

## Oxidation of Aryldialkylamines with Cerium(IV) Ammonium Nitrate and Thallium(III) Nitrate

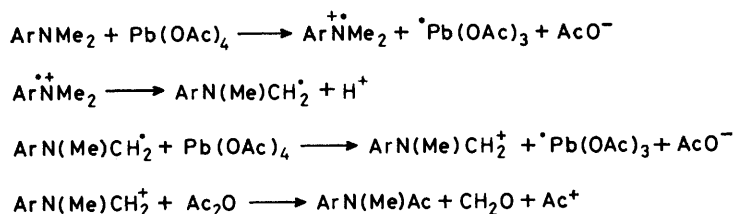
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Nine alkylmethylanilines were oxidised with cerium(IV) ammonium nitrate and thallium(III) nitrate in acetic acid, acetonitrile, and methanol. Reaction products were those deriving from demethylation, dealkylation, and aromatic nitration at positions *ortho* and *para* to the amino-group. The ratio between demethylation and dealkylation and between them and aromatic nitration is discussed in terms of (i) the oxidising power and electrophilicity of the reagent and (ii) the co-ordinative properties of the solvent.

CONSIDERABLE interest has been shown recently in the oxidation reactions effected by cerium(IV) salts.<sup>1</sup> The value of the redox couple  $\text{Ce}^{\text{IV}}-\text{Ce}^{\text{III}}$  is high; thus intermediates formed during the oxidation of organic compounds can rarely be isolated. Further complications arise when a salt such as cerium(IV) ammonium nitrate (CAN) is used. The nitrate group is sometimes found to

occurred (Scheme 2). In all cases demethylation was preferred to dealkylation.<sup>8</sup>

When dimethylaniline was treated with cerium(IV) sulphate in dilute sulphuric acid a *para-para* coupling occurred and a tetramethylbenzidine,  $\text{Me}_2\text{N}-\text{Ar}-\text{Ar}-\text{NMe}_2$ , was obtained.<sup>9</sup> The dimethylaniline cation radical may be intermediate in this reaction and a

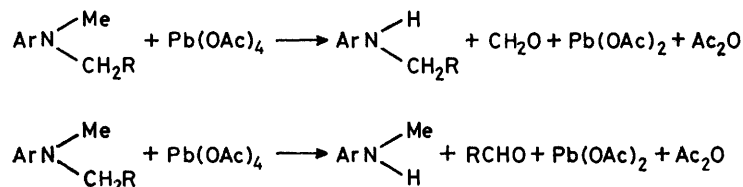


SCHEME 1

trap reaction intermediates, giving nitrate esters which often undergo further disproportionation reactions, *e.g.* the isolation of benzyl nitrate and benzaldehyde or 9,10-dihydro-10-oxo-9-anthryl nitrate and anthraquinone or acridone in the oxidation of toluene,<sup>2</sup> anthracene,<sup>3</sup> or acridine<sup>4</sup> with CAN. Similar behaviour is shown by thallium(III) nitrate (TTN), which has, however, a value for the redox couple  $\text{Tl}^{\text{III}}-\text{Tl}^{\text{I}}$  lower than that of Ce.

similarity between the oxidation mechanisms of LTA and  $\text{Ce}(\text{SO}_4)_2$  may be suggested.

Preliminary results showed that when oxidising agents were the nitrate-ligand-bearing cerium(IV) ammonium nitrate (CAN) and thallium(III) nitrate (TTN) the demethylation reaction was concurrent with the introduction of nitro-groups at the aromatic nucleus.<sup>10</sup> We report now the results of the oxidation of nine aryldi-



SCHEME 2

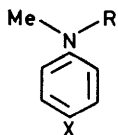
The oxidation of organic substrates with TTN has been recently reviewed.<sup>5</sup>

