Organic Oxidation Processes. Part III. The Reaction of Lead Tetra-acetate with Some Phenyl Ethers.*

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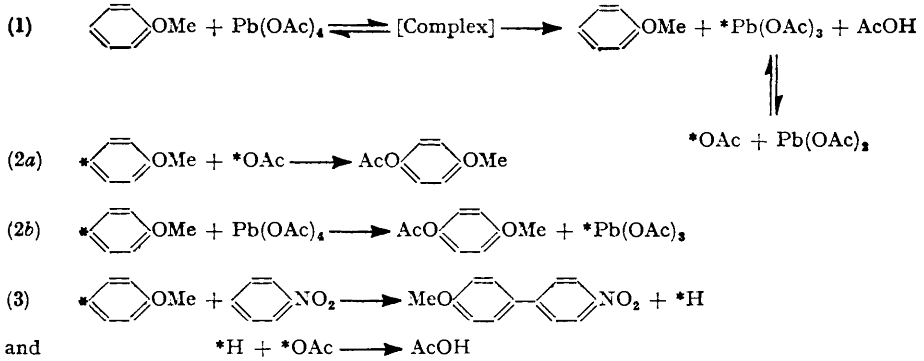
The *p*-acetoxylation of anisole and of related phenyl ethers by lead tetra-acetate is described. The mechanism of the reaction is discussed, especially with reference to solvent effects.

Alkylphenols are readily oxidised by lead tetra-acetate in acetic acid or benzene at room temperature (Part I, *J.*, 1954, 2785), but phenol derivatives such as anisole or benzyl phenyl ether not at all. At 80°, benzyl phenyl ether yields *p*-acetoxyphenyl benzyl ether together with the expected product of oxidation at the α-methylene group (Barron, Cavill, Cole, Gilham, and Solomon, *Chem. and Ind.*, 1954, 76).

The *p*-acetoxylation of phenyl ethers, and related reactions, are now reported in detail. Anisole, phenetole, and phenyl *iso*propyl ether with lead tetra-acetate in acetic acid at 80° give the *p*-acetoxy-ethers: the yields are small, unchanged ether is recovered, and no attack on the alkyl group is observed. Anisole yields as additional products 4-methoxydiphenyl in benzene, 4-methoxy-4'-nitrodiphenyl in nitrobenzene, and 4 : 4'-dimethoxydiphenyl in excess of anisole, which, since they result from an attack on the solvent, indicate a free-radical mechanism.

We suggest a primary dehydrogenation by lead tetra-acetate to give *p*-methoxyphenyl and acetate radicals with acetic acid and lead acetate. Subsequent reactions are as in (2*a* and *b*). Kharasch, Friedlander, and Urry (*J. Org. Chem.*, 1951, **16**, 533) proposed a similar mechanism for the initial breakdown of lead tetra-acetate in di*iso*propyl ether. Reaction with the solvent is exemplified for nitrobenzene in (3); other isomers may have been formed but were not identified. The 4 : 4'-dimethoxydiphenyl formed in absence of added solvent may result from attack on anisole by the *p*-methoxyphenyl radical (3) or from dimerisation of the radical.



No chlorinated anisole derivative was detected on oxidation in carbon tetrachloride, which gave *p*-acetoxyanisole and *p*-methoxyphenyl *p*-anisoate. That no attack on the solvent occurs indicates that the *p*-methoxyphenyl is less reactive than the phenyl radical [cf. Kharasch, Kane, and Brown's observations (*J. Amer. Chem. Soc.*, 1942, **64**, 1621) on the relative reactivity of free radicals]. The formation of the *p*-anisoate, although indicative of the *p*-methoxyphenyl radical in solution, is unexpected and the mechanism is not yet understood.

Wessely, Kotlan, and Metlisics (*Monatsh.*, 1954, **85**, 69) showed that methyl α-naphthyl ether is oxidised to the 4-acetoxy-1-naphthyl methyl ether with lead tetra-acetate in acetic acid at room temperature, and suggest that primary attack of an acetate radical (from

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* Part II, *J.*, 1954, 3943.

lead tetra-acetate at room temperature) yields the 4-methoxy-1-naphthyl radical and acetic acid; 4-acetoxy-1-naphthyl methyl ether then results from a combination of the naphthyl and acetate radicals. 4 : 4'-Dimethoxydi-1-naphthyl was also isolated. As we have treated anisole with acetyl peroxide in acetic acid–ether to 80° without apparent oxidation we believe that the acetate radical is not responsible for the primary dehydrogenation of phenyl ethers.

