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SELECTIVE DEMETHYLATION IN THE OXIDATION OF ARYLALKYLMETHYLAMINES WITH METAL ACETATES

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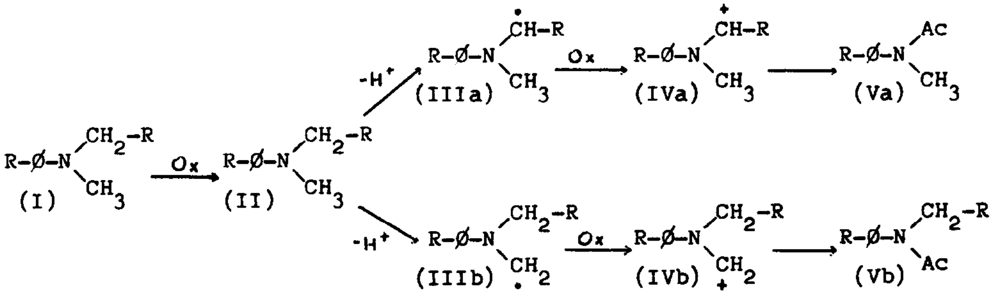
In a previous paper(1) we reported the oxidation of dimethylaniline, ethylmethylaniline and n-butylmethylaniline with lead tetraacetate (LTA), manganese triacetate (MTA), cobalt triacetate (CTA) and thallium triacetate (TTA) in chloroform-acetic anhydride 1:1 at room temperature under nitrogen atmosphere. The results obtained indicated a preference for demethylation over dealkylation. This fact was more apparent for the n-butyl derivative. Literature data referred to the anodic or Fe (III) oxidation of tertiary amines suggest that the product-determining step is the loss of a proton from the initial radical-ion (II) to give the radical (IIIa,b)(2,3)(Scheme 1). In methylalkylanilines the factors driving the reaction toward demethylation have been suggested to be of statistical origin or to derive from the major acidity of the $>N-CH_3$ protons toward the $>N-CH_2-R$ hydrogens of the substrates, based on the inductive effect(4,5). In all cases the initial electron-abstraction process was indicated to be the rate-determining step.

Scheme 1



Here we report the results obtained by oxidation of the amines (VI-XIV) with LTA, MTA, CTA and TTA (Table 1)(6).

Compounds (VI-VIII) and (XII-XIV) were prepared by alkylation of the corresponding arylmethylamines. Compounds (IX-XI) were prepared by treatment of 4-nitrofluorobenzene with the appropriate aliphatic secondary amine.

Some observations can be derived from the data reported in Table 1:

a) The preference for the demethylation reaction increases passing from ethylmethyl to n-butylmethyl derivatives.

b) The demethylation/dealkylation ratio is relatively unaffected by changing the para substituent at the aromatic nucleus (Electron donating substituents para to the aromatic nucleus had been indicated in one case(4) to increase the demethylation/dealkylation ratio).

c) The selectivity of the demethylation reaction by changing the metal oxidant follows the order MTA $>$ CTA $>$ LTA.

d) TTA is the least reactive oxidant. Its reactivity parallels that of the other oxidants, showing its ability to react via two successive monoelectronic steps

These observations seem to indicate that the selectivity of demethylation over dealkylation does not depend only on acidity or statistical factors. Neither the statistical factor nor acidity effects could account for the increase of selectivity when passing from ethylmethyl to n-butylmethyl derivatives. The acidity effect could be invoked in a concerted electron abstraction-proton loss mechanism. Kinetic data from the oxidation of dimethylaniline, (IX) and (XII) with LTA exclude this possibility(7). The increase of selectivity passing from LTA to MTA (i. e. following the decrease of the redox couple) suggests that product formation could be governed by the different oxidation rate of the radicals (IIIa or b) to the cations (IVa or b). The known stability and reactivity differences among alkyl radicals could account for a faster oxidation of (IIIb) over (IIIa). In this process the steric factor could play a role since the radical

Table 1

Substrate	Product	LTA	MTA	CTA	TTA
p-MeO-Ø-NMe$_2$	p-MeO-Ø-NMeAc	46%	55%	43%	39%
(VI)	p-MeO-Ø-NHAc	-	-	16%	-
p-MeO-Ø-NMeEt	p-MeO-Ø-NEtAc	48%	69%	41%	*
(VII)	p-MeO-Ø-NMeAc	9%	8%	4%	
p-MeO-Ø-NMeBu	p-MeO-Ø-NBuAc	32%	50%	40%	71%
(VIII)	p-MeO-Ø-NMeAc	3%	4%	4%	5%
p-NO$_2$-Ø-NMe$_2$	p-NO$_2$-Ø-NMeAc	32%	36%	40%	**
(IX)	p-NO$_2$-Ø-NHMe	-	25%	13%	
	p-NO$_2$-Ø-NHAc	-	-	19%	
p-NO$_2$-Ø-NMeEt	p-NO$_2$-Ø-NEtAc	33%	43%	***	**
(X)	p-NO$_2$-Ø-NMeAc	2%	5%		
	p-NO$_2$-Ø-NHEt	27%	-		
	p-NO$_2$-Ø-NHMe	3%	-		
p-NO$_2$-Ø-NMeBu	p-NO$_2$-Ø-NBuAc	59%	33%	***	**
(XI)	p-NO$_2$-Ø-NMeAc	7%	3%		
p-Cl-Ø-NMe$_2$	p-Cl-Ø-NMeAc	42%	72%	57%	45%
(XII)					
p-Cl-Ø-NMeEt	p-Cl-Ø-NEtAc	56%	67%	30%	23%
(XIII)	p-Cl-Ø-NMeAc	10%	12%	7%	6%
p-Cl-Ø-NMeBu	p-Cl-Ø-NBuAc	56%	53%	16%	38%
(XIV)	p-Cl-Ø-NMeAc	9%	3%	2%	5%

* The small amount of material recovered was constituted of a mixture of products.

** Quantitative recovery of the starting material.

*** The most part of the starting material was recovered. No definite reaction products could be isolated.

(IIIb) is more exposed to further attack than (IIIa). An eventual interconversion between radicals (IIIa and b) or cations (IVa and b) will be tested by isotopic labelling. The presence of double dealkylation products in some instances could be ascribed to a competition between acetylation and further dealkylation. The latter process has no precedents in the reaction of secondary amines with metal oxidants(8). Further work is in progress to show an eventual relation between the oxidative dealkylation effected by TTA and the possible aromatic thallation.

REFERENCES AND NOTES

1) B. Rindone and C. Scolastico, Tetrahedron Letters 3379, (1974).

2) M. Masui, H. Sayo and Y. Tsuda, J. Chem. Soc. (B), 973 (1968).

3) J. R. Lindsay Smith and L. A. V. Mead, J. Chem. Soc. (Perkin II), 206 (1973).

4) C. A. Audeh and J. R. Lindsay Smith, J. Chem. Soc. (B), 1741 (1971).

5) M. Masui and H. Sayo, J. Chem. Soc. (B), 1593 (1971).

6) The reaction yields were determined by quantitative NMR analysis of fractions obtained by silica-gel chromatography. 1 mole/mole of LTA and TTA and 2 moles/mole of MTA and CTA were used. Bu = n-Butyl.

7) Unpublished results.

8) R. Criegee, "Oxidations with lead tetraacetate" in K. B. Wiberg, "Oxidations in organic chemistry", Vol. 5A, Academic Press (1965).

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