GLOBAL JOURNAL OF PURE AND APPLIED SCIENCES VOL. 9, NO.4, SEPTEMBER 2003: 481 - 489
COPYRIGHT(C) BACHUDO SCIENCE CO. LTD. PRINTED IN NIGERIA. ISSN 1118-0579

KINETICS AND MECHANISM OF THE BASE-CATALYSED REACTION OF 4-NITROPHENYL (4-METHYLPHENOXY) FORMATE IN BENZENE.

GODDY NKEM ONUOHA and EDWARD EFFIONG

(Received 20 September 2002; Revision accepted 2 June 2003)

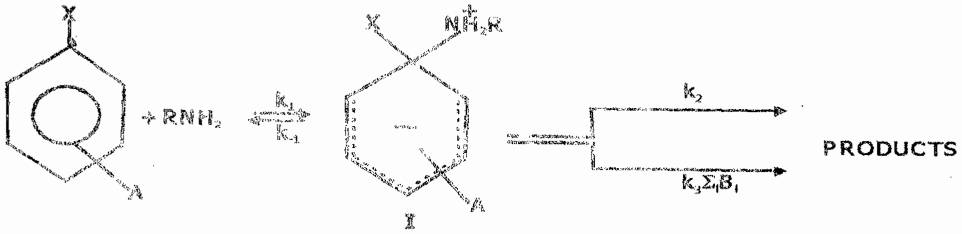
ABSTRACT.

The kinetics of n-butylaminolysis of 4-nitrophenyl (4-methylphenoxy) formate (NPMPF) in benzene has been investigated at 27°C and in the presence of functionally similar, but structurally different addenda, namely; imidazole, pyridine and triethylamine. The reaction is catalysed by the nucleophile and imidazole in a linear fashion across the entire range of concentrations employed, giving values of k_3/k_2 ratio of 398 and 267.5 respectively. In the presence of pyridine and triethylamine, which respectively gave k_3/k_2 values of 260 and 780, the modes of catalyses differed very significantly. While the observed second order rate constant, k_A, showed a quadratic dependence on pyridine concentration, it manifested a curvilinear (downward) dependence on the concentration of triethylamine. Analyses of the kinetic data have revealed that all additives, regardless of their differing modes of activity, manifested genuine base catalyses of the reaction in accord with a Bunnett-type (Specific Base-General Acid, SB-GA) mechanism in which electrophilic catalyzing models assist the detachment of the leaving group.

INTRODUCTION.

The proof of the existence of a difference between the mechanism of the nucleophilic aromatic substitution, S_NAr reaction and the aliphatic analogue, S_N2 was provided by the observed order of nucleofugality of halogens at the aromatic and saturated carbon centers. It had been shown (Ingold, 1953, p.453) that in protic solvents, the order of frangibility of the halogens in S_N2 reactions is I > Br > Cl >> F, a trend that is the reverse of the order of inductive effect of these atoms. In S_NAr reactions however, the often observed order is F>> Cl ≅ Br > I (Bunnette, 1978, p.413). Since kinetic data on their own alone, do not offer any distinction between the S_N2-type mechanism and the intermediate complex mechanism for aromatic nucleophilic substitutions, it became necessary that experiments capable of discriminating between the two were designed and investigated.

The reaction of activated aromatic substrates with primary or secondary amines invariably involves proton transfer at one stage or the other along the reaction coordinate and therefore offers the possibility of observing base catalysis. The intermediate complex (IC) mechanism for such reactions can be represented as in Scheme 1, where I is the first formed intermediate that is zwitterionic in nature.



x = leaving group
A = activating group
B = added base
R = alkyl group of the amine.

SCHEME 1.

Application of the steady-state approximation to scheme 1 gives the observed second order rate

---

GODDY NKEM ONUOHA, Department of Chemistry, Federal University of Technology, Owerri, Nigeria
EDWARD EFFIONG, Department of Chemical Engineering, Federal University of Technology, Owerri, Nigeria

constant, k_A, as shown in equation 1, where B is either a molecule of the nucleophile or of an added base.

$$k_A = \frac{k_1 k_{21} + k_1 k_3 \Sigma_i B}{k_{-1} + k_2 + k_3 \Sigma_i B} \qquad \ldots\ldots\ldots\ldots \qquad (1)$$

Depending on the relative magnitudes of the rate coefficients k_{-1} and $k_2 + k_3\Sigma_i B$, three possible kinetic forms are observable.