As noted in our preliminary communication (*loc. cit.*, p. 76) two competitive reactions occur with benzyl phenyl ether, *viz.*, *p*-acetoxylation and attack at the α-methylene group. The nuclear substitution is analogous to that in anisole. Attack at the α-methylene group yields α-phenoxybenzyl acetate, identified by hydrolysis in alkali to benzaldehyde and phenol. The yield in this reaction is small compared with that of benzyl acetate from toluene (cf. Part II, *loc. cit.*), and it is of further significance that benzyl *p*-tolyl ether is oxidised to *p*-benzyloxybenzyl acetate (isolated as the alcohol) in high yield, no attack at the α-methylene group being observed.

In conclusion we emphasise that the primary process in the oxidation of phenyl ethers is an attack by the lead tetra-acetate which results in the dehydrogenation of the substrate. The final products isolated are determined by interactions of the intermediate radicals and/or by their reaction with oxidant, substrate, and solvent.

The acetoxylation of phenyl ethers contrasts with Fieser, Clapp, and Daudt's methylations of benzenoid compounds (*J. Amer. Chem. Soc.*, 1942, **64**, 2052). They reported that benzene was converted into benzyl acetate, nitrobenzene into *o*- and *p*-nitrotoluene, and chlorobenzene into a mixture of chlorobenzyl acetates, the *para*-isomer being identified. [Their isolation of nitrotoluenes and not nitrobenzyl acetates is explicable, for the nitro-group strongly deactivates the toluene towards further oxidation (cf. Part II, *loc. cit.*).] Thus nuclear acetoxylation by lead tetra-acetate occurs in benzenoid compounds containing a powerful electron-donating substituent but methylation, by methyl radicals from decomposition of lead tetra-acetate, is favoured in compounds having electron-attracting substituents. Acetoxylation of the side-chain may be the preferred reaction of lead tetra-acetate with an alkylbenzene.

EXPERIMENTAL

Oxidation of Anisole with Lead Tetra-acetate.—(*a*) Anisole (32·4 g.; freshly distilled over sodium) with lead tetra-acetate (133 g.) in " AnalaR " acetic acid (120 ml.) was heated at 80° (oil-bath) until no positive test (starch–iodide) for the oxidant was obtained (40 hr.). Acetic acid was distilled off under reduced pressure, and the residue was then extracted with ether (6 × 50 ml.), lead acetate remaining. The ethereal solution, washed with water, sodium hydrogen carbonate solution, water, and then dried ($MgSO_4$) and evaporated, gave a viscous yellow oil, which, under reduced pressure, yielded unchanged anisole, n_D^{20} 1·5171, and *p*-acetoxyanisole (7·0 g., crude), b. p. 96°/3 mm., colourless needles, m. p. 32°, from light petroleum (b. p. 40—60°) (Found: C, 65·4; H, 6·1. Calc. for $C_9H_{10}O_3$: C, 65·1; H, 6·1%). Klemenc (*Monatsh.*, 1914, **35**, 85) records m. p. 31—32°. No formaldehyde was detected.

(*b*) Anisole (7·0 g.) with lead tetra-acetate (28·8 g.) in acetic acid (40 ml.) was heated at 80° (111 hr.). The mixture, hydrolysed with excess of aqueous sodium hydroxide, was then steam-distilled to yield anisole (5·0 g., n_D^{20} 1·5180), recovered by extraction with ether. Similar extraction of the residual solution, after acidification, gave *p*-hydroxyanisole (1·2 g.), obtained as colourless needles, m. p. and mixed m. p. 50—51°, from water.

(*c*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in benzene (120 ml.; freshly distilled over sodium) was heated at 80° (90 hr.). The mixture, worked up as in (*a*), gave unchanged anisole, n_D^{20} 1·5176, *p*-acetoxyanisole (3·0 g., crude), and a semisolid residue (0·5 g.). On re-distillation, the *p*-acetoxyanisole was obtained as an almost colourless oil, b. p. 94°/3 mm. (Found: C, 65·2; H, 6·2%). The semisolid residue, after chromatography on alumina from light petroleum, yielded 4-methoxydiphenyl (0·1 g.), colourless needles, m. p. 88—89° (from aqueous ethanol) (Found: C, 84·4; H, 6·6. Calc. for $C_{13}H_{12}O$: C, 84·8; H, 6·6%). Werner (*Annalen*, 1902, **322**, 135) records m. p. 90°. Further elution with benzene gave an unidentified oil (0·4 g.).

