

Nucleophilic Attacks on Carbon-Carbon Double Bonds. Part XVII.¹ Base-catalysis in the Displacement of Vinylic Ethoxy-, Fluoro-, and Cyano-leaving Groups by Amines

By Zvi Rappoport* and Pnina Peled, Department of Organic Chemistry, The Hebrew University, Jerusalem, Israel

The observed second-order rate coefficients k_{obs}^2 for the displacement of the leaving group X of $p\text{-Me}_2\text{N}\cdot\text{C}_6\text{H}_4\cdot\text{C}(\text{X})\text{:C}(\text{CN})_2$ [(1) when X = OEt, CN, and F] by piperidine and morpholine in MeCN, and of compound (I; X = OEt) also in EtOH and PrOH and of (I; X = OEt) with di-isobutylamine in MeCN, increase with the increase in the amine concentration. Two types of kinetic behaviour are (a) a linear dependence, $k_{\text{obs}}^2 = k' + k''[\text{Amine}]$, observed for all the reactions of compounds (I; X = CN) and (I; X = F) and for (I; X = OEt) with piperidine in MeCN and EtOH, and (b) curved plots of k_{obs}^2 against [Amine], which yield linear inversion plots of $1/k_{\text{obs}}^2$ against $1/[\text{Amine}]$, found for the other reactions. The reactions of (I; X = OEt) in MeCN are not catalysed by pyridine, p -phenylenediamine, and N -methylpiperidine, but the reaction with piperidine + morpholine is faster than the combination of the two separate reactions. The reaction of the cyano-compound (I; X = CN) with di-isobutylamine is faster in 1 : 3 $\text{CCl}_4\text{-MeCN}$ than in 1 : 1 $\text{CCl}_4\text{-MeCN}$. A mechanism is suggested in which the amine attacks the double bond (k_1) forming a zwitterion, which can either revert to the reactants (k_{-1}), expel the leaving group in an uncatalysed route (k_2), or react with a second amine molecule in a catalysed (k_{3B}) route, where a rapid proton transfer equilibrium is followed by a slow electrophilically assisted detachment of the leaving group by the ammonium ion. Linear plots are obtained when $k_{-1} \gg k_2 + k_3[\text{Amine}]$ and curved plots which yield linear inversion plots when $k_{-1} \sim k_2 + k_3[\text{Amine}]$. The catalysed route predominates in MeCN ($k_{3B}/k_2 = 5 \rightarrow 2300$) but the uncatalysed route becomes more important in the alcohols. The effects of the changes in the nucleophile, the solvent, and the leaving group [relative k_{3B} in MeCN: (I; X = OEt), $1 <$ (I; X = CN), $10^4 <$ (I; X = F), 10^7] are consistent with the mechanism suggested, and are in accord with a multistep mechanism for nucleophilic vinylic substitution.

THE nucleophilic vinylic displacement *via* the addition-elimination route² of a leaving group X by amines is of the first order in amine when X = Cl,^{1,3} X = Br,^{1,3b-d} X = OSO_2Me or $\text{OSO}_2\text{C}_6\text{H}_4\text{Me-}p$,¹ or second order in amine with 1,1-dicyano-2- p -dimethylaminophenyl-2-fluoroethylene (I; X = F),⁴ or with several polycyanoolefins when X = CN,⁵ and exhibits an order between one and two in the amine with 2-chloro-1,1-dicyano-2- p -dimethylaminophenylethylene (I; X = Cl).⁴ These features are accommodated by Scheme 1,⁴ which is illustrated by the 1,1-dicyano-2- p -dimethylaminophenyl-2-X system (I). The initial nucleophilic attack (k_1) forms the zwitterion (II), where the C-X bond cleavage should be slower than that in (III) owing to the electron-attraction by the substituted ammonium ion, which is also a good leaving group (*i.e.*, k_{-1} is high). With a good leaving group the expulsion of X from (II) to give

(IV) is fast and uncatalysed (k_2) and k_1 is rate-determining. However, with a poor leaving group, when the C-X bond cleavage is slow, deprotonation of the ammonium ion of (II) by a second amine molecule (with a rate coefficient k_{3B}) may precede the C-X bond cleavage. The expulsion of X from the resulting carbanion (III) will be enhanced since the electron-attracting $^+\text{NHR}_2$ group is replaced by the mesomerically electron-donating NR_2 group. Alternatively, primary or secondary amines may serve as electrophilic (k_{3A}) or bifunctional catalysts for the formation of (IV), by hydrogen bonding to X. Evidence for base catalysis is derived from the fact that pyridines catalyse the formation of (V) from the fluoro-compound (I; X = F) and p -toluidine.^{4,6}

Steady-state treatment of Scheme 1, the electrophilically-assisted k_{3A} route being neglected (the derived equations would have the same form with $k_{3A} + k_{3B}$ replacing k_{3B}), gives the second-order rate coefficient k_{obs}^2 of equation (1). A more detailed description of the k_{3B} route where the C-X bond cleavage is involved in the rate-determining step (Scheme 3) will be discussed later. For a good leaving group, the forward reactions are

¹ Part XVI, Z. Rappoport and A. Topol, *J.C.S. Perkin II*, 1972, 1823.

² (a) Z. Rappoport, *Adv. Phys. Org. Chem.*, 1969, 7, 1; (b) G. Modena, *Accounts Chem. Res.*, 1971, 4, 73.

³ (a) G. Modena, P. E. Todesco, and S. Tonti, *Gazzetta*, 1959, 89, 878; (b) G. Modena, F. Taddei, and P. E. Todesco, *Ricerca Sci.*, 1960, 30, 894; (c) L. Maioli, G. Modena, and P. E. Todesco, *Boll. sci. Fac. Chim. ind. Bologna*, 1960, 18, 66; (d) A. Campagni, G. Modena, and P. E. Todesco, *Gazzetta*, 1960, 90, 694; (e) F. Scotti and E. J. Frazza, *J. Org. Chem.*, 1964, 29, 1800; (f) F. Beltrame, G. Favini, M. G. Cattania, and F. Guella, *Gazzetta*, 1968, 98, 380.

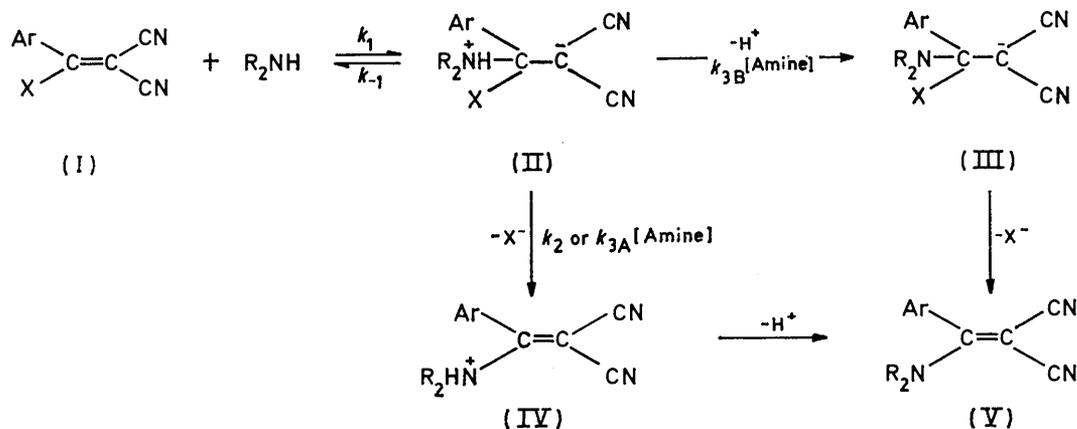
⁴ Z. Rappoport and R. Ta-Shma, *J. Chem. Soc. (B)*, 1971, 871.

⁵ Z. Rappoport and D. Ladkani, *J.C.S. Perkin II*, in the press; Abstracts of the 72nd Meeting of the Israel Chemical Society, Rehovoth, 1972, p. 6.

⁶ Z. Rappoport and N. Ronen, *J.C.S. Perkin II*, 1972, 955.

faster than the reversal of the nucleophilic attack, *i.e.*, $k_2 + k_{3B}[\text{Amine}] \gg k_{-1}$, so equation (1) reduces to equation (2) and no amine-catalysis is observed. With sluggish leaving groups the reversal is faster than the

(I; X = Cl)] with piperidine, morpholine, and di-isobutylamine in several solvents. The reaction of the cyano-analogue, *NN*-dimethyl-*p*-tricyanovinylaniline (I; X = CN)¹⁰ was also investigated briefly.



