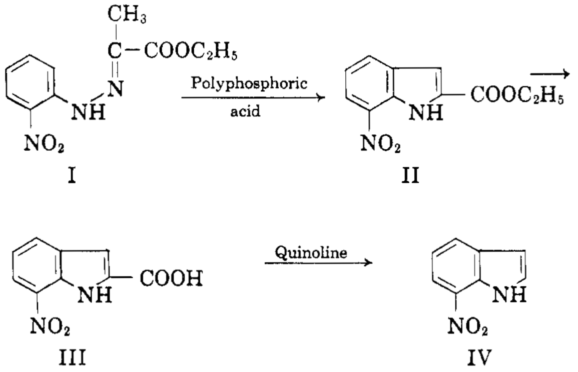
During the course of some recent work with indolecarboxylic acids,[4,5] we also attempted ring closure of ethyl pyruvate *o*-nitrophenylhydrazone. In essence, results analogous to those of Rydon and Siddappa were obtained including the formation of a material isomeric with ethyl pyruvate *o*-nitrophenylhydrazone.

Recently Rydon and Tweddle[6] were successful in the cyclization of some substituted phenylhydrazones by means of polyphosphoric acid. We, therefore, re-investigated the ring closure of ethyl pyruvate *o*-nitrophenylhydrazone (I) with this reagent and were able to isolate ethyl 7-nitro-2-indolecarboxylate (II). Hydrolysis of this product gave 7-nitro-2-indolecarboxylic acid (III) which was decarboxylated to form 7-nitroindole (IV).



7-Nitroindole at a concentration of 100 γ per ml. inhibits the growth of *Lactobacillus arabinosus* 17–5. However, the growth inhibition is not reversed by anthranilic acid, indole, tryptophan or 7-indolecarboxylic acid.

EXPERIMENTAL[7]

Ethyl 7-nitro-2-indolecarboxylate. To 10 g. of polyphosphoric acid was added 2 g. of ethyl pyruvate *o*-nitrophenylhydrazone, and the mixture was stirred on a steam bath until it was homogeneous. The dark brown colored reaction mixture was then heated in an oil bath until a bath temperature of 195° was attained. The reaction mixture was allowed to remain at this temperature for 5 minutes and then removed from the oil bath. When the temperature of the mixture had decreased to 50°, 25 ml. of water was added and the mixture was heated on a steam bath. The solid material was broken by stirring and the suspension poured into a beaker. The remainder of the deep brown insoluble gum was stirred with an additional 25 ml. of water on the steam bath, and the aqueous mixture was combined with the first water suspension.

The water phase which contained a considerable amount of dark solid was extracted with three 50-ml. portions of ether The ether layer, orange colored, was washed with 5% sodium bicarbonate, with water, and finally dried over sodium sulfate. After drying, the ether was removed on a steam bath, and the residual oil was dissolved in 95% ethanol. To this solution, water was added until it became quite cloudy. This mixture was allowed to cool for several hours in a refrigerator. The yellow-orange needles separating were filtered and recrystallized from aqueous ethanol after treatment with charcoal. On cooling, lemon yellow needles were obtained. Yield of material melting at 92–93° was 250 mg. (13.4%).

Anal. Calc'd for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.30; N, 11.96. Found: C, 56.50; H, 4.35; N, 11.95.

7-Nitro-2-indolecarboxylic acid. Ethyl 7-nitro 2-indolecarboxylate (100 mg.) was added to 10 ml. of a 10% aqueous solution of potassium hydroxide. The mixture was heated with stirring on a steam bath for several minutes. At the end of this time the deep red solution was filtered and allowed to cool. An equal volume of water was added to the mixture which was then vigorously shaken. This mixture was filtered and the filtrate was acidified with 6*N* hydrochloric acid. The cream-yellow solid was removed by filtration and recrystallized twice from aqueous ethanol. The very pale yellow needles were dried at 140° for 4 hours. Yield of material melting at 271–272° was 49.5 mg. (56%).

Anal. Calc'd for $C_9H_6N_2O_4$: C, 52.43; H, 2.93; N, 13.59. Found: C, 52.54; H, 3.24; N, 13.62.

7-Nitroindole. To 3 ml. of redistilled quinoline containing a trace of copper chromite was added 100 mg. of 2-carboxy-7-nitroindole. This mixture was heated in an oil bath at 205° for 2 hours with occasional stirring. At the end of this time, the hot black mixture was poured into a solution of 4 ml. of concentrated hydrochloric acid and ice. The mixture was filtered, and both the precipitate and the filtrate were extracted several times with ether. The ether extracts were combined and dried over sodium sulfate. Evaporation of the ether on a steam bath with subsequent cooling gave deep yellow needles. This material was recrystallized from aqueous ethanol. Yield of material melting at 95–96° was 39 mg. (49.5%); λ_{max} (95% ethanol): 232 mμ, 364 mμ; a plateau at 242–251 mμ with a slight maximum at 248–250 mμ; λ_{min}: 285 mμ. This solid when dissolved in Kovac reagent (Ehrlich reagent using isoamyl alcohol as solvent) gave a deep red color.

