Oxidation of Aromatic Anils with Lead Tetra-acetate

By **Bruno Rindone** * and **Carlo Scolastico,** Istituto di Chimica Organica dell'Università, Via Saldini 50, Milano, Italy

Aromatic anils are oxidised by lead tetra-acetate under mild conditions to the corresponding aldehydes, amines, and azo-derivatives. In some instances, nuclear acetoxylation products and *N*-acetylamines are also formed.

THE acetoxylation reaction of metal acetates is well known.[1] The oxidation of organic nitrogen compounds with lead tetra-acetate (LTA) [2] and the behaviour of azomethines towards this oxidant have been reviewed.[3]

The reactivity of aromatic anils toward LTA has been explored to some extent. When these compounds contain labile *ortho*-substituents such as NH_2 or OH in the *N*-aryl ring, oxidative cyclisation to benzimidazoles

[1] D. J. Rawlinson and G. Sosnovsky, *Synthesis*, 1973, 567.
[2] J. B. Aylward, *Quart. Rev.*, 1971, **25**, 407.

[3] R. N. Butler, F. L. Scott, and T. A. F. O'Mahony, *Chem. Rev.*, 1973, **73**, 93.

and benzoxazoles occurs.[4] The reaction of N-benzyl-idenebenzylamine with LTA has been discussed.[5] Triarylmethyl- and diphenylmethyl-amines are oxidised by LTA with rearrangement to give anils which are largely unaffected under the reaction conditions used.[6] We now report the behaviour of some aromatic anils toward LTA.[7]

The substrates (1)—(4) were oxidised with 1 mol. equiv. of LTA in benzene solution at room temperature. The corresponding aldehyde, aniline, and azobenzene were the products, except in the case of compound (4), which did not react. The Table summarises the yields obtained.

$RC_6H_4 \cdot CH = NPh$ 　(1) R = H 　　(3) R = p - Ph
　　　　　　　　　　　　(2) R = p - OMe 　(4) R = p - NO$_2$
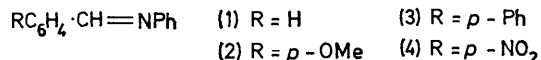
The oxidation of compounds (1) and (2) was inhibited by the presence of acrylamide which polymerised. In control experiments, neither the substrates nor LTA alone caused polymerisation of acrylamide under these conditions.

p-Methoxybenzaldehyde resulting from the oxidation of the 2,6-dideuterio-analogue of the 4'-methoxy-compound (2) retained the deuterium completely.

The reaction of compounds (1) and (2) with LTA in isopropylbenzene solution gave, together with the normal products, $\alpha\alpha\alpha'\alpha'$-tetramethylbibenzyl in 12 and 4% yield, respectively.

Oxidation of the N-biphenylyl compounds (5) and (6) in benzene with 1 mol. equiv. of LTA gave the results

$RC_6H_4 \cdot CH = N \cdot C_6H_4Ph-o$ 　(5) R = H
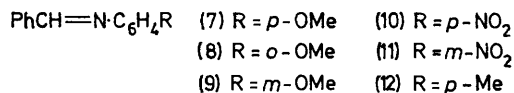　　　　　　　　　　　　　　　　　(6) R = p - OMe
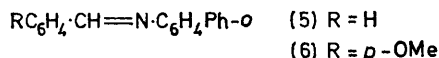
shown in the Table. Compound (6) also gave 1% of carbazole.

TABLE

Yields (mol %) of the products of oxidation of the anils (1)—(3), (5), and (6) by LTA

Substrate	Anil	Aldehyde	Azo-derivative	Amine
(1)	23	11	9	ca. 1
(2)	8	30	21	ca. 1
(3)	10	27	18	ca. 1
(5)	62	11	4	14
(6)	26	25	6	28

The anils (7)—(12), having a substituted N-aryl ring, were oxidised with 1.2 mol. equiv. of LTA in the hope