SCHEME 1 Ar = *p*-Me₂N·C₆H₄; X = F, Cl, OEt, or CN

forward reactions ($k_{-1} \gg k_2 + k_{3B}[\text{Amine}]$) and equation (3) which calls for linearity in a plot of k_{obs} against

$$k_{\text{obs}}^2 = k_1 (k_2 + k_{3B}[\text{Amine}]) / (k_{-1} + k_2 + k_{3B}[\text{Amine}]) \quad (1)$$

$$k_{\text{obs}}^2 = k_1 \quad (2)$$

[Amine] is obtained. Equation (3) includes terms both for the 'catalysed' and the 'uncatalysed' reaction, and their relative importance, *i.e.*, k_{3B}/k_2 is obtained from the (Slope):(Intercept) ratio of the above plot. When k_{3B}/k_2 is high the reaction is of the second order in the amine, and when it is low the reaction is mainly uncatalysed.

$$k_{\text{obs}}^2 = k_1 k_2 / k_{-1} + (k_1 k_{3B} / k_{-1}) [\text{Amine}] \quad (3)$$

The observation of catalysis argues for the multi-step nature of the vinylic substitution,² but the argument would be strengthened if equation (1) would be obeyed in a vinylic system. A promising leaving group is ethoxy, since it was recently demonstrated that equation (1) is followed in nucleophilic aromatic substitution when X = OEt or OAr.⁷ Other mechanistic questions, which were little or not at all explored, cover the relative importance of the catalysed and the uncatalysed routes and the relative magnitude of the rate coefficients in the catalysed route as a function of a change in the nucleophile,^{4,8} the leaving group, and the solvent,^{4,8} and whether the catalysis is basic, electrophilic, or bifunctional.

For these reasons we studied the reactions of 1,1-dicyano-2-*p*-dimethylaminophenyl-2-ethoxyethylene (I; X = OEt)⁹ [the ethoxy-analogue of (I; X = F) and

RESULTS

Reaction of the Ethoxy-compound (I; X = OEt) with Piperidine, Morpholine, and Di-isobutylamine in Acetonitrile.—The reaction of (I; X = OEt)⁹ with the three amines was followed spectrophotometrically by monitoring the decrease in the absorption of (I; X = OEt) at 410 nm. The amine was always in large excess and its concentration was changed 3–32 fold. The reactions were followed up to 70–90% and showed pseudo-first-order kinetics in each run. The rate coefficients k_{obs}^1 were obtained from the linear plots of $\log(D_t - D_\infty)$ against time where D_t and D_∞ are the optical densities at the time t and after 10 or more half-lives, respectively. The D_∞ values remained constant when the cold reaction mixtures were kept in the dark in order to avoid oxidation. The second-order coefficients k_{obs}^2 were obtained by dividing k_{obs}^1 by the amine concentration. Most of the runs were conducted with the same concentration of (I; X = OEt), but occasional change in its concentration showed that the reaction order in (I; X = OEt) is unity.

Table 1 shows that k_{obs}^2 values increase with the increase in the amine concentration. For piperidine and di-isobutylamine the increase is linear according to equation (4) (Figure 1). The least-squares intercepts (the 'uncatalysed' rate coefficients) k' and slopes (the 'catalysed' rate

$$k_{\text{obs}}^2 = k' + k''[\text{Amine}] \quad (4)$$

coefficients) k'' , their ratios, and the derived activation parameters are in Table 2. The reactions of di-isobutylamine were much slower than those with the cyclic amines, and the k_{obs}^2 values are based on initial rate coefficients k_{obs}^1 .

The increase in k_{obs}^2 values for morpholine with the amine concentration (Table 1) is not linear, as demonstrated in Figure 2. The relative increase with the addition of a

⁷ (a) J. F. Bunnett and C. Bernasconi, *J. Amer. Chem. Soc.*, 1965, **87**, 5209; (b) C. R. Hart and A. N. Bourns, *Tetrahedron Letters*, 1966, 2995; (c) C. F. Bernasconi, *J. Org. Chem.*, 1967, **32**, 2947; (d) J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, 1965, **87**, 3875; *J. Org. Chem.*, 1968, **33**, 2320; (e) F. Pietra, D. Vitali, and S. Frediani, *J. Chem. Soc. (B)*, 1968, 1595.

⁸ Z. Rappoport and R. Ta-Shma, *J. Chem. Soc. (B)*, 1971, 1461.

⁹ A. D. Josey, C. C. Dickinson, K. C. Dewhirst, and B. C. McKusick, *J. Org. Chem.*, 1967, **32**, 194.

¹⁰ B. C. McKusick, R. E. Heckert, T. L. Cairns, D. D. Coffman, and H. F. Mower, *J. Amer. Chem. Soc.*, 1958, **80**, 2806.

TABLE 1

Second-order rate coefficients (k^2_{obs}) for the reaction of 10^{-4}M -(I; X = OEt) with amines in acetonitrile

$10^2[\text{Piperidine}]/\text{M}$	2.5	5.0	7.5	10	20	20 ^b	30	40	50			
$10^3 k^2_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$ at 30 °C ^a	0.46	0.77	1.15	1.36	2.62	2.71	3.88	4.77	6.21			
$10^3 k^2_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$ at 45 °C ^a				1.73	3.36		4.94	6.21	7.77			
$10^2[\text{Morpholine}]/\text{M}$	2.5	5.0	7.5	10	20	20 ^b	30	40	50	60	70	80
$10^3 k^2_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$ at 30 °C ^a	2.69	2.79	3.21	3.45	3.80	3.76	4.07	4.20	4.38	4.45	4.54	4.56
$10^3 k^2_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$ at 45 °C ^a				5.68	6.52		7.09	7.41				
$10^2[\text{Di-isobutylamine}]/\text{M}$	20	30	30 ^b	40	50	60						
$10^4 k^2_{\text{obs}}/\text{l mol}^{-1} \text{s}^{-1}$ at 30 °C ^c	1.44	1.73	1.74	2.04	2.53	2.79						

^a Correlation coefficient (r) for the first-order plot ≥ 0.9991 . ^b $[(\text{I}; \text{X} = \text{OEt})] = 5 \times 10^{-5}\text{M}$. ^c Initial rate coefficients; $r \geq 0.983$.

TABLE 2

Kinetic parameters for the reactions of (I; X = OEt) with piperidine and di-isobutylamine in acetonitrile

Amine	$t/^\circ\text{C}$	$10^4 k'$ $\text{l mol}^{-1} \text{s}^{-1}$	$10^4 k''$ $\text{l}^2 \text{mol}^{-2} \text{s}^{-1}$	k''/k' l mol^{-1}	'Uncatalysed' reaction ^a		'Catalysed' reaction ^a	
					ΔH^\ddagger kcal mol^{-1}	$\Delta S^\ddagger (30^\circ\text{C})$ $\text{cal mol}^{-1} \text{K}^{-1}$	ΔH^\ddagger kcal mol^{-1}	$\Delta S^\ddagger (30^\circ\text{C})$ $\text{cal mol}^{-1} \text{K}^{-1}$
Piperidine	30	2.0	119	60	5.4 ± 0.9	-58 ± 3	2.3 ± 0.5	-60 ± 2
	45	3.2	149	46.5				
Di-isobutylamine	30	0.71	3.5	4.95				

^a The errors were calculated according to Peterson *et al.* (see Table 10).

certain concentration of amine is lower with morpholine than with piperidine, and a plateau in the curve of k^2_{obs} against $[\text{Amine}]$ is obtained at high amine concentration. Consequently, the reaction with morpholine is faster at low amine concentrations [*e.g.*, $k^2_{\text{obs}}(\text{morpholine})/k^2_{\text{obs}}(\text{piperidine}) = 6$ at 0.025M -amine at 30°C] while that with piperidine is faster at high amine concentrations [$k^2_{\text{obs}}(\text{morpholine})/k^2_{\text{obs}}(\text{piperidine}) = 0.7$ at 0.5M -amine at 30°C]. A plot of

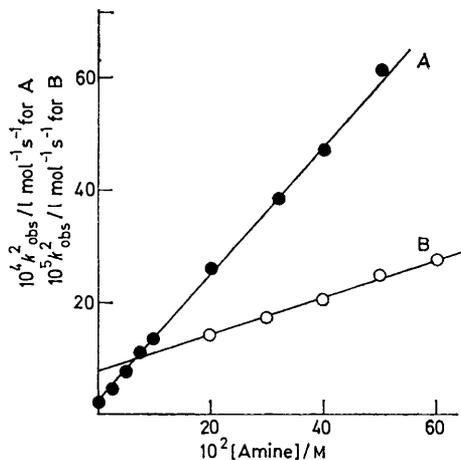


FIGURE 1 Dependence of k^2_{obs} for the reaction of (I; X = OEt) with A, piperidine and B, di-isobutylamine in acetonitrile at 30°C on the concentration of the amine

$1/k^2_{\text{obs}}$ against $1/[\text{Morpholine}]$ was found to be linear [equation (5), Figure 3], and the k''' and k^{IV} values, their reciprocals (see Discussion section), and the derived activation

$$1/k^2_{\text{obs}} = k''' + k^{\text{IV}}/[\text{Amine}] \quad (5)$$

parameters are in Table 3.

