

ORGANIC SYNTHESSES

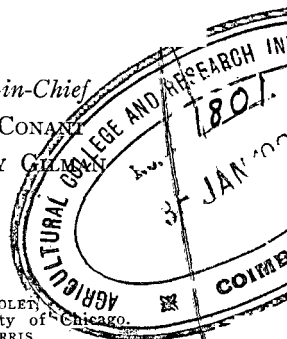
AN ANNUAL PUBLICATION OF SATISFACTORY
METHODS FOR THE PREPARATION
OF ORGANIC CHEMICALS

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VOL. VII

NEW YORK
JOHN WILEY & SONS, INC.
LONDON: CHAPMAN & HALL, LIMITED

1927

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PREFACE TO VOLUME VII

THE general plan of this series as set forth in the preceding volumes has been followed in the present volume. It is a great pleasure to acknowledge the help of former and new contributors both in this and other countries. In this volume twenty-six of the thirty preparations have been submitted by twenty-four contributors, four of whom are of foreign countries.

Of the special features included in previous volumes, all have been retained except the collection of later references to preparations in preceding volumes. This will appear again in Volume VIII. A few corrections to some of the earlier preparations are included in the Appendix. The editors acknowledge their appreciation of the help given by those submitting the corrections, and invite any comments on the preparations in any of the volumes.

In the present volume, seventeen of the preparations use as starting materials substances for which directions appear in this or earlier volumes. By the use of these preparations it is possible to arrange interesting series of preparations each of which starts from the product of the preceding one.

In addition to all other thanks which are due, the editor-in-chief of this volume wishes to thank his colleague, Louis Ehrenfeld, for his invaluable assistance especially in checking all computations.

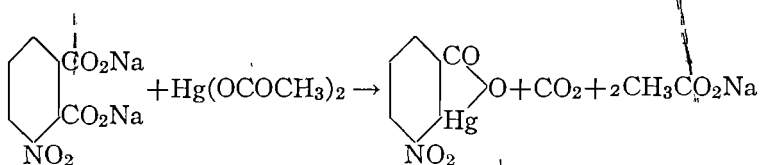
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ORGANIC SYNTHESSES

I

ANHYDRO-2-HYDROXYMERCURI-3-NITROBENZOIC ACID



Submitted by FRANK C. WHITMORE, P. J. CULHANE and H. T. NEHER
 Checked by HENRY GILMAN and C. C. VERNON.

1. Procedure

A SOLUTION of 80 g. (2 moles) of sodium hydroxide in 800 cc. of water is prepared in a 2-l. beaker. To the warm solution is added 211 g. (1 mole) of 3-nitrophthalic acid (p. 70) (Note 1). A small amount of insoluble material is removed by filtration through a large preheated Büchner funnel (Note 2). A solution of 350 g. (1.1 moles) of mercuric acetate (Note 3) in a mixture of 50 cc. of glacial acetic acid and 700 cc. of water is prepared by heating and filtering while hot (Note 4). The two hot solutions are poured into a 3-l. long-necked flask and mixed by shaking. No precipitate should separate (Note 5). The flask is clamped in a large oil bath (Note 6) with the level of the oil almost to the neck of the flask. It is fitted with a reflux condenser provided with a tube leading to a large beaker placed on the desk (Note 7). The temperature of the oil bath is raised to 170° over a period of about one hour. If any considerable amount of material

is driven through the condenser, it is poured back through the top of the condenser as soon as the reaction slackens. The heating at $165-175^{\circ}$ is continued for about seventy hours. After about sixty hours the end of the tube leading from the top of the condenser is introduced below the surface of about 1 cc. of mercury in a small test tube. The evolution of carbon dioxide can be followed by observing the bubbles which pass through the mercury. When not more than one or two bubbles escape per minute, the heating is discontinued (Note 8).

