Kinetics of the Reaction of Chloromethylated Phenols with Aniline and Substituted Anilines

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The kinetics of the reaction of several chloromethylated phenols with substituted anilines, mainly *p*-nitroaniline, were studied for dimethyl sulphoxide solution by conductivity measurements. Substitution of the chlorine atoms proceeds in two steps. In a reversible step hydrogen chloride is eliminated by a suitable base to form a quinone methide. The aniline is added to this intermediate in the second step, forming the anilinomethylphenol as the product. The base in the first step may be the solvent, if weakly basic anilines (*e.g. p*-nitroaniline) are used, or the aniline, if the reaction is carried out with more basic anilines (*e.g.* aniline itself).

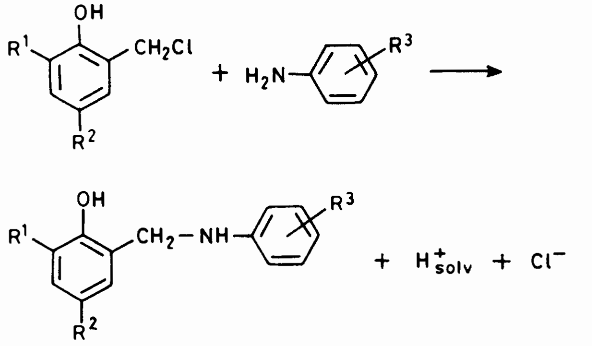
Benzylation of anilines with benzyl halides in protic solvents such as alcohols[1] or mixtures containing alcohol[2] was found to be a second-order process, first order in both reactants. In aprotic solvents such as acetonitrile or benzene a third-order reaction was found, second-order with respect to the amine;[3] however, in dimethyl sulphoxide the overall order is two again.[4] Although the reaction of (substituted) benzyl chlorides with (substituted) anilines was first investigated kinetically nearly 60 years ago,[5] it has remained the subject of kinetic[6] and mechanistic[7] studies. Recently for instance this reaction was chosen to elucidate the steric influence of alkyl substituents on the reaction rate.[8]

Although the reactivity of benzyl chlorides[9] or similar alkyl halides[10] in nucleophilic substitutions has been studied intensively, not much is known about the reactivity of chloromethylated phenols (hydroxybenzyl chlorides). We have studied the methanolysis of substituted hydroxybenzyl chlorides. An S_N1 solvolysis reaction was found for the undissociated phenol, while the reaction rate of the phenolate anion was much too high for the usual kinetic techniques.[11] To obtain some insight into the reactivity of chloromethylated phenols towards more basic nucleophiles, we have examined the reaction with substituted anilines in dimethyl sulphoxide. This was carried out with an excess of the aniline and followed by measuring the conductivity.

Results and Discussion

Products.—Most reactions were carried out with *p*-nitroaniline for experimental reasons. The more reactive anilines (*e.g.* aniline itself) led to high reaction rates with some chloromethylated phenols which were unmeasurable with the available technique. The reaction may be represented by the overall equation (1). The increase of the conductivity is caused by the hydrogen chloride formed which is completely dissociated in Me_2SO[12] and consequently also in Me_2SO solutions containing anilines in excess.

Preparative runs with some representative chloromethylphenols (**4**)—(**6**), (**9**), and (**10**) showed that only monobenzylation occurs under the reaction conditions, even if only a 3—5-fold amount of *p*-nitroaniline is taken. The expected products (**11**)—(**13**), (**15**), and (**16**) were characterized by elemental analysis, vapour pressure osmometry, i.r., ^1H n.m.r., and mass spectra, and no further reaction products could be detected by t.l.c. With aniline under the same conditions the dibenzylated product (**17**) is obtained from (**4**). With a 100-fold excess of aniline, however, present at least in the kinetic runs, only the monobenzylated aniline (**14**) is formed again.



(1)

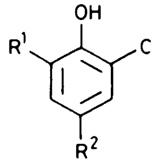
Kinetic Studies.—In spite of the large excess of *p*-nitroaniline a first-order plot of ln $c_\infty/(c_\infty - c_t)$ *versus* t (c_t and c_∞ being the concentrations of HCl at time t and at the end of the reaction) does not show the expected linearity. Figure 1a shows a typical kinetic run. The curved line with decreasing slope finally, after 75—85% conversion, becomes a straight line with constant slope m_e. Similar behaviour was found for the methanolysis of these chloromethylated phenols. This can be explained by slight dissociation of the phenolic hydroxy-group which is suppressed by the hydrogen chloride formed during the reaction.[11] In this case m_e would correspond to the first-order rate constant for the undissociated compound.

However, there are some striking differences between the aminolysis and the methanolysis reaction. (a) The final slope m_e decreases with increasing concentration $[P]_0$ of the chloromethylated phenol (Figure 2a), while a first-order rate constant would be independent, as was found indeed for the methanolysis.[11] (b) The reaction rate for the aminolysis is not only decreased by the addition of acids (*e.g.* HCl, H_2SO_4, CH_3COOH) as for the methanolysis, but also, in contrast to the methanolysis, by added chlorides [*e.g.* NaCl, $(CH_3)_4NCl$]. Indifferent salts (*e.g.* $LiNO_3$, Li_2SO_4) do not change the reaction rate. (c) While the rate of the methanolysis reaction is decreased, the rate of aminolysis is increased by electron-withdrawing substituents R^1 and R^2 in the phenolic compound.

