Organic Oxidation Processes. Part IV.* The Reaction of Lead Tetra-acetate with Some Carbonyl Compounds.

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Lead tetra-acetate readily effects the α-acetoxylation of simple ketones and of β-dicarbonyl systems (cf. Dimroth and Schweizer, *Ber.*, 1923, **56**, 1375). The process involves a primary attack by lead tetra-acetate on the enolic form of the carbonyl compound, and the products isolated are then determined by the further reactions of the intermediate carbonyl radical.

SIMPLE ketones, *e.g.*, acetone and acetophenone, readily form the corresponding acyloin acetate on treatment with lead tetra-acetate in hot acetic acid (Dimroth and Schweizer, *Ber.*, 1923, **56**, 1375). This process has not been used generally for the synthesis of acyloins (cf. McElvain, " Organic Reactions," Vol. IV, Wiley and Sons, New York, 1948, p. 256) although it has been used, with advantage, in the preparation of mixed benzoins from the corresponding deoxybenzoin (Badcock, Cavill, Robertson, and Whalley, *J.*, 1950, 2961). As the present investigation is primarily concerned with the mechanism of such oxidations, simple carbonyl compounds, including some previously reported by Dimroth and Schweizer (*loc. cit.*), have been studied.

*cyclo*Hexanone is oxidised in acetic acid at 80° (no reaction at room temperature) to form 2-acetoxy*cyclo*hexanone, whilst *cis*-2 : 6-diacetoxy*cyclo*hexanone is obtained as an additional product in benzene solution or in excess of substrate. The structure and configuration of this compound are confirmed by its catalytic reduction and acid hydrolysis to *cis-cyclo*hexane-1 : 2 : 3-triol (Posternak and Ravenna, *Helv. Chim. Acta*, 1947, **30**, 441). In benzene, at 80°, acetophenone and ethyl malonate yield the α-acetoxy-derivatives as the sole oxidation products, whereas diethyl ketone gives a mixture of 1-acetoxy- and 1 : 1'-diacetoxy-diethyl ketone (cf. Dimroth and Schweizer's reactions in acetic acid). The 1-acetoxy-ketone is readily converted into the osazone; the structure of the diacetoxy-ketone is confirmed by its reduction and acetylation to a pentane-2 : 3 : 4-triol acetate (Reif, *Ber.*, 1908, **41**, 2739). Since 2-acetoxy*cyclo*hexanone is further oxidised, it appears that diacetoxy-compounds result from an attack by lead tetra-acetate at a second active centre in the monoacetoxy-derivative; disubstitution at the same carbon atom has not been noted. Although oxidation is slower in benzene than in acetic acid, the yields of acetoxylated products are considerably greater.

Ichikawa and Yamaguchi (*J. Chem. Soc. Japan*, 1952, **73**, 415), who studied the kinetics of the reactions between lead tetra-acetate and acetone, and acetophenone and its *p*-chloro- and *p*-bromo-derivatives in acetic acid, note that the process is of first order with respect to the ketone and independent of the oxidant. In benzene–acetic acid the rate is proportional to $[\text{AcOH}]^{\frac{1}{2}}$. These results indicate that enolisation of the ketone is the rate-determining step. Similarly, ketones are attacked by other oxidants (*e.g.*, potassium permanganate, Drummond and Waters, *J.*, 1955, 497) *via* the enolic form.

The ease of oxidation of β-diketones and β-oxo-esters supports the above hypothesis. In addition, the dimeric products isolated from these oxidations indicate a free-radical

mechanism. Thus ethyl acetoacetate, in benzene at 10°, readily gives ethyl α-acetoxy-acetoacetate and ethyl αα'-diacetylsuccinate, m. p. 91—91·5° (cf. Dimroth and Schweizer, *loc. cit.*, who obtained the α-acetoxy-derivative and an unidentified compound, m. p. 95—101°). Similarly, oxidation of acetylacetone yields 3-acetoxypentane-2 : 4-dione and 3 : 4-diacetylhexane-2 : 5-dione.