$PhCH = N \cdot C_6H_4R$ 　(7) R = p-OMe 　(10) R = p-NO$_2$
　　　　　　　　　　　(8) R = o-OMe 　(11) R = m-NO$_2$
　　　　　　　　　　　(9) R = m-OMe 　(12) R = p-Me

of obtaining higher yields. Compounds (10) and (11) were not attacked under these conditions. The reaction mixture from (7) consisted of benzaldehyde (43%), and two isomeric monoacetyl derivatives (32%). One

of the latter, separated by chromatography showed $\nu_{max.}$ 3 430 (OH) and 1 685 cm^{-1} (CO·NH). This and its analytical and n.m.r. data agreed with the formula (13). The second isomer showed $\nu_{max.}$ 1 735 cm^{-1} (ester) and its mass spectrum contained a molecular ion at the same m/e value as (13). Acetylation of the mixture of isomers gave the diacetate (15), which was also prepared by catalytic reduction of 2-nitro-5-methoxyphenol (16) followed by acetylation. Hence the second component of the isomer mixture had structure (14). Addition of acrylamide to the reaction mixture resulted in its polymerisation and inhibition of the oxidation. In isopropylbenzene solution, the normal products were accompanied by 7% of $\alpha\alpha\alpha'\alpha'$-tetramethylbibenzyl.
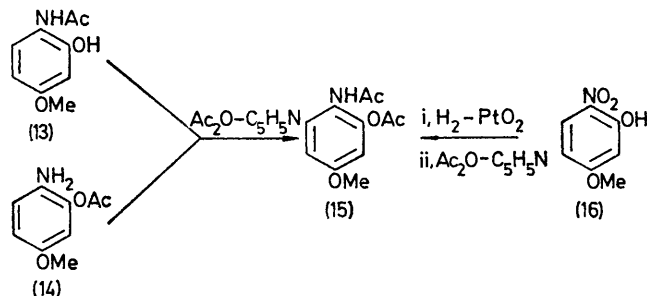
The reaction mixture from compound (8) contained five components: benzaldehyde (18%), 4-acetamido-3-methoxyphenyl acetate (17) (7%), 2-acetamido-3-methoxyphenol (18) (19%), the anil (19) (12%), and N-(2-methoxyphenyl)benzamide (20) (3%). Compounds (11)—(19) were identical with material prepared by independent syntheses. Catalytic reduction of 3-methoxy-4-nitrophenyl acetate gave the unstable amine, which was acetylated to give (17) or condensed with benzaldehyde to give (19). Catalytic reduction of 2-nitro-3-methoxyphenyl acetate gave (18) via transposition of the acetyl group [$\nu_{max.}$ 3 210 (OH) and 1 635 cm^{-1} (CO·NH)].
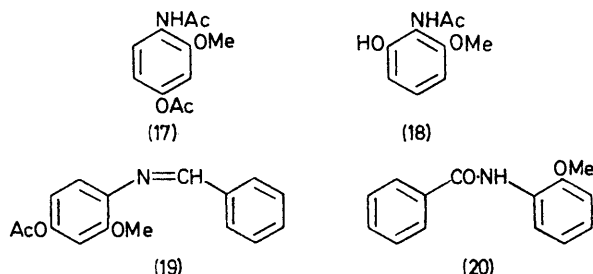
The reaction mixture from compound (9) contained benzaldehyde (16%), N-acetyl-m-anisidine (4%), 3,3'-dimethoxyazobenzene (14%), and starting material (62%).

The anil (12) gave a mixture of benzaldehyde (14%), N-acetyl-p-toluidine (14%), starting material (43%), and traces of 4,4'-dimethylazobenzene.

[4] F. F. Stevens and J. D. Bower, J. Chem. Soc., 1949, 2971; 1950, 1772; F. F. Stevens, Nature, 1949, 164, 342.
[5] A. Stojiljkovic, V. Andrejevic, and M. Mihailovic, Tetrahedron, 1967, 33, 721.
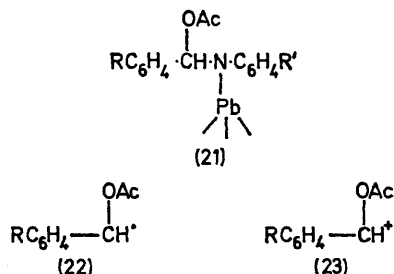
[6] A. J. Sisti, Chem. Comm., 1968, 1272.
[7] Preliminary reports, (a) B. Rindone, E. Santaniello, and C. Scolastico, Tetrahedron Letters, 1972, 19; (b) A. Catto, F Corbani, B. Rindone, and C. Scolastico, ibid., 1973, 2723.