Aromatic tertiary amines have been oxidised with many oxidising agents. Among them, we have studied the reaction products and kinetics of oxidations with lead tetra-acetate (LTA) and thallium triacetate (TTA) in chloroform-acetic anhydride. The reaction products were an aromatic secondary amine and an aldehyde<sup>6</sup> and it was shown that LTA reacted with dimethylanilines with the mechanism depicted in Scheme 1.<sup>7</sup> When alkylarylmethylamines were treated with this reagent both demethylation and dealkylation reactions

alkylamines with CAN and TTN at room temperature in acetic acid, acetonitrile, and methanol. The mixtures from reactions with CAN were treated with urea and sulphuric acid in order to transform the *N*-nitroamines into secondary amines, this stage not being necessary in the case of oxidation by TTN since *N*-nitroamines were not formed. The reaction products were isolated by chromatography on silica gel. 4-Methoxy-*NN*-dimethylaniline (I) was converted by CAN in acetic acid or acetonitrile or by TTN in acetic acid into the mono-demethylated dinitroamine (10). Compound (I) gave (11) when treated with TTN in acetonitrile. This

derived from nitration of the material. Compound (1) polymerised on reaction with CAN or TTN in methanol.

4-Methoxy-*N*-methyl-*N*-*n*-butylaniline (2) underwent



(1) R = Me; X = OMe

(2) R = Bu<sup>n</sup>; X = OMe

(3) R = Me; X = Cl

(4) R = Bu<sup>n</sup>; X = Cl

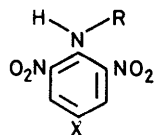
(5) R = Me; X = NO<sub>2</sub>

(6) R = Bu<sup>n</sup>; X = NO<sub>2</sub>

(7) R = Et; X = OMe

(8) R = Et; X = Cl

(9) R = Et; X = NO<sub>2</sub>



(10) R = Me; X = OMe

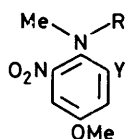
(15) R = H; X = OMe

(17) R = Me; X = Cl

(20) R = Bu<sup>n</sup>; X = Cl

(28) R = Et; X = OMe

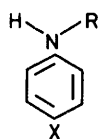
(30) R = Et; X = Cl



(11) R = Me; Y = H

(13) R = Bu<sup>n</sup>; Y = NO<sub>2</sub>

(14) R = Bu<sup>n</sup>; Y = H

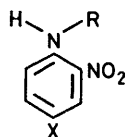


(18) R = Me; X = Cl

(21) R = Bu<sup>n</sup>; X = Cl

(24) R = Me; X = NO<sub>2</sub>

(26) R = Bu<sup>n</sup>; X = NO<sub>2</sub>



(12) R = Bu<sup>n</sup>; X = OMe

(16) R = Me; X = Cl

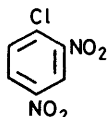
(19) R = Bu<sup>n</sup>; X = Cl

(25) R = Me; X = NO<sub>2</sub>

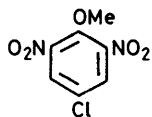
(27) R = Bu<sup>n</sup>; X = NO<sub>2</sub>

(29) R = Et; X = Cl

(31) R = Et; X = NO<sub>2</sub>



(22)



(23)

demethylation and dealkylation accompanied by nitration when treated with CAN in acetic acid. TTN in acetic acid caused nitration with or without concurrent

demethylation or dealkylation. TNN in acetonitrile gave only nitration of the starting material. Again, compound (2) polymerised on reaction with CAN or TTN in methanol.

Compound (12) was identified by oxidation with CrO<sub>3</sub> which yielded the amine (15). Compounds (13) and (14) were identified by their conversion with CAN in acetic acid into a mixture of (10) and (12). 4-Chloro-*NN*-dimethylaniline (3) gave compound (16), derived from demethylation and nuclear nitration. The dinitro-compound (17) was also obtained from oxidation by CAN. The reaction of (3) with CAN in methanol gave polymers, whereas TTN in methanol gave the demethylated amine (18). 4-Chloro-*N*-methyl-*N*-*n*-butylaniline (4) underwent demethylation and dealkylation accompanied by nitration when treated with CAN or TTN in acetic acid. TTN in methanol or acetonitrile gave demethylation. Compounds (19) and (20) were prepared by reaction of (22) and (23) with *n*-butylamine. *NN*-dimethyl-4-nitroaniline (5) gave demethylation. The reaction with CAN in acetic acid gave also (25), deriving from demethylation and nitration. Also *N*-methyl-*N*-*n*-butyl-4-nitroaniline (6) gave mainly demethylation along with small amounts of dealkylated products. As before, CAN in acetic acid gave also (27), deriving from demethylation and nitration.

The ratio between demethylation and dealkylation was tested also in the oxidation of some *N*-ethyl-*N*-methylanilines.

