third and fifth hours. After standing overnight the reaction mixture was heated to boiling and filtered. The filter cake was dissolved in water, made slightly alkaline with dilute sodium hydroxide and acidified with acetic acid to precipitate 3.3 g. (36%) unreacted *p*-dimethylaminobenzoic acid. The xylene filtrate was concentrated and cooled to yield 4.1 g. of crystals, m. p. 147–160°. This material was taken up in chloroform, extracted with sodium bicarbonate solution and dried. Stripping of the solvent followed by recrystallization of the residue from benzene gave 2.6 g. (30%) of *p*-dimethylaminobenzoic anhydride, m. p. 157–159° (cor.).

Anal. Calcd. for $C_{18}H_{20}O_3N_2$: C, 69.3; H, 6.4; N, 9.0. Found: C, 69.6; H, 6.4; N, 8.8.

Method B.—To a solution of 16.0 g. of *p*-dimethylaminobenzoic acid and 60 ml. of triethylamine in 150 ml. of chloroform there was added dropwise 11.7 g. (7.0 ml.) of phosphorus oxychloride. After the initial reaction subsided the solution was heated to reflux for ten minutes and allowed to stand one hour at room temperature. The chloroform solution was extracted with ice-cold dilute sodium hydroxide solution and filtered through anhydrous sodium sulfate. Upon concentration and cooling the chloroform solution deposited 9.6 g. of crystals, m. p. 148–157°. Two recrystallizations of this material from benzene gave 7.5 g. (50%) of *p*-dimethylaminobenzoic anhydride, m. p. 157–159° (cor.), identical with that obtained by method A as evidenced by mixed melting point determination.

Acidification of the alkali extract with acetic acid did not yield any recovery of *p*-dimethylaminobenzoic acid.

Methyl *p*-Dimethylaminobenzoate.—In a sealed tube there was heated for three hours at 100° 0.5 g. of *p*-dimethylaminobenzoic anhydride and 25 ml. of methanol. The reaction mixture was poured into cold dilute sodium hydroxide to dissolve the *p*-dimethylaminobenzoic acid and to precipitate the ester which was collected by filtration. There was thus obtained 0.23 g. (80%) of methyl *p*-dimethylaminobenzoate, m. p. 99–102° (lit. 102°).[3] Acidification of the alkali extract gave 0.18 g. of *p*-dimethylaminobenzoic acid.

***p*-Dimethylaminobenzamide.**—A solution of 0.53 g. of *p*-dimethylaminobenzoic anhydride in 25 ml. of chloroform was saturated with ammonia and then heated in a sealed tube for two hours at 70° and two additional hours at 100°. The chloroform was stripped and the residue recrystallized from water to give 0.21 g. (76%) amide, m. p. 203–206° (lit. 206°).[4]

NATIONAL CANCER INSTITUTE
NATIONAL INSTITUTE OF HEALTH
BETHESDA 14, MARYLAND

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Preparation of 2-Phenylbenzoxazole

BY LUCAS C. GALATIS

The preparation of 2-substituted benzoxazoles by heating appropriately *o*-substituted anilines with an organic acid is a well-known reaction. In the case of benzoxazole, apparently the reaction has been used only for the preparation of the parent compound from *o*-aminophenol and formic acid.[1] It has now been found that 2-phenylbenzoxazole (I) may be prepared by the general method by heating *o*-aminophenol with benzoic acid. Purification of crude I presents difficulty especially because of the persistence of a highly fluorescent by-product which has been commonly encountered when I was prepared by heating aminophenol with various benzoyl derivatives.[2] By choosing ligroin as a solvent, I could be extracted from the reaction product free from other by-products, except traces of the above mentioned fluorescent substance, which were in their turn eliminated by taking advantage of a difference in basicity between I and the latter. The fluorescent matter accumulated in the residue of the ligroin extraction was then easily separated and identified as triphen-dioxazine, an oxidation product of *o*-aminophenol.[3]