(1) when $k_{-1} >> k_2 + k_3\Sigma_i B$, then equation 1 reduces to equation 2 and the system is susceptible to base catalysis.

$$k_A = \frac{k_1 k_2}{k_{-1}} + \frac{k_1 k_3 \Sigma_i B}{k_{-1}} \qquad \ldots\ldots\ldots \qquad (2)$$

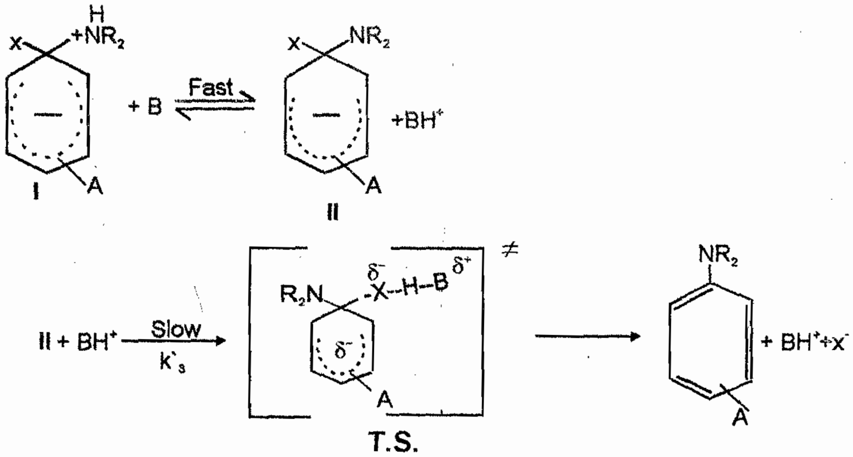
(2) when $k_{-1} << k_2 + k_3\Sigma_i B$, then equation 3 results from equation 1 and the system is rendered insensitive to base catalysis.

$$k_A = k_1 \qquad \ldots\ldots\ldots\ldots\ldots \qquad (3)$$

(3) when the magnitudes of k_{-1} and $k_2 + k_3\Sigma_i B_i$ are comparable, there is no further simplification of equation 1 and the system responds to a curvilinear dependence of the rate constant on nucleophile concentration.

That these three distinct classes of kinetic forms exist have already been reported (Onuoha *et al* 2000 p.79), and just a few examples will be cited. In the reaction of 2,4-dinitrophenylphenyl ether with n-Butylamine in 10% dioxane-90% water, Bernasconi and Schmid, 1973, showed that $k_A = k_1$, hence attack of the nucleophile on the substrate was rate limiting and the system was insensitive to base catalysis. With the same substrate however, and in the same solvent, Bernasconi, 1967, showed that the observed second-order rate constant, k_A, is linearly dependent on morpholine concentration, indicating that the breakdown of the first-formed intermediate was kinetically more significant across the entire range of base concentration studied, hence the first kinetic condition operates. The same substrate reacting with piperidine in the same solvent has been shown by Bunnett and Bernasconi, 1965, to be curvilinearly dependent on piperidine concentration, corresponding to the third kinetic condition.

The mechanism of base catalysed pathway in aprotic solvents of medium to high dielectric constant is widely accepted as that shown in scheme 2 (Bunnette and Davies, 1960, p 5958).



SCHEME 2

According to the scheme, the first formed intermediate, I, is rapidly deprotonated by the base to give its conjugate base, II. The resulting conjugate acid of the base then electrophilically catalyses the expulsion of the leaving group via a transition state, (T.S.) This mechanism is formally designated the specific base, general acid, (SB-GA).

In non-polar aprotic solvents, the involvement of hydrogen-bonded aggregates, namely homo- and heteroconjugates in the catalysis of S_NAr reactions has been demonstrated (Hirst et al, 1988, p. 79). While Nudelman and coworkers (Nudelman et al, 1983, p.1607) put forward the dimer nucleophile mechanism, Banjoko and coworkers (Banjoko et al, 1982, p.1356) proposed a modification of the cyclic transition state. (Capon et al, 1963, p. 277). Further evidence for the involvement of hydrogen-bonded aggregates has been reported (Onuoha et al, 2000, p. 79).

