172. *A New Reagent for the Oxidation of Acyloins to Diketones.*

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Acyloins are efficiently oxidised to 1 : 2-diketones by heating them with bismuth oxide (Bi_2O_3) in solutions containing acetic acid, the oxide being reduced to the metal. The reagent is specific and the reaction often virtually quantitative : yields from the sensitive acyloins, furoin and piperoin, are better than those obtained by standard methods. The reaction serves as a qualitative test. The preparation of bismuth triacetate has been improved.

During an earlier investigation it was noticed that, when benzoin was oxidised at moderate temperatures by sodium bismuthate in acetic acid, the " normal " fission reaction occurred exclusively, but that, when the materials were boiled together, some metallic bismuth was precipitated. The presence of phosphoric acid prevented this further oxidation, even at the higher temperatures, and that was the reason for adding phosphoric acid to the acetic acid solution when acyloins were being oxidised (Rigby, *J.*, 1950, 1907). It was obvious that in the side-reaction the primary product of the bismuthate reduction, some compound of tervalent bismuth, was being further reduced.

It has now been found that acyloins are readily oxidised to 1 : 2-diketones by warming them, in media containing acetic acid, with bismuth oxide (Bi_2O_3) which is reduced to metallic bismuth; the reaction is smooth and rapid and appears to be specific for the $-CH(OH)\cdot CO-$ group of acyloins. Apart from its general utility, this mild, selective oxidising agent might have special value in the case of sensitive acyloins : it has been noted on several occasions that the usual copper reagents are not entirely satisfactory in all cases (cf., *e.g.*, Campbell, Dunsmuir, and Fitzgerald, *J.*, 1950, 2744). It is noteworthy that by the bismuth method piperil can be produced in almost quantitative yield—an improvement on the copper-catalysed ammonium nitrate–acetic acid reagent of Weiss and Appel (*J. Amer. Chem. Soc.*, 1949, **71**, 2269). Furil is obtained in 92% yield, compared with 63% by the copper–pyridine method (Hartmann and Dickey, *ibid.*, 1933, **55**, 1228), or 90% (m. p. 162°) by nitrobenzene (Nisbet, *J.*, 1928, 3124).

A convenient qualitative test for acyloins consists in heating, at 100° (or at its boiling point), a solution of *ca.* 0·1 g. of the substance in a few ml. of acetic acid with a little bismuth oxide, a black precipitate of finely divided bismuth being produced almost immediately.

For preparative purposes, acetic acid may be used alone as solvent; with use of a slight excess of the oxide, reaction then is complete in about 15—30 minutes at 95—100°, and yields are usually 90% or more; with benzoin, the oxidation is appreciable at about 70—75°. However, as some acyloins are discoloured slightly when heated with the undiluted acid, addition of technical 2-ethoxyethanol is desirable, although this slows the reaction somewhat; for the oxidation of furoin, dilution of the acetic acid with water was also effective in diminishing the marked discoloration which occurred under the usual conditions. Mineral acids or large amounts of water inhibit the reaction. Stirring the acyloin with a 20% excess of bismuth oxide in a mixture of acetic acid with 1—3 volumes of 2-ethoxyethanol at about 100° for 1¼ hours gave the following % yields of diketone : benzil 96; anisil 95; piperil 97; furil 92. Isolation of the products is very simple. Typical aliphatic 1 : 2-diketones were readily obtained by an analogous procedure.

Presumably bismuth triacetate is formed initially and is the actual compound reduced : a solution of bismuth triacetate in acetic acid can be used instead of the extemporaneous mixture of oxide and acid, but normally offers no advantage, and the reaction is not appreciably more rapid. The triacetate is easily prepared and is stable under ordinary, good conditions of storage. It seems likely that union of the acyloin and bismuth compound through $-C-O-Bi$ linkages, perhaps involving the enediol, occurs before the oxidation.

While all the simple acyloins investigated readily reduce the bismuth oxide–acetic acid reagent, sugars gave no precipitate of bismuth; ascorbic acid also failed to reduce the reagent, and this was not due to its acidity as there was no reduction when sodium acetate was added. The simultaneous presence of glucose inhibits the reduction of bismuth oxide by benzoin in acetic acid unless an excess of the oxide is used; catechol has a similar effect, but resorcinol and quinol have not. It would appear that bismuth oxide reacts preferentially in the usual way with neighbouring hydroxyl groups of these polyhydroxy-compounds.