(*d*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in " AnalaR " nitrobenzene (120 ml.) was heated at 80° as above (83 hr.). The product, worked up as in (*a*), gave a mixture of anisole, nitrobenzene, and *p*-acetoxyanisole, b. p. to 120°/1 mm., and a small residue which was chromatographed on alumina from light petroleum to yield 4-methoxy-4′-nitrodiphenyl (0·2 g.), yellow needles (from light petroleum–benzene), m. p. 109—110° (Found: C, 68·3; H, 4·95; N, 6·2. Calc. for $C_{13}H_{11}O_3N$: C, 68·1; H, 4·8; N, 6·1%). Bell and Kenyon (*J.*, 1926, 3044) record m. p. 111°. An amber-coloured oil (0·2 g.) was eluted with benzene. The presence of *p*-acetoxyanisole (2·0 g., estimated by sap. val.) was indicated by the isolation of *p*-hydroxyanisole (1·2 g.), m. p. and mixed m. p. 50—51°, on hydrolysis of the original mixture.

(*e*) Anisole (32·4 g.) with lead tetra-acetate (133 g.) in carbon tetrachloride (120 ml.; freshly distilled) was heated at 80° (100 hr.). The mixture, extracted as in (*a*), yielded anisole, *p*-acetoxyanisole (1·0 g., crude), b. p. 80—84°/1 mm., and a semisolid residue (0·5 g.). Hydrolysis of the *p*-acetoxyanisole gave *p*-hydroxyanisole (0·5 g.), m. p. and mixed m. p. 52°. The residue was chromatographed on alumina, elution with light petroleum–benzene (1 : 1) giving a compound (0·4 g.), forming colourless prisms, m. p. 123°, from ethanol [Found: C, 70·3, 69·3; H, 5·8, 5·3; Ac, 2·2%; *M* (Rast), 254. Calc. for $C_{15}H_{14}O_4$: C, 69·8; H, 5·5%, *M*, 258]; the mixed m. p. with *p*-methoxyphenyl *p*-anisoate was 123—124°.

(*f*) Anisole (150 g.) and lead tetra-acetate (133 g.) were heated at 80° for 70 hr. The mixture, after removal of excess of anisole, n_D^{20} 1·5176, gave *p*-acetoxyanisole (3·0 g., crude), b. p. 78—80°/1 mm., and 4 : 4′-dimethoxydiphenyl (2·3 g.), b. p. 134°/1 mm. A residue (0·3 g.) was not distilled. *p*-Acetoxyanisole was finally obtained as colourless needles (2·3 g.), m. p. 32°, from light petroleum (Found: C, 65·2; H, 6·1%). The 4 : 4′-dimethoxydiphenyl formed colourless needles, m. p. and mixed m. p. 174°, from alcohol after sublimation under reduced pressure (Found: C, 78·3; H, 6·8. Calc. for $C_{14}H_{14}O_2$: C, 78·5; H, 6·6%).

p-*Methoxyphenyl* p-*Methoxyphenylacetate and* p-*Anisate.*—*p*-Methoxyphenylacetyl chloride (6·0 g.) (Cain, Simonsen, and Smith, *J.*, 1913, **103**, 1035) was added to sodium *p*-methoxyphenoxide [from sodium (0·8 g.) and *p*-hydroxyanisole (4·1 g.)] in toluene (20 ml.), and the mixture heated at reflux for 15 min. After working up in the usual manner, p-*methoxyphenyl* p-*methoxyphenylacetate* was obtained as colourless plates (6·5 g.), m. p. 74—74·5°, from ethanol (Found: C, 70·3; H, 5·7. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

Similarly, *p*-anisoyl chloride (5·0 g.) and sodium *p*-methoxyphenoxide gave p-*methoxyphenyl* p-*anisate* (8·0 g.), colourless prisms, m. p. 123—124°, from ethanol (Found: C, 69·5; H, 5·5. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%).

Attempted Oxidation of Anisole with Acetyl Peroxide.—Anisole (16·2 g.) in acetic acid (60 ml.) was added to acetyl peroxide (18·0 g.) (Gambarjan, *Ber.*, 1909, **42**, 4003) in ether (300 ml.). The ether was distilled off and the temperature of the mixture slowly raised to 80°. No positive test for the oxidant was obtained after 1 hr. The mixture was then hydrolysed with aqueous sodium hydroxide. Steam-distillation, followed by extraction of the distillate with ether, gave unchanged anisole (16·0 g.), b. p. 154—155°, n_D^{20} 1·5176. A sweet-smelling oil (1·0 g.), presumably resulting from oxidation of the solvent, was isolated from the acidified residue, but no phenolic products. Acetaldehyde, also from oxidation of the solvent, was isolated as the 2 : 4-dinitrophenylhydrazone (1·0 g.), m. p. and mixed m. p. 147° (Found: N, 24·9. Calc. for $C_8H_8O_4N_4$: N, 25·0%).