*N*-Ethyl-4-methoxy-*N*-methylaniline (7) gave with CAN in acetic acid a mixture of the dealkylated compound (10) and the demethylated compound (28),

TABLE I

Physical and analytical data for new compounds

Product	M.p. or b.p. (°C) [mmHg]	Found (%)			Required (%)		
		C	H	N	C	H	N
(26)	79—81	44.85	4.85	17.55	44.8	4.6	17.4
(5)	33—34	48.75	5.9	15.55	49.05	5.6	15.6
(14)	100 [0.01]	52.5	5.4	12.35	52.65	5.7	12.3
(15)	160 [0.01]	44.2	4.5	15.35	43.95	4.4	15.4

identified by chromic oxidation to the amine (15). 4-Chloro-*N*-ethyl-*N*-methylaniline (8) gave compounds (16), (17), (29), and (30). The latter two compounds were also prepared by reaction of (22) and (23) with ethylamine. *N*-Ethyl-*N*-methyl-4-nitroaniline (9) gave the dinitroamine (31). The results from compounds (1)—(4), (7), and (8) are summarised in Table 2, with those from compounds (5), (6), and (9) being in Table 3. Melting or boiling points and elemental analyses of all new compounds are reported in Table 1.

These results indicate that the reaction of CAN or TNN on these substrates has two effects: the oxidative dealkylation process and the nitration reaction. Dealkylation processes of aromatic tertiary amines could be the result of an electron abstraction mechanism such as that suggested for LTA: the oxidant could abstract one electron from the substrate giving a cation

radical (32). The loss of a hydrogen ion from this would give rise to an  $\alpha$ -arylalkylamino-carbon radical (33) with subsequent oxidation to an immonium ion (34) followed by solvolysis to a secondary amine (Scheme 3). In the case of TTN oxidations the intermediate  $Ti^{II}$  species could abstract one electron from the original

4-methoxy-derivatives, nitration would be the only reaction.

The two reagents are also not equivalent with regard to selectivity between demethylation and dealkylation. With the more reactive 4-methoxy-derivatives, CAN leads to a preference for dealkylation over demethylation

TABLE 2  
Reaction conditions and product yields in the oxidation of compounds (1)—(4), (7), and (8)

Compound	Oxidant	Solvent <sup>a</sup>	Products [% yield]				
			Demethylation		Dealkylation		Other
			Mononitro	Dinitro	Mononitro	Dinitro	
(1)	CAN	AC		(10) [40]			
(1)	CAN	AN		(10) [35]			
(1)	TTN	AC		(10) [59]			
(1)	TTN	AN	(11) [59]				
(2)	CAN	AC		(12) [12]			
(2)	TTN	AC		(12) [16]	(10) [56]	(13) [30]	
(2)	TTN	AN			(10) [12]	(4) [72]	
(3)	CAN	AC	(16) [15]	(17) [2]			
(3)	CAN	AN	(16) [15]	(17) [22]			
(3)	TTN	AC	(16) [69]				
(3)	TTN	AN	(16) [60]				
(3)	TTN	ME				(18) [36]	
(4)	CAN	AC	(19) [15]	(20) [1]	(16) [29]	(17) [2]	
(4)	TTN	AC	(19) [69]		(16) [27]		
(4)	TTN	AN				(21) [47]	
(4)	TTN	ME				(2) [36]	
(7)	CAN	AC		(28) [9]		(10) [31]	
(8)	CAN	AC	(29) [21]	(30) [7]	(16) [19]	(17) [4]	

<sup>a</sup> AC = acetic acid; AN = acetonitrile; ME = methanol.

substrate or the carbon radical (33) more efficiently than the  $Ti^{III}$  reagent.  $Ti^{II}$  species are in fact expected to be more powerful oxidants than  $Ti^{III}$  salts.<sup>11</sup>

CAN and TTN appear to be largely equivalent as oxidising agents towards aromatic tertiary amines. The main differences are noted in the ratios of dealkylation to nitration and in the selectivity between demethylation and dealkylation. In CAN oxidations the nitroamine eventually obtained has invariably lost one alkyl group.

irrespective of the nature of the alkyl group (ethyl or n-butyl), whereas with TTN these two processes are equivalent. The less reactive 4-chloro-derivatives give nearly equimolar amounts of demethylated and dealkylated products with CAN, whereas demethylation is preferred with TTN. With the least reactive 4-nitro-derivatives both CAN and TTN give preference to demethylation. The chemical and electrochemical oxidation of tertiary amines has been reported to give pre-