Experimental

In a large test-tube an intimate mixture of 10.9 g. of *o*-aminophenol and 15 g. of benzoic acid is melted in an oil-bath at 160°. The tube is then fitted with a stopper carrying a gas inlet tube and an exit tube bent downward. The temperature is raised to 195° while passing carbon dioxide through the tube, at which temperature rapid evolution of water occurs. After two hours the temperature is raised to 200–205° and held at that point for ten hours. Every two or three hours the sublimate is melted down from the walls of the tube. After cooling to 130° the melt is poured with stirring into cold water. The insoluble material is ground in a mortar with 2 *N* sodium hydroxide. The dark colored residue is warmed with 300 ml. of ligroin (b. p. 80–120°) until extraction of 2-phenylbenzoxazole from contaminating black material is complete. After filtering, the solution which is strongly fluorescent, although it does not contain but traces of the fluorescent matter, is shaken with two drops of concd. hydrochloric acid which removes the fluorescent impurity as a violet-blue solution. The ligroin solution is filtered through a dry gravity filter and shaken with 80 ml. of concd. hydrochloric acid which removes the benzoxazole. The acid extract is diluted with stirring with four or five volumes of cold water yielding 14 g. (72%) of 2-phenylbenzoxazole as a white or slightly green powder melting at 101°. A perfectly white product may be obtained by distillation of the material after the sodium hydroxide treatment with superheated steam (180°) followed by the treatment with hydrochloric acid in ligroin.

In order to isolate the main quantity of the fluorescent substance, the black residue from the ligroin extraction is repeatedly extracted with boiling alcohol for removal of a red contaminant, and then with boiling xylene. On cooling, the intensively fluorescent xylene solution deposits small red brown needles with a metallic cast. This shows all the properties of triphen-dioxazine including the characteristic production of green vapor on heating at 300°.

Acknowledgement.—The author is indebted to Mr. Nicholas G. Dovletis for his assistance during this work.

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[1] Ladenburg, *Ber.*, **10**, 1124 (1877).

[2] Skraup, *Ann.*, **419**, 76 and 82 (1919).

[3] Seidel, *Ber.*, **23**, 182 (1890).

CHEMICAL LABORATORY
OF THE ADMIRALTY
ATHENS, GREECE

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Synthesis of 2,3-Diketopiperazine

BY C. E. GOULDING, JR.,[1] AND C. B. POLLARD

Two prior methods for the preparation of 2,3-diketopiperazine by the reaction between diethyl oxalate and 1,2-ethanediamine[2,3] have been reinvestigated in this Laboratory and found to afford yields of only about 1 and 10%, respectively. A new method involving the reaction of oxamide and 1,2-ethanediamine in 1,4-dioxane was therefore

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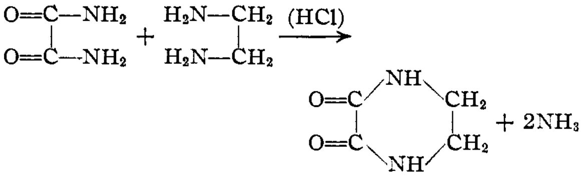
[1] Present address: Caracas, Venezuela.

[2] Hofmann, *Ber.*, **5**, 247 (1872).

[3] Van Alphen, *Rec. trav. chim.*, **54**, 937 (1935).

undertaken which, using anhydrous reagents and vigorous stirring, has afforded yields of approximately 50%. The reaction is presumably



Procedure.—To 63 g. of finely powdered oxamide in a three-necked flask, 60 g. of anhydrous 1,2-ethanediamine in 250 ml. of anhydrous 1,4-dioxane, and thereafter as a catalyst, 2 ml. of concentrated hydrochloric acid was added. The mixture was heated to reflux and stirred with a collapsible, stainless steel stirrer which swept the sides of the flask for twenty-four hours until ammonia was no longer evolved.

The 1,4-dioxane was removed by evaporation *in vacuo*, the solid material macerated in 3 liters of boiling water and filtered. The filtrate was evaporated on a steam-bath to 300 ml. and the solid 2,3-diketopiperazine removed by filtration. The yield was 41.1 g. (or 50.3%) melting with decomposition at 285°. The product was identified by means of the 1,4-dinitrate-2,3-diketo derivative, m. p. 150°, which, mixed with an authentic sample of the 1,4-dinitrate derivative, melted at 149–150°.

UNIVERSITY OF FLORIDA
GAINESVILLE, FLORIDA
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Trifluoroethanol

BY ALBERT L. HENNE, ROBERT M. ALM AND MALCOLM SMOOK

CF_3CH_2OH has been prepared by Swarts[1] by reduction of trifluoroacetic anhydride under pressure, on a platinum catalyst. Although no one has ever voiced any doubt, this reduction has never been successfully repeated, due apparently to Swarts' failure appropriately to describe his catalyst. The reduction of CF_3CONH_2 is also mentioned by Swarts, and has been successfully developed by Gilman[2]; we duplicated Gilman's 77% yield, but had to consume 5 g. of platinum per mole of amide. Scherer[3] has made trifluoroalcohol by treating CF_3CH_2Cl with fused potassium acetate at 225°, and saponifying the resulting acetate. We have repeated this work and found the yields exceedingly sensitive to the reaction temperature, an experience duplicated by other laboratories.

