

yield in addition the three mixed compounds, $R_3R'Pb$, $R_2R'_2Pb$ and RR'_3Pb .

A mixture of Me_6Pb_2 and Et_6Pb_2 without the addition of any catalyst was heated in an atmosphere of nitrogen at 100° for five hours. No appreciable gas evolution was observed, and at the end of that period no R_6Pb_2 was found in the product, which was composed only of R_4Pb and metallic lead. The R_4Pb product was separated from the metallic lead and fractionated.

The amount of metallic lead recovered was only 5% greater than that called for by eq. 1. This is striking proof of how small a quantity of alkyl group is lost through side reactions, in spite of the rather profound change in structure which has taken place, and shows that the over-all disproportionation of R_6Pb_2 compounds is correctly represented by eq. -1.

The composition of the R_4Pb product is given in Table I and shows that it contained not only tetramethyllead and tetraethyllead, which obviously would have been expected, but in addition the other three possible lead alkyls, namely, trimethylethyllead, dimethyldiethyllead and methyltriethyllead. Since it is known¹ that tetraalkyllead compounds do not undergo redistribution in the absence of a catalyst, this indicates that the interchange of alkyl radicals in the present experiment took place either before or during, but not after, the decomposition of the R_6Pb_2 compounds.

TABLE I

COMPOSITION OF THE R_4Pb PRODUCT OBTAINED BY THERMAL DECOMPOSITION OF A MIXTURE OF Me_6Pb_2 AND Et_6Pb_2

Compound	Mole per cent. ^a
Me_4Pb	18
Me_3EtPb	15
Me_2Et_2Pb	23
$MeEt_3Pb$	31
Et_4Pb	13

^a Determined from the distillation curve.³

Experimental

Preparation of Hexamethyldilead and Hexaethyldilead.

—Hexaethyldilead was prepared by the method of Hein and Klein,⁴ and hexamethyldilead by the method of Calingaert and Soroos.⁵ *Anal.* Calcd. for Me_6Pb_2 : Pb, 82.1. Found: Pb, 81.8. Calcd. for Et_6Pb_2 : Pb, 70.4. Found: Pb, 70.2.

Decomposition of Hexamethyldilead and Hexaethyldilead.—The decomposition of the mixture of R_6Pb_2 compounds was carried out in two runs; 0.070 mole each of hexamethyldilead and hexaethyldilead was used in the

first, and 0.080 mole of each in the second. The materials were introduced into a 100-cc. 3-neck round-bottomed flask equipped with a nitrogen inlet, thermometer, and reflux condenser to which was connected, in series, a dry-ice trap and mercury bubbler. Each mixture was maintained at $100 \pm 5^\circ$ for five hours while maintaining a nitrogen atmosphere within the system. Decomposition with the deposition of metallic lead and without any noticeable evolution of gas set in immediately and proceeded smoothly; there was also a noticeable evolution of heat.

After cooling to room temperature, the reaction products were filtered, and the metallic lead residues were extracted with several portions of ether. The ether solutions and the lead alkyl products from the two runs were combined and analyzed by distillation.³ Table I gives the composition of the R_4Pb product. The metallic lead residues were dissolved in nitric acid and analyzed for lead. Found: total Pb, 32.5 g. (0.157 mole).

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RECEIVED JULY 14, 1941

The Preparation of 4(5)-Hydroxymethylimidazole

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4(5)-Hydroxymethylimidazole is a valuable intermediate for the synthesis of histidine, histamine, and related imidazole derivatives. Pyman's method² has been widely used for the preparation of this compound, but it is complicated and gives poor yields. Parrod³ reported the formation of 4(5)-hydroxymethylimidazole during the prolonged aerobic oxidation of fructose or dihydroxyacetone in ammoniacal copper solution, but made no attempt to develop a preparative method. The procedure of Weidenhagen and Herrmann⁴ affords good yields, but the dihydroxyacetone employed as starting material is difficult to secure in quantity. Weidenhagen, *et al.*,⁵ later reported that 4(5)-hydroxymethylimidazole could be obtained from fructose in a yield of 38% of theoretical. Some difficulty was experienced in inducing crystallization of the free base. No analysis was recorded; identification rested solely on the melting point of the picrate. Akabori, *et al.*,⁶ were unable to duplicate the yields reported by Weidenhagen and co-workers.

(1) This work was completed during current appointment as a Fellow in the Medical Sciences of the National Research Council, Department of Biochemistry, College of Physicians and Surgeons, Columbia University, New York, N. Y.

(2) Pyman, *J. Chem. Soc.*, **99**, 668 (1911).

(3) Parrod, *Bull. soc. chim. (Mem.)*, **51**, 1424 (1932).

(4) Weidenhagen and Herrmann, *Ber.*, **68**, 1953 (1935).

(5) Weidenhagen, Herrmann and Wegner, *ibid.*, **70**, 570 (1937).

(6) Akabori, Ose and Kanedo, *Proc. Imp. Acad. (Tokyo)*, **16**, 191 (1940).

(3) Calingaert, Beatty and Neal, *THIS JOURNAL*, **61**, 2755 (1939).

(4) Hein and Klein, *Ber.*, **71B**, 2381 (1938).

(5) Calingaert and Soroos, *J. Org. Chem.*, **2**, 535 (1938).