TABLE 3  
Reaction conditions and product yields in the oxidation of compounds (5), (6), and (9)

Compound	Oxidant	Solvent <sup>a</sup>	Products [% yield]		
			Demethylation	Dealkylation	Other
(5)	CAN	AC	(24) [23]		(25) [11]
(5)	CAN	AN	(24) [60]		
(5)	CAN	ME	(24) [89]		
(5)	TTN	AC	(24) [40]		
(5)	TTN	AN	(24) [60]		
(5)	TTN	ME	(24) [87]		
(6)	CAN	AC		(26) [5]	(27) [24]
(6)	TTN	AC	(24) [3]	(26) [20]	
(6)	TTN	AN	(24) [2]	(26) [32]	
(6)	TTN	ME	(24) [3]	(26) [30]	
(9)	CAN	AC			(31) [33]

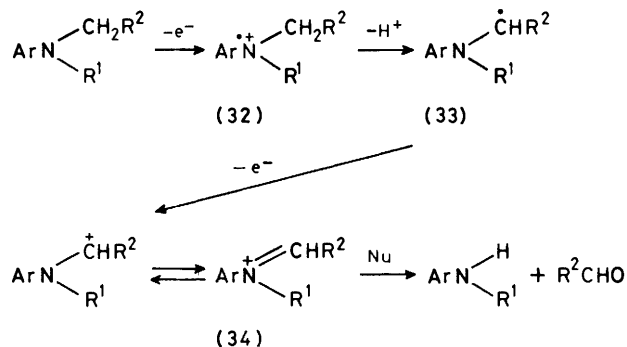
<sup>a</sup> AC = acetic acid; AN = acetonitrile; ME = methanol.

This suggests the oxidative reaction precedes nitration. On the contrary, treatment with TTN leads in some instances to nitration without concurrent dealkylation. The fact that this is noted only with the 4-methoxy-anilines where the methoxy-group exerts a powerful +M and +I electronic effect suggests that the nitration is more sensitive to electronic factors than the oxidation reaction, so that in very reactive substrates, such as the

ference to demethylation over dealkylation, for which acidity<sup>12</sup> or probability<sup>13</sup> factors have been suggested to be responsible. In our case, the ratio between demethylation and dealkylation effected by the powerful oxidant CAN depended on the nature of the nuclear substituent, whereas demethylation was always preferred with the weaker oxidant TTN. This indicates that this ratio is sensitive to the oxidising power, thus

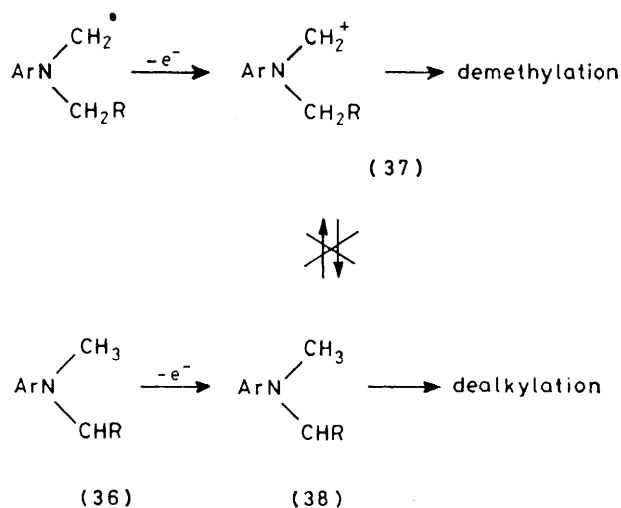
suggesting that the prevalence of demethylation often observed could be attributed to the easier oxidation of the primary carbon radical (35) over the secondary carbon radical (36), effected by sufficiently selective reagents, such as LTA or TTN.