Oxidation of an equimolecular mixture of (2) and (9) with 1 mol. equiv. of LTA in benzene gave a mixture of the products obtained from the individual substrates: benzaldehyde (9%), *p*-methoxybenzaldehyde (18%), azobenzene (4%), *N*-acetyl-*m*-anisidine (3%), 3,3'-dimethoxyazobenzene (8%), and starting materials (29%). In addition, 3-methoxyazobenzene (3%) and the anils (1) (12%) and *N*-4-methoxybenzylidene-*m*-anisidine (20%) were also present. These anils were also formed by equilibration of an equimolecular mixture of (2) and (9) in benzene.

That the nitro-derivatives (4), (10), and (11) are not oxidised by LTA suggests that the reaction is inhibited by electron-withdrawing substituents, implying an electrophilic attack of LTA on the substrates.

The retention of the deuterium atoms in the oxidation of *N*-(2,6-dideuterio-4-methoxybenzylidene)aniline rules out the possibility of an intermediate having a metal–*ortho*-carbon bond.[8]

The intermediate (21) derived from electrophilic attack of LTA on the anils could be cleaved *via* a homolytic or a heterolytic path, giving rise respectively to the radical (22) or the cation (23), which could be converted into the corresponding aldehydes by acetyl radical or acetyl cation loss. Moreover, acetyl radical loss from (22) could be concurrent with the oxidation

$$\underset{(21)}{RC_6H_4 \cdot \overset{\overset{\displaystyle OAc}{|}}{CH} \cdot N \cdot C_6H_4R'}$$
$$\underset{\diagup \,|\, \diagdown}{\overset{|}{Pb}}$$

$$\underset{(22)}{RC_6H_4 \overset{\overset{\displaystyle OAc}{|}}{—CH^\bullet}} \qquad \underset{(23)}{RC_6H_4 \overset{\overset{\displaystyle OAc}{|}}{—CH^+}}$$

(22) ⟶ (23) effected by LTA itself. The *gem*-diacetates which might be expected to be formed from (23) were not detected. A control experiment indicated that they are stable under the reaction conditions. This and the polymerisation and inhibition effects observed when acrylamide was added supported the occurrence of homolytic rupture of (21) to yield (22).

The nitrogenous reaction products were azo-derivatives, amines, *N*-acetyl amines, and their nuclear acetoxylation products. This, together with the production of tetramethylbibenzyl in isopropylbenzene solution and of carbazole in the oxidation of compound (6), suggested the intervention of an arylnitrenoid species as inter-

mediate. Nitrene-forming photolysis or thermal decomposition of aryl azides is known to yield anilines and azo-derivatives.[9] Carbazole has been found as a product of pyrolytic or photolytic cleavage of *o*-biphenylyl azide[10] and of photolysis of a quinone imine *N*-oxide,[11] and was suggested to be derived from an intramolecular insertion reaction effected by *o*-biphenylylnitrene. The deoxygenation of nitrobiphenyls in isopropylbenzene solution has been shown to give quantities of tetramethylbibenzyl[12] *via* hydrogen abstraction from the solvent effected by the intermediate nitrene. In our case, the arylnitrenoid could be constituted from a species containing a metal–nitrene bond.[13] Such structures have been suggested for intermediates in the photolysis or pyrolysis of ferrocenyl azide[14] and in the reduction of azobenzene derivatives by transition metal oxalates.[15]

The substrates having an *o*- or *p*-methoxy-group in the *N*-aryl ring gave also anilines bearing an acetoxy-group at the *ortho*- or *para*-position relative to the amino-group. Here, the 1:1 ratio between (17) + (19) and (18) (*i.e.* equimolecular *ortho* and *para* attack) indicates a radical mechanism, ruling out the possibility of nucleophilic attack such as that noted in the photolysis of aryl azides in the presence of dimethylamine,[16] or of a rearrangement such as that reported when this reaction was performed in acetic anhydride solution[17] (only the *ortho*-isomer was obtained). The radical acetoxylation could occur at the nitrenoid stage. Direct acetoxylation of the substrate anils takes place only in LTA oxidations at reflux temperature.[18]

