

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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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).

droxylamine hydrochloride method as before. In these cases, the catalyst was caused to react with the acid chloride previous to the addition of the aromatic compound.

The curves in Fig. 1, compared to those of the earlier work in which the catalyst was added to a mixture of the acid chloride and aromatic compound, indicate that performing the reaction under these conditions improves the yield given by catalysts previously found good, but lowers that produced by those previously found poor or only mediocre. Titanium tetrachloride is the lone and conspicuous exception to this generalization. Additional experiments have shown that the Perrier procedure followed by heating at 80–110° produces yields better than those reported in the previous paper, but not so good as those represented in Fig. 1.

The tests of antimony pentachloride at two concentrations were undertaken to learn whether an increased amount of catalyst would have the same effect as prolonged reaction time. It will be seen that the maximum yield is the same for both cases, but is produced more rapidly by more catalyst.

This is the first report of columbium pentachloride as a catalyst for the ketone synthesis, although it has been tested for alkylation.⁴ It is evidently equal to aluminum chloride in maximum yield produced but not in speed. The unexpected earlier finding that tellurium dichloride is a better catalyst than tellurium tetrachloride at temperatures of the steam-bath is not duplicated here. The single trial with beryllium chloride was not performed at the optimum conditions under which Brederick, Lehman, Fritzsche and Schonfeld⁵ secured a yield of 80%. Selenium tetrachloride is to be added to the list of chlorides having no catalytic effect upon this reaction.

Schroeder and Brewster⁶ have reported mercuric chloride to catalyze the Friedel-Crafts reaction of benzoyl chloride with diphenyl ether, whereas earlier work in this Laboratory² showed that this halide would not cause the formation of *p*-methylacetophenone. To test the indispensability of mercuric chloride in the former reaction, a run was made following the procedure of Schroeder and Brewster in all particulars except that no catalyst was added. The resulting mix-

ture, evaporated to about 1 ml. under reduced pressure, liberated hydrochloric acid from hydroxylamine hydrochloride and gave a solid derivative with phenylhydrazine. It cannot be said that mercuric chloride is not a catalyst, however, since the yield without it was far inferior to that obtained by Schroeder and Brewster.

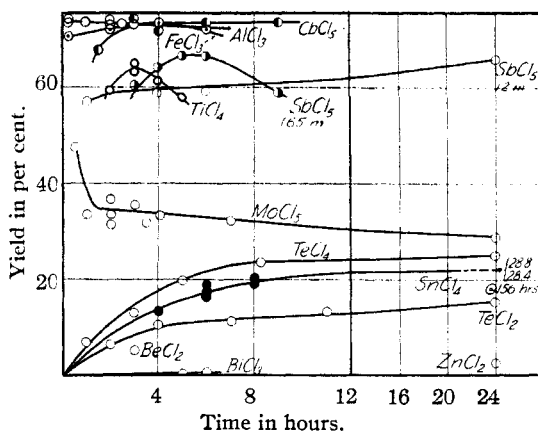


Fig. 1.—Relation between reaction time and yield. Ratios of catalyst/acid chloride were as follows: AlCl_3 , 1.6; CbCl_5 , 1.3; FeCl_3 , 1.2; SbCl_5 (a), 1.65; SbCl_5 (b), 1.2; TiCl_4 , 3.0; MoCl_5 , 1.2; TeCl_4 , 1.0; SnCl_4 , 2.0; TeCl_2 , 1.8; BeCl_2 , 1.2; ZnCl_2 , 0.8; BiCl_3 , 1.0.

Experimental

Most of the reagents were those described in the previous article. Columbium pentachloride and selenium tetrachloride were prepared by chlorinating the element at elevated temperatures, but the beryllium chloride was purchased.

Only two significant deviations from the original procedure were adopted. When the Perrier order of combining reagents is used, initial cooling in ice water is necessary to prevent loss of acetyl chloride, since there is usually an exothermic reaction producing a molecular compound of the catalyst and the acid chloride. The dripping of toluene down through a scrubber plug in the reflux condenser proved unnecessary, since the addition compound binds acid chloride and since reactions were in general less vigorous at the lower temperatures.

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The Rate Equations for Consecutive Reactions

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The purpose of the present note is to point out explicitly the way in which several well-known procedures in differential equations may be of use in providing a completely general method of attack in solving the system of first order dif-

(4) Grosse and Ipatieff, *J. Org. Chem.*, **1**, 559 (1937).

(5) Brederick, Lehman, Fritzsche and Schonfeld, *Ber.*, **72**, 1414 (1939); *Angew. Chem.*, **52**, 445 (1939).

(6) Schroeder and Brewster, *THIS JOURNAL*, **60**, 752 (1938).