In non-polar aprotic solvents, various medium effects are known to apply. These include negative activation energy resulting from inverse dependence of k_A on temperature (Banjoko et al, 1982, p.1356), curvilinear (upwards) dependence of k_A on base concentration (Bamkole et al 1982, Bernasconi *et al*, 1966, p. 2570) and acceleration of reaction rates by neutral species which have no formal basic properties (Hirst et al, 1988). It has already been pointed out (Hirst et al 1988) that because of the range of electrostatic forces in these media, several mechanisms and solvent effects are feasible.

The results and discussion in this paper focus on the n-butylaminolysis of 4-nitrophenyl (4-methylphenoxy) formate in benzene. Aminolysis of various activated aromatic amines in non-polar solvents by n-Butylamine have been investigated and reported by several groups of workers (Onuoha and Onyido, 2000, Onuoha 2001, Ayediran et al, 1976). But there is paucity of information with carbonates, thiocarbonates and formates as the substrates (Castro et al, 2002). Benzene was chosen as the solvent, not just because it is among the common non-polar solvents available, but also because there is reasonable amount of literature on S_NAr reactions in this solvent. In addition, its dielectric constant of 2.27 and pKa < 1 (Weast, 1968) make its choice reasonable, since the effects of aggregation can be investigated without complications arising from high solvent polarity and basicity.

MATERIALS AND METHOD.

Materials

Analar grade imidazole, pyridine and triethylamine were purchased from Aldrich Chemicals, and were used as received.t The substrate 4-nitrophenyl (4-methylphenoxy) formate was synthesized as reported.(Castro et al , 2002, p. 309). n-Butylamine was purchased from BDH and purified by standard method (Onuoha et al, 2000,).

Benzene was purchased from Fischer. The solvent was soaked with 15% of its volume of sulphuric acid for 24 hours with occasional shaking. After discarding the acid layer, the solvent was washed thrice with water and 10% sodium carbonate. It was then dried with anhydrous calcium chloride, filtered and distilled. The middle fraction boiling at 80-81°C was collected and stored over sodium wire.

Method

The reactions were monitored at 400nm, with the nucleophile in large enough excess to ensure pseudo-first order kinetics, using a Pye-Unicam sp-6-200 spectrophotometer and employing the pipette technique already described (Bamkole et al, 1968).

Constant temperature during kinetic runs was achieved by the use of a Techne water thermostat. This was set at the required temperature of 27°C and was left working continuously. The temperature of the bath was monitored with a standard thermometer that was permanently fixed to the water volume.

Observed second order rate constants were obtained by dividing the pseudo first-order rate constants by the nucleophile concentration.

RESULTS AND DISCUSSION.

The values of the observed second order rate constant, k_A, from the kinetics of the title reaction are assembled in Tables 1-4.

Table 1: Values of observed second order rate constants, k_A, ($M^{-1}s^{-1}$) for the n-butylaminolysis[a] of 4-nitrophenyl (4-methylphenoxy) formate[b] in Benzene at 27°C and in the absence of added base.

10^3[n-ButNH$_2$.]/M	2.00	3.00	5.00	7.50
10^2k_A	1.86	2.20	2.80	3.98
10^3[n-ButNH$_2$.]/M	10.00	12.50	15.00	17.50
10^2k_A	4.80	6.60	7.20	8.19
10^3[n-ButNH$_2$]/M	20.00	25.00	30.00	35.00
10^2k_A	9.00	11.41	13.05	15.40
10^3[n-ButNH$_2$]/M	40.00	45.00	50.00	
10^2k_A	17.72	20.15	22.25	

Table 2: Values of observed second order rate constants, k_A, ($M^{-1}s^{-1}$) for the n-butylaminolysis[a] of 4-nitrophenyl (4-methylphenoxy) formate[b] in Benzene at 27°C and in the presence of pyridine.