Steric parameters related to complex formation could be involved in this selectivity; CAN is too strong an oxidising agent to exhibit selectivity. Furthermore, the prototropic equilibrium (37)  $\rightleftharpoons$  (38) does not occur (Scheme 4). For the nitration reaction it can be



SCHEME 3

noted that the nitro-groups are introduced in the aromatic nucleus in the same position as by electrophilic nitration. Also, the number of nitro-groups introduced parallels the electrophilic nitration. Thus, the CAN or TTN nitration is a non-redox process similar to that noted with other metal nitrates such as the nitrate-complexes of  $\text{Ti}^{\text{IV}}$ ,<sup>14</sup>  $\text{Zr}^{\text{IV}}$ , and  $\text{Fe}^{\text{III}}$ .<sup>15</sup> The behaviour of the nitrate-group as a bidentate ligand has been indicated to be a condition for the nitration reaction.<sup>16</sup> In fact, the co-ordination number of twelve in CAN



SCHEME 4

indicates that this condition is fulfilled.<sup>17</sup> It could be suggested that the nitration reaction occurs with a molecular rearrangement within a co-ordination complex of the substrate with a metal-containing species.<sup>14</sup> In fact, CAN is known to form complexes with amines by displacement of one of the nitrate-ligands.<sup>18</sup> The same

situation could be valid for TTN. The redox couple  $\text{Ti}^{\text{III}}-\text{Ti}^{\text{I}}$  is enough low and the electrophilicity of TTN high enough to allow the nitration and not the oxidative dealkylation to occur. The less reactive nitroamines thus formed could largely survive in the reaction conditions. The absence of nitration reactions in methanol solution could be ascribed to the fact that methanol co-ordinates to the metal.<sup>19</sup> This prevents formation of the metal-substrate complex which is suggested to be necessary for aromatic nitrations to occur.

In conclusion, the oxidative dealkylation effected by CAN and TTN seems to depend on the oxidising power of the metal, whereas the nuclear nitration appears to correlate with the electrophilicity of these bidentate nitrate-ligand-bearing species. The balance between these two effects gives rise in acetic acid or in acetonitrile to prevalence of nitration with TTN and prevalence of oxidation with CAN. In acetonitrile, the different abilities of CAN and TTN to nitrate organic substrates are more apparent, whereas in methanol their oxidising efficiencies can be evaluated.

## EXPERIMENTAL

Microanalyses were performed with a Perkin-Elmer 240 elemental analyser. I.r. spectra were measured with a Perkin-Elmer 257 spectrophotometer for Nujol mulls. Melting points were determined with a Büchi apparatus. Chromatography was performed with silica gel G Merck 0.05–0.2 mm ( $R = 100$ ) with heptane and benzene as eluants.

*Oxidation of Substrates.*—0.04M-Solutions of the substrate in the appropriate solvent were treated with CAN (2 mol. equiv.) or TTN (1 mol. equiv.) at room temperature with stirring. After consumption of the oxidant the solvent was evaporated off under reduced pressure and the residue was dissolved in water and extracted with chloroform. The extracts were dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated under reduced pressure. For oxidations with TTN, the residue was chromatographed on silica gel. For oxidations with CAN, the residue (0.2 g) was dissolved in concentrated sulphuric acid (1.5 ml), urea (0.1 g) was added, and the mixture was kept at 80 °C for 20 h. After dilution with water (50 ml), neutralisation with aqueous  $\text{NaHCO}_3$ , and extraction with chloroform, the reaction products were isolated by chromatography on silica gel.

*Preparation of Compounds (29) and (19).*—The appropriate amine (5 mmol) was added to compound (22) (0.5 mmol) in benzene (10 ml) and the solution was left at room temperature for 20 h. After evaporation of the solvent under reduced pressure the residue was purified by distillation.

*Preparation of Compounds (30) and (20).*—Compound (23) (0.43 mmol) was dissolved in benzene (10 ml) containing the appropriate amine (0.5 mmol) and the solution was left at room temperature for 24 h. After evaporation of the solvent under reduced pressure the residue was distilled.

*Oxidation of Compounds (12) and (28).*—Chromium trioxide (1 mmol) was added to the substrate (1 mmol) in acetic acid (10 ml) and the solution was left at room temperature for 48 h. After evaporation of the solvent under reduced pressure, the residue was dissolved in water and extracted with chloroform, and the extracts were dried

(Na<sub>2</sub>SO<sub>4</sub>) and evaporated under reduced pressure to give compound (15).

*Oxidation of Compounds* (11), (13), and (14).—These oxidations were performed in acetic acid under the conditions previously reported for oxidations of the substrates by CAN. After oxidation and treatment with urea-sulphuric acid the reaction products were isolated as usual.

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