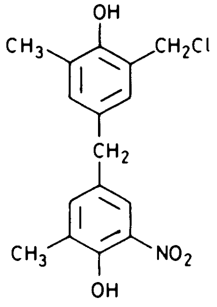
These results suggest a completely different reaction mechanism for aminolysis than for methanolysis. They can be entirely explained by the kinetic scheme (2) and (3). In a

$$P + B \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} I + BH^+ + Cl^- \tag{2}$$

$$I + An \xrightarrow{k_2'} Z \tag{3}$$



(1) $R^1 = R^2 = CH_3$
(2) $R^1 = Br,\ R^2 = CH_3$
(3) $R^1 = R^2 = Br$
(4) $R^1 = NO_2,\ R^2 = CH_3$
(5) $R^1 = NO_2,\ R^2 = Br$
(6) $R^1 = Br,\ R^2 = NO_2$
(7) $R^1 = R^2 = NO_2$



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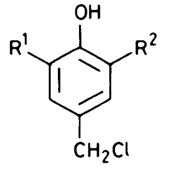
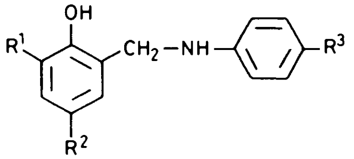
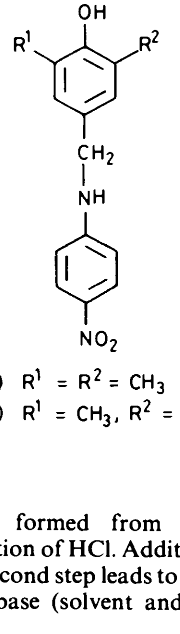


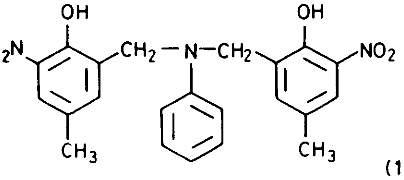
(9) $R^1 = R^2 = CH_3$
(10) $R^1 = CH_3,\ R^2 = NO_2$



(11) $R^1 = R^3 = NO_2,\ R^2 = CH_3$
(12) $R^1 = R^2 = R^3 = NO_2$
(13) $R^1 = R^3 = NO_2,\ R^2 = Br$
(14) $R^1 = NO_2,\ R^2 = CH_3,\ R^3 = H$



(15) $R^1 = R^2 = CH_3$
(16) $R^1 = CH_3,\ R^2 = NO_2$



(17)

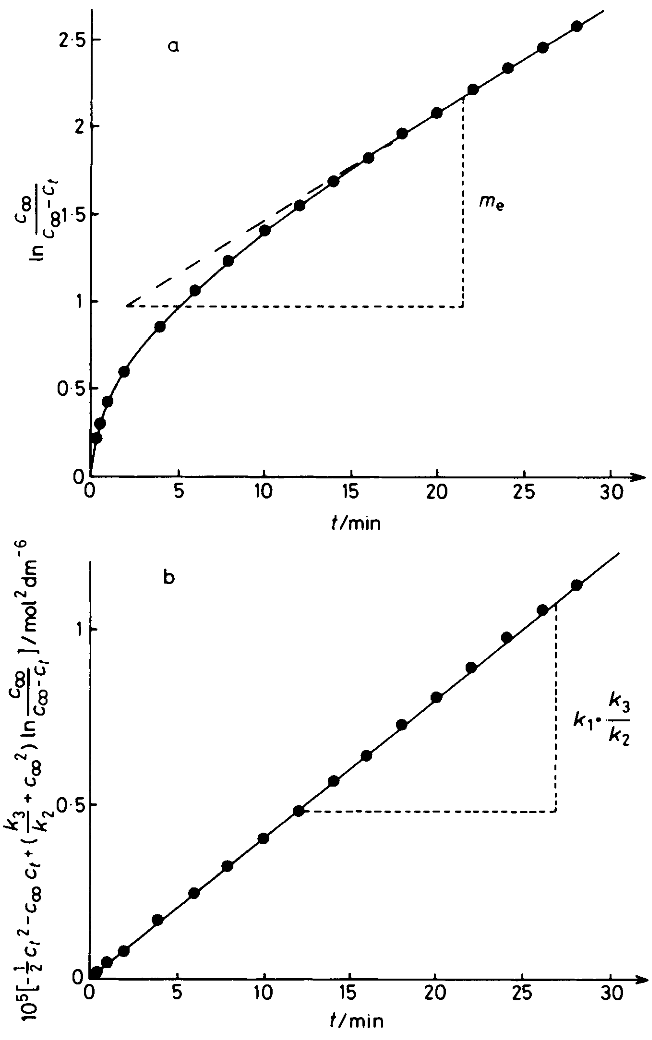


Figure 1. a, First-order plot for the reaction of (4) (2.72 mmol dm^{-3}) with *p*-nitroaniline (0.338 mol dm^{-3}). b, Plot according to equation (9) for the same reaction

reversible step an intermediate I is formed from the chloromethylated phenol P by the elimination of HCl. Addition of the aniline An to the intermediate in a second step leads to the reaction product Z. B or BH^+ is any base (solvent and/or aniline) in the basic or protonated form.

Application of the steady-state principle to the concentration of I gives equation (4) which may be simplified under first-order

$$k_1'[P]_t[B] = k_2'[I]_t[BH^+]_t[Cl^-]_t + k_3'[I]_t[An] \qquad (4)$$

conditions where [B] and [An] remain constant to give equation (5) (with $k_1 = k_1'[B]$, $k_2 = k_2'$, $k_3 = k_3'[An]$, and

$$k_1[P]_t = k_2[I]_tc_t^2 + k_3[I]_t \qquad (5)$$

$[BH^+]_t = [Cl^-]_t = c_t$, the concentration of HCl at time t). The general mass balance for the whole process is (6). Under the

$$[P]_t + [I]_t + [Z]_t = [P]_t + c_t = [P]_0 = c_\infty \qquad (6)$$

most probable condition $[I]_t \ll [Z]_t$ we further obtain equation (7). Combination of equations (5)—(7) with elimination of $[I]_t$

$$[Z]_t = c_t;\ d[Z]/dt = dc_t/dt = k_3[I]_t \qquad (7)$$

and $[P]_t$ leads to (8) which may be integrated to (9).