The reactions of piperidine and morpholine in the presence of added amines are summarised in Table 4. No significant rate change was observed either with pyridine or with *p*-phenylenediamine except at high concentrations, where

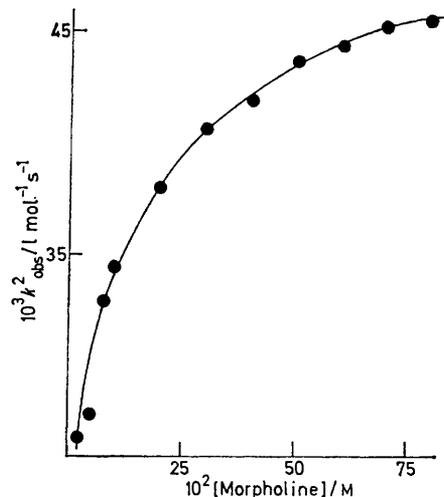


FIGURE 2 Dependence of k^2_{obs} for the reaction of (I; X = OEt) with morpholine in acetonitrile at 30°C on the morpholine concentration

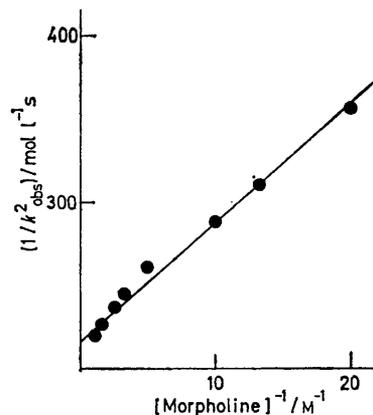


FIGURE 3 Inversion plot [equation (5)] for the reaction of (I; X = OEt) with morpholine in acetonitrile at 30°C

oxidation of the amine complicates the spectrophotometric measurements. The stronger base, *N*-methylpiperidine, was practically ineffective when the [*N*-methylpiperidine] : [Morpholine] ratios were changed from 0.33 to 20.

TABLE 3

Kinetic parameters for the reaction of (I; X = OEt) with morpholine in acetonitrile

	At 30 °C	At 45 °C
$k'''/\text{mol l}^{-1} \text{ s}$	215	127
$k^{IV}/\text{mol}^2 \text{ l}^{-2} \text{ s}$	7.27	4.92
$(10^3/k''')/\text{l mol}^{-1} \text{ s}^{-1}$	4.65	7.86
$(10/k^{IV})/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$	1.38	2.03
$(k'''/k^{IV})/\text{l mol}^{-1}$	29.6	25.8

For the 'uncatalysed' process: $\Delta H^\ddagger = 6.1 \pm 0.4 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger (30^\circ \text{C}) = -49.4 \pm 1.3 \text{ cal mol}^{-1} \text{ K}^{-1}$ ^a

For the 'catalysed' process: $\Delta H^\ddagger = 4.3 \pm 1.3 \text{ kcal mol}^{-1}$; $\Delta S^\ddagger (30^\circ \text{C}) = -48.4 \pm 5.2 \text{ cal mol}^{-1} \text{ K}^{-1}$ ^b

^a Based on $1/k'''$. ^b Based on $1/k^{IV}$.

TABLE 4

Pseudo-first-order coefficients (k^1_{obs}) for the reaction of (I; X = OEt) with morpholine and piperidine in the presence of added amines in acetonitrile at 30 °C

$10^2[\text{Piperidine}]/\text{M}$	30	30	30	30	30
$10^2[p\text{-Phenylenediamine}]/\text{M}$		0.1	0.5	1.0	10
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	1.10	1.16	1.12	1.20	1.67 ^a
$10^2[\text{Piperidine}]/\text{M}$	20	20	20	20	20
$10^2[\text{Pyridine}]/\text{M}$		5	10	20	30
$10^4k^1_{\text{obs}}/\text{s}^{-1}$	5.37	5.06	5.35	5.36	5.47
$10^2[\text{Piperidine}]/\text{M}$	30	30	30	30	30
$10^2[\text{N-Methylpiperidine}]/\text{M}$		10	20	40	50
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	1.10	1.04	1.01	0.98	1.08
$10^2[\text{Morpholine}]/\text{M}$	30	30	30	30	30
$10^2[p\text{-Phenylenediamine}]/\text{M}$		0.1	0.5	1.0	1.5
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	1.27	1.30	1.33	1.33	1.46
$10^2[\text{Morpholine}]/\text{M}$	20	20	20	20	20
$10^2[\text{Pyridine}]/\text{M}$		5	10	20	30
$10^4k^1_{\text{obs}}/\text{s}^{-1}$	7.71	8.13	7.87	7.99	8.28
$10^2[\text{Morpholine}]/\text{M}$	2.5	2.5	2.5	2.5	2.5
$10^2[\text{N-Methylpiperidine}]/\text{M}$		5	20	40	50
$10^4k^1_{\text{obs}}/\text{s}^{-1}$	6.69	6.80	5.47	5.49	6.37
$10^2[\text{Morpholine}]/\text{M}$	30	30	30	30	30
$10^2[\text{N-Methylpiperidine}]/\text{M}$		10	20	40	50
$10^4k^1_{\text{obs}}/\text{s}^{-1}$	10.7	10.9	11.0	11.0	10.7

^a Oxidation of the amine after long reaction times (observed by u.v.) obscures the infinity reading.

TABLE 5

Pseudo-first-order coefficients for the reaction of (I; X = OEt) (10^{-4}M) with morpholine (0.4M) and piperidine in acetonitrile at 30 °C

$10^2[\text{Piperidine}]/\text{M}$	5	10	20	30	40
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	1.91	2.23	3.04	3.92	5.09
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	0.038	0.13	0.52	1.16	1.91
$10^3k^1_{\text{obs}}/\text{s}^{-1}$	1.60	1.60	1.60	1.60	1.60
$10^3\Delta k^1_{\text{obs}}/\text{s}^{-1}$ ^a	0.27	0.49	0.92	1.15	1.58

^a $\Delta k^1_{\text{obs}} = k^1_{\text{obs}}^{p+m} - (k^1_{\text{obs}}^p + k^1_{\text{obs}}^m)$.

In order to use a stronger catalytic base with morpholine, the reactions of mixtures containing 0.4M -morpholine and varying concentrations of piperidine were compared with the reactions in the presence of each amine alone. Only the disappearance of (I; X = OEt) was followed, since the spectra of the morpholino- and the piperidino-enamines (V) are similar. Table 5 gives the pseudo-first-order coefficients for the individual reactions with piperidine and morpholine ($k^1_{\text{obs}}^p$ and $k^1_{\text{obs}}^m$), for the reactions with the mixtures of the

amines ($k^1_{\text{obs}}^{p+m}$), and the difference $k^1_{\text{obs}}^{p+m} - (k^1_{\text{obs}}^p + k^1_{\text{obs}}^m) = \Delta k^1_{\text{obs}}$ which reflects the sum of catalysis by morpholine to the piperidine reaction and the catalysis by piperidine to the morpholine reaction. The linear increase in Δk^1_{obs} values with the increase in the piperidine concentration (Figure 4) shows the presence of catalysis by the cyclic amines.

Reactions of the Ethoxy-compound (I; X = OEt) with Piperidine and Morpholine in Ethanol and in Propan-2-ol.—The reactions of (I; X = OEt) with the cyclic amines in ethanol and propan-2-ol were followed similarly to those in acetonitrile. Again, the reaction of (I; X = OEt) with

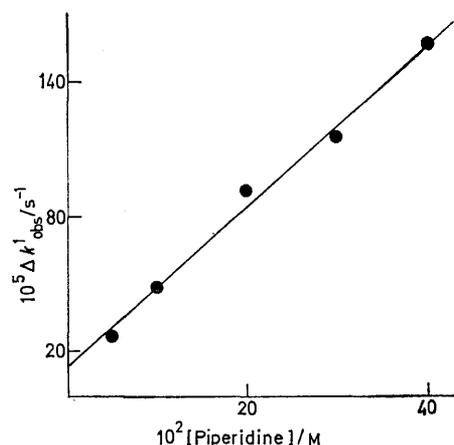


FIGURE 4 Dependence of Δk^1_{obs} in the reaction of (I; X = OEt) with piperidine + morpholine on the piperidine concentration

piperidine followed equation (4) (Table 6), but the contribution of the catalysed process expressed in the $k'' : k'$ ratios was lower than in acetonitrile.