The product is allowed to settle and the hot supernatant liquid is poured through a preheated suction filter. The filtrate deposits less than 10 g. of crude product on cooling. The product in the flask is shaken with several 100-cc. portions of water, and all the fine material is transferred to the filter. Some lumpy material is usually left in the flask. This is transferred to a large mortar and ground to a paste with a little water and then transferred to the filter. After sucking as dry as possible, the suction is shut off, and 100 cc. of alcohol is poured over the material on the filter. After standing a few minutes, suction is again applied. The product is then dried to constant weight (Note 9). The yield of anhydro-2-hydroxymercuri-3-nitrobenzoic acid is 300-330 g. (82-90 per cent of the theoretical amount based on the 3-nitrophthalic acid used). It is a cream-colored powder which dissolves in an excess of dilute sodium hydroxide, leaving only a slight turbidity (Notes 10 and 11).

2. Notes

1. 3-Nitrophthalic acid melting above 200° (sealed tube) is pure enough for this preparation.
2. Although the insoluble material is very small in amount, filtration without suction is too slow.
3. Commercial mercuric acetate, about 90 per cent pure, was used. The equivalent amounts of mercuric oxide and acetic acid may be used if the acetate is not available.
4. A small amount of mercurous compounds is removed by the filtration.

5. If more concentrated solutions are used, the mercuric salt precipitates and the reaction runs less smoothly.

6. A large galvanized pail containing extra heavy lubricating oil was used. This oil does not fume even after heating for long periods.

7. This beaker serves to catch any material which is carried over during a slightly violent reaction which sometimes takes place at the beginning.

8. If a more accurate indication of the end of the reaction is desired, a tube of mercury may be inverted in a small beaker of mercury and any gas evolved during the later stages of the reaction may be collected over the mercury.

9. The wet material may be used without drying for the preparation of 2-bromo-3-nitrobenzoic acid (p. 12).

10. To dissolve the mercury compound, it should be dusted into boiling sodium hydroxide solution.

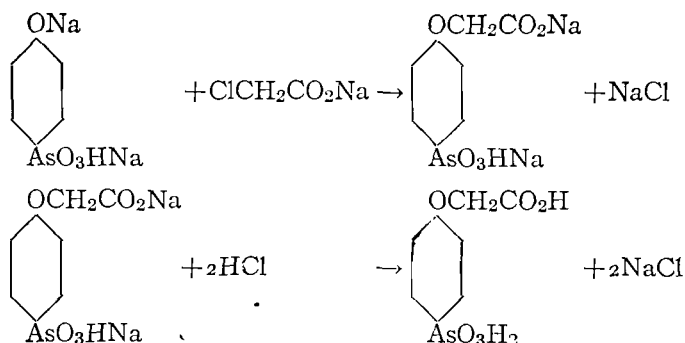
11. By a similar procedure phthalic anhydride may be converted into anhydro-2-hydroxymercuribenzoic acid. Thus, 300 g. (2 moles) of phthalic anhydride and 750 g. (2.2 moles) of commercial mercuric acetate (Note 3) gives 550 g. of the mercury compound (85 per cent of the theoretical amount). With phthalic anhydride the reaction is complete in six to ten hours.

3. Other Methods of Preparation

The preparation of anhydro-2-hydroxymercuri-3-nitrobenzoic acid does not appear in the literature.

II

p-ARSONOPHENOXYACETIC ACID



Submitted by C. S. PALMER and E. B. KESTER.
 Checked by J. B. CONANT.

1. Procedure

IN a 2-l. round-bottom flask is placed 218 g. (1 mole) of *p*-hydroxyphenylarsonic acid (Note 1) and 375 cc. of water. A solution of 180 g. (4.5 moles) (Note 2) of sodium hydroxide in 375 cc. of water is added, and the mixture shaken until a homogeneous solution is obtained. After cooling to 40–50° there is added 189 g. (2 moles) of chloroacetic acid in small portions (Note 3) with stirring, and the clear solution is refluxed for four hours. At the end of this time the mixture is cooled to 20°, filtered to remove a slight flocculent precipitate, and the *p*-arsonophenoxyacetic acid precipitated (Note 4) by the addition of 200 cc. (2.1 moles) of hydrochloric acid (sp. g. 1.19). The product is filtered on a 10-cm. Büchner funnel and washed with three successive 100-cc. portions of cold water. It is then crystallized from 2 l. of hot water (Note 5), filtered, and washed

twice with 100-cc. portions of cold water, once with 25 cc. of acetone, and once with 25 cc. of ether. After drying at 110° for one hour, there remains a pure white, anhydrous product weighing 110–120 g. (40–43 per cent of the theoretical amount) (Note 6). An arsenic analysis shows the product to be about 99 per cent pure.