Comparative studies with acetyl peroxide show that acetylacetone and acetophenone are not oxidised in benzene at room temperature, thereby demonstrating stability to acetate radicals. However, at 80°, acetylacetone yielded 3 : 4-diacetylhexane-2 : 5-dione, and acetophenone gave an unidentified oil. Kharasch, McBay, and Urry (*J. Amer. Chem. Soc.*, 1948, **70**, 1269) who had previously obtained dimeric products from the attack of acetyl peroxide at 130° on acetylacetone and *cyclo*hexanone and were unable to identify the products of oxidation of acetophenone, suggest that methyl radicals (from the thermal decomposition of acetyl peroxide) are responsible for these dehydrogenations. Such processes would involve an initial abstraction of hydrogen from the active methylene group of the ketonic form of the carbonyl compound.

The oxidation of carbonyl compounds by lead tetra-acetate, although free-radical in nature, clearly differs from the above processes, and the following mechanism is proposed :

$$R\cdot CH_2\cdot COR' \rightleftharpoons R\cdot CH{:}CR'\cdot OH \text{ (rate-determining)}$$

Initiation : $R\cdot CH{:}CR'\cdot OH + Pb(OAc)_4 \longrightarrow$ Complex

$$R\cdot CH{:}CR'\cdot O\cdot + \cdot Pb(OAc)_3 + AcOH$$

$$R\cdot \overset{\cdot}{C}H\cdot CO\cdot R' \qquad \cdot OAc + Pb(OAc)_2$$

Propagation : $R\cdot \overset{\cdot}{C}H\cdot CO\cdot R' + Pb(OAc)_4 \longrightarrow AcO\cdot CHR\cdot CO\cdot R' + \cdot Pb(OAc)_3$

Termination : (i) $R\cdot \overset{\cdot}{C}H\cdot CO\cdot R' + \cdot OAc \longrightarrow AcO\cdot CHR\cdot CO\cdot R'$

(ii) $2R\cdot \overset{\cdot}{C}H\cdot COR' \longrightarrow (R'\cdot CO\cdot CHR\cdot)_2$

The failure to isolate dimeric products from the oxidation when the percentage of enol is very small is not inconsistent with the proposed mechanism, as termination (i) takes charge. The lead tetra-acetate, which is always in excess, would readily effect the transformation of the carbonyl radicals available into the corresponding acetoxy-derivative. However, dimeric products are isolated [termination (ii)] from the oxidation of β-dicarbonyl systems in which the percentage of enol and the rate of enolisation are appreciable. These features are summarised in the annexed Table :

Compound	Enol (%) (in liquid)	Lead tetra-acetate oxidation products	
		Acetoxy	Dimeric
Ethyl malonate	0·01 [b]	Mono	—
*cyclo*Hexanone	0·02 [a]	Mono and di	—
Acetophenone	0·025 [c]	Mono	—
Triethoxycarbonylmethane	0·2 [b]	?	+
Ethyl acetoacetate	7·5 [a]	Mono	+
Acetylacetone	80·4 [a]	Mono	+

[a] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, 1953, pp. 530 *et seq.* [b] Meyer, *Ber.*, 1912, **45**, 2852. [c] Smith and Guss, *J. Amer. Chem. Soc.*, 1937, **59**, 804.

The above mechanism for the oxidation of carbonyl compounds with lead tetra-acetate has obvious similarities to that postulated for the oxidation of phenols (cf. Part I, *J.*, 1954, 2785).

Cavill, Dean, McGookin, Marshall, and Robertson (*J.*, 1954, 4573) reported the conversion of chromanones into the 3-acetoxy-derivatives, whilst flavanones give a mixture in

which the flavone is invariably present, and the corresponding *iso*flavone and/or 3-acetoxy-flavanone may be additional products. The present studies thus confirm the suggestion that the acetoxylation of chromanones and flavanones in the 3-position proceeds by a free-radical process, whilst attack at the 2-position in the latter series may be compared with the oxidation of toluene derivatives and benzyl ethers (cf. Parts II and III, *locc. cit.*).