TABLE 6

Second order coefficients for the reaction of 10^{-4}M - (I; X = OEt) with amines in EtOH and in Pr ⁱ OH ^a						
$10^2[\text{Piperidine}]/\text{M}$	10	20	30	40	50	60
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in EtOH at 30 °C	1.93	3.30	3.66	4.51		
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in EtOH at 45 °C		4.40	5.20	5.90	6.60	
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in Pr ⁱ OH at 30 °C	3.99	5.89	7.03	8.03	8.72	9.12
$10^2[\text{Morpholine}]/\text{M}$	10	20	30	40	50	60
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in EtOH at 30 °C	0.78	1.11	1.28	1.34	1.43	
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in EtOH at 45 °C			2.28	2.34	2.56	2.60
$10^3k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ in Pr ⁱ OH at 30 °C	0.99	1.14	1.26	1.35	1.38	1.44

^a For the first order plots $r \geq 0.9993$.

The reactions with morpholine in ethanol and propan-2-ol and the reaction with piperidine in propan-2-ol gave non-linear plots of k^2_{obs} against [Amine] (Figure 5). An inverse plot according to equation (5) gave linear correlations in all cases (Figure 6) except for the reaction with morpholine in propan-2-ol which showed curvature. The k^2_{obs} values are in Table 6 and the parameters of the above plots and the activation parameters are in Tables 7 and 8.

Reaction of NN-Dimethyl-p-tricyanovinylaniline (I; X = CN) and 1,1-Dicyano-2-p-dimethylaminophenyl-2-fluoroethylene (I; X = F) with Morpholine and Piperidine in Acetonitrile.—The effect of the leaving group was studied in the

TABLE 7
Kinetic parameters for the reaction of (I; X = OEt) with piperidine in ethanol

$t/^\circ\text{C}$	'Uncatalysed' reaction ^a			'Catalysed' reaction ^a			
	$10^3k'$ l mol ⁻¹ s ⁻¹	$10^3k''$ l ² mol ⁻² s ⁻¹	k''/k' l mol ⁻¹	ΔH^\ddagger kcal mol ⁻¹	$\Delta S^\ddagger(30^\circ\text{C})$ cal mol ⁻¹ K ⁻¹	ΔH^\ddagger kcal mol ⁻¹	$\Delta S^\ddagger(30^\circ\text{C})$ cal mol ⁻¹ K ⁻¹
30	1.32	8.12	6.15	9.7 ± 0.3	-40 ± 1	-2.0 ± 0.3	-75 ± 1
45	2.96	7.31	2.46				

^a The errors were calculated according to Peterson *et al.*, (see Table 10).

substitutions of (I; X = CN) and (I; X = F) with the cyclic amines in acetonitrile. The reaction of (I; X = CN)

The reaction of (I; X = F) with morpholine at 45 °C is very fast and the data are less accurate than in the other experiments. The reaction with piperidine was very fast

TABLE 8
Kinetic parameters for the reaction of (I; X = OEt) with amines in EtOH and in PrⁱOH

	Piperidine in Pr ⁱ OH		Morpholine in EtOH		in Pr ⁱ OH	
	at 30 °C	at 30 °C	at 45 °C	at 30 °C	at 30 °C	at 30 °C
$k'''/\text{mol l}^{-1} \text{ s}$	82.2	547	315	654		
$k^{IV}/\text{mol}^2 \text{ l}^{-2} \text{ s}$	17	73	17.6	37.4		
$(10^3/k''')/\text{l mol}^{-1} \text{ s}^{-1}$	12.16	1.83	3.18	1.53		
$(10^2/k^{IV})/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$	5.9	1.37	5.7	2.68		
$(k'''/k^{IV})/\text{l mol}^{-1}$	4.8	7.5	17.9	17.5		
$\Delta H^\ddagger/\text{kcal mol}^{-1}$ ('catalysed' reaction) ^a		6.5 ± 0.5				
$\Delta S^\ddagger(30^\circ\text{C})/\text{cal mol}^{-1} \text{ K}^{-1}$ ('catalysed' reaction) ^a		-50 ± 1.5				
$\Delta H^\ddagger/\text{kcal mol}^{-1}$ ('uncatalysed' reaction) ^b		17.5 ± 1.0				
$\Delta S^\ddagger(30^\circ\text{C})/\text{cal mol}^{-1} \text{ K}^{-1}$ ('uncatalysed' reaction) ^b		-9 ± 3				

^a Based on $1/k'''$. ^b Based on $1/k^{IV}$.

was followed at 510 nm and that of (I; X = F) at 420 nm. Except for the reaction of (I; X = F) with piperidine all the reactions were studied under pseudo-first-order conditions, and k^1_{obs} values were independent of a change in the substrate concentrations. Several amine concentrations were studied and k^2_{obs} values increased linearly with the increase in the amine concentration (Table 9). Since the catalysis is very important, Table 9 includes also the third-order coefficients $k^3_{\text{obs}} = k^2_{\text{obs}}/[\text{Amine}]$. Treatment according to equation (4) gives sometimes intercepts k' of ca. 0. The data are in Table 10.

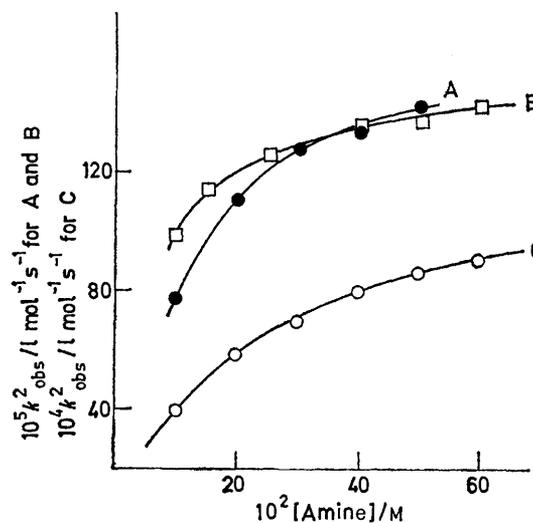


FIGURE 5 Dependence of k^2_{obs} for the reaction of (I; X = OEt) with amines on the amine concentration at 30 °C; A, with morpholine in EtOH; B, with piperidine in PrⁱOH; and C, with morpholine in PrⁱOH

under pseudo-first-order conditions, but third-order coefficients with correlation coefficients of $r = 0.998$ for each run were obtained by using the third-order equation: Rate = $k^3_{\text{obs}}(a-x)(b-2x)^2$ where x , $a-x$, and $b-2x$

TABLE 9
Second-order (k^2_{obs}) and third-order (k^3_{obs}) rate coefficients for the reactions of $3 \times 10^{-5}\text{M}$ -(I; X = CN) and -(I; X = F) with amines in acetonitrile

(I; X = CN)									
$10^3[\text{Morpholine}]/\text{M}$	4	8	12	16	18	20	20 ^a	24	28
$10^2k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 30 °C		1.04	1.82	2.87		3.89	3.86	5.01	6.05
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 30 °C		1.30	1.52	1.79		1.95	1.93	2.08	2.16
$10^2k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 45 °C	4.0	6.6			13.6			15.8	17.6
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 45 °C	10	8.3			7.6			6.6	6.3
$10^4[\text{Piperidine}]/\text{M}$	4	8	12	16	20	20 ^a	24		
$10^2k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 30 °C	17.0	25.5	32.3	40.8	47.7	47.9	52.4		
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 30 °C	425	318	269	255	238	239	218		
$10^2k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 45 °C		14.4	21.9	29.6			46.0		
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 45 °C		180	183	185			192		
(I; X = F)									
$10^4[\text{Morpholine}]/\text{M}$	4	6	8	9	10	10 ^b	12	15	16
$k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 30 °C	0.39	0.64	0.88		1.29	1.34	1.45		2.18
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 30 °C	975	1067	1100		1290	1340	1208		1363
$k^2_{\text{obs}}/\text{l mol}^{-1} \text{ s}^{-1}$ at 45 °C	1.08			1.44				2.00	
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 45 °C	1800			1600				1333	
$10^4[\text{Piperidine}]/\text{M}$	1.2	1.5	1.8	2.1	2.4				
$k^3_{\text{obs}}/\text{l}^2 \text{ mol}^{-2} \text{ s}^{-1}$ at 30 °C	34,800	60,900	73,900	87,800	97,600				

^a [(I; X = CN)] = $1.5 \times 10^{-5}\text{M}$. ^b [(I; X = F)] = $1.5 \times 10^{-5}\text{M}$.

are the concentrations of (V), (I; X = F), and piperidine, respectively. The involvement of two amine molecules in the stoichiometry is shown by the formation of only

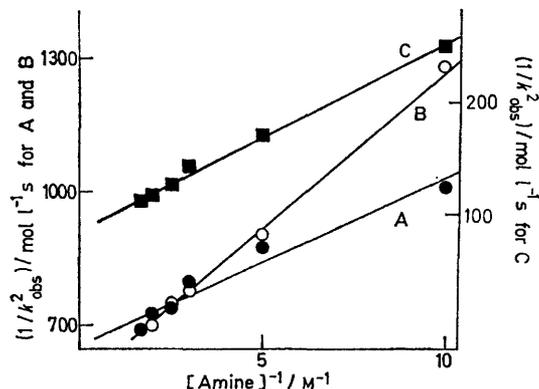


FIGURE 6 Inversion plots [equation (5)] for the reactions of (I; X = OEt) at 30 °C with A, morpholine in Pr^oOH; B, morpholine in EtOH; and C, piperidine in Pr^oOH

half an equivalent of (V) when equimolar amounts of the reactants are used. However, the k_{obs}^3 values increased with the amine concentrations.