Anal. Calc'd for $C_8H_6N_2O_2$: C, 59.26; H, 3.73; N, 17.28. Found: C, 59.61; H, 4.03; N, 17.21.

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Palladium Catalyzed Reduction of *p,p'*-Dihydroxybenzophenone

M. LEVINE AND S. C. TEMIN

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Hydrogenation of *p,p'*-dihydroxybenzophenone (I) to *p,p'*-dihydroxydiphenylmethane(II) was carried out in excellent yield with palladium on carbon black. No report had previously been made on the use of a palladium catalyst in the reduction of a dihydroxybenzophenone. Bradlow and Van der

Werf[1] reported the only previous reductive system used on (I), a modified Clemmensen method which was unsatisfactory because of the formation of resinous products.

In general, the Clemmensen[1] and the Wolff-Kishner,[2] or modifications of these, are used for the reduction of aromatic ketones. Benzophenone has been reduced in excellent yield by both of these methods.[1,2] Using the techniques of the modified Clemmensen method, however, Bradlow and Van der Werf[1] obtained only a 25% yield of (II). The Wolff-Kishner reduction has apparently not been applied to (I), but the reduction of p,p'-dichlorobenzophenone[3] by this method gave only 21% of p,p'-dichlorodiphenylmethane.

Although catalytic methods have not been widely used for the reduction of ketones, a number of studies have been made. Hartung and Crossley[4] reduced a number of propiophenones with palladized carbon, and the work was extended to a few aromatic systems by Baltzly and Buck.[5] Horning and Reisner[6] described the palladium catalyzed reduction of several β-aroylpropionic acids to the α-arylbutyric acids.

As a result of the limited number of hydrogenations previously reported using palladium, it was not possible to predict what effect hydroxyl substituents on benzophenone would have on the reduction. Thus, it was interesting that catalytic reduction of (I) with palladium-carbon catalyst absorbed 100% of the theoretical hydrogen uptake. On using platinum under similar conditions, the hydrogenation resulted in the reduction of the aromatic ring.

EXPERIMENTAL

To a solution of 10.7 g. (0.05 mole) of p,p'-dihydroxybenzophenone in 100 ml. isopropyl alcohol was added 3 g. of 5% palladium on carbon powder (Baker and Co., Inc.). The reduction, carried out in a low pressure Parr hydrogenator, was complete in about 5 hours at 25°C. with a 100% theoretical hydrogen uptake. The catalyst was removed by filtration, and after the filtrate was reduced to a small volume, a crystalline solid settled out upon addition of an equal volume of water. Recrystallization of this material from water gave a 95% yield of p,p'-dihydroxydiphenylmethane, m.p. 161–162°.[7] A diacetoxy derivative was prepared, m.p. 70–71°.[7]

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Some New Quaternary-Substituted Alkyl Morpholinium Chlorides and Pyrrolidinium Alkyl Sulfates[1]

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Studies in the fields of morpholinium halides and alkyl sulfates and thiamorpholinium alkyl sulfates[2] have been extended to include a group of N-alkyl-N-substituted alkyl morpholinium chlorides and two series of symmetrical, N,N-dialkyl pyrrolidinium alkyl sulfates prepared from a group of five N-alkyl pyrrolidines. These quaternary morpholinium and pyrrolidinium compounds were prepared for the purpose of determining their bactericidal properties in comparison with those of quaternary morpholinium and thiamorpholinium compounds previously described. The results of these bacteriological tests are as yet not complete.

No systematic study of the longer chain N-alkyl pyrrolidines and the corresponding N-alkyl pyrrolidinium alkyl sulfates has been made. A recent German patent[3] describes the preparation of N-*n*-dodecyl-N-methyl pyrrolidinium methosulfate. Ames, Bowman, Buttle and Squires[4] have described the preparation of N-*n*-dodecyl pyrrolidine and the hydrochloride of this compound. Jerchel and Kimmig[5] have prepared N-*n*-dodecyl-N-phenyl pyrrolidinium bromide. Erickson and Keps[6] have recently described the preparation of N-*n*-dodecyl and N-*n*-octadecyl pyrrolidine and N,N-di-*n*-dodecyl and N,N-di-*n*-octadecyl pyrrolidinium chlorides by the reaction of the appropriate primary or secondary amine with 1,4-dichlorobutane in the presence of excess sodium carbonate in butyl alcohol solution. The N-alkyl pyrrolidines were analyzed as their picrates.

EXPERIMENTAL

N-Alkyl morpholines were prepared by the method previously described.[2]

N-Alkyl-N-substituted alkyl morpholinium chlorides were prepared by reacting equimolar quantities (approximately 0.02 mole) of the N-alkyl morpholine and the substituted alkyl chloride without solvent or in an equal volume of dry

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[1] Presented before the Division of Organic Chemistry, Delaware Valley Regional Meeting of the AMERICAN CHEMICAL SOCIETY, Philadelphia, Feb. 16, 1956.

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