes in the pathway of the S_NAr reactions. When protic amines are used, the kinetic features observed may be reasonably explained by both mechanisms (or by their superimposition).[3,8]

We present here some data concerning a reaction involving the formation of a Meisenheimer-like complex in a system lacking a leaving group on the substrate and a proton on the reacting nitrogen of the nucleophile. 1,3,5-Trinitrobenzene (TNB) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) offer a simple model which we recently studied in dimethyl sulphoxide.[9]

RESULTS

The visible spectrum, recorded immediately after mixing appropriate solutions of TNB and DBU in toluene, shows a feeble absorbance maximum at 505 nm (first maximum). After variable times (under the conditions $[\mathrm{DBU}]_0 \gg [\mathrm{TNB}]_0$), the spectrum is modified and a new absorbance maximum is recorded at 468 nm (second maximum). This maximum is stable (in the dark) for a time longer than that which it takes to appear.

The presence of the first maximum (505 nm) is also observed in the reaction mixtures under the experimental conditions $[\mathrm{TNB}]_0 \gg [\mathrm{DBU}]_0$. In this case, the rate of formation of the second maximum (468 nm) is very slow and we can make a quantitative evaluation of the first interaction which is reasonably ascribed to the formation of a molecular complex (MC) between TNB and DBU in an equilibrium preceding the Meishenheimer complex formation. Even if the statistical errors calculated as standard deviations (see 'Experimental') are high, the Benesi–Hildebrand plot ($[\mathrm{DBU}]_0/A_0$ vs $[\mathrm{TNB}]_0^{-1}$, where A_0 is the absorbance at zero reaction time) is linear and K^{MC} values of equilibrium (1) were calculated by the least-squares method, at several temperatures.

$$\mathrm{TNB} + \mathrm{DBU} \xrightleftharpoons{K^{\mathrm{MC}}} \text{molecular complex (MC)} \qquad (1)$$

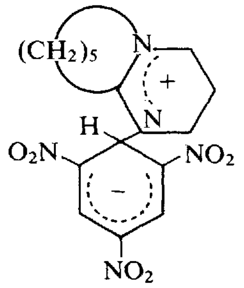
At $\lambda = 510$ nm, K^{MC} ($\mathrm{mol}^{-1}\mathrm{l}$) $= 12{\cdot}0$ ($\varepsilon = 198$) at 18 °C, $7{\cdot}3$ ($\varepsilon = 208$) at 25 °C and $5{\cdot}7$ ($\varepsilon = 220$) at 33 °C. The K^{MC} value is clearly depressed by an increase in temperature. This fact and the related thermodynamic parameters ($\Delta H = -39 \pm 3$ kJ mol^{-1}; $\Delta S = -357 \pm 10$ J mol^{-1} K^{-1}) agree well with the usual observed parameters of the equilibria of formation of molecular complexes.[5,10]

Under the experimental conditions $[\mathrm{TNB}]_0 \ll [\mathrm{DBU}]_0$($[\mathrm{TNB}]_0 = 2{\cdot}5 \times 10^{-3}$ $\mathrm{mol\,l}^{-1}$, $[\mathrm{DBU}]_0 = 8 \times 10^{-3}$–$1{\cdot}5 \times 10^{-2}$ $\mathrm{mol\,l}^{-1}$), $K^{\mathrm{MC}} = 4.8$ $\mathrm{mol\,l}^{-1}$ at 25 °C. This value is calculated by extrapolation of the experimental absorbance at zero reaction time. For higher values of the ratio $[\mathrm{DBU}]_0/[\mathrm{TNB}]_0$, unsatisfactory reproducibility of the A_0 values was observed.

The absorbances of the maximum at 468 nm are independent of the initial concentration of DBU ($= [\mathrm{DBU}]_0$). In the range of concentrations of DBU used here (1×10^{-2}–1×10^{-1} $\mathrm{mol\,l}^{-1}$), the formation of the species related to the second maximum is complete and for $[\mathrm{TNB}]_0$ values from $5{\cdot}0 \times 10^{-5}$ to $2{\cdot}0 \times 10^{-4}$ $\mathrm{mol\,l}^{-1}$ the Lambert–Beer law is followed ($\varepsilon = 1{\cdot}4 \times 10^{4}$). Addition of $\mathrm{CF_3COOH}$ to the reaction mixtures resulted in fading of the colour.