DISCUSSION

The increase of k_{obs}^2 values with the amine concentration in our reactions fulfills the prediction that amine-assisted routes of the intermediate (II) which carries sluggish leaving groups (F, CN, or OEt) are important. Two distinct types of kinetic behaviour are (a) a linear dependence of k_{obs}^2 on [Amine] [equation (4)] observed in the reactions of piperidine with (I; X = OEt), (I; X = CN), and (I; X = F) in acetonitrile and with (I; X = OEt) in EtOH, and with morpholine with (I; X = CN) and (I; X = F) in acetonitrile, and (b) curved plots of k_{obs}^2 against [Amine], observed in all the reactions of morpholine with (I; X = OEt) and of piperidine with (I; X = OEt) in Pr^oOH. We will use the superscripts p, m, and d in conjunction with the rate coefficients for piperidine, morpholine, and di-isobutylamine, respectively.

The linear dependence is predicted by Scheme 1 when $k_{-1} \gg k_2 + k_{3B}[\text{Amine}]$ and comparison of the slopes and the intercepts of equations (3) and (4) gives $k' = k_1 k_2 / k_{-1}$, $k'' = k_1 k_{3B} / k_{-1}$, and $k''/k' = k_{3B}/k_2$. The contribution of the catalysed route (k_{3B}) is very high ($k_{3B}/k_2 = 274 - > 2300$, Table 10) with (I; X = CN) and (I; X = F),

TABLE 10

Kinetic parameters for the reactions of (I; X = CN) and (I; X = F) with amines in acetonitrile

Compound	Amine	t/°C	$10^2 k'$ l mol ⁻¹ s ⁻¹	k'' l ² mol ⁻² s ⁻¹	k''/k' l mol ⁻¹	'Catalysed' process ^a	
						ΔH^\ddagger kcal mol ⁻¹	ΔS^\ddagger (30 °C) cal mol ⁻¹ K ⁻¹
(I; X = CN)	Morpholine	30	0	2.55	Very high	9.7 ± 1.8	-26 ± 6
		45	2.09	5.74	274.3		
	Piperidine	30	10.8	180	1672	0.6 ± 0.4	-46 ± 1.5
		45	0	197.5	Very high		
(I; X = F)	Morpholine	30	0	1480	Very high	-3.2 ± 2.6	-55 ± 9
		45	48	1100	2305		

^a The errors were calculated according to R. C. Peterson, J. H. Markgraf, and S. D. Ross, *J. Amer. Chem. Soc.*, 1961, **83**, 3819.

The reaction of (I; X = CN) with di-isobutylamine in 1 : 1 and in 1 : 3 CCl₄-MeCN mixtures is faster in the solvent with the higher dielectric constant. k_{obs}^2 and k_{obs}^3 are in Table 11. From the linear plots of k_{obs}^2 against [Di-iso-

TABLE 11

Second-order (k_{obs}^2) and third-order (k_{obs}^3) coefficients for the reaction of (I; X = CN) with di-isobutylamine at 30 °C

$10^2[\text{Amine}]/\text{M}$	In 1 : 1 CCl ₄ -MeCN ^a					
	2.0	2.5	3.0	3.5	4.0	5.0
$10^4 k_{\text{obs}}^2 / \text{l mol}^{-1} \text{s}^{-1}$	4.4	5.2	5.8	7.1	8.3	11.0
$10^3 k_{\text{obs}}^3 / \text{l}^2 \text{mol}^{-2} \text{s}^{-1}$	2.2	2.1	2.0	2.0	2.1	2.2
$10^2[\text{Amine}]/\text{M}$	In 1 : 3 CCl ₄ -MeCN ^b					
	3.0	3.5	4.0	5.0	6.0	
$10^4 k_{\text{obs}}^2 / \text{l mol}^{-1} \text{s}^{-1}$	1.26	1.43	1.51	1.90	2.23	
$10^3 k_{\text{obs}}^3 / \text{l}^2 \text{mol}^{-2} \text{s}^{-1}$	4.2	4.1	3.8	3.8	3.7	

^a [(I; X = CN)] = 7.5 × 10⁻⁵M. ^b [(I; X = CN)] = 3 × 10⁻⁵M.

butylamine] $k' = 1.47 \times 10^{-5}$ l mol⁻¹ s⁻¹, $k'' = 2.01 \times 10^{-3}$ l² mol⁻² s⁻¹, and $k''/k' = 137$ l mol⁻¹ in 1 : 1 CCl₄-MeCN mixtures at 30 °C, and $k' = 27 \times 10^{-5}$ l mol⁻¹ s⁻¹, $k'' = 3.25 \times 10^{-3}$ l² mol⁻² s⁻¹, and $k''/k' = 12$ l mol⁻¹ in 1 : 3 CCl₄-MeCN mixtures at 30 °C.

where the reactions are of almost of the second order in the amine, as also found with substituted anilines with (I; X = F)⁴ or with 2-dicyanomethyleneindane-1,3-dione.⁵ The uncatalysed route (k_2) is relatively more important with (I; X = OEt), but since $k_{3B}^p/k_2^p = 46.50-60$ the catalysed route predominates at all our amine concentrations. Only with di-isobutylamine is the catalysis moderate, *i.e.*, at amine concentrations < 0.2M the uncatalysed route predominates.

Curvature in the plot of k_{obs}^2 against [Amine] is predicted by Scheme 1 when $k_{-1} \sim k_2 + k_{3B}[\text{Amine}]$ [equation (1)], with a plateau at high amine concentrations when $k_{-1} \ll k_2 + k_{3B}[\text{Amine}]$. Inversion of equation (1), coupled with the assumption $k_{3B}[\text{Amine}] \gg k_2$ as found for piperidine, gives equation (6), according to which $1/k_{\text{obs}}^2$ is linear in $1/[\text{Amine}]$. Indeed, all except

$$1/k_{\text{obs}}^2 = 1/k_1 + (k_{-1}/k_1 k_{3B})/[\text{Amine}] \quad (6)$$

one of the reactions which showed curvature in the plots of k_{obs}^2 against [Amine] gave linear inversion plots [equation (5)]. This is the first demonstration of such behaviour in a vinylic system, and it is in excellent

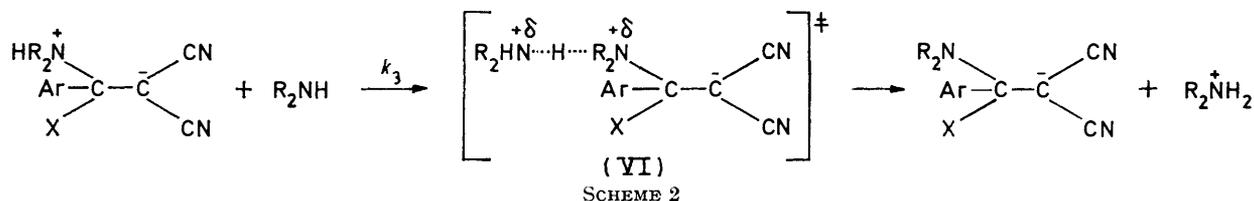
accord with, and strengthens, the multistep mechanism of Scheme 1.

Comparison of equations (5) and (6) gives $k''' = 1/k_1$, $k^{IV} = k_{-1}/k_1 k_{3B}$ ($= 1/k''$), and $k'''/k^{IV} = k_{3B}/k_{-1}$. Consequently, the value of k_{obs}^2 at the plateau (*e.g.*, of Figure 2) should be [equation (2)] and indeed is equal to $1/k'''$. The k_{3B}^m/k_{-1}^m values of 25.8—29.6 with (I; X = OEt) show that with morpholine as nucleophile in acetonitrile, the forward reaction is much favoured over the expulsion of morpholine from the zwitterion (II), while with piperidine the opposite is true.

