Kinetics of the Oxidation of Some *meta*- and *para*-Substituted Dimethylanilines with Lead Tetra-acetate

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The second-order kinetics of the oxidation of some aryldimethylamines with lead tetra-acetate in chloroform–acetic anhydride (1 :1 v/v) to give acetamides and formaldehyde follow the equation $-d[LTA]/dt = k[LTA][amine]$. The obtained ρ value ($-2.4 \pm 0.5$) is consistent with the presence of a positive charge in the transition state.

AROMATIC tertiary amines have been subjected to reaction with a variety of oxidising agents.[1] In most cases, dealkylation to give a secondary amine was noted. Interest in the oxidation of these substrates with metal oxidants is stimulated by the importance of biological oxidation of the amine nitrogen atom.[2] An important approach to this problem is the study of the reactivity of different metal oxidants and their influence on the structure and the solvation of the transition state.

Two preliminary communications[3,4] reported the reactivity of the acetates of Pb^{IV}, Mn^{III}, Co^{III}, and Tl^{III} with various aryldialkylamines. Here we report the kinetics of the oxidation of six dimethylanilines with lead tetra-acetate (LTA) to give an acetylated secondary amine and formaldehyde.[5]

The reactivity of this reagent with nitrogen compounds has been reviewed[6] and it is thought that LTA can behave either as a one or two electron oxidant according to the substrate and the reaction conditions. Kinetic support for the mechanism and for the intermediates proposed (nitrenes, nitrenium ions, aminiumyl cation-radicals, aminyl radicals) has rarely been reported.[6] Simple substrates such as tertiary amines should be good models for more complex substrates.

RESULTS

Products.—Table 1 summarises the results of the oxidation of amines (1)—(6) with LTA in chloroform–acetic anhydride (1 : 1 v/v) at room temperature to give the amides (7)—(12)

$XC_6H_4NMe_2$
(1) $X = H$
(2) $X = 4\text{-Cl}$
(3) $X = 4\text{-I}$
(4) $X = 3\text{-I}$
(5) $X = 3\text{-NO}_2$
(6) $X = 4\text{-NO}_2$
XC_6H_4NMeAc
(7) $X = H$
(8) $X = 4\text{-Cl}$
(9) $X = 4\text{-I}$
(10) $X = 3\text{-I}$
(11) $X = 3\text{-NO}_2$
(12) $X = 4\text{-NO}_3$
$4\text{-ClC}_6H_4N(CX_2CH_3)_2$
(13) $X = H$
(14) $X = D$

and formaldehyde. All the oxidations were carried out for 5×10^{-2}M solutions of the substrates in the presence of 1 mol. equiv. of LTA (heterogeneous conditions since LTA is not completely solubilised). Yields reported refer to the isolated reaction products. When the oxidation was performed in 10^{-4}M solution for both reagents (homogeneous conditions) the reaction showed 1 : 1 stoicheiometry.

TABLE 1

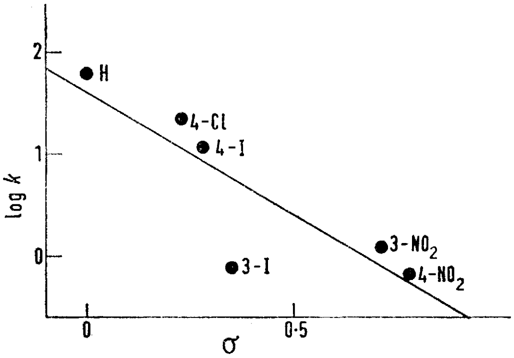
Yields (%) in the reactions between amine (5×10^{-2}M) and LTA (1 mol. equiv.) in chloroform–acetic anhydride (1 : 1 v/v) at room temperature

Substrate	Amide (%)
(1)	33
(2)	42
(3)	24
(4)	29
(5)	39
(6)	32

Kinetics.—The reaction of substrates (1)—(6) with LTA (both 10^{-4}M) in chloroform–acetic anhydride (1 : 1 v/v) was followed spectrophotometrically at 285 nm. The linearity of the relationship between the absorption at 285 nm and LTA concentration was confirmed. The reaction follows the kinetic relationship (1). In all the kinetic

$$-d[LTA]/dt = k_{obs}[LTA][amine] \qquad (1)$$

studies the reactions were followed to 2–3 half-times. A computer was used to obtain the kinetic data by means of least squares regression analysis (Table 2) and also to calculate the activation parameters (Table 3). The correlation coefficients for the second-order rate constants were ⩾0.99.