Oxidation of Phenetole and Phenyl iso*Propyl Ether with Lead Tetra-acetate.*—(*a*) Phenetole (36·6 g.; freshly distilled over sodium) with lead tetra-acetate (133 g.) in acetic acid (120 ml.) was heated at 80° for 40 hr. Working up as for anisole (*a*) gave unchanged phenetole, n_D^{16} 1·5080, then p-*acetoxyphenetole* (3·0 g., crude), b. p. 100°/4 mm., colourless plates (1·5 g.), m. p. and mixed m. p. 54° (from light petroleum) (Found: C, 66·5; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

p-Hydroxyphenetole (1·4 g.) with acetic anhydride–pyridine gave *p*-acetoxyphenetole (1·4 g.) as colourless plates, m. p. 54° (from light petroleum) (Found: C, 66·8; H, 6·8%).

(*b*) Similarly phenyl *iso*propyl ether (10·8 g.) with lead tetra-acetate (35 g.) in acetic acid (30 ml.) gave unchanged ether, n_D^{16} 1·4990, and p-*acetoxyphenyl* iso*propyl ether* (1·3 g.), b. p. 120°/3 mm. (Found: C, 68·2; H, 7·1. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·3%). No acetone was detected during the oxidation or the working-up.

Oxidation of Benzyl Phenyl Ether with Lead Tetra-acetate.—(*a*) Benzyl phenyl ether (14·8 g.) with lead tetra-acetate (37·6 g.) in acetic acid (80 ml.) was heated at 80° for 16 hr. Working up as for anisole (*a*) gave a yellow semisolid material, which by chromatography on alumina with light petroleum yielded unchanged benzyl ether (9·3 g.), m. p. and mixed m. p. 39—40°, and then p-*acetoxyphenyl benzyl ether* (0·8 g.), colourless plates, m. p. and mixed m. p. 110—111° (from aqueous ethanol) (Found: C, 74·2; H, 5·7. $C_{15}H_{14}O_3$ requires C, 74·4; H, 5·8%).

Quinol monobenzyl ether (0·3 g.; m. p. 122°) (Schiff and Pellizzari, *Annalen*, 1883, **221**,

370) with acetic anhydride–pyridine gave *p*-acetoxyphenyl benzyl ether (0·2 g.), colourless plates, m. p. 111° (from benzene–light petroleum) (Found : C, 74·5; H, 5·6%).

(*b*) Benzyl phenyl ether (14·8 g.) with lead tetra-acetate (37·6 g.) was oxidised as in (*a*) but for 12 hr. Excess of acetic acid was removed and the ether-soluble residue hydrolysed with aqueous sodium hydroxide. Steam-distillation of the alkaline solution gave benzaldehyde, isolated as the 2 : 4-dinitrophenylhydrazone (1·0 g., corresponding to 4·4% of α-phenoxybenzyl acetate), m. p. and mixed m. p. 238° (Found : N, 19·6. Calc. for $C_{13}H_{10}O_4N_4$: N, 19·6%). The acidified solution was extracted with ether, and the product, after removal of solvent, was chromatographed on alumina with light petroleum, giving unchanged benzyl phenyl ether (8·5 g.), m. p. and mixed m. p. 39—40°. Elution with chloroform yielded quinol monobenzyl ether (1·1 g.) as almost colourless plates, m. p. and mixed m. p. 121—122° (from water). In a further experiment phenol (from α-phenoxybenzyl acetate) was identified as 2 : 4 : 6-tribromophenol, colourless prisms, m. p. 93—94° (from aqueous methanol).

Oxidation of Benzyl p-*Tolyl Ether with Lead Tetra-acetate.*—Benzyl *p*-tolyl ether (7·0 g.; m. p. 41°) (Staedel, *ibid.*, 1883, **217**, 40) with lead tetra-acetate (15·9 g.) in acetic acid (40 ml.) was heated at 80° for 6 hr. The product (6·4 g.), worked up as above, was chromatographed on alumina. Elution with benzene–light petroleum (1 : 1) gave unchanged benzyl *p*-tolyl ether (3·4 g.), m. p. and mixed m. p. 40—41°, then chloroform yielded p-*benzyloxybenzyl alcohol* (2·8 g.), colourless plates, m. p. 88—89° (from ethyl acetate–light petroleum) (Found : C, 78·5; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·6%). Hydrogenation (Raney nickel) of this compound gave a quantitative yield of *p*-hydroxybenzyl alcohol, recrystallised as colourless needles, m. p. 110°, from water (Found : C, 67·7; H, 6·4. Calc. for $C_7H_8O_2$: C, 67·7; H, 6·5%). Auwers and Daecke (*Ber.*, 1899, **32**, 3373) record m. p. 124·5—125·5°; Sugimoto (*Reports Osaka Ind. Research Inst.*, 1929, **10**, No. 10; *Chem. Abs.*, 1930, **24**, 837) gives m. p. 110°.

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