[Py]/M	0.05	0.10	0.15	0.20
10^2k_A	2.42	3.65	4.61	5.80
[Py]/M	0.25	0.30	0.35	0.40
10^2k_A	7.20	8.56	12.43	14.61
[Py]/M	0.45	0.50		
10^2k_A	17.40	21.05		

Table 3: Values of observed second order rate constants, k_A, ($M^{-1}s^{-1}$) for the n-butylaminolysis[a] of 4-nitrophenyl (4-methylphenoxy) formate[b] in Benzene at 27°C and in the presence of triethylamine (Et_3N)

$10^3[Et_3N]$/M	2.00	5.00	7.50	10.00	
10^2k_A	1.83	2.08	2.26	2.38	
$10^3[Et_3N]$/M	12.50	15.00	18.00	20.00	
10^2k_A	2.65	2.78	3.04	3.06	
$10^3[Et_3N]$/M	25.00	30.00	35.00	40.00	50.00
10^2k_A	3.35	3.48	3.60	3.60	3.75

Table 4: Values of observed second order rate constants, k_A, ($M^{-1}s^{-1}$) for the n-butylaminolysis[a] of 4-nitrophenyl (4-methylphenoxy) formate[b] in Benzene at 27°C and in the presence of imidazole (imid).

10^3[Imid.]/M	1.00	2.00	3.00	4.00
10^2k_A	2.10	2.62	2.98	3.59
10^3[Imid.]/M	5.00	7.00	9.00	12.00
10^2k_A	3.78	4.80	5.40	6.88
10^3[Imid.]/M	15.00			
10^2k_A	8.18			

[a] $[N\text{-}ButNH_2.] = 2.5\times10^{-3}M$, [b] $[NPMPF] = 2.4\times10^{-4}M$

The reaction is linearly catalysed by the nucleophile, as shown in Figure 1. A k3/k2 ratio of 398 as calculated from the plot shows that the nucleophile strongly catalysed the reaction.

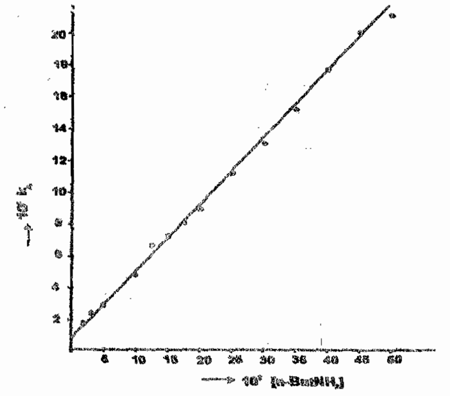


FIG 1: Plot of k_A against Nucleophile concentration.

Figure 2 shows the variation of the second order rate constant, k_A, with varying concentrations of imidazole as an added base. Just as with the nucleophile, the reaction is linearly catalysed by imidazole. The k_3/k_2 ratio of 267.5 also reveals genuine base catalysis. ❖

❖ According to Bunnett, (Bunnette et al, 1965) cases in which $k_3/k_2 \geq 50$ 1 mol^{-} represent true base catalysis.

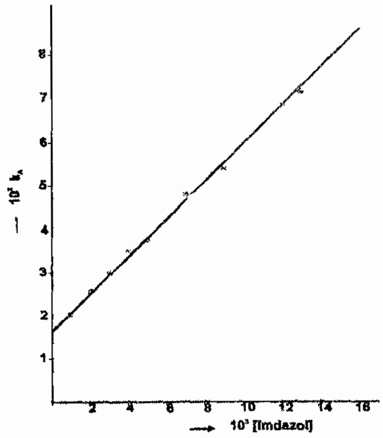


FIG 2: Plot of k_A against [imidazole]

This mode of catalysis by the nucleophile and imidazole has been explained to derive from electrophilic catalysis by homo- and heteroconjugates during the expulsion of the leaving group (Hirst *et al*, 1988).

The second kinetic form observed was exhibited by pyridine in which a plot of k_A against pyridine concentration is curved upwards as shown in Figure 3.

Since this plot is not typical of kinetic forms usually observed in S_NAr reactions, the criterion usually employed i.e. the k_3/k_2 ratio cannot be used to decide whether the reaction is genuinely catalysed or otherwise.

A different approach is therefore adopted in considering the reaction in the presence of this catalyst. It is seen that a five – fold increase in pyridine concentration also increases k_A five – fold. Moreover, the upward curving arm of the plot increases rapidly with pyridine concentration.