Comparison of the rate coefficients of the catalysed route in MeCN for the cyclic amines (Tables 2 and 3) gives $k''^m/k''^p = k_{3B}^m(k_1^m/k_{-1}^m)/k_{3B}^p(k_1^p/k_{-1}^p) = 11.6$ at 30 °C and 13.6 at 45 °C. Since the steric bulk of the two amines is similar, their carbon basicities (k_1/k_{-1}) should follow their relative hydrogen basicities (230 in MeCN) and nucleophilicities. The k_1^p/k_1^m ratios for attack on the structurally related *p*-O₂N·C₆H₄·C(OTs)·C(CO₂Et)₂ and the corresponding *p*-bromobenzenesulphonate are 13.7—16.2,¹ and the ratios are 7—17 for their addition to *p*-tolylvinylsulphone.¹¹ Moreover, $k_1^p/k_1^m = 8$ for the addition of (I; X = OEt) in PrⁱOH (Table 8). If a Brønsted relationship exists between the carbon nucleophilicities and the carbon basicities, the $(k_1^p/k_{-1}^p) : (k_1^m/k_{-1}^m)$ ratio should be higher (*i.e.*, ≥ 10) than the above ratio and then $k_{3B}^m/k_{3B}^p > 100$. If k_{3B} is given its

bond cleavage X is hydrogen-bonded to the amino-hydrogen of a second amine molecule), or more complex base-catalysed.

Catalysis by tertiary amines which can serve only as base catalysts was used for distinguishing between electrophilic catalysis and base catalysis in the reactions of (I; X = F).^{4,6} The added amine competes with the second amine molecule in the proton abstraction, and k_{3B} of Scheme 1 is replaced by $\sum_B k_{3B}^B$ for all the amines B in solution. We used this approach in the reactions of (I; X = OEt). That pyridine (pK_a 5.25)¹² catalysis does not compete with the self-catalysis by piperidine (pK_a 11.2)¹² or morpholine (pK_a 8.32)¹² is not surprising. However, *N*-methylpiperidine (mp) is a stronger base (pK_a 10.08)¹² and if we assume that $pK_a^p - pK_a^{mp}$ is the same in water and in acetonitrile, and that the catalysis is efficient (*e.g.*, Brønsted $\beta = 0.7$) the reaction with piperidine should be accelerated by 30% at our highest *N*-methylpiperidine concentration. Although *N*-methylpiperidine is a stronger base than morpholine, the reaction with morpholine is already near the plateau region, and the maximum rate enhancements expected are therefore only 10% at 0.3M-morpholine and 70% at 0.025M-morpholine. However, no catalysis was observed in either reaction, even with high excess of *N*-methylpiperidine. This is ascribed to reduction of the catalytic efficiency of the tertiary amine by steric effects,



simplest mechanistic interpretation as the rate constant for proton transfer between zwitterion and amine we reach the surprising conclusion that for (I; X = OEt) the deprotonation of the morpholinium zwitterion by morpholine is much faster than the deprotonation of the piperidinium zwitterion by piperidine. However, this fits the detailed mechanism of the k_{3B} step discussed below.

Since k_1^m is 23 times larger than $k_1^p k_2^p / k_{-1}^p$, k_{-1}^p / k_2^p is estimated as 230 by using the tentative value $k_1^p / k_1^m = 10$ and, since $k_{3B}^p / k_2^p = 46.5-60$, $k_{-1}^p / k_{3B}^p = 4-5$, and for (I; X = OEt) $k_{-1}^p > k_{3B}^p > k_2^p$.

The Nature of the Catalysed Reaction.—That under conditions where $k_{3B}[\text{Amine}] \gg k_2$, $k_{-1}^m < k_{3B}^m$ while $k_{-1}^p > k_{3B}^p$ seems incompatible with k_{3B} being a one-step proton abstraction [Scheme 2, transition state (VI)], since morpholinium should be a better leaving group than piperidinium, *i.e.*, $k_{-1}^m > k_{-1}^p$. The effect of the leaving group discussed below leads to a similar conclusion. The reaction is therefore either electrophile-catalysed (where in the transition state for the C-X

A similar explanation was invoked for the absence of catalysis by *N*-methylaniline,⁴ or for the lower than expected catalysis by *ortho*-substituted pyridines⁶ in the reaction of (I; X = F) with *p*-toluidine.

Catalysis was observed in the reaction of piperidine and morpholine together where $\Delta k_{obs}^1 = k_{obs}^{1,p+m} - (k_{obs}^{1,p} + k_{obs}^{1,m})$ increased linearly with the piperidine concentration (Figure 4). This cannot be mainly due to catalysis by the piperidine to the morpholine reaction since $k_{obs}^{1,m}$ is close to k_1 , and cannot be mainly due to catalysis by morpholine to the piperidine reaction which should be constant at 0.4M-morpholine (Table 5). These arguments also hold for electrophilic catalysis. The absence of catalysis with *p*-phenylenediamine which should be a better proton donor than the cyclic amines argues against electrophilic catalysis.

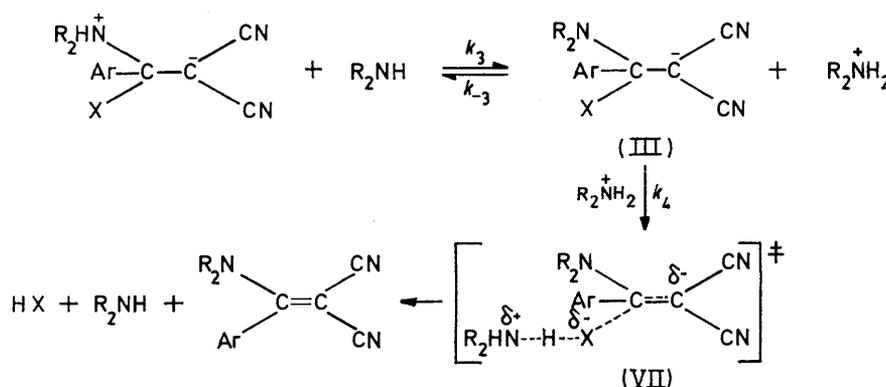
In the absence of conclusive evidence we still believe that the catalysis is basic *via* transition state (VII) rather than electrophilic, since base-catalysis was shown for (I; X = F) which is *a priori* more prone to electrophilic catalysis.^{4,6} We suggest a multistep route

¹¹ S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1967, 343.

¹² Z. Rappoport, 'Handbook of Tables for Organic Compounds Identification,' The Chemical Rubber Co., Ohio, 3rd edn., 1967.

(Scheme 3) in which a reversible fast proton transfer to the base, forming the carbanion (III), is followed by a rate-determining ammonium ion-assisted detachment of the leaving group. An analogous mechanism for the replacement of sluggish leaving groups is favoured in nucleophilic aromatic substitution⁷ and was recently observed in the reaction of 2,4-dinitro-1-naphthyl ethyl ether with amines in dimethyl sulphoxide.¹³ A similar scheme was suggested for the replacement of the fluorine of (I; X = F) by amines in alcoholic solvents⁸ and the k_4 step was discussed for the E1cB elimination of cyanide ion from carbanions structurally related to (III) in the presence of amines.^{14,15}

The use of Scheme 3 requires replacement of k_{3B} in equations (1), (3), and (6) by the product $(k_3/k_{-3})k_4$.



SCHEME 3

Since the equilibrium constant k_3/k_{-3} is determined by the difference in pK_a between the unsubstituted and the $\text{Ar}[\bar{\text{C}}(\text{CN})_2]\text{XC}^-$ substituted ammonium ion it should be similar for both amines and $k_3^p/k_{-3}^p \sim k_3^m/k_{-3}^m$, resulting in a high $k_4^m:k_4^p$ ratio. This is reasonable since morpholinium ion is a stronger acid than piperidinium ion and hence it is a better proton donor in the k_4 step.

Moreover, it follows that $k_{-1}^m \ll k_4^m$ and $k_{-1}^p \gg k_4^p$ and to comply with $k_{-1}^p > k_{-1}^m$, k_4^m/k_4^p is higher than k_{-1}^p/k_{-1}^m , i.e., the C-N bond cleavage is less sensitive than the ammonium ion-assisted detachment of the leaving group to the nature of the ammonium ion. This is understood if the degree of the C-N bond cleavage of the good leaving group ($-\overset{+}{\text{NHR}}_2$) in the transition state is small, while the degree of the N-H bond cleavage in the catalysed proton transfer is high.

The rate enhancement in the morpholine-piperidine mixtures is in accord with the involvement of low concentrations of morpholinium ion (formed in the piperidinium ion + morpholine \rightleftharpoons morpholinium ion + piperidine equilibrium) as a general acid in the reaction of the piperidinium carbanion (III). This is

¹³ J. A. Orvik and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1970, **92**, 2417.

¹⁴ Z. Rappoport and E. Shohamy, *J. Chem. Soc. (B)*, 1971, 2060.

¹⁵ M. Albeck, S. Hoz, and Z. Rappoport, *J.C.S. Perkin II*, 1972, 1249.

more likely than catalysis in the k_1 step, which requires a change in the nature of the nucleophile either by replacing intermolecular hydrogen bonding between like amine molecules by morpholine-piperidine hydrogen bonds, or by forming low concentrations of the highly reactive morpholide ion by the piperidine + morpholine \rightleftharpoons piperidinium ion + morpholide ion equilibrium.