2. Notes

1. Commercial phenolarsonic acid may be used, or 240 g. of sodium *p*-hydroxyphenylarsonate (Org. Syn. 4, 65) and 140 g. of sodium hydroxide may be substituted for the acid and the larger amount of base.

2. The use of less than 4.5 moles of alkali lowers the yield, while an increase in the alkali concentration does not increase the yield.

3. Unless the chloroacetic acid is added cautiously, there may be a violent reaction and the yield of *p*-arsonophenoxyacetic acid is lowered.

4. The product sometimes does not precipitate readily without vigorous agitation and rubbing the inside wall of the vessel with a stirring rod.

5. It is sometimes necessary to use decolorizing carbon in order to get a white recrystallized product.

6. The odor of phenol is strong at the end of the reaction, but most of the *p*-hydroxyphenylarsonic acid which does not react with the chloroacetic acid is not hydrolyzed and can be recovered in the filtrate from the *p*-arsonophenoxyacetic acid.

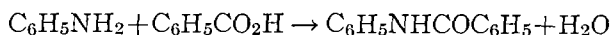
3. Other Methods of Preparation

p-Arsonophenoxyacetic acid has been made by heating aqueous sodium *p*-hydroxyphenylarsonate, two moles of chloroacetic acid, and four moles of sodium hydroxide.¹

¹ Ger. pat. 216,270; Frdl. 9, 1047 (1908–10).

III

BENZANILIDE



Submitted by CARL N. WEBB.

Checked by C. S. MARVEL and P. L. SALZBERG.

1. Procedure

IN a 3-l. round-bottom flask are placed 750 g. (8.1 moles) of aniline (Note 1) and 1 kg. (8.2 moles) of benzoic acid. When about two-thirds of the benzoic acid is in the flask the mixture is melted to make room for the rest. The flask is placed in a large oil bath and connected to a condenser for distillation. The temperature of the oil is raised quickly to 180–190°, at which point distillation starts. The bath is held at this temperature until practically no more aniline and water distil (about two hours), and then the temperature is slowly raised to 225° and maintained at this temperature until no further distillation takes place (one to two hours). The oil bath is now removed and the contents of the flask are allowed to cool below 180° and 550 g. (5.9 moles) of aniline is added. The distillations at 190° and 225° are repeated (about six hours). The hot mixture is poured into two 20-cm. evaporating dishes (hood) and is allowed to cool. The crude product weighs 1600–2000 g., depending on the amount of aniline retained.

The purplish-gray solid is ground (Note 2) in a large mortar and is poured with vigorous stirring into a 12-l. (3-gal.) crock containing 6 l. of approximately normal hydrochloric acid (5.5 l. of water and 500 cc. of concentrated hydrochloric acid). The stirring is continued for one hour after all the benzanilide has been added, and then the solid is filtered on a 20-cm. Büchner funnel. The process of stirring with acid and filtering is repeated twice to remove the excess of aniline. The solid is stirred for two hours with 6 l. of water and is filtered. It is stirred for one

hour with 6 l. of normal sodium hydroxide solution to remove the excess of benzoic acid and is then filtered. The stirring with alkali and filtering is repeated. The solid is next stirred for two hours with 7 l. of water and is filtered, sucked dry, and air-dried over night on paper.

After drying on paper the purplish solid is dried to constant weight in three 20-cm. evaporating dishes at 90–100° (about two days) and is then repowdered. The product is light purplish-gray and weighs 1270–1325 g. (80–84 per cent of the theoretical amount). It melts at 157–160°. The product is pure enough for use in the preparation of *p*-dimethylamino-benzophenone (p. 24) and for most synthetic purposes. When 100 g. of benzanilide is dissolved in 750 cc. of hot alcohol (Note 3) and the solution is boiled with about 10 g. of decolorizing carbon (Norite), filtered, and cooled to 10° over night, 80–86 g. of an almost colorless product melting at 160–161° separates. A second crystallization from alcohol using decolorizing carbon gives a white product with approximately the same loss in the mother liquors as in the first crystallization.