EXPERIMENTAL

Light petroleum had b. p. 60—80°.

Carbonyl compounds were purified by distillation, then treated with ferrous sulphate, dried (MgSO$_4$), and redistilled. Acetic acid was purified by Orton and Bradfield's method (*J.*, 1924, **125**, 960). Lead tetra-acetate was prepared as in Part II.

Oxidation of cyclo*Hexanone.*—(*a*) *cyclo*Hexanone (19·6 g.) with lead tetra-acetate (88·6 g.) in acetic acid (150 ml.) was heated at 80° (bath) until no positive test for the oxidant (starch-iodide) was obtained (2 hr.). Acetic acid was distilled from the mixture, and the residue extracted with ether (3 × 50 ml.). The ethereal layer was washed with water, sodium hydrogen carbonate solution, and water, dried (MgSO$_4$), and evaporated. Distillation under reduced pressure gave unchanged *cyclo*hexanone, b. p. 54—58°/11 mm., n_D^{20} 1·4497, and 2-acetoxy*cyclo*-hexanone (8·0 g.), b. p. 99—100°/6 mm., prisms, m. p. 40—41° (from light petroleum) (Found : C, 61·6; H, 7·7. Calc. for C$_8$H$_{12}$O$_3$: C, 61·5; H, 7·75%). Bergmann and Gierth (*Annalen*, 1926, **448**, 48) record m. p. 41—42°.

(*b*) *cyclo*Hexanone (19·6 g.) and lead tetra-acetate (88·6 g.) in benzene (150 ml.; freshly distilled from sodium) were heated at 80° until no test for the oxidant was obtained (8 hr.). The mixture was washed with water (4 × 50 ml.), and the organic layer separated and dried (MgSO$_4$). Removal of solvent, and then distillation under reduced pressure, yielded *cyclo*hexanone (3·6 g.), b. p. 67—70°/15 mm., n_D^{20} 1·4499, and 2-acetoxy*cyclo*hexanone (19·0 g.), b. p. 123—126°/16 mm., prisms, m. p. 39—40° (from light petroleum) (Found : C, 61·2; H, 7·4%). Further distillation gave *cis*-2 : 6-diacetoxy*cyclo*hexanone (1·1 g.), b. p. 158—160°/10 mm., needles, m. p. 145—146° (from light petroleum) (Found : C, 56·1; H, 6·35. C$_{10}$H$_{14}$O$_5$ requires C, 56·1; H, 6·6%). Posternak and Ravenna (*loc cit.*) report m. p. 147—148°. Hydrogenation (Adams catalyst) of this compound, followed by acid hydrolysis, gave *cis*-*cyclo*hexane-1 : 2 : 3-triol, purified by recrystallisation from alcohol and isolated as needles, m. p. 145—146°, from ethyl acetate (Found : C, 54·7; H, 9·2. Calc. for C$_6$H$_{12}$O$_3$: C, 54·5; H, 9·15%). A mixed m. p. of the *cis*-triol with *cis*-*cyclo*hexane-1 : 2 : 3-triol, kindly supplied by Professor T. Posternak, gave no depression.

(*c*) *cyclo*Hexanone (126 g., large excess) with lead tetra-acetate (88·6 g.), treated as in (*b*) (2 hr.), gave *cyclo*hexanone (104 g.), b. p. 50—52°/14 mm., n_D^{20} 1·4489, 2-acetoxy*cyclo*hexanone (12·0 g.), b. p. 112—114°/9 mm., prisms, m. p. 39—40° (from light petroleum) (Found : C, 61·6; H, 7·65%), and *cis*-2 : 6-diacetoxy*cyclo*hexanone (1·1 g.), b. p. 150—152°/9 mm., needles, m. p. 145—146° (from light petroleum) (Found : C, 56·3; H, 6·5%).