The nature of the observed red colour (second maximum) cannot be directly investigated by the usual ^{1}H NMR spectroscopic measurements, because the related compounds is poorly soluble in toluene. In this solvent, at usual NMR concentrations, a dark red, sticky compound precipitated, but all attempts to crystallize it failed. In any case, the crude compound is soluble in dimethyl sulphoxide (DMSO) and its ^1H NMR spectrum in DMSO-d_6 is identical with that obtained[9,11] directly by mixing the solutions of TNB and DBU in DMSO. In addition, the zwitterionic complex obtained in DMSO, when dissolved in toluene, presents the same absorbance maximum (= 468 nm) as that obtained by mixing the solutions of TNB and DBU in toluene. We conclude that the appearance of the second maximum in toluene is due to the equilibrium

TNB + DBU $\rightleftharpoons$



(I)

(2)

The formation of the red colour is strongly depressed by sunlight, but it is unaffected by the light of the sectrophotometer used in the determinations.

The kinetic data for the formation of the second maximum at 468 nm are reported in Table 1. The k_{obs} values are increased by increasing $[DBU]_0$. Under the experimental conditions, $[TNB]_0 = 4 \times 10^{-2}$ mol l^{-1}, $[DBU]_0 = 5 \times 10^{-4}$ mol l^{-1}, a very low k_{obs} value of $\leqslant 1 \times 10^{-5}$ s^{-1} mol^{-1} was tentatively evaluated at 25 °C. This is of the order of one hundredth of the k_{obs} when DBU is in excess.

Table 1. Kinetic data for the reactions between TNB and DBU in toluene

Conditions	Parameter	Values
$T = 25\,^{\circ}C$, $[TNB]_0 = 8{\cdot}13 \times 10^{-5}$ mol l^{-1}	$10^2[DBU]_0$ (mol l^{-1})	1·29 2·19 2·59 4·39 6·59 8·72
	$10^4 k_{obs}$ (s^{-1} mol^{-1} l)	2·70 3·03 3·36 4·72 6·21 7·30
$T = 35\,^{\circ}C$, $[TNB]_0 = 1{\cdot}03 \times 10^{-4}$ mol l^{-1}	$10^2[DBU]_0$ (mol l^{-1})	1·97 2·29 3·94 4·60 5·91 7·88 9·20
	$10^3 k_{obs}$ (s^{-1} mol^{-1} l)	1·20 1·25 1·38 1·50 1·67 1·83 1·95
$T = 45\,^{\circ}C$, $[TNB]_0 = 1{\cdot}00 \times 10^{-4}$ mol l^{-1}	$10^2[DBU]_0$ (mol l^{-1})	2·30 4·59 9·18
	$10^3 k_{obs}$ (s^{-1} mol^{-1} l)	2·45 2·71 3·30

DISCUSSION

We relate the first interaction to the molecular complex in equilibrium (1). In principle, several substrate–nucleophile interactions are possible, with different stoichiometries (2:1, 1:1, 1:2).[5,12] The obtainment of similar K^{MC} values (within the experimental errors) under both sets of experimental conditions $[\mathrm{DBU}]_0 \ll [\mathrm{TNB}]_0$ and $[\mathrm{DBU}]_0 \gg [\mathrm{TNB}]_0$ indicates that the two reagents interact in a 1:1 stoichiometric ratio, as required by equilibrium (1).

The nature of the molecular complex may be questioned, but owing to the structure of the reagents, we think that the main interaction may be a donor–acceptor type. The kinetic features reported here are the same as observed in S_NAr reactions between nitro derivatives and amines, in poorly polar solvents, and it is usually explained[2] by the so-called base catalysis, as shown in Scheme 1, where L is the leaving group and B is the racting amine or other catalyst.

In the present system, the base-catalysed step for departure of HL does not exist and the increase in k_{obs} values with the initial concentration of DBU must be explained by a mechanisms different from that shown in Scheme 1.

Under the experimental conditions $[\mathrm{DBU}]_0 \ll [\mathrm{TNB}]_0$, the k_{obs} value is much lower than under the conditions $[\mathrm{DBU}]_0 \gg [\mathrm{TNB}]_0$. Under these conditions, the amount of DBU complexed by TNB is unavailable for the nucleophilic attack. The low reactivity indicates that the molecular complex has very little tendency to rearrange to the zwitterionic complex.