$$dc_t/dt = \frac{k_3k_1(c_\infty - c_t)}{k_2c_t^2 + k_3} \qquad (8)$$

$$-\frac{1}{2}c_t^2 - c_\infty . c_t + \left(\frac{k_3}{k_2} + c_\infty^2\right)\ln\frac{c_\infty}{c_\infty - c_t} = \frac{k_1k_3}{k_2}t \qquad (9)$$

Figure 1a can now be explained as follows. For high conversions, that is $c_t \longrightarrow c_\infty$, the additive part $(0.5c_t^2 + c_\infty c_t)$ obviously does not change very much in relation to the logarithmic part and equation (9) gives approximately (10). From this follows (11). Thus, if these considerations are correct,

$$\ln\frac{c_\infty}{c_\infty - c_t} = \frac{k_1k_3}{k_3 + k_2c_\infty^2}t + \text{const.} = m_et + \text{const.} \qquad (10)$$

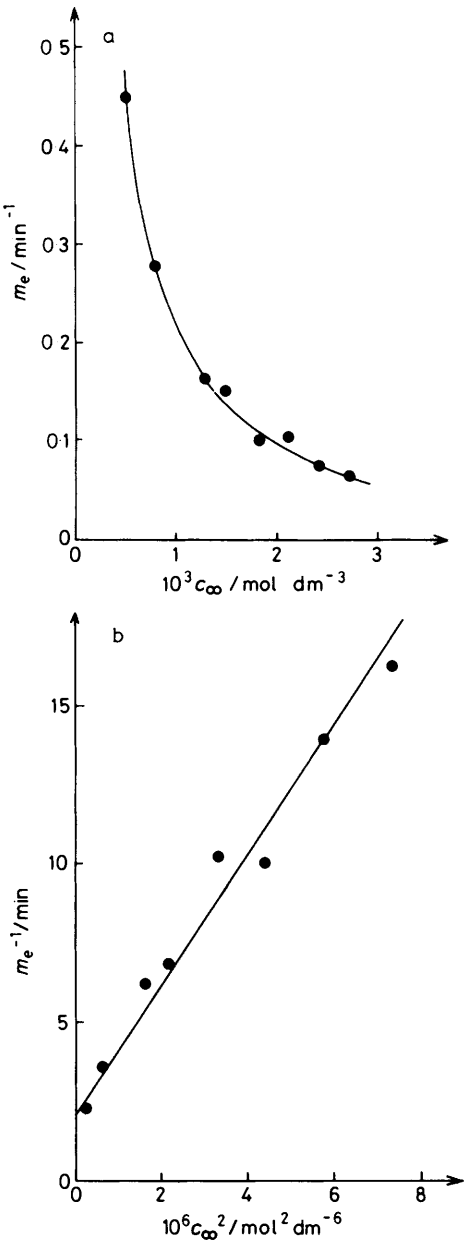


Figure 2. a, Dependence of the final slope m_e in first-order plots as in Figure 1a from the initial concentration of (4) which is equal to c_∞, the final concentration of HCl (concentration of *p*-nitroaniline 0.338 mol dm^{-3}). b, Plot according to equation (11) for the same experiments

$$\frac{1}{m_e} = \frac{1}{k_1} + \frac{k_2}{k_1 k_3} c_\infty^2 \qquad (11)$$

a plot of $1/m_e$ from different reactions with different c_∞ (which is equal to the starting concentration $[P]_0$ of the chloromethylated compound) against c_∞^2 will give a straight line. Figure 2b shows such a plot which is fairly linear.

From the slope and the intercept of those straight lines we can now calculate k_1 and the ratio k_3/k_2. Knowing this ratio a plot according to the complete equation (9) becomes possible. This is shown in Figure 1b for the experiment presented in Figure 1a. We obtain a straight line from the beginning of the reaction up to conversions higher than 90% which may be regarded as an excellent proof for the reaction scheme proposed in equations (2) and (3).

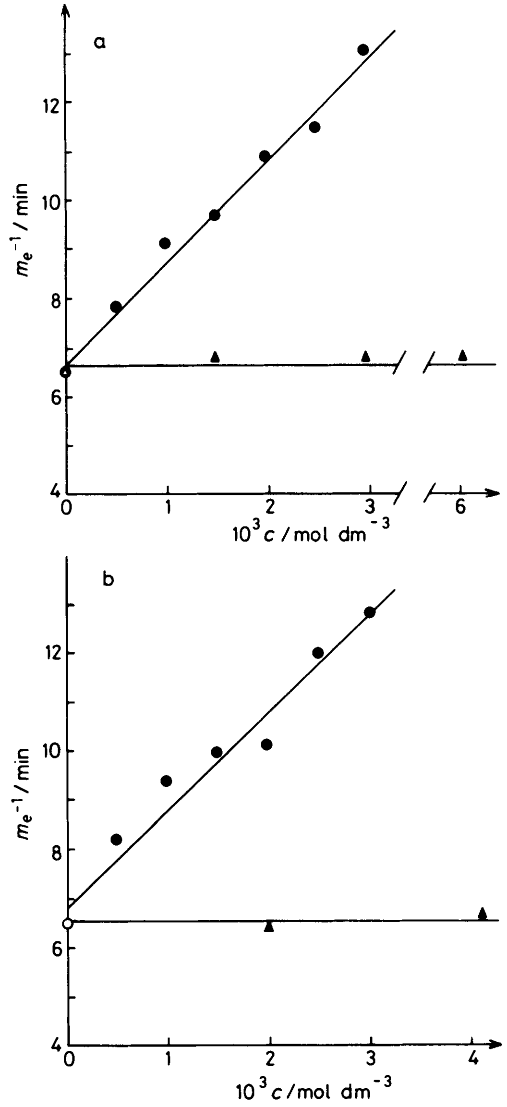


Figure 3. a, Plot according to equation (17), *i.e.* $1/m_e$ *versus* salt concentration *c*, for the reaction of (4) (1.49 mmol dm^{-3}) with *p*-nitroaniline (0.338 mol dm^{-3}) in the presence of LiCl (●) or $LiNO_3$ (▲). b, Plot according to equation (18) for the reaction of (4) (1.49 mmol dm^{-3}) with *p*-nitroaniline (0.338 mol dm^{-3}) in the presence of CF_3COOH (●) or CF_3COONa (▲)