*Oxidation of 2-Acetoxy*cyclo*hexanone.*—2-Acetoxy*cyclo*hexanone (15·6 g.) and lead tetra-acetate (44·3 g.) in benzene (75 ml.) were heated at 80° (14 hr.). The mixture, worked up as in (*b*), yielded 2-acetoxy*cyclo*hexanone (7·0 g.), b. p. 110—120°/8 mm., m. p. and mixed m. p. 40—41°, and *cis*-2 : 6-diacetoxy*cyclo*hexanone (5·0 g.), b. p. 152—160°/8 mm., plates, m. p. 147—148° (from alcohol) (Found : C, 56·0; H, 6·7%).

Oxidation of Acetophenone.—(*a*) Acetophenone (11·0 g.) and lead tetra-acetate (44·3 g.) in benzene (75 ml.) were heated at 80° as above (9 hr.). The mixture, worked up as in (*b*), gave acetophenone (4·0 g.), b. p. 50—56°/2 mm., n_D^{20} 1·5346, and ω-acetoxyacetophenone (8·2 g.), b. p. 110—114°/2 mm., prisms, m. p. 46° (from light petroleum) (Found : C, 67·7; H, 5·7. Calc. for C$_{10}$H$_{10}$O$_3$: C, 67·4; H, 5·7%). Hunnius (*Ber.*, 1877, **10**, 2006) records m. p. 40°, and Nef (*Annalen*, 1904, **335**, 268) m. p. 49°.

Oxidation of Ethyl Malonate.—Ethyl malonate (16·0 g.) was treated with lead tetra-acetate (44·3 g.) in benzene (75 ml.) (8 hr.), then worked up as described for acetophenone, giving diethyl α-acetoxymalonate (17·2 g.), b. p. 114—116°/5 mm., n_D^{20} 1·4263 (Found : C, 49·1; H, 6·2. Calc. for C$_9$H$_{14}$O$_6$: C, 49·5; H, 6·5%). Conrad and Brückner (*Ber.*, 1891, **24**, 2993) report b. p. 235—245°.

Oxidation of Diethyl Ketone.—Diethyl ketone (86·0 g.) with lead tetra-acetate (443 g.) in benzene (750 ml.) was oxidised (50 hr.), then worked up as above, to yield 1-*acetoxydiethyl ketone* (45·0 g.), b. p. 56—57°/3 mm., n_D^{20} 1·4181 (Found : C, 58·4; H, 8·5. C$_7$H$_{12}$O$_3$ requires C, 58·3;

H, 8·4%), and 1 : 1'-*diacetoxydiethyl ketone* (15·0 g.), b. p. 80°/1 mm. (Found : C, 54·1 ; H, 6·7. $C_9H_{14}O_5$ requires C, 53·5 ; H, 7·0%).

Acid hydrolysis of the 1-acetoxy-compound yielded 2-hydroxy-3-pentanone, identified as the osazone, yellow prisms, m. p. 166—167° (from alcohol) (Found : C, 72·7 ; H, 7·05 ; N, 20·0. Calc. for $C_{17}H_{20}N_4$: C, 72·8 ; H, 7·2 ; N, 20·0%). Von Peckmann (*Ber.*, 1888, 21, 1411) records m. p. 166—167°. Hydrogenation (Adams catalyst) of 1 : 1'-diacetoxydiethyl ketone, then acetylation (acetic anhydride–sodium acetate), gave a pentane-2 : 3 : 4-triol triacetate, needles, m. p. 123—124° (from ether). Reif (*loc. cit.*) records m. p. 121°. Acid hydrolysis of the hydrogenation product yielded a pentane-2 : 3 : 4-triol, which, on treatment with lead tetra-acetate (2 mols.), gave acetaldehyde (1·3 mols.), isolated as the 2 : 4-dinitrophenylhydrazone, m.p. and mixed m.p. 163·5—164° (Found : N, 25·2. Calc. for $C_8H_8O_4N_4$: N, 25·0%).