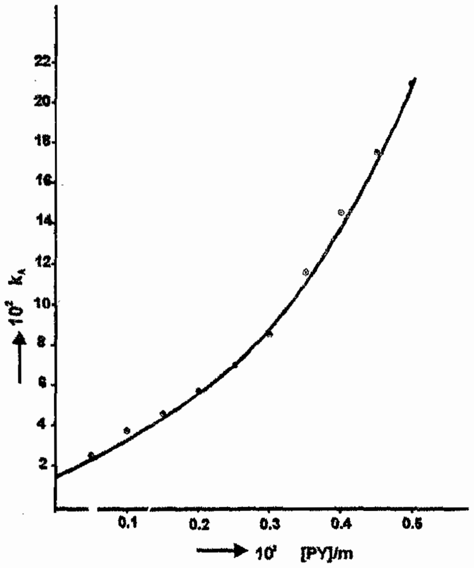


Fig 3: Plot of k_A against pyridine concentration.

Hence, even on the basis of the magnitudes of increments of k_A with increasing pyridine concentration, it is reasonable to conclude that pyridine genuinely catalysed the reaction.

Again, when a quadratic dependence of k_A on pyridine concentration is assumed, the plot given in Figure 4 results. The plot of k_A versus $[\text{pyridine}]^2$ gives a good correlation, ($r = 0.987$) with slope = 260. This behaviour is easily explained if it is assumed that, in the high concentration of pyridine employed in this study (0.05-0.50M), there is dimerization of the type in equation 4 where K_d is the formation constant of the dimer equilibrium, and that it is the dimer that participates in the heteroconjugation that finally catalyses the detachment of the leaving group according to equation 5. There is evidence already (Robinson, B. H., 1975, p. 138.) that extensive self-association of amines occurs in aprotic solvents.

$$P + P \overset{K_d}{\rightleftharpoons} P_2 \qquad ....(4)$$

$$P_2 + NH^+ \rightleftharpoons [N....H....P_2]^+ \qquad ....(5)$$

P = pyridine molecule.

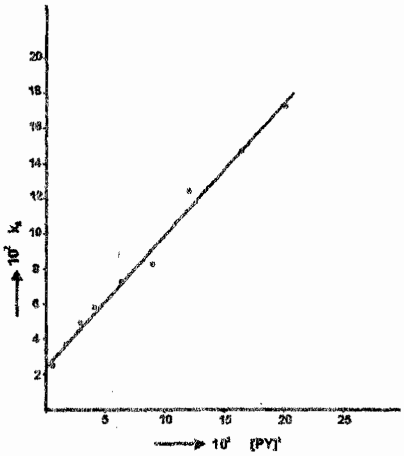


Fig 4: Plot of k_A against $[PYRIDINE]^2$

The third class of the catalysed reactions involves Et_3N, which manifested a downward curvilinear kinetic form as shown in Figure 5. The results for this additive are analysed in accordance with standard procedures usually employed for this kinetic form (Taft, 1952, p. 2729).

This kinetic form is equivalent to the kinetic condition $k_{-1} \cong k_2 + k_3\Sigma_i[B_i]$, in which the first formed intermediate is approximately equally partitioned between the product – forming steps and k_{-1} i.e. the step for the reversion to reactants, showing that equation (2) holds. If equation 2 is inverted and it is assumed that $k_3\Sigma_i[B_i] > k_2$, then equation (6) results.

$$\frac{1}{k_A} = \frac{1}{k_1} + \frac{1}{k_1 k_3 [B]} \qquad .... (6)$$

A plot of $1/k_A$ versus $1/[Et_3N]$ should give a straight line except under conditions where initial assumption is not valid, i.e. at low catalyst concentration. Hence this plot is expected to be initially deviating towards the 1/[B] axis. Such a plot is actually obtained and is given in Figure 6 and analysis of the intercept gives $k_1 = 4.16 \times 10^{-2}\ M^{-1}\ s^{-1}$. Using this value of k_1, another plot can be constructed which makes no simplifying assumption, using equation (7) obtained by rearranging equation (2).

$$\frac{k_A}{k_1 - k_A} = \frac{k_2}{k_1} + \frac{k_3 \Sigma_i B_i}{k_1} \qquad ....(7)$$

A plot of $k_A/(k_1 - k_A)$ versus triethylamine concentration should be linear across the entire range of triethylamine concentration employed in the study. Such a plot, given in Figure 7, is indeed linear with slope = 160 and intercept = 0.205.