Plot of log k at 40.0 °C against σ in the reaction between $XC_6H_4NMe_2$ and LTA in chloroform–acetic anhydride (1 : 1 v/v)

The values of the rate constants obtained for different concentrations of substrates (2) and (6) and LTA (Table 4) confirmed that the reaction is first order in each reactant. The logarithms of the second-order rate constants at 38.5 °C for substrates (1)—(3), (5), and (6) were plotted against the σ

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TABLE 2

Second-order rate constants for the reaction between XC_6H_4NMe (10^{-4}M) and LTA (10^{-4}M) in chloroform–acetic anhydride (1 : 1 v/v)

X	t/°C	k_{obs}/l mol^{-1} s^{-1}
H	23.5	15.8
	29.3	28.1
	30.2	29.3
	33.8	35.7
	40.5	64.6
4-Cl	18.9	2.74
	20.8	3.92
	26.4	7.20
	31.6	10.3
	37.7	17.5
4-I	23.2	1.43
	28.3	2.85
	33.4	5.46
	38.5	9.70
3-I	28.6	0.224
	32.2	0.329
	34.8	0.449
	43.6	1.11
3-NO_2	32.7	0.486
	35.0	0.660
	41.9	1.59
	43.0	1.90
	48.5	3.45
4-NO_2	25.0	0.0818
	30.6	0.212
	36.7	0.465
	41.2	0.738
	44.6	1.25

TABLE 3

Enthalpy and entropy of activation for the reaction of $XC_6H_4NMe_2$ with LTA in chloroform–acetic anhydride (1 : 1 v/v)

X	$\Delta H^‡$/ kcal mol^{-1}	$\Delta S^‡$/ cal mol^{-1} K^{-1}
H	14.3 ± 0.5	−4.9 ± 1.8
4-Cl	16.5 ± 0.8	0.2 ± 2.6
4-I	22.4 ± 0.5	17.7 ± 1.7
3-I	19.6 ± 0.2	3.6 ± 0.6
3-NO_2	23.8 ± 0.3	17.9 ± 1.0
4-NO_2	24.7 ± 0.7	19.8 ± 2.2

TABLE 4

Comparison of rate constants for the reaction between $XC_6H_4NMe_2$ and LTA in chloroform–acetic anhydride (1 : 1 v/v) at different concentration of the reactants

X	[amine]/M	[LTA]/M	t/°C	k/ l mol^{-1} s^{-1}
H	10^{-4}	5×10^{-5}	27.8	25.1
H	10^{-4}	10^{-4}	27.8	23.6
H	5×10^{-5}	10^{-4}	27.8	25.7
4-NO_2	2×10^{-4}	10^{-4}	46.4	1.45
4-NO_2	10^{-4}	10^{-4}	46.4	1.55
4-NO_2	5×10^{-5}	10^{-4}	46.4	1.56

values for the substituents[7] (Figure). The slope of the linear plot obtained gave ρ −2.4 ± 0.5. From the slope of the plot of $-\Delta H^‡$ against $\Delta S^‡$ for these five substrates a value of $\beta = 419 \pm 22$ K in the isokinetic relationship $\delta\Delta H^‡ = \beta\delta\Delta S^‡$ was obtained. The kinetic isotope effect k_H/k_D from the oxidation of 4-chlorodiethylaniline (13) and its tetradeuterio-analogue (14) was 1.44.

DISCUSSION

The ability of LTA to act both as a one- and two-electron oxidant has been summarised in many reviews.[6,8] In the oxidation of aromatic tertiary amines with this reagent the similarity of the oxidation products with those obtained for typical one-electron oxidants such as $Mn(OAc)_3$ and $Co(OAc)_3$[3,4] and $K_3Fe(CN)_6$[9] suggested the mechanism shown in equations (2)—(5) and a rate-determining electron transfer. The e.s.r. signals of cation-radicals such as (15) have been observed in the LTA oxidation of aromatic amines.[10] Aminiumyl cation-radicals are suggested as being formed in various reactions involving electron transfer such as photolysis of the mixtures *NN*-dimethylaniline–bromobenzene[11] and *NN*-dimethylaniline–nitrobenzene,[12] the γ-irradiation of aromatic tertiary amines[13] or treatment with Cu^{II},[14] tetracyanoethylene,[15] or tris-(p-bromophenyl)-ammoniumyl perchlorate.[16]

$$XC_6H_4NMe_2 + Pb(OAc)_4 \xrightarrow{k_1} \underset{(15)}{XC_6H_4\overset{+\cdot}{N}Me_2} + {}^{\cdot}Pb(OAc)_3 + AcO^- \qquad (2)$$