Another proof can be derived from the dependence of the reaction rate from the concentration of added chlorides or acids. In the presence of chlorides equation (12) applies at any time

$$[Cl^-]_t = c_t + [Cl^-]_0 \qquad (12)$$

where $[Cl^-]_0$ is the concentration of added chloride. Instead of equations (5) and (8) we obtain (13) and (14) which may be

$$k_2[P]_t = k_2[I]_t c_t(c_t + [Cl^-]_0) + k_3[I]_t \qquad (13)$$

$$dc_t/dt = \frac{k_1 k_3 (c_\infty - c_t)}{k_2 c_t (c_t + [Cl^-]_0) + k_3} \qquad (14)$$

integrated to (15). In this case the slope of a first-order plot is given by equation (16) from which finally follows (17).

$$-\frac{1}{2}c_t^2 - (c_\infty + [\mathrm{Cl}^-]_0)c_t + \left\{\frac{k_3}{k_2} + c_\infty(c_\infty + [\mathrm{Cl}^-]_0)\right\}\ln\frac{c_\infty}{c_\infty - c_t} = \frac{k_1k_3}{k_2}t \quad (15)$$

$$m_e = \frac{k_1k_3}{k_2c_\infty^2 + k_2c_\infty[\mathrm{Cl}^-]_0 + k_3} \quad (16)$$

$$\frac{1}{m_e} = \left(\frac{1}{k_1} + \frac{k_2}{k_1k_3}c_\infty^2\right) + \frac{k_2c_\infty}{k_1k_3}[\mathrm{Cl}^-]_0 \quad (17)$$

Figure 3a shows the corresponding plot for a series of measurements in the presence of various amounts of LiCl. As expected, we find a linear increase of $1/m_e$ with increasing concentration of LiCl. It can be also seen that $LiNO_3$ has no measurable influence on the reaction rate, even if a double quantity is taken. Thus, the influence of Li^+ cation or salt effects can be neglected.

For measurements in the presence of strong acids we obtain the analogous relation (18). {This equation can be derived

$$\frac{1}{m_e} = \left(\frac{1}{k_1} + \frac{k_2}{k_1k_3}c_\infty^2\right) + \frac{k_2c_\infty}{k_1k_3}[\mathrm{BH}^+]_0 \quad (18)$$

exactly as for equation (17), starting from the relation $[\mathrm{BH}^+]_t = c_t + [\mathrm{BH}^+]_0$ where $[\mathrm{BH}^+]_0$ is the concentration of added acid.} A corresponding plot for measurements in the presence of trifluoroacetic acid is shown in Figure 3b. Again we find the expected linear dependence, whereas sodium trifluoroacetate has no influence. Thus the kinetic scheme presented in equations (2) and (3) is well established by various experimental evidence.

It should be mentioned, however, that this kinetic scheme represents the simplest one to fit all the experimental data. A more complicated scheme (19)—(21) where the elimination of hydrogen chloride to form the intermediate occurs in two steps cannot be entirely excluded.

$$\mathrm{P} + \mathrm{B} \rightleftharpoons \mathrm{P}^- + \mathrm{BH}^+ \quad (19)$$

$$\mathrm{P} \rightleftharpoons \mathrm{I} + \mathrm{Cl}^- \quad (20)$$

$$\mathrm{I} + \mathrm{An} \longrightarrow \mathrm{Z} \quad (21)$$

The Table contains the kinetic constants k_1 and k_3/k_2 for the aminolysis of several chloromethylated phenols with *p*-nitroaniline. Constants were determined by plots according to equation (11) (Figure 2b), and improved values were obtained using equation (9) (Figure 1b), as described in the Experimental section. There is a large increase in k_1, caused by electron-withdrawing substituents R^1 and R^2, *e.g.* the bromo-nitro-substituted compounds (**5**) and (**6**) show a *ca.* 10^3-times higher value of k_1 than the dimethyl-substituted compound (**1**). For the dinitro-compound (**7**) k_1 is even higher and, therefore, cannot be determined in the manner described. For compounds (**1**)—(**6**) $\lg k_1$ may be fairly well correlated with $\Sigma\sigma_m$ according to Jaffé's equation,[13] leading to a reaction constant ρ of +2.5. This dependence implies that the cleavage of the OH bond, *i.e.* the transfer of a proton, is more important in the formation of the intermediate than the cleavage of the C–Cl bond leading to the elimination of a chloride ion. And this means that a correlation using σ_m values is not quite justified, since the substituents R^1 and R^2 are *meta* to the chloromethyl group, but *ortho* and *para* to the phenolic hydroxy-group. And since the influence of an *ortho*-substituent cannot be described entirely by σ constants, this also explains the difference in k_1 of the isomeric compounds (**5**) and (**6**). The ratio k_3/k_2 decreases when electron-withdrawing substituents are introduced which means that the addition of HCl to the intermediate forming the starting compound is favoured over the addition of *p*-nitroaniline forming the product. It seems too early to draw further mechanistic conclusions from this result, especially since nothing can be said on the dependence of k_2 or k_3 itself. However, it is clear that the general increase of the overall reaction rate produced by electron-withdrawing substituents is clearly caused by the increase in k_1.