In order to examine the specificity of the reaction, various readily-oxidisable substances and substances showing some structural similarity to acyloins were heated with the bismuth oxide–acetic acid reagent: namely, hydrazine hydrate, formaldehyde, paraformaldehyde, metaldehyde, catechol (yellow solid produced), resorcinol, quinol, pyrogallol (yellow solid produced), *p*-phenylenediamine, ethyl lactate, pyruvic acid, glucose, sorbose, and diosphenol—but with negative results.

EXPERIMENTAL.

Bismuth Oxide.—Material of the ordinary laboratory grade was used : it was an impalpable yellow powder which lost 1·2% of its weight on ignition. A very old sample which had become almost white by exposure to air was unsatisfactory, as bismuth carbonate is not dissolved by hot acetic acid.

Bismuth Triacetate.—Bismuth oxide (50 g.) was heated at 140—150° with acetic acid (300 ml.) and acetic anhydride (35 ml.) until it dissolved (1½—2 hours), to leave only a light suspension of (presumably) the small amount of carbonate contaminant. After filtration, the triacetate separated on cooling as glistening, colourless, elongated six-sided tablets (75 g., 90%) [Found : Bi (by ignition after moistening with concentrated nitric acid), 54·4. Calc. for $BiC_6H_9O_6$: Bi, 54·1%]. The substance is insoluble in, and hydrolysed by, water, but is soluble in aqueous acetic acid of above *ca.* 60% strength; it is insoluble (milky) in alcohol or 2-ethoxyethanol. The acetic acid can easily be driven off by gentle heating with concentrated nitric acid before ignition; the material then ignites to oxide without trouble. Ignition before removal of the acetic acid entails volatilisation of bismuth, but Salkowsky's procedure (*Biochem. Z.*, 1917, **79**, 99) appears to be unnecessary and undesirable.

General Procedures.—(a) *In the mixed solvent.* To a briskly stirred solution of the acyloin in a mixture of acetic acid with ½—3 volumes of technical 2-ethoxyethanol, heated at 105—110°, was added 1·2 times the theoretical amount of bismuth oxide, and stirring and heating were continued for 70—80 minutes : as wide-mouthed open flasks were used, the temperature in the reaction mixture was a few degrees lower than the bath-temperature; the initially black precipitate was partly converted (by oxidation) into a yellowish suspension before the end of the experiment. The mixture was then heated to boiling and filtered, and on cooling deposited the major part of the diketone, which was removed (ice-cooling brought about some contamination with bismuth compounds). The filtrate was distilled to dryness from the water-bath under reduced pressure, the residue was boiled with benzene, and the hot benzene solution clarified by filtration through 2 g. of aluminium oxide which removed residual traces of bismuth compounds. Evaporation to low bulk allowed the remainder of the diketone to crystallise. The solutions and products had the clear yellow colour of the pure diketone (except furil, which in the crude state was slightly discoloured).

(b) *In acetic acid alone.* The acyloin, dissolved in 2—5 times its weight of acetic acid, was similarly treated with 1·2 times the theoretical quantity of bismuth oxide; 15—30 minutes' stirring usually sufficed for a mixture heated in a water-bath. After filtration from bismuth, the diketone deposited at room temperature was removed and the filtrate, after addition of water (¾ the volume of the acetic acid used), was extracted with a similar quantity of benzene; alternatively, the whole of the original hot filtrate was extracted with warm benzene after the addition of warm water. After being washed with water and filtered through 2 g. of aluminium oxide, the benzene solution was concentrated and a further crop of diketone crystallised. The solutions and crude products had a slight orange tint instead of the yellow of the pure diketone, and the yields were usually a few per cent. lower than when the mixed solvent was used.

Benzil.—Benzoin (10·6 g.) with acetic acid (10 ml.), 2-ethoxyethanol (15 ml.), and bismuth oxide (9·3 g.) (internal temp. 104°; 1 hour) gave benzil, m. p. 95° (10·1 g., 95%). Benzoin (10·6 g.) with acetic acid (22 ml.) and bismuth oxide (9·3 g.) (95—97°; 30 minutes) gave benzil (9·8 g., 93%; an orange-coloured syrup from which benzoic acid could be isolated remained after the crystallisations. An analogous experiment in which a hot solution of bismuth triacetate (15 g.) in acetic acid (45 ml.) was used gave a similar result.

Anisil.—Anisoin (4·7 g.) with acetic acid (9 ml.), 2-ethoxyethanol (18 ml.), and bismuth oxide (3·7 g.) (105°; 1 hour) gave anisil, m. p. 133° (4·42 g., 95%), 87% being obtained in the first crystallisation. Anisoin (12·4 g.) with acetic acid (40 ml.) and bismuth oxide (9·3 g.) (100°; 20 minutes) gave anisil (91%), a little anisoin remaining. There was only slight discoloration.