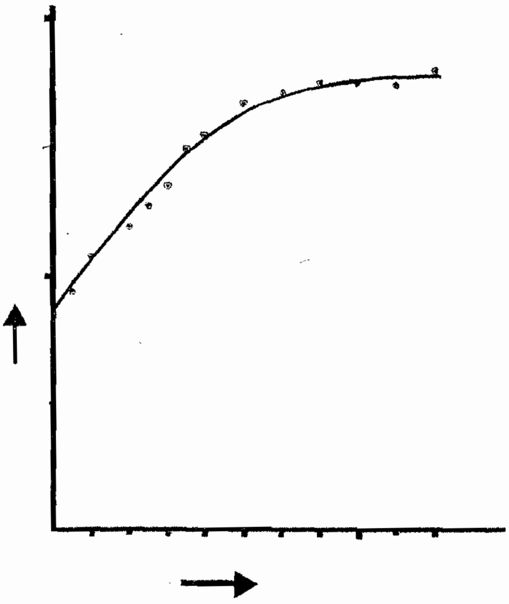


Fig 5: Plot of k_A against $[Et_3N]$.

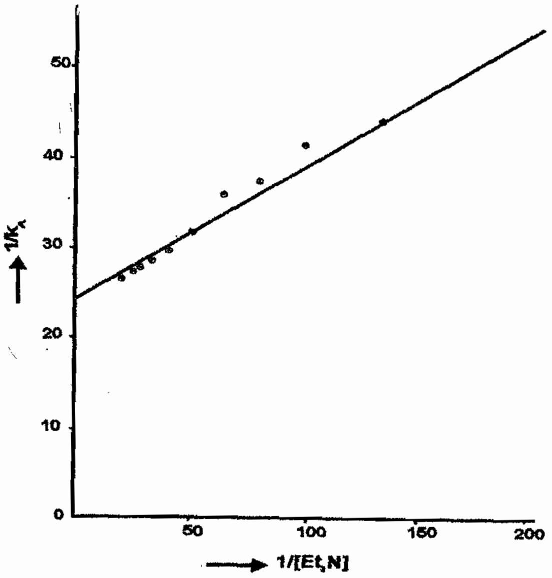


Fig 6: Plot of $1/k_A$ against $1/[Et_3N]$.

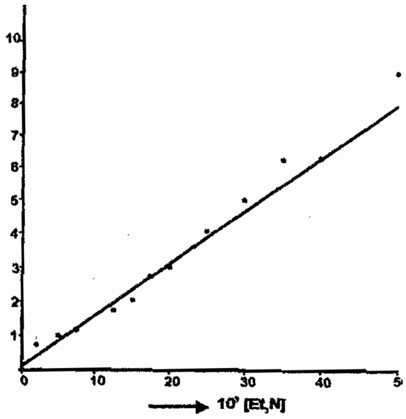
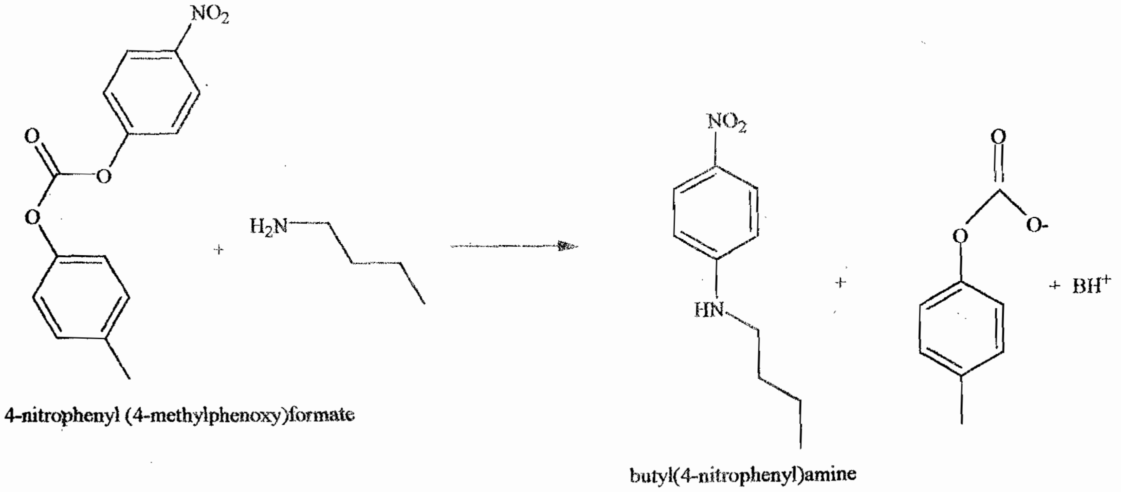