Table. Rate constants for the reaction of several chloromethylated phenols with 4-nitroaniline (c 0.3378 mol dm^{-3}) in dimethyl sulphoxide at 25 °C

Compound	$10^4\, k_1$/min^{-1}	$10^8\, k_3k_2^{-1}$/ mol^2 dm^{-6}
(**1**)	16	2 230
(**2**)	182	1 170
(**3**)	13 700	71
(**4**)	4 420	116
(**5**)	7 940	95
(**6**)	31 200	115

A variation of the excess of *p*-nitroaniline used provides an insight into the dependence of the rate constants on the aniline concentration. For increasing concentrations of *p*-nitroaniline we see in Figure 4a that plots according to equation (11) lead to straight lines with decreasing slope but obviously a constant intercept, even if [An] is changed by a factor of 30. This indicates that k_1 is independent of the concentration of *p*-nitroaniline and that k_3/k_2 rises with increasing concentration. With $k_3 = k_3'[\mathrm{An}]$, as we expected from the kinetic scheme [equation (13)], equation (11) leads to (22).

$$\frac{1}{m_e} = \frac{1}{k_1} + \frac{k_2c_\infty^2}{k_1k_3'}\frac{1}{[\mathrm{An}]} \quad (22)$$

Figure 4b contains plots of $1/m_e$ against $1/[\mathrm{An}]$, showing that equation (22) is well fulfilled for *p*-nitroaniline. Other possible dependences of k_1—k_3 on [An] are not in accord with the experimental results.

There are two possibilities of explaining the independence of k_1 from [An]. Either *p*-nitroaniline is not involved in the first reaction step, *i.e.* it does not act as a base under the reaction conditions, or a rapid equilibrium $\mathrm{P} + \mathrm{An} \rightleftharpoons \mathrm{P}\cdots\mathrm{An}$ exists which is completely shifted to the right by an excess of *p*-nitroaniline. Then the complex $\mathrm{P}\cdots\mathrm{An}$, whose concentration could not be increased further by increasing the concentration of *p*-nitroaniline, would be transformed to $\mathrm{I} + \mathrm{HAn}^+ + \mathrm{Cl}^-$. Such complexes between phenols and amines, hydrogen bonded or in form of ion pairs, are described for different aprotic solvents.[14] If the latter explanation were correct, k_1 should be independent of the concentration (not of the kind) of all anilines which are stronger bases than *p*-nitroaniline. However, compared with *p*-nitroaniline aniline itself shows quite different behaviour (Figure 5a). Here k_1 is directly proportional to the concentration of aniline (Figure 5b). Furthermore the ratio k_2/k_3 goes to zero (Figure 5a) which means that the addition of aniline to the intermediate is very much faster than the addition of hydrogen chloride. Consequently, the overall rate is determined only by the k_1 step and clear first-order reactions are observed for the single runs ($m_e = k_1$).

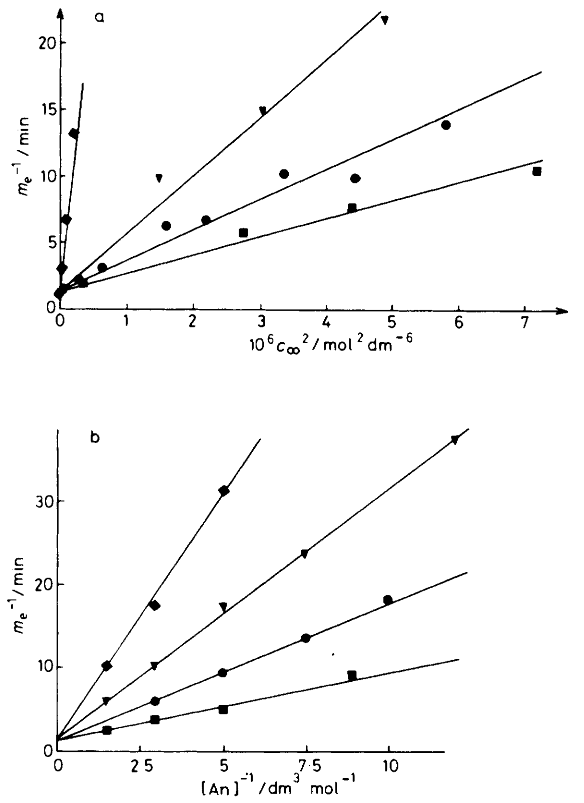


Figure 4. a, Plots of $1/m_e$ *versus* c_∞^2 according to equation (11) for the aminolysis of (**4**) and different concentrations of *p*-nitroaniline (0.0211 mol dm^{-3} ◆, 0.20 mol dm^{-3} ▼, 0.338 mol dm^{-3} ●, 0.676 mol dm^{-3} ■). b, Plots of $1/m_e$ *versus* 1/[An] according to equation (22) for different initial concentrations of (**4**) (2.536 mmol dm^{-3} ◆, 1.794 mmol dm^{-3} ▼, 1.268 mmol dm^{-3} ●, 0.897 mmol dm^{-3} ■)

The first step of the aminolysis reaction becomes quite clear from Figure 6. It shows a plot of lg k_1 *versus* $\Sigma\sigma$ according to Jaffé's relation[13] for substituted anilines. We find a linear dependence with the expected negative slope (ρ −4.6) only for the more strongly basic anilines, and in this range we also find the direct proportionality between k_1 and the concentration of the aniline. For weakly basic anilines ($\Sigma\sigma > 0.6$) k_1 is independent of the substituents in the aniline molecule. This suggests that in this range the solvent Me_2SO acts as the base and is protonated instead of the aniline in the first reaction step.

There is not much known on the basicity of substituted anilines in Me_2SO. For aniline itself pK_s 3.6 is reported.[15] With this value and a typical concentration during the kinetic runs of 0.3 mol dm^{-3} the ratio [HAn^+]/[Me_2SOH^+] is *ca.* 1 200. Preliminary conductivity measurements for various concentrations of HCl and *p*-nitroaniline lead to K_s *ca.* 1 mol dm^{-3}, and thus, for the same concentration of *p*-nitroaniline the ratio [HAn]/[Me_2SOH^+] is *ca.* 0.3. This confirms the kinetic data.