We are now recommending the reduction of a derivative of trifluoroacetic acid (the ester or the acyl halide) with lithium aluminum hydride as the most convenient and efficient way to make the alcohol. Our preferred procedure is given.

Preparation of CF_3COCl.—A two-liter, three-necked flask was fitted with a dropping funnel, a mercury-sealed stirrer and a coiled reflux condenser with outlet leading to a 500-cc. receiver cooled in Dry Ice. The apparatus was thoroughly dried by flaming while sweeping with dry nitrogen; the inlet and outlet were protected by drying tubes. Benzoyl chloride (679 g. or 4.83 moles) was delivered into the flask; then over a one-hour period, trifluoroacetic acid (417 g. or 3.66 moles) was dropped in, with constant stirring. After completing the addition, the dropping funnel was replaced by a thermometer and the mixture heated overnight, up to 150°. The crude trifluoroacetyl chloride distilled through the reflux condenser; its rectification gave 380 g. (2.87 moles = 79%) of pure product, b.p. −27°, and 47 g. (0.41 mole = 11%) of unreacted acid.

Preparation of CF_3CH_2OH.—A five-liter, three-necked flask was fitted with a Dry Ice reflux condenser, a sealed stirrer and a gas inlet tube. The equipment was dried by flaming and sweeping with dry nitrogen. Solid lithium aluminum hydride (54 g. or 1.42 moles) was placed in the flask and covered with three liters of rigorously dried ether; while continuously stirring, CF_3COCl was led into the liquid as fast as the return from the reflux condenser would permit; the addition of 350 g. (2.64 moles) took about three and one-half hours. After this the mixture was refluxed for one more hour on an electric heating mantle. The inlet tube was replaced by a dropping funnel, then 200 cc. of water was slowly added to hydrolyze the excess of hydride. This made a clear solution and a precipitate of white curds. The solution was decanted into 1500 cc. of 6 *N* sulfuric acid containing ice. The ether layer was separated, then used in three portions for extractions of the aqueous layer; the latter was poured back onto the solid residue in the flask, then ether extracted. From the ether extracts, distillation isolated 285 g. of material boiling at 74–75°, which is a mixture of the trifluoroalcohol with 5–10% of water. Distilling from concentrated sulfuric acid gives the desired anhydrous alcohol, CF_3CH_2OH, b. p. 74°. The net yield is 85%.

In later experiments an excess of trifluoroacetyl chloride was used instead of an excess of hydride, because the latter was not readily available; a utilization of about 95% of the hydride was thus obtained, but this procedure is not recommended.

DEPARTMENT OF UNIVERSITY
OHIO STATE UNIVERSITY
COLUMBUS, OHIO
RECEIVED FEBRUARY 16, 1948

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[1] Swarts, *Bull. soc. chim. Belg.*, **43**, 471 (1934).

[2] Gilman, THIS JOURNAL **70**, 1281 (1948).

[3] Scherer, Scientific Zetko Exchange, P. B. Report No. 765.

Production of Radioactive Carbon Monoxide and Phosgene from Barium Carbonate

BY J. L. HUSTON[1] AND T. H. NORRIS[1]

Recently Kummer[2] has recommended the preparation of radioactive carbon monoxide by exchanging over a hot tungsten filament the C^{14} in a small amount of carbon dioxide with the inactive carbon in a large quantity of ordinary carbon monoxide. Some time ago we had occasion to prepare radioactive carbon monoxide ($C^{14}O$) as the first step in the preparation of radioactive phosgene which was to be used in biological experiments. Since our procedure involves no dilution of the radioactive carbon, and can be accomplished in less time than Kummer's procedure, we are presenting it at this time.

Our method involved the reduction of carbon dioxide to carbon monoxide by hot zinc, which was discovered by Noack.[3] Although this method was considered the most suitable for our purposes it should be pointed out that carbon monoxide can be prepared in good yield by heating alkaline earth

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[1] Present address: Chemistry Department, Oregon State College, Corvallis, Oregon.

[2] Kummer, THIS JOURNAL, **69**, 2239 (1947).

[3] E. Noack, *Ber.*, **16**, 75 (1883).