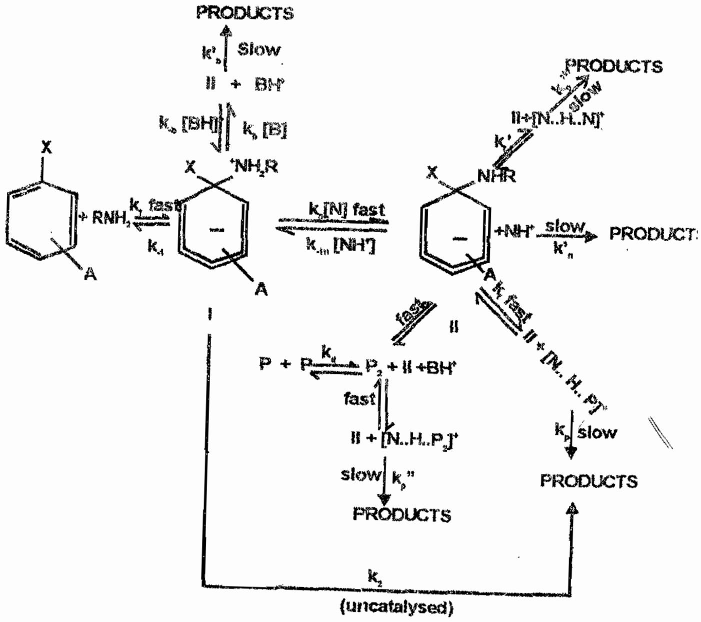
Fig 7: Plot of k_A/k_1-k_A against $[Et_3N]$

Since the slope in this plot = k_3/k_{-1} and its intercept = k_2/k_{-1} the ratio slope/ intercept gives k_3/k_2 = 780 which shows (i) that the reaction is strongly catalysed by Et_3N and (ii) that the catalytic efficiency of Et_3N is greater than those of imidazole and pyridine both of which have been shown to catalyse the reaction by a heteroconjugate mechanism. There is reason to believe, both from the magnitude of its k_3/k_2 ratio and its kinetic form that the mechanism of catalysis by Et_3N is entirely different from those of imidazole and pyridine. A homoconjugate formed by Et_3N will be bulky and Et_3N will not catalyse the reaction via the homoconjugation mechanism.

It is to be pointed out that Et_3N is a strong base; pKa in water = 10 (Taft, 1952) and has been known to catalyse several A_N+D_N reactions (March, J., 1991). Hence its catalysis is mainly via its activity as a Bronsted base since proton abstraction from the first – formed intermediate by Et_3N will be favoured. Similar argument holds for n-butylamine. On this basis, pyridine and imidazole being much weaker bases would not compete favourably for the deprotonation of the first formed intermediate with the nucleophile, hence their catalytic activity is mainly through the heteroconjugation mechanism.

In conclusion, the observed kinetics conform to an SB-GA type mechanism in which the nucleophile catalysed the reaction via homoconjugation. While imidazole and pyridine catalysed by heteroconjugation, triethylamine catalysed purely as a Bronsted base. The stoichiometric equation for the conversion of reactants to products is shown below, while the detailed mechanistic pathway, as postulated, is as illustrated in Scheme 3.





SCHEME 3

REFERENCES.

Ayediran, D. , T. O. Bamkole and Hirst, J., 1976. The kinetics of the reaction of piperidine, n-Butylamine, Morpholine and Benzylamine with 1-fluoro and chloro- 2,4-dinitrobenzenes,
J. Chem. Soc, Perkin Trans II, 1396.