Working independently, the present authors also have found it impossible to obtain good yields of a pure material by the method of Weidenhagen, *et al.*,⁵ which yields a mixture of imidazole derivatives. In the most favorable runs the desired product makes up less than half of the total upon which Weidenhagen, *et al.*, based their yields.

The following procedure has repeatedly proved reliable for the rapid preparation of considerable quantities of 4(5)-hydroxymethylimidazole picrate.

Experimental

Preparation of 4(5)-Hydroxymethylimidazole Picrate.—

Into a 6-liter round-bottom flask was weighed 222 g. of basic cupric carbonate, 1500 cc. of distilled water added, followed by 800 cc. of ammonium hydroxide (28%, sp. gr. 0.90). The flask was rotated, and most of the cupric carbonate dissolved. One hundred cc. of a 37–40% solution of formaldehyde was added with shaking, and then a solution of 90 g. of fructose (95%) in 200 cc. of water added immediately. The solution was well mixed and placed on a steam-bath under a hood. The mixture was shaken at intervals and, after one-half hour of heating, a moderate current of air was bubbled through. The heating and aeration were continued for two hours, and aeration for an additional two hours. The mixture was then chilled in an ice-bath, the olive to brown precipitate of the sparingly soluble copper complex of imidazole derivatives filtered off and washed. The moist precipitate was suspended in 1 liter of water, and concentrated hydrochloric acid (about 40 cc.) added until the suspension was just acid to litmus. Hydrogen sulfide was bubbled through the suspension with frequent shakings until precipitation of the copper was complete (two to three hours). The precipitate was filtered off and extracted two or three times with a total of 500 cc. of water.

The clear, light brown to reddish-brown filtrate and washings were boiled for fifteen minutes, and then 60 g. of picric acid was added with stirring and heating continued until solution was complete. The slightly greenish-yellow plates, which separated as the solution was cooled to room temperature, were filtered off, washed three times, and air dried. The filtrate and first washings were combined and heated, 10 g. of picric acid was added, and the mixture cooled and filtered. This process was repeated, using 10-g. portions of picric acid, until the air-dried picrate fraction so obtained melted below 195°. All fractions melting above 200° were combined and recrystallized from water. This was most efficiently accomplished by adding 700 cc. of water for each 30 g. of crystals, heating in a covered beaker until solution occurred, treating with charcoal, and filtering through a warm funnel. The crystals deposited upon the slightest cooling. After cooling, the yellow needles (occasionally plates) were filtered, washed, and air dried; melting point 204° (dec.) (uncor.) or higher. The fractions melting at 195–200° were recrystallized in like manner. If the melting point was not raised to 203°, the process was repeated. The yield of crude picrate was 95–100 g. (61–

64%); of recrystallized picrate, 85–94 g. Equally good yields were obtained with double the above quantities. The melting point varies slightly with the rate of heating between 203.5° and 203° (dec.) (uncor.).

In the same bath, the picrate melted simultaneously with an authentic sample of 4(5)-hydroxymethylimidazole picrate prepared by Pyman's method² and with a mixture of the two. A definite melting point depression occurred when either sample was mixed with imidazole picrate.

Anal. Picric acid calcd.: 70.0. Found: 69.9 (Nitron method of Busch and Blume⁷).

4(5)-Hydroxymethylimidazole and its hydrochloride were readily prepared in excellent yields from the picrate by the methods of Pyman² and of Koessler and Hanke.⁸ Samples so prepared gave the following constants: 4(5)-hydroxymethylimidazole hydrochloride, m. p. 107.5–108.5° (uncor.); free base, m. p. 91–92° (uncor.). Imidazole-4(5)-formaldehyde which was prepared by oxidation of the free base according to Pyman's directions⁹ melted at 172–173° (uncor.).

The picrates of at least two other imidazole derivatives may be obtained from the reaction mixture after the precipitation of the 4(5)-hydroxymethylimidazole picrate. One of these is soluble in water, and may be identical with the 4(5)-[*d*-arabino]-tetrahydroxybutylimidazole picrate isolated by Parrod.³

(7) Busch and Blume, *Z. angew. Chem.*, **21**, 354 (1908).

(8) Koessler and Hanke, *This Journal*, **40**, 1716 (1918).

(9) Pyman, *J. Chem. Soc.*, **109**, 186 (1916).

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LITTLE ROCK, ARKANSAS RECEIVED NOVEMBER 25, 1941

Comparison of Metallic Chlorides as Catalysts for the Friedel-Crafts Ketone Synthesis. II¹

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In continuation of earlier work,² some anhydrous metallic chlorides have been further tested for ability to catalyze the Friedel-Crafts synthesis of *p*-methylacetophenone. In the present instance all reactions were carried out at 20–25°, with consistent use of the Perrier³ sequence of combining reagents. For all but one catalyst (antimony pentachloride) it was assumed that the optimum ratio of catalyst to acid chloride under these conditions would be the same as in the earlier work. Yields of ketone at various time intervals were measured acidimetrically by the hy-

(1) This paper is based upon a thesis submitted by R. A. B. in partial fulfillment of the requirements for the degree of Master of Science at the Oklahoma Agricultural and Mechanical College in 1941.

(2) Dermer, Wilson, Johnson and Dermer, *This Journal*, **63**, 2881 (1941).

(3) Perrier, *Ber.*, **33**, 815 (1900).