Oxidation of Triethoxycarbonylmethane.—Triethoxycarbonylmethane (23·2 g.) (Adickes, Brunnert, and Lucker, *J. prakt. Chem.*, 1931, 130, 163) and lead tetra-acetate (44·3 g.) in benzene (100 ml.) were heated at 80° (6 hr.). The colour changed to orange. The mixture, treated as above, yielded triethoxycarbonylmethane (20 g.), b. p. 110—112°/2 mm., m. p. and mixed m. p. 28°, then an oil (2·0 g.), b. p. 158—160°/4 mm. (Found : C, 54·6 ; H, 6·5%). The residue (1·1 g.) slowly solidified to yield hexaethoxycarbonylethane, plates, m. p. 101° (from light petroleum) (Found : C, 52·3 ; H, 6·5. Calc. for $C_{20}H_{30}O_{12}$: C, 51·9 ; H, 6·5%). Mulliken (*Amer. Chem. J.*, 1893, 15, 530) reports m. p. 101°.

Oxidation of Ethyl Acetoacetate.—Lead tetra-acetate (44·3 g.) was slowly added (20 min.) to a solution of ethyl acetoacetate (13·0 g.) in benzene (75 ml.) at 10°. On each addition of oxidant a colour change to orange, fading to pale yellow, occurred. The oxidation was exothermic. The mixture, worked up in the usual manner, gave unchanged ester (3·5 g.), b. p. 80—90°/15 mm., n_D^{20} 1·4176, ethyl α-acetoxyacetoacetate (8·0 g.), a pale yellow oil, b. p. 120—22°/ 15 mm. (Found : C, 51·2 ; H, 6·55. Calc. for $C_8H_{12}O_5$: C, 51·1 ; H, 6·4%) (Dimroth and Schweizer, *loc. cit.*, report b. p. 118—125°/16 mm.), and ethyl αα'-diacetylsuccinate (2·2 g.), b. p. 148—150°/15 mm., prisms, m. p. 91—91·5° (from light petroleum) (Found : C, 55·7 ; H, 6·9. Calc. for $C_{12}H_{18}O_6$: C, 55·8 ; H, 7·0%). Morton and Rogers (*J.*, 1926, 713) record m. p. 92° for one form of ethyl αα'-diacetylsuccinate.

Oxidation of Acetylacetone.—Acetylacetone (30·0 g.) with lead tetra-acetate (133 g.) in benzene (225 ml.) was treated as above (identical colour changes, reaction instantaneous) to give 3-acetoxypentane-2 : 4-dione (12·0 g.), a pale yellow oil, b. p. 84—90°/7 mm. (Found : C, 52·9 ; H, 6·4. Calc. for $C_7H_{10}O_4$: C, 53·2 ; H, 6·3%), and 3 : 4-diacetylhexane-2 : 5-dione (4·8 g.), b. p. 130—132°/1 mm., prisms, m. p. 190—191° (from benzene–light petroleum) (Found : C, 60·5 ; H, 7·0. Calc. for $C_{10}H_{14}O_4$: C, 60·6 ; H, 7·1%). Combes (*Compt. rend.*, 1890, 111, 422) gives b. p. 111°/21 mm. for 3-acetoxypentane-2 : 4-dione and Mulliken (*loc. cit.*) reports m. p. 191·2° for 3 : 4-diacetylhexane-2 : 5-dione.

Oxidations with Acetyl Peroxide.—(a) Acetylacetone (5·0 g.) in benzene (50 ml.) was added to acetyl peroxide (6·0 g.) in ether (100 ml.) (cf. Part III, *loc. cit.*). A positive test for the oxidant was still obtained after 30 hr. at room temperature. Ether was then distilled off and the temperature raised to 80° (negative test after 1 hr.). The mixture was washed with water (2 × 50 ml.) and dried (MgSO₄). Removal of benzene, followed by distillation under reduced pressure, gave 3 : 4-diacetylhexane-2 : 5-dione (1·0 g.), b. p. 148°/2 mm., prisms, m. p. 190° (from benzene–light petroleum) (Found : C, 60·8 ; H, 7·2%). A gum (3·0 g.) did not distil.

(b) Acetophenone (6·0 g.) in benzene (75 ml.) was added to acetyl peroxide (6·0 g.) in ether (100 ml.). The mixture, treated as for acetylacetone (4 hr.), gave an intractable gum.

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