Bamkole, T.O., C.W.L.Bevan and J. Hirst, 1968, Aromatic Nucleophilic Replacement, Part Xii., Nigeria J. of Science, 2: 11-22.

Bamkole, T.O., Hirst J. and Onyido, I., 1982, Base catalysis of Aromatic Nucleophilic Substitutio Reactions in Aprotic and Dipolar aprotic solvents, J. Chem. Soc., Perkin Trans II 889-893.

Banjoko, O. and Ezeani, C., 1982. Kinetics of the reactions of phenyl-2, 4, 6-trinitrophenylether with various substituted anilines in benzene. J. Chem. Soc., Perkin trans II 1356.

Bernasconi, C.F., 1967. Kinetics of the reactions of amines with ethers of 2,4-dinitrophenol in 10% dioxane-90% water. Dependence of base catalysis on entering amine and on leaving group, J. Org. Chem. 32: 2947-2952.

Bernasconi, C.F. and Schmid, P., 1973, Base-catalysis of the reaction of morpholine with 2,4-dinitrophenylphenyl ether in 10% dioxane-90% water, J. Org. Chem., 32: 2953-2956.

Bernasconi, C.F. and Zollinger, H., 1966. Catalytic effect in the reaction of 2,4-dinitrofluoro and –chloro benzenes with morpholine, Helv. Chem. Acta 49 2570.

Bunnett, J.F. and Bernasconi, C.F., 1965. Kinetics of the reactions of piperidine with ethers of 2,4-dinitrophenol in 10% dioxane-90% water. Dependence of base catalysis on the group displaced, J. Am. Chem. Soc., 87: 5209-5218.

Bunnett, J.F. and Garst, R.H., 1965, Kinetics of reactions of aniline and n-butylamine with 2,4-dinitrofluorobenzene.J Am. Chem. Soc. 87: 3875.

Bunnett, J.F. and Davies, G. T. . 1960. The mechanism of aminolysis of Esters. J. of Am. Chem. Soc., 99: 5958-64.

Bunnett, J. F., 1978. Aromatic Substitution by the $S_{RN}1$ Mechanism Acc. of Chem. Res., 11: 413.

Capon, B. and C.W. Rees,1963, Reaction Mechanisms. Ann. Reports, 60: 277-282

Castro, E.A., Andujar, M. and Campodonico, P., 2002. Kinetics of the reaction of alicyclic amines with 4-nitrophenyl and 2,4-dinitrophenyl carbonates, Int J. Chem. Kinet. 34: 309..

Hirst, J., Onuoha, G.N., and Onyido, I., 1988. Mechanism of nucleophilic Aromatic Substitution in non-polar media. J. chem. Soc. Perkin Trans II: 971-974

Ingold, C.K., 1969. Structure and Mechanism in Organic Chemistry, Bell, London, 2nd Edition p.453

March, Jerry 1991. Advanced Organic Chemistry: Reactions, Mechanisms and Structure. 4th. Ed, Wiley & Sons Interscience Publication, New York, 641-676

Nudelman, N.S and D. Palleros,1983, Reactions of nitroanisoles 4. Reaction of 2,4- and 2,6-dinitroanisoles with cyclohexylamine. Evidence of a dimmer nucleophile. J. Org. Chem. 48: 1607.

Onuoha, G. N. and Ikenna Onyido, 2000, Kinetics of the reaction of 1 phenoxy-2, 4 dinitrobenzene with n-Butylamine in Benzene: Evidence of catalysis by hydrogen bond acceptors, J. Chem. Soc. Nigeria 25: 79-84.

Onuoha, G. N., 2001. The effects of added Bases on the reactions of 2,4,6 trinitrophenylphenyl ether with Aniline in Benzene: Further evidence of electrophilic catalysis. J. Chem. Soc. Nigeria 26 (2): 199-204.

Robinson, B. H., 1975. Ed. Calvin, E and V. Gold. Hydrogen bonding and Proton transfer reactions in aprotic solvents. Chapman and Hall Ltd, London, pp121-152.

Taft, R. W., 1952. Linear free energy relationships from rates of esterification and hydrolysis of aliphatic and ortho-substituted Benzoate esters. J. Am. Chem. Soc. 74: 272.

Weast, R. C., 1968. Handbook of Chemistry and Physics, 4th Ed. McGraw-Hills Book Company, New York.