In agreement with our previous findings, Scheme 2 may be proposed.[13]

Under our experimental conditions the obtainment of absorbances at 'infinite' reaction time that are independent of $[\mathrm{DBU}]_0$ indicates that the equilibria in Scheme 2 are completely shifted towards **I**. Consequently, $K = k_1/k_{-1}$ (and k_1^0/k_{-1}^0) are very large, i.e. $k_1 \gg k_{-1}$ (and $k_1^0 \gg k_{-1}^0$). This conclusion agrees with previously reported data in DMSO. In this way, the equations

$$K^{\mathrm{MC}} = [\mathrm{MC}]/([\mathrm{TNB}]_0 - [\mathrm{MC}])[\mathrm{DBU}]_0 \tag{3}$$

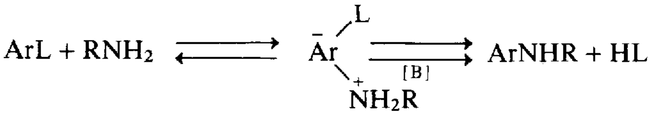
and

$$v = k_1[\mathrm{MC}]\,[\mathrm{DBU}]_0 + k_1^0([\mathrm{TNB}]_0 - [\mathrm{MC}])[\mathrm{DBU}]_0 \tag{4}$$

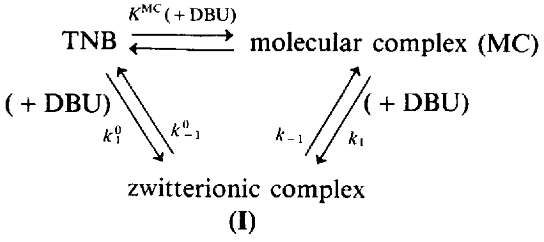
allow us to obtain equation (5) under the experimental conditions $[\mathrm{DBU}]_0 \gg [\mathrm{TNB}]_0$:

$$k_{\mathrm{obs}}(1 + K^{\mathrm{MC}}[\mathrm{DBU}]_0) = k_1^0 + k_1 K^{\mathrm{MC}}[\mathrm{DBU}]_0 \tag{5}$$

K^{MC} values are known from independent absorbance values at various temperatures (or they are extrapolated values), and k_1^0 (referred to the reactivity of the substrate 'free' from DBU,



Scheme 1



Scheme 2

Table 2. k_1^0 and k_1 values[a] calculated by equation (5)

Temperature (°C)	k_1^0 ($\mathrm{s^{-1}\,mol^{-1}\,l}$)	k_1K^{MC} ($\mathrm{s^{-1}\,mol^{-2}\,l}$)	k_1 ($\mathrm{s^{-1}\,mol^{-1}\,l}$)	r[b]
25	$(9{\cdot}5 \pm 2) \times 10^{-5}$	$0{\cdot}012 \pm 2 \times 10^{-5}$[c]	$1{\cdot}64 \times 10^{-3}$	0·9979
35	$(8{\cdot}8 \pm 0{\cdot}3) \times 10^{-4}$	$0{\cdot}021 \pm 3 \times 10^{-5}$[d]	$4{\cdot}28 \times 10^{-3}$	0·9985
45	$(2{\cdot}04 \pm 0{\cdot}06) \times 10^{-3}$	$0{\cdot}024 \pm 5 \times 10^{-5}$[e]	$7{\cdot}74 \times 10^{-3}$	0·9992

$k_1^0: \Delta H^* = 118\ \mathrm{kJ\,mol^{-1}}$; $\Delta S^* = -75\ \mathrm{J\,mol^{-1}\,K^{-1}}$

$k_1: \Delta H^* = 58\ \mathrm{kJ\,mol^{-1}}$; $\Delta S^* = -102\ \mathrm{J\,mol^{-1}\,K^{-1}}$

[a] Errors are standard deviations.

[b] Correlation coefficient.

[c] $K^{MC} = 7{\cdot}3\ \mathrm{mol^{-1}\,l}$.

[d] $K^{MC} = 4{\cdot}9\ \mathrm{mol^{-1}}$ (extrapolated value).

[e] $K^{MC} = 3{\cdot}1\ \mathrm{mol^{-1}\,l}$ (extrapolated value).

in the uncatalysed process) and k_1 values (referred to the reactivity of the molecular complex) are calculated and are reported in Table 2, which also gives the thermodynamic parameters.