$$XC_6H_4\overset{+\cdot}{N}Me_2 \xrightarrow{k_2} XC_6H_4NMeCH_2^{\cdot} + H^+ \qquad (3)$$

$$XC_6H_4NMeCH_2^{\cdot} + Pb(OAc)_4 \xrightarrow{k_3} XC_6H_4NMeCH_2^+ + {}^{\cdot}Pb(OAc)_3 + AcO^- \qquad (4)$$

$$XC_6H_4NMeCH_2^+ + Ac_2O \xrightarrow{k_4} XC_6H_4NMeAc + CH_2O + Ac^+ \qquad (5)$$

A steady state approximation for equations (2)—(5) predicts that (6) obtains if k_2 and k_4 are much greater

$$-d[LTA]/dt = k_1[LTA][amine] \qquad (6)$$

than k_1 and k_3.[9] $k_{obs} = k_1$ assuming the fast disproportionation of ${}^{\cdot}Pb(OAc)_3$ to LTA and lead diacetate.[8,17] The kinetic data fit this mechanistic scheme and give information on step (2). An inspection of the values of the second-order rate constants shows that $-I$ and $-M$ substituents retard the reaction rate relative to hydrogen and suggests a rate-controlling electron abstraction process.

The ρ value, −2.4 ± 0.5, obtained in this study, and particularly its negative sign, indicates a transition state structure bearing a high degree of positive charge on nitrogen. This fact and the lack of primary kinetic

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isotope effect in the oxidation of 4-chlorodiethylaniline rules out the possibility of a concerted loss of an electron and a proton. A ρ value of -1.83 was reported in the photoreduction of aromatic ketones with aromatic amines.[18] ρ Values of -0.989 and -0.924 were obtained in ferricyanide[9] and ClO_2 oxidation of cyclic amines.[19]

The values of the enthalpy of activation are in line with an increasing destabilisation of the positively charged transition state effected by electron-withdrawing substituents throughout the series.

Also the values of the entropy of activation appear to correlate with the substrate series with the exclusion of the 3-I derivative, which does not fit the Hammett plot. A decrease of the tightness of the ionic pair in the transition state could explain the observed increase in activation entropy. This fact is deduced from the influence of the substituent in solvation of the transition state and could be important in any correlation among different metal oxidants on these substrates. A solvent effect study would further clarify this point.

In conclusion, LTA seems to react with tertiary amines by substantially the same mechanism as other oxidants. The results of the study of the transition state structure and of the activation parameters are useful for a comparison among metal oxidants.

EXPERIMENTAL

Materials.—The amines were prepared by known methods and purified by distillation under vacuum before use. LTA was a B.D.H. product and was freed from acetic acid by vacuum drying. Its purity was estimated spectrophotometrically[20] and by iodimetric titration. Anhydrous chloroform was prepared by distillation over anhydrous calcium chloride and pure acetic anhydride was obtained by distillation of the Carlo Erba reagent grade product.

The tetradeuterio-analogue (14) of 4-chlorodiethylaniline was prepared by $LiAlD_4$ reduction of the corresponding acetamide. This was in turn prepared by acetylation of the dideuterio-analogue of 4-chloro-*N*-ethylaniline synthesised by $LiAlD_4$ reduction of *N*-acetyl-4-chloroaniline. The content of deuterium was estimated by mass spectrometry using a LKB 9000 instrument operating at 70 eV and was $>99\%$.

Product Studies.—Substrate (1 mmol) was dissolved in chloroform–acetic anhydride (1 : 1 v/v; 30 ml) and LTA (1 mmol) was added. The resulting suspension was stirred at room temperature under nitrogen until the oxidant was consumed (starch–iodine paper), then evaporated to dryness under reduced pressure, dissolved in benzene (50 ml), and filtered to remove lead diacetate. The residue from evaporation of the filtrate was chromatographed on silica gel G (Merck; 0.05—0.2 mm; 5 g) eluting with chloroform (10 ml fractions). The fractions containing pure product were collected and weighed.

Kinetic Studies.—Reactants were weighed, dissolved in chloroform–acetic anhydride (1 : 1 v/v), and transferred to a series of tubes which were stoppered with screw caps. The temperature in the thermostat was constant to within 0.1 °C. Tubes were withdrawn at intervals and the contents quenched by cooling. Absorbance was measured at 285 nm using a Hitachi–Perkin-Elmer 124 spectrophotometer.

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