There is still the question of the structure of the intermediate, the existence of which was deduced from the kinetic data. In accord with the literature[16] this is most probably a quinone methide, which is also demonstrated by the following experiments. Addition of a sterically hindered tertiary amine such as di-isopropylethylamine which is not substituted immediately causes an increase in the conductivity. Subsequent addition of an aniline, even after several hours, yields the normal aminolysis product. If triethylamine is taken in [$^2H_6$]Me_2SO, an i.r. absorption at 1 680 cm^{-1} appears, which is stable for at least 24 h.

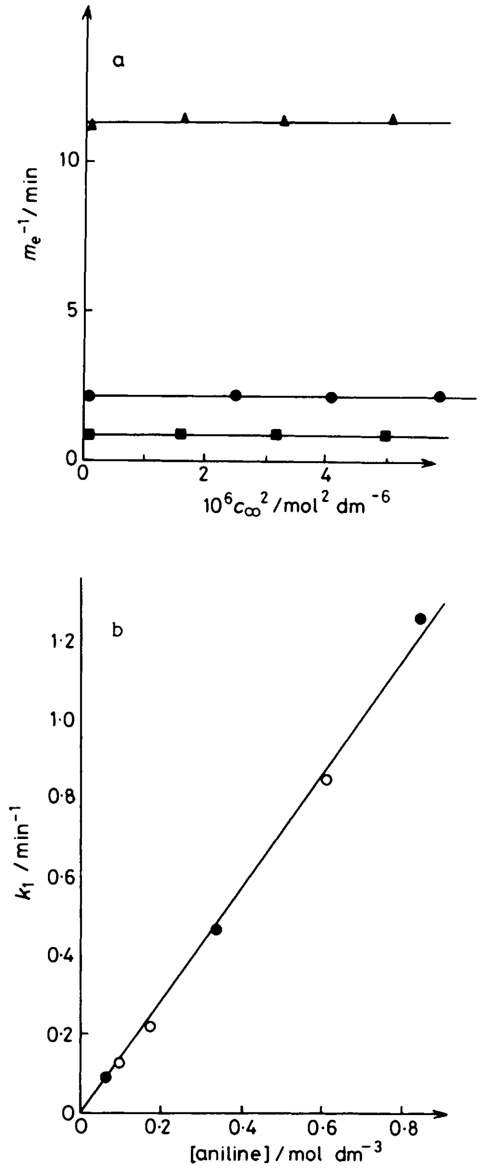


Figure 5. a, Plot of $1/m_e$ *versus* c_∞^2 according to equation (11) for the aminolysis of (**8**) and different concentrations of aniline (0.0676 mol dm^{-3} ▲, 0.338 mol dm^{-3} ●, 0.845 mol dm^{-3} ■). b, Dependence of k_1 from the concentration of aniline for (**8**): ●, from intercepts of Figure 5a; ○, single experiments with c_∞ 1.27 mmol dm^{-3}

Conclusions.—The mechanism for the first step in the reaction of chloromethylated phenols with anilines may be formulated as in the Scheme. The base B may be the solvent, the aniline, or any added base. The increase in k_1 caused by electron-withdrawing substituents can be understood by shifting the initial rapid equilibria towards the ion pair or even to the phenolate ion, probably depending on the nature of the phenolic compound. Of course, the kinetic data are also in accord with simultaneous cleavage of the O–H and C–Cl bonds, but this would mean that the proton transfer occurs in the rate-limiting step with rate constants as low as k_1 1.6×10^{-3} min^{-1}.

Nothing in detail can be said on the addition of aniline to the intermediate. However, experiments are in progress to elucidate this reaction step as well as to differentiate further the cleavage of hydrogen chloride.

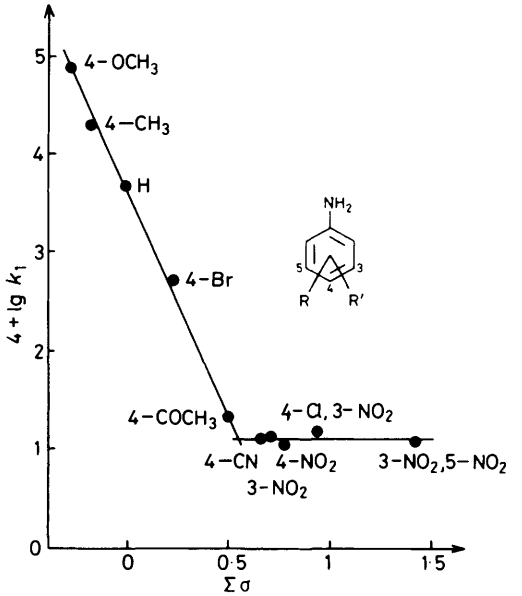
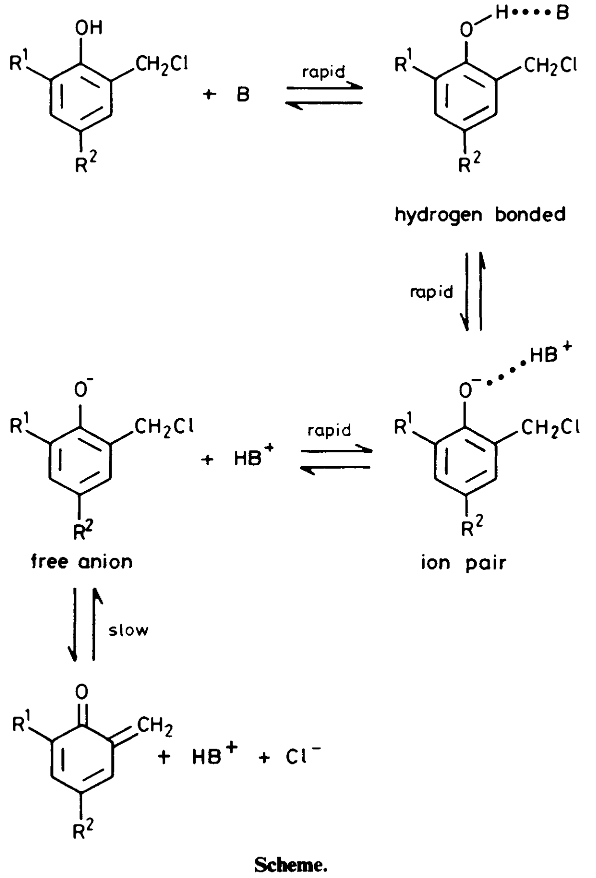


Figure 6. Jaffé's plot for the aminolysis of (**8**) and substituted anilines (0.338 mol dm^{-3})



Scheme.