In the literature there are several examples[14–16] of the dependence of the catalysed and uncatalysed processes on temperature. In some cases the experimental reaction rate constant is decreased by increasing the temperature.[16] This unusual behaviour may be easily explained by the present data, by considering that the second term in equation (5) includes the substrate–nucleophile association constant (K^{MC}), which is clearly decreased by increasing the temperature. The data (see Table 2) indicate that both k_1^0 and k_1 are increased on increasing the temperature, as required by Scheme 2. The activation parameters of both processes agree well with the usual parameters for S_NAr reactions. The activation energy for the reactivity of MC (measured by k_1 value) is lower than the activation energy of the 'free' TNB (k_1^0 value), as expected considering that $k_1 > k_1^0$.

When the nucleophile is a protic amine, the self-association of the amine (or the association between the amine and the catalyst) was reported to be operative in the reaction pathway.[17] Previously, we reported[18] some experimental details against this interpretation which, obviously, may be ruled out in the present system.

An increase in temperature reduces the possibility of observing catalytic effects by reducing the amount of the complexed substrate. In any case, the observation of catalytic phenomena is related to the difference in the rate of the free substrate with respect to the complexed substrate:[13] in our case when k_1 is higher than k_1^0, the k_{obs} value is increased on raising $[\mathrm{DBU}]_0$. When k_1 is lower than (or equal to) k_1^0, the k_{obs} value is decreased (or unaffected) on increasing the initial nucleophile concentration $[\mathrm{DBU}]_0$, as observed in very polar solvents (DMSO).[9]

In conclusion, not only the model of Scheme 2 is consistent with the kinetic data reported here, but also it is a starting point for reconsidering the 'anomalous' kinetic features of S_NAr reactions.

EXPERIMENTAL

Materials

TNB and DBU were commercial samples (Carlo Erba, RPE) purified by the usual procedures. Toluene was refluxed for 1 day over sodium and freshly distilled.[19]

Table 3. A_0 (absorbance at zero reaction time) values for TNB–DBU mixtures in toluene at 18 °C ($\lambda = 510$ nm); $[\mathrm{DBU}]_0 = 3\cdot89 \times 10^{-3}$ mol l^{-1})

$[\mathrm{TNB}]_0 \times 10^{-2}$ mol l^{-1}	1·93	3·01	3·89	4·75	9·45	2·53[a]
A_0	0·144	0·210	0·240	0·278	0·409	0·091

[a] $[\mathrm{DBU}]_0 = 1\cdot95 \times 10^{-3}$ mol l^{-1}.

Determination of the formation constant of the molecular complex between TNB and DBU

Extrapolation at zero reaction time of the experimental absorbance values was performed by the usual procedures. Table 3 reports an example of the values obtained which were used in the Benesi–Hildebrand plots. The linear relationship between $[\mathrm{DBU}]_0/A_0$ and $1/[\mathrm{TNB}]_0$ can be expressed algebraically by the following equations: at 18 °C, $[\mathrm{DBU}]_0/A_0 = (5\cdot06 \pm 0\cdot3) \times 10^{-3} + (4\cdot2 \pm 3) \times 10^{-4} \times 1/[\mathrm{TNB}]_0$ (number of points = 6, $r = 0\cdot9986$); at 25 °C, $[\mathrm{DBU}]_0/A_0 = (4\cdot79 \pm 0\cdot4)^{-3} + (6\cdot59 \pm 6) \times 10^{-4} \times 1/[\mathrm{TNB}]_0$ (number of points = 12, $r = 0\cdot9995$), $[\mathrm{TNB}]_0/A_0 = (2\cdot82 \pm 0\cdot9) \times 10^{-3} + (5\cdot91 \pm 5) \times 10^{-4} \times 1/[\mathrm{DBU}]_0$ (number of points = 5, $r = 0\cdot9996$); at 33 °C, $[\mathrm{DBU}]_0/A_0 = (4\cdot55 \pm 0\cdot6) \times 10^{-3} + (7\cdot96 \pm 7) \times 10^{-4} \times 1/[\mathrm{TNB}]_0$ (number of points = 6, $r = 0.9990$). At the λ value used here (510 nm), the starting materials (in separate solutions) did not show appreciable abosrbance values.

Kinetics

Kinetic runs were performed by following the appearance of the reaction product at 468 nm. The pseudo-first-order rate constants were divided by $[\mathrm{DBU}]_0$ to give second-order rate constants, k_{obs}. The reproducibility of k_{obs} values was ±4%. The values of the apparent coefficient of absorbance at infinite reaction time ($A_\infty/[\mathrm{TNB}]_0$) were unaffected by the temperature used within experimental error (±3%) and by changes in $[\mathrm{DBU}]_0$ values.

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