EXPERIMENTAL

N.m.r. spectra were recorded for solutions in CDCl₃ unless otherwise specified, with a Perkin-Elmer R10 instrument (Me₄Si as internal reference). I.r. spectra were measured for Nujol mulls with a Perkin-Elmer 257 spectrophotometer. U.v. spectra were measured with a Perkin-Elmer 130 spectrophotometer. Analytical g.l.c. was performed with a Varian 1740 gas chromatograph equipped with a glass column (6 ft × 0.3 in) packed with 3% silicone SE30 on Chromosorb W (oven temp. 70—220 °C, injection temp. 200 °C, flame ionisation detector temp. 200 °C, carrier gas N₂ at 26 ml min⁻¹), with anthracene as internal standard. Product yields were determined by tracing the curves on paper and cutting out and weighing the paper. Mass spectra were obtained with an LKB 9000 (70 eV) g.l.c.-linked instrument. M.p.s were obtained with a Büchi apparatus.

Oxidation of Substrates.—To a 0.05M-solution of the substrate in anhydrous benzene the appropriate amount of LTA free from acetic acid was added, and the resulting suspension was stirred at room temperature until the oxidant had disappeared. After removal of lead diacetate by

[8] I. Jardine and F. J. McQuillin, *Tetrahedron Letters*, 1972, 459.

[9] (*a*) P. A. Smith, in 'Nitrenes,' ed. W. Lwowski, Interscience, New York, 1970, p. 99; (*b*) R. A. Abramovitch in 'Organic Reactive Intermediates,' ed. S. P. McManus, Academic Press, New York, 1973, p. 127.

[10] (*a*) J. S. Swenton, *Tetrahedron Letters*, 1968, 3421; (*b*) P. A. S. Smith and J. H. Hall, *J. Amer. Chem. Soc.*, 1962, **84**, 480; (*c*) A. Reiser, G. Bowes, and R. J. Horne, *Trans. Faraday Soc.*, 1966, **62**, 3162.

[11] A. R. Forrester, M. M. Ogilvy, and R. H. Thompson, *J.C.S. Chem. Comm.*, 1973, 483.

[12] J. I. G. Cadogan and M. J. Todd, *Chem. Comm.*, 1967, 178.

[13] Ref. 13*b*, p. 150.

[14] R. A. Abramovitch, C. I. Azogu, and R. G. Sutherland, *Chem. Comm.*, 1971, 134.

[15] R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, 1964, **64**, 149; *J. Chem. Soc.* (*C*), 1968, 119.

[16] R. A. Odum and A. M. Aaronson, *J. Amer. Chem. Soc.*, 1969, **91**, 5680.

[17] R. K. Smalley and H. Suschitzky, *J. Chem. Soc.*, 1963, 5571.

[18] Unpublished results.

filtration, the reaction mixtures were analysed by g.l.c.–mass spectrometry, by quantitative g.l.c., and by quantitative n.m.r. The azo-derivatives were also detected by filtering 50 mg of reaction mixture dissolved in n-hexane–chloroform (4 : 1; 5 ml) over silica gel (3 g; Merck 0.05—0.2 mm). Elution with 35 ml of the same solvent mixture gave the pure azo-derivatives, which were estimated quantitatively by visible spectroscopy.

The crude reaction mixture from compound (7) (1 g) was chromatographed on silica gel (Merck 0.05—0.2 mm; 30 g) with chloroform (150 ml) and chloroform–ethyl acetate (4 : 1; 50 ml fractions) as eluants. Fractions 9—12 contained N-(2-*hydroxy*-4-*methoxyphenyl*)*acetamide* (13), m.p. 156—160° (from chloroform); δ (C_5D_5N) 2.19 (3 H, s, NAc), 3.63 (3 H, s, OMe), 4.69 and 6.62 (1 H, dd, J 9 and 2.5 Hz, aromatic H), 6.86 (1 H, d, J 2.5 Hz, aromatic H), and 7.93 (1 H, d, J 9 Hz, aromatic H) (Found: C, 59.4; H, 6.1; N, 7.65. $C_9H_{11}NO_3$ requires C, 59.65; H, 6.1; N, 7.75%). Fractions 13—15 contained a mixture of compounds (13) and (14) (0.078 g). This was dissolved in pyridine (0.05 ml) and acetic anhydride (1 ml) and left overnight at room temperature. Evaporation, and crystallisation from heptane–benzene gave 2-*acetamido*-5-*methoxyphenyl acetate* (15) (0.087 g), m.p. 114—117°, $\nu_{max.}$ 1 740 and 1 690 cm^{-1} (Found: C, 59.05; H, 5.7; N, 6.0. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.85; N, 6.3%).