Experimental

Materials.—Dimethyl sulphoxide (dried; analytical grade; Riedel–de Haen; max. 0.1% water) was further purified by fractional distillation over calcium hydride. The conductivity of this solvent at 25 °C was $<2.5 \times 10^{-7}$ mho cm^{-1}. The aniline derivatives (Fluka; Riedel–de Haen) were purified either by three-fold recrystallization from water or by two-fold fractionation *in vacuo* (*p*-toluidine, aniline). LiCl, LiNO$_3$, CF$_3$COOH, CF$_3$COONa, and (CH$_3$)$_4$NCl (analytical grade; Merck–Schuchardt) were used without further purification. The preparation of the chloromethylated phenols was described previously.[11]

Kinetic Measurements.—All kinetic experiments were done in a thermostatted glass vessel at 25 ± 0.1 °C using dimethyl sulphoxide as solvent. The concentration of the chloromethylated phenol was 3×10^{-3} mol dm^{-3} or lower and the excess of aniline was at least 100-fold. For each run a sample of the chloromethylated phenol was exactly weighed, dissolved in Me$_2$SO (2 cm^3) and added (t 0) to a solution (30 cm^3) of the aniline derivative. Mixing was complete after *ca.* 2 s. The reaction was followed by measuring the conductivity until a constant value was obtained for complete conversion (conductivity cells: LTA 100, WTW, cell constant 1.08 cm^{-1} or Tacussel CM 05/Cr, cell constant 1.15 cm^{-1}; apparatus DIGI 610, WTW; recorder RE 541.8 or RE 511, Metrawatt, for automatic registration of the conductivity as a function of time.) Since HCl is completely dissociated in Me$_2$SO, the same is true for the system HCl–aniline–Me$_2$SO. However, the dependence of the conductivity on the HCl concentration was not exactly linear and thus a calibration curve was used to deduce c_t, the concentration of HCl at time t, from L_t the observed conductivity at this time. To establish the relation between c and L, gaseous HCl was bubbled into Me$_2$SO, the concentration of the stock solution so obtained was determined by titration and different compositions of the system HCl–aniline–Me$_2$SO were obtained by mixing the appropriate volumes. No contribution of the phenolic hydroxy-group to the conductivity was observed under the relevant conditions.

The concentration of the chloromethylated phenol P is given by the relation $[P]_t = [P]_0 - c_t = c_\infty - c_t$. Thus, for a first-order plot $\ln c_\infty/(c_\infty - c_t)$ was plotted against t. However, only slight deviations of 2% or less were found, if $\ln L_\infty/(L_\infty - L_t)$ was plotted against t, assuming direct proportionality between c_t and L_t.

Evaluation of the Rate Constants.—The rate constant k_1 and the ratio k_3/k_2 [compare equations (2) and (3)] were determined as follows. For different concentrations of the chloromethylated phenol ($[P]_0 = c_\infty$) a plot according to equation (11) was carried out. Slope and intercept were determined such that the squares sum of the relative deviations, was minimized.[17]

$$S_r \sum_{i=1}^{n} [(ax_i + b - y_i)/y_i]^2,$$

If the usual procedure was taken, low values of m_e, *i.e.* high values of $1/m_e$, would be overestimated in their statistical weight, leading to obviously wrong values for the intercept. The ratio of intercept and slope thus obtained (k_3/k_2) was taken to produce linear plots (correlation coefficient >0.998) according to equation (9) for each value of c_∞, and the slope of these straight lines through the origin was divided by k_3/k_2. The values so obtained for k_1 show deviations of ±10% from the average $\bar{k}_1$ which thus was determined using all measurements with different concentrations c_∞. The ratio k_3/k_2 was finally determined from the slope of a plot according to equation (11) where $1/\bar{k}_1$ was taken as a fixed value for the intercept. Thus the uncertainty in k_3/k_2 is somewhat higher than in k_1.

For aminolysis by the strongly basic aniline derivatives where the reaction is pure first order, k_1 could be determined with a reproducibility of ±2%

Preparation of N-*Benzyl-substituted Anilines.*—To confirm the structure of the compounds which are formed according to equation (1) some representative chloromethylated phenols were treated with 4-nitroaniline or aniline in dimethyl sulphoxide. The products were characterized by m.p. (Mettler FP 1), elemental analysis, i.r., ^1H n.m.r. (Bruker WH 90; solvent $[^2H_6]Me_2SO$; standard Me_4Si), and mass spectra (Varian MAT MS-711; ionisation energy 70, sometimes 20 eV). The most important fragmentation occurs between the C and N atoms of the $-CH_2-NH-$ group. Most characteristic in the n.m.r. spectra is the coupling (J 4.7—5.6 Hz) of the CH_2 protons (doublet) and the NH proton (triplet).

Reaction with 4-*nitroaniline.* A solution of 0.6—6 mmol of the chloromethylated phenol in Me_2SO (10 cm^3) was added with vigorous stirring to a 3—5-fold excess of *p*-nitroaniline in Me_2SO (5—50 cm^3). According to the reactivity of the chloromethylated phenol after a reaction time of 1 h to 1 week at room temperature the solution was dropped into water (1 dm^3) to remove the excess of *p*-nitroaniline. (This procedure had to be repeated in some cases.) The 4-nitrophenylaminomethylphenols were separated as yellow precipitates in chromatographically pure form (t.l.c. on silica gel plates). They were finally purified by recrystallization.