Piperil.—Piperoin (3·75 g.) with acetic acid (8 ml.), 2-ethoxyethanol (24 ml.), and bismuth oxide (2·4 g.) (103—105°; 1¼ hours) gave piperil, m. p. 173—174° (3·63 g., 97%), 92% being obtained in the first crystallisation : even the evaporated liquors were barely discoloured. (Weiss and Appel, *loc. cit.*, report an 89% yield on oxidation by ammonium nitrate–copper acetate.)

Furil.—Furoin (2·4 g.) with acetic acid (8 ml.), 2-ethoxyethanol (24 ml.), and bismuth oxide (2·4 g.) (water-bath; ¾ hour) gave furil, m. p. 166° (2·2 g., 92%), 84% being obtained in the first crystallisation. Furoin (5·1 g.) with acetic acid (30 ml.), water (15 ml.), and bismuth oxide (5·1 g.) (water-bath; 10

minutes) gave furil (4·5 g., 88%); the crude product was only slightly discoloured. Undiluted acetic acid at 80—85° gave an inferior product (79%), and at 100° the initial product was bronze-coloured. Hartmann and Dickey (*loc. cit.*) reported a 63% yield by the copper–pyridine method, and their initial crude product was described as black.

Diacetyl.—A mixture of commercial acetoin (a light brown syrup) (22 g.), acetic acid (35 ml.), and bismuth oxide (40 g.) was distilled from an oil-bath through a small Fenske column, with a variable-ratio take-off head, at atmospheric pressure until the distillate was no longer yellow, the distillation temperature being finally allowed to rise to 107°. The distillate (*ca.* 35 g.) was redistilled, through the same column, whereupon fractionation was much more effective; practically the whole of the diacetyl distilled as an azeotrope at *ca.* 79·5° (presumably owing to water present in the starting material) and this, together with the next approx. 2 ml. which distilled up to about 100° and accounted for all the remaining yellow material, was dried ($CaCl_2$) and redistilled in the same apparatus, the fraction boiling at 89—91° being collected (yield, 12·5 g.). Condensation with *o*-phenylenediamine gave 2 : 3-dimethylquinoxaline, double m. p. 85° and 107°. No attempt was made to improve the yield by varying the experimental conditions as had been done in the case of furil; the purity of the starting material was unknown.

*Octane-*4 : 5*-dione.*—Butyroin, b. p. 80—86°/12 mm. (*Org. Synth.*, **13**, 24) (21·6 g.), acetic acid (75 ml.), and bismuth oxide (25 g.) were stirred together in a boiling water-bath for 15 minutes, and bismuth and its compounds were filtered off. Removal of the acetic acid by distillation was unsatisfactory, appreciable amounts of the volatile ketone being carried over with it; accordingly the acetic acid solution was diluted with its own volume of water and extracted with benzene. After washing of the solution with water the benzene was very easily removed under reduced pressure, and the octanedione collected at 94—95°/65 mm. (13·8 g.). A colourless residue remained. The product, on condensation with *o*-phenylenediamine, gave 2 : 3-di-*n*-propylquinoxaline, m. p. 44° (lit., 42·9°). A sample of the starting material on careful fractionation yielded 84% of material distilling within the ranges of octanedione (of which a few per cent. was present) and butyroin. No attempt was made to improve the yield of the oxidation reaction by varying the conditions.

Qualitative Tests.—Approx. 0·1 g. of the substance was gently boiled with acetic acid (2—3 ml.) and bismuth oxide (*ca.* 0·1 g.). With resorcinol, quinol, 40% formaldehyde, paraformaldehyde, metaldehyde, ethyl lactate, pyruvic acid, ascorbic acid, diosphenol, *p*-phenylenediamine, and hydrazine hydrate there was no visible change; catechol and pyrogallol gave yellow precipitates of (presumably) the bismuth derivative; the glucose solution gradually became light brown on continued boiling—there was no precipitate—L-sorbose reacted similarly but rather more rapidly; a mixture of glucose (*ca.* 0·1 g.) and benzoin (0·05 g.) in acetic acid (2—3 ml.) with bismuth oxide (*ca.* 0·02 g.) gave only a slight turbidity of bismuth on boiling, but on further addition of bismuth oxide (*ca.* 0·1 g.) more bismuth was precipitated; addition of bismuth oxide to a boiling solution of catechol (0·1 g.) with benzoin (*ca.* 0·05 g.) in acetic acid gave at first only a precipitate of the yellow bismuth–catechol compound, but further additions of bismuth oxide in excess of that required by the catechol resulted in reduction to metallic bismuth.

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