2. Notes

1. The ordinary "pure" aniline of commerce gives as good yields and as pure a product as redistilled aniline.
2. The benzanilide must be finely ground in order that aniline and benzoic acid may be completely extracted.
3. Very little of the solid fails to go into solution. The hot solution must be filtered rapidly as the benzanilide crystallizes easily.

3. Other Methods of Preparation

Benzanilide has been prepared by the treatment of aniline with benzoyl chloride,¹ benzoic anhydride,² or benzoic acid.³ The method described in the procedure is essentially that of Nägeli.

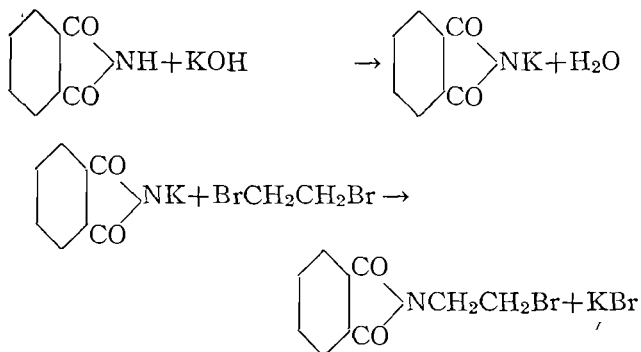
¹ Gerhardt, Ann. **60**, 311 (1846); Dehn and Ball, J. Am. Chem. Soc. **36**, 2096 (1914).

² Meyer and Sundmacher, Ber. **32**, 2123 (1899).

³ Hübner, Ann. **208**, 291 (1881); Nägeli, Bull. soc. chim. [3] **11**, 892 (1894).

IV

β -BROMOETHYLPHTHALIMIDE



Submitted by P. L. SALZBERG and J. V. SUPNIEWSKI.
 Checked by F. C. WHITMORE and H. C. BENEDICT, JR.

1. Procedure

A. Potassium Phthalimide.—In a 2-l. round-bottom flask fitted with a reflux condenser are placed 80 g. (0.54 mole) of phthalimide (Note 1) and 1600 cc. of absolute alcohol. (Org. Syn. 5, 56.) The mixture is gently boiled for about fifteen minutes or until no more of the phthalimide dissolves (Note 2). The hot solution is decanted from any solid into a specially prepared solution of 30.5 g. (0.54 mole) of potassium hydroxide (Note 3). A precipitate of potassium phthalimide separates at once. The mixture is stirred and cooled quickly to room temperature, and the precipitate is filtered with suction. To the alcoholic mother liquors a second 80-g. portion of phthalimide is added, and the entire process is repeated. The two crops of crystals are united (Note 4) and washed with 200 cc. of acetone

to remove any unchanged phthalimide. The yield of air-dried potassium phthalimide is 160-180 g. (79-89 per cent of the theoretical amount).

B. β -Bromoethylphthalimide.—In a 1-l. two-necked round-bottom flask fitted with an efficient stirrer and a reflux condenser are placed 150 g. (0.8 mole) of potassium phthalimide and 450 g. (2.4 moles) of ethylene dibromide (Note 5). The stirrer is started and the mixture is heated for about twelve hours in an oil bath maintained at 180-190°. The condenser is then set for distillation, and the excess of ethylene dibromide is distilled under reduced pressure. The recovery of the bromide amounts to 290-295 g. (Note 6).

The crude bromoethylphthalimide is extracted from the potassium bromide by refluxing with 300 cc. of alcohol (98-100 per cent) (Note 7) until the dark oil is entirely dissolved. This requires about one-half hour. The hot solution is filtered with suction, and the residue of salt is washed with a little hot alcohol. The alcohol is distilled under reduced pressure, and the dry residue