2-*Nitro*-6-(4-*nitrophenylaminomethyl*)-p-*cresol* (**11**). This was formed in 95% yield, yellow needles from benzene, m.p. 160.3 °C (Found: C, 55.35; H, 4.35; N, 13.9. $C_{14}H_{13}N_3O_5$ requires C, 55.45; H, 4.3; N, 13.85%); δ_H 2.27 (3 H, s, Me), 4.47 (2 H, d, J 4.9 Hz, CH_2), 7.71 (1 H, t, J 4.9 Hz, NH), 7.46, 7.76 (1 H each, d, J 1.5 Hz, ArH), 6.72, 8.02 (2 H each, d, J 9.2 Hz, ArH), and 10.62 (1 H, s, OH); m/z 303 (M^+, 62%), 166 ($M^+ - 137$, 100), and 138 (64).

2,4-*Dinitro*-6-(4-*nitrophenylaminomethyl*)*phenol* (**12**). This was formed in 97% yield, orange crystals from benzene, m.p. 203.1 °C (Found: C, 46.75; H, 2.85; N, 16.8. $C_{13}H_{10}N_4O_7$ requires C, 46.7; H, 3.0; N, 16.75%); δ_H 4.55 (2 H, CH_2), 8.17 (1 H, NH), 8.29, 8.69 (1 H each, d, J 2.7 Hz, ArH), and 6.73, 8.02 (2 H each, d, J 9.1 Hz, ArH); m/z 334 (M^+, 100%), 197 ($M^+ - 137$, 68), and 138 (90).

4-*Bromo*-2-*nitro*-6-(4-*nitrophenylaminomethyl*)*phenol* (**13**). This was formed in 98% yield, pale yellow needles from benzene, m.p. 161.7 °C (Found: C, 42.2; H, 2.75; N, 11.5. $C_{13}H_{10}BrN_3O_5$ requires C, 42.4; H, 2.75; N, 11.4%); δ_H 4.46 (2 H, d, J 5.6 Hz, CH_2), 7.66, 8.07 (1 H each, d, J 2.4 Hz, ArH), and 6.70, 8.02 (2 H each, d, J 9.4 Hz, ArH); m/z 367/369 (M^+, 60%), 230/232 ($M^+ - 137$, 37), and 138 (100).

4-(4-*Nitrophenylaminomethyl*)-2,6-*xylenol* (**15**). This was formed in 93% yield, yellow needles from benzene, m.p. 206.9 °C (Found: C, 65.95; H, 5.8; N, 10.5. $C_{15}H_{16}N_2O_3$ requires C, 66.15; H, 5.9; N, 10.3%); δ_H 2.17 (3 H, s, Me), 4.21 (2 H, d, J 5.6 Hz, CH_2), 7.63 (1 H, t, J 5.6 Hz, NH), 6.90 (2 H, s, ArH), 6.66, 7.98 (2 H each, d, J 9.2 Hz, ArH), and 8.15 (1 H, s, OH); m/z 272 (M^+, 30%), 135 ($M^+ - 137$, 100), and 138 (23).

6-*Nitro*-4-(4-*nitrophenylaminomethyl*)-o-*cresol* (**16**). This was formed in 83% yield, small yellow needles from benzene, m.p. 198.8 °C (Found: C, 55.4; H, 4.3; N, 13.9. $C_{14}H_{13}N_3O_5$ requires C, 55.45; H, 4.3; N, 13.85%); δ_H 2.27 (3 H, s, Me), 4.38 (2 H, d, J 5.6 Hz, CH_2), 7.73 (1 H, t, J 5.6 Hz, NH), 7.54, 7.89 (1 H each, d, ArH), 6.68, 7.97 (2 H each, d, J 9.2 Hz, ArH), and 10.56 (1 H, s, OH); m/z 303 (M^+, 42%), 166 ($M^+ - 137$, 100), and 138 (32).

2-*Nitro*-6-(*phenylaminomethyl*)-p-*cresol* (**14**). A solution of (**4**) (1.5 g, 7.44 mmol) in Me_2SO (20 cm^3) was dropped at room temperature into aniline (70 g, 0.75 mol) in Me_2SO (480 cm^3). Excess of aniline and Me_2SO were removed *in vacuo*, and the remaining red oil was purified by column chromatography (silica gel; $CHCl_3$ as eluant) to yield (**14**) (1.88 g, 98%) as a red oil which finally solidified to form orange crystals, m.p. 92.1 °C (Found: C, 65.3; H, 5.5; N, 10.85. $C_{14}H_{14}N_2O_3$ requires C, 65.1; H, 5.45; N, 10.85%); δ_H 2.23 (3 H, s, Me), 4.29 (2 H, CH_2), 7.45, 7.71 (1 H each, d, J 1.5 Hz, ArH), 6.50—7.15 (5 H, m, ArH); m/z 258 (M^+, 93%), 166 ($M^+ - 92$, 45), and 93 (100).

4,4′-*Dimethyl*-6,6′-*dinitro*-2,2′-(*phenyliminodimethylene*)-*diphenol* (**17**). A solution of (**4**) (0.244 g, 1.21 mmol) in Me_2SO (10 cm^3) was added to aniline (0.388 g, 3.62 mmol) in Me_2SO (10 cm^3). This mixture was dripped into diluted HCl (1 dm^3), and (**17**) was obtained as a yellow precipitate, yield 47%, m.p. 187.3 °C (Found: C, 61.95; H, 4.9; N, 9.75. $C_{22}H_{21}N_3O_6$ requires C, 62.4; H, 5.0; N, 9.95%), δ_H 2.22 (6 H, s, Me), 4.68 (4 H, CH_2), 7.24, 7.72 (2 H each, d, J 1.5 Hz, ArH), 6.57—7.22 (5 H, m, ArH), and 10.6 (2 H, s, OH); m/z 423 (M^+, 38%), 258 (84), 166 (51), and 93 (100).

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