2-*Acetamido*-5-*methoxyphenyl Acetate* (15).—A solution of the nitrophenol (16) (1 g) in acetic acid (20 ml) was hydrogenated at ambient pressure and temperature over platinum oxide (50 mg). After the uptake of 3 mol. equiv. of hydrogen the suspension was filtered and evaporated to dryness. The residue was immediately dissolved in pyridine (2 ml) and acetic anhydride (5 ml) and left overnight. Evaporation, and crystallisation from heptane–benzene gave compound (15) (0.765 g, 58%), identical with the sample obtained from the oxidation products of (8).

4-*Acetamido*-3-*methoxyphenyl Acetate* (17) *and its* 4-*Benzylideneamino-analogue* (19).—A solution of 3-methoxy-4-nitrophenol (0.8 g) in pyridine (2 ml) and acetic anhydride (5 ml) was left overnight at room temperature. The *acetate* obtained after evaporation and crystallisation from heptane–benzene had m.p. 82—84 °C (Found: C, 50.9; H, 4.4;

N, 6.55. $C_9H_9NO_5$ requires C, 51.2; H, 4.3; N, 6.65%)· A solution of the acetate (0.5 g) in acetic acid (10 ml) was hydrogenated at ambient pressure and temperature over platinum oxide (25 mg). After the uptake of 3 mol. equiv. of hydrogen the suspension was filtered and evaporated to dryness. The amine thus obtained (0.128 g) was dissolved in pyridine (1 ml) and acetic anhydride (2 ml) and left overnight. Evaporation, and crystallisation from heptane–benzene gave the *amide* (17) (0.102 g, 65%), m.p. 173—176° (Found: C, 59.5; H, 5.65; N, 6.1. $C_{11}H_{13}NO_4$ requires C, 59.2; H, 5.85%; N, 6.3%). To the amine (0.437 g) in anhydrous benzene (10 ml) were added benzaldehyde (0.25 ml) and Linde 4 Å molecular sieves (2 g), and the mixture was stirred for 1 day at room temperature. Filtration, evaporation, and distillation of the residue at 130 °C and 10^{-5} mmHg yielded the *imine* (19) (0.280 g, 43%) (Found: C, 71.1; H, 5.9; N, 4.9. $C_{16}H_{15}NO_3$ requires C, 71.35; H, 5.6; N, 5.2%).

N-(2-*Hydroxy*-6-*methoxyphenyl*)*acetamide* (18).—A solution of 3-methoxy-2-nitrophenol (0.2 g) in pyridine (0.2 ml) and acetic anhydride (0.5 ml) was left overnight, then evaporated to dryness and the residue was distilled at 130 °C and 3 mmHg. The acetate thus obtained (0.157 g, 63%), dissolved in acetic acid (5 ml), was hydrogenated at ambient pressure and temperature over platinum oxide (5 mg). After the uptake of 3 mol. equiv. of hydrogen the suspension was filtered and evaporated and the residue was chromatographed on silica gel (16 g; Merck 0.05—0.2 mm; 50 ml fractions) with chloroform (fractions 1—6) and chloroform–ethyl acetate (9 : 1; fractions 7—10) as eluants. Fractions 6—9 contained the *amide* (18) (0.030 g, 22%), m.p. 89—90° (from heptane–benzene) (Found: C, 59.95; H, 6.4; N, 7.85. $C_9H_{11}NO_3$ requires C, 59.6; H, 6.1; N, 7.75%).

N-(2,6-*Dideuterio*-4-*methoxybenzylidene*)*aniline*.— 2,6-Dideuterio-4-methoxybenzonitrile, prepared [19] from *p*-anisidine, was converted into the aldehyde by reduction with nickel alloy and 75% formic acid.[20] The aldehyde was then condensed with aniline under the usual conditions.

[4/1867 *Received, 11th September*, 1974]

[19] F. Langenbucher, R. Mecke, and E. D. Schmid, *Annalen*, 1963, **669**, 11.
[20] T. Van Es and B. Staskun, *J. Chem. Soc.*, 1965, 5775.