Steric effects are apparent in the reactivity ratios of piperidine and the slightly weaker base (pK_a 10.91)¹² but more crowded di-isobutylamine. The ratio $k'^p:k'^d$ of ca. 3 is much lower than the reactivity ratios (265—285)¹⁶ in the substitution of 1-chloro-2,4-dinitrobenzene. We believe that this results from a compensation of $(k_1^p/k_{-1}^p)/(k_1^d/k_{-1}^d)$ and k_2^d/k_2^p terms which are both large owing to steric reasons. However, $k''^p/k''^d = 34$

since the steric retardation to the approach of the bulky nucleophile (or its conjugate acid) results in $k_4^p > k_4^d$. Consequently, $k_{3B}^d/k_2^d = 5$ and the uncatalysed route predominates at low amine concentrations.

The very low and even negative [with (I; X = F) and morpholine] activation enthalpies ($\Delta H^\ddagger = 9.7$ to -3.2 kcal mol⁻¹) and the high negative activation entropies ($\Delta S^\ddagger = -55$ to -26 cal mol⁻¹ K⁻¹) are consistent with the composite nature of k' and k'' as discussed earlier.^{4,17} The main contributors to the activation parameters are ΔH_1^\ddagger and ΔS_1^\ddagger since the value of ΔH^\ddagger and ΔS^\ddagger for the k_1 step in the reaction of (I; X = OEt) with morpholine in acetonitrile, or for the addition of piperidine to *p*-tolyl vinyl sulphone,¹⁸ are similar to those based on k_{3B} . This fact suggests a cancellation of the contributions of ΔH_1^\ddagger (ΔS_1^\ddagger) on the one hand and ΔH_2^\ddagger (ΔS_2^\ddagger) or ΔH_{3B}^\ddagger (ΔS_{3B}^\ddagger) on the other.

The Effect of the Leaving Group.—Data on the relative reactivities of systems with different leaving groups X other than chloride and bromide are scarce for nucleophilic vinylic substitutions and absent for sluggish X.^{1,2a} The base catalysis found in the present work shows that

¹⁶ J. J. Blanksma and H. H. Schreinemachers, *Rec. Trav. chim.*, 1933, **52**, 498; O. L. Brady and F. R. Cropper, *J. Chem. Soc.*, 1950, 507.

¹⁷ Z. Rappoport, P. Greenzaid, and A. Horowitz, *J. Chem. Soc.*, 1964, 1334.

¹⁸ S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1967, 351.

cyanide, fluoride, and ethoxy are indeed 'sluggish' leaving groups. The reason for the increase in k^3_{obs} for piperidine with (I; X = F) is not yet clear.

Comparison of k_{3B} for (I; X = OEt) and (I; X = CN) with piperidine and for (I; X = CN) and (I; X = F) with morpholine gives the reactivity order: (I; X = OEt), $1 < (I; X = \text{CN})$, $10^4 < (I; X = \text{F})$, 10^7 , and since k_2 is negligible, this is also the overall relative reactivity. Since $k_{3B}(\text{I; X = F})/k_{3B}(\text{I; X = Cl})$ is ca. 50 for substituted anilines,⁴ the relative order of k_{3B} is (I; X = F) > (I; X = Cl) > (I; X = CN) > (I; X = OEt). Since for Scheme 2 only inductive and steric effects are of importance while in Scheme 3 an element effect is apparent, this order and the enormous reactivity difference between X = OEt and X = F argue strongly for Scheme 3. For Scheme 2, $k_{3B} = (k_1/k_{-1})k_3$ and for Scheme 3, $k_{3B} = (k_1/k_{-1})(k_3/k_{-3})k_4$. We therefore evaluated the effect of X on (a) the k_1/k_{-1} term, (b) the k_3 and k_3/k_{-3} terms, and (c) the k_4 term and found that our conclusion is borne out by a detailed consideration of (a)–(c).

(a) The $k_1 : k_{-1}$ ratios should be in the order $\text{F} > \text{Cl} > \text{OEt}$ if the electronegativity [$\text{F}(4.0) > \text{O}(3.5) > \text{Cl}(3.0)$] governs k_1 ,^{7a,19} and if k_{-1} is governed by steric effects²⁰ (where $\text{OEt} > \text{F}$). The $\log(k_1/k_{-1})$ values for the reaction of OH^- with C(1) of 2,4,6-trinitro-1-substituted benzenes^{21,22} are Cl, 0.10; MeO, 0.00; and H, 0.33, although it was questioned whether the attack is on C(1) for X = Cl and X = MeO.²² Data for the 1-fluoro-compound are absent, but the above suggests that k_1/k_{-1} would not be more than two orders of magnitude higher than for the chloro-compound. This is also in line if k_1/k_{-1} values are mainly governed by k_1 . In most nucleophilic aromatic substitutions $k_1(\text{OEt})$ and $k_1(\text{Cl})$ do not differ much,^{7a,23} while the highest $k_1(\text{F})/k_1(\text{Cl})$ ratios observed or extrapolated in nucleophilic vinylic substitutions are < 300 .^{2a,3f,24}

(b) We evaluated the relative k_3/k_{-3} values in water for the zwitterions (II) with different X groups by using Taft's relationship for tertiary amines $\text{p}K_a = -3.30 \Sigma \sigma^* + 9.61$,²⁵ by using the values $\sigma^*(\text{CH}_2\text{CN}) = 1.30$, $\sigma^*(\text{CH}_2\text{F}) = 1.10$, $\sigma^*(\text{CH}_2\text{Cl}) = 1.05$, and $\sigma^*(\text{OMe}) = 0.52$,²⁶ since the only structural change is in the $\text{Ar}[\text{C}(\bar{\text{C}}\text{N})_2]\text{XC}^-$ substituent. Compound (II; X = CN) is the most acidic, while (II; X = F) is 2 $\text{p}K_a$ units stronger acid than (II; X = OEt). The relative k_3 values would be lower on the assumption of a normal Brønsted relationship between k_3 and k_3/k_{-3} .

Hence, a combination of k_1/k_{-1} and k_3 and Scheme 2 is

¹⁹ J. Sauer and R. Huisgen, *Angew. Chem.*, 1960, **72**, 91; H. Suhr, *Chem. Ber.*, 1964, **97**, 3268.

²⁰ J. F. Bunnett and J. J. Randall, *J. Amer. Chem. Soc.*, 1958, **80**, 6020.

²¹ R. Gaboriaud and R. Schaal, *Bull. Soc. chim. France*, 1969, 2683.

²² J. Hine, *J. Amer. Chem. Soc.*, 1971, **93**, 3701.

²³ J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, Amsterdam, 1968, ch. 5.

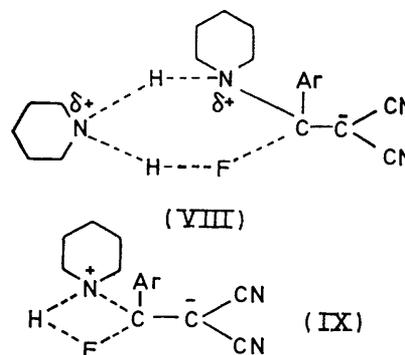
²⁴ P. Beltrame and G. Favini, *Gazzetta*, 1963, **93**, 757; E. F. Silversmith and D. Smith, *J. Org. Chem.*, 1958, **23**, 427.

²⁵ H. K. Hall, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 5441.

incompatible with the ratio $k^3_{\text{obs}}(\text{I; X = F}) : k^3_{\text{obs}}(\text{I; X = OEt}) = 10^7$, while (I; X = CN) is expected to react more rapidly than observed. The results are compatible with Scheme 3 if k_4 involves an appreciable element effect.

(c) The scattered data on $E1cB$ eliminations^{14,15,27} shows that the C-X bond cleavage from the carbanions $\text{>C(X)-}\bar{\text{C}}\text{<}$ is highly sensitive to the nature of X. For the C-X bond cleavage in the $\text{RCX=N-}\bar{\text{N}}\text{Ar}$ anions²⁸ it was estimated that the variation in the reactivity on a logarithmic scale is roughly half the variation in the $\text{p}K_a$ of HX . Such an estimate in our system ($\text{p}K_a$ values in water are: HF, 3.45; HCN, 9.3; EtOH, 16.29) gives for an unassisted k_4 step the reactivity order $\text{OEt}(1) < \text{CN}(5 \times 10^3) < \text{F}(10^6)$ which is close to that observed experimentally. It is highly probable that this order would remain the same in the electrophilically assisted k_4 step, and the leaving-group effect therefore supports Scheme 3. A bifunctional catalysis (transition state VIII) fits qualitatively (c) above, but it is discarded since tertiary amines catalyse the reaction of (I; X = F) with *p*-toluidine.^{4,6}

The 'Uncatalysed' Route.—The high solvation energy of F^- and EtO^- makes unassisted expulsion highly unlikely in acetonitrile. However, by analogy with Scheme 3, an internal assistance *via* the four-membered transition state (IX) is possible. The preference for catalysis then reflects the unfavourable entropy terms



associated with (IX), the absence of the inductive effect of the ammonium ion in (VII), and the higher basicity of the external base than of the group X towards the N-H proton.

The Solvent Effect.—The increase in both k' and k'' on changing the solvent from 1 : 1 $\text{CCl}_4\text{-MeCN}$ to 1 : 3

²⁶ R. W. Taft, in 'Steric Effects in Organic Chemistry,' ed. M. S. Newman, Wiley, New York, 1956, ch. 13.

²⁷ T. I. Crowell, R. T. Kemp, R. E. Lutz, and A. A. Wall, *J. Amer. Chem. Soc.*, 1968, **90**, 4638; L. R. Fedor, *ibid.*, 1969, **91**, 908; A. Berndt, *Angew. Chem. Internat. Edn.*, 1969, **8**, 613; W. K. Kwok, W. G. Lee, and S. I. Miller, *J. Amer. Chem. Soc.*, 1969, **91**, 468; L. R. Fedor and W. R. Glave, *J. Amer. Chem. Soc.*, 1971, **93**, 985; F. G. Bordwell, K. C. Yee, and A. C. Knipe, *J. Amer. Chem. Soc.*, 1970, **92**, 5945.

²⁸ A. F. Hegarty, M. P. Cashman, and F. L. Scott, *J.C.S. Perkin II*, 1972, 44.

²⁹ R. C. Weast, 'Handbook of Chemistry and Physics,' The Chemical Rubber Co., Ohio, U.S.A., 51st edn., 1970–1971.

CCl_4 -MeCN in the reaction of (I; X = CN) with diisobutylamine is expected. When acetonitrile (dielectric constant $D^{25} = 37.5$)²⁹ was replaced by the protic EtOH ($D^{25} = 32$)²⁹ the importance of the catalysed route for (I; X = OEt) decreased, but it increased again by a further change to propan-2-ol ($D^{25} = 18.3$).²⁹ The relative k'' are MeCN (10) > EtOH (1) < PrⁱOH (2) for morpholine, and MeCN (1.5) > EtOH (1) < PrⁱOH (7.3) for piperidine.

The k_{3B}^p/k_2^p values decrease from 46.5–60 in MeCN to 2.5–6.15 in EtOH where the catalysis is recognised only owing to the high piperidine concentrations used. Similar behaviour was observed for (I; X = F) with anilines.⁸

In the protic solvents k_2 would be enhanced compared with acetonitrile since the solvent competes with the amine as a base and also serves as an electrophilic catalyst. Apparently this is more important than the increase in k_{3B} ,³⁰ in the acidity of (II),³¹ and in k_4 [since for $^+ \text{NR}_2\text{H}_2$ $pK_a(\text{MeCN}) > pK_a(\text{ROH})$].

From the data of Table 7 and the assumption that $k_1^p(\text{EtOH})/k_1^p(\text{Pr}^i\text{OH}) = 1.21$ [from Table 8, $k_1^m(\text{EtOH})/k_1^m(\text{Pr}^i\text{OH}) = 1.21$] we find at 30 °C in EtOH that $k_2^p/k_1^p = 0.9$, $k_{3B}^p/k_1^p = 5.5$, and $k_{3B}^p/k_2^p = 6.15$.

Since $k^p(\text{EtOH})/k^p(\text{MeCN}) = 6.5$ – 9.0 and we suggested above that $k_2^p(\text{EtOH}) > k_2^p(\text{MeCN})$ it follows that $(k_1^p/k_1^p)(\text{EtOH})/(k_1^p/k_1^p)(\text{MeCN}) \lesssim 1$. It is difficult to predict the change in k_1/k_{-1} between MeCN and EtOH since both (II) and the amine form hydrogen bonds with EtOH. However, we predict a somewhat higher k_1/k_{-1} in EtOH than in PrⁱOH.

The more negative $\Delta S^\ddagger(\text{EtOH})$ than $\Delta S^\ddagger(\text{MeCN})$ for the uncatalysed process fits the presence of an EtOH molecule in the transition state.

The similarity of $k''(\text{EtOH})$ and $k''(\text{MeCN})$ would result in $k_{3B}(\text{MeCN})/k_{3B}(\text{EtOH}) = ca. 1$. This seems reasonable since in the k_{-1} and the k_{3B} processes the zwitterion gives neutral molecules. However, the change EtOH \rightarrow PrⁱOH increases k'' , which calls for $k_{3B}(\text{Pr}^i\text{OH}) > k_{3B}(\text{EtOH})$ for both amines. This is contradictory to the behaviour of (I; X = F) where $k''(\text{Pr}^i\text{OH}) > k''(\text{Bu}^t\text{OH})$.⁸

For piperidine in PrⁱOH $k_{-1} \sim k_2^p + k_{3B}^p[\text{Amine}]$, and since equation (6) is obeyed $k_{3B}^p > k_2^p$ and $k_3^p/k_{-1}^p = 4.8$ (Table 8), while in EtOH where equation (3) is obeyed $k_3^p/k_{-1}^p(\text{EtOH})$ is low. Since k_{-1}^p would be

favoured in the less polar solvent we find again that $k_{3B}^p(\text{Pr}^i\text{OH}) > k_{3B}^p(\text{EtOH})$.

Since the reactivity ratios $k''^p/k''^m = 2.2$, $(k_{3B}^p/k_{-1}^p)/(k_{3B}^m/k_{-1}^m) = 0.27$ in PrⁱOH are only qualitatively understood, it is important that the k_1^p/k_1^m ratio of 8 at 30 °C in PrⁱOH is reasonable in view of the hydrogen basicities of the two amines, and is similar to the values obtained where k_1 is rate-determining.^{1,11} Since this ratio is derived from the inversion plots, it supports strongly Scheme 1 in the alcoholic solvents.

EXPERIMENTAL

Solvents and Materials.—Dry acetonitrile was prepared as described.⁴ Dry ethanol and propan-2-ol were prepared according to Vogel^{32a} and the middle fractions of the distillate were used. Carbon tetrachloride was purified according to Vogel,^{32b} dried (CaCl_2), and distilled, b.p. 76.5 °C. The amines were distilled before use and the middle fractions were used. The b.p.s agree with literature values.¹² 1,1-Dicyano-2-*p*-dimethylaminophenyl-2-fluoroethylene and the 2-ethoxy-analogue were prepared according to Josey *et al.*⁹ [(I; X = F), orange needles (from chloroform-methylcyclohexane), m.p. 161–164 °C, λ_{max} (MeCN) 424 (ϵ 51,500), 315 (1360), 263 (7100), and 240sh nm (5400); (I; X = OEt), yellow needles (dilute MeOH), m.p. 91 °C, λ_{max} (MeCN) 377 nm (ϵ 25,000)]. *NN*-Dimethyl-*p*-tricyanovinylaniline was prepared as yellow needles, m.p. 173–175 °C (from AcOH), λ_{max} (MeCN) 514 nm (ϵ 41,000), according to McKusick *et al.*¹⁰

The enamines were prepared by adding 10 mol. equiv. of the amine to one equivalent of (I; X = OEt) or (I; X = F) in acetonitrile. The solutions were left to stand overnight, evaporated, and the residues were crystallised from aqueous ethanol, giving >90% of yellow crystals of 1,1-dicyano-2-*p*-dimethylaminophenyl-2-morpholinoethylene, m.p. 173 °C, λ_{max} (MeCN) 348 (ϵ 18,600), and 340sh nm (18,300), ν 2200 cm^{-1} (doublet, C≡N) (Found: C, 67.9; H, 6.43; N, 19.7. $\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}$ requires C, 68.1; H, 6.38; N, 19.8%) and white crystals of 1,1-dicyano-2-*p*-dimethylaminophenyl-2-piperidinoethylene, m.p. 166 °C, λ_{max} (MeCN) 335 (ϵ 21,000) and 322 nm (21,000), ν 2180 cm^{-1} (doublet, C≡N) (Found: C, 72.7; H, 7.22; N, 19.7. $\text{C}_{17}\text{H}_{20}\text{N}_4$ requires C, 72.8; H, 7.19; N, 20.0%).

Kinetic Procedure.—This was similar to that described.⁴ The first-order rate coefficients were calculated by using the KINDAT programme.³³

[2/1993 Received, 21st August, 1972]

³⁰ M. Cocivera, *J. Amer. Chem. Soc.*, 1966, **88**, 672; J. J. Delpeuch, B. Bianchin, and C. Beguin, *Chem. Comm.*, 1970, 1186.

³¹ J. F. Coetzee, *Progr. Phys. Org. Chem.*, 1967, **4**, 45.

³² A. I. Vogel, 'Practical Organic Chemistry,' Longmans, London, 1956, (a) p. 168; (b) p. 176.

³³ R. C. Williams and J. M. Taylor, *J. Chem. Educ.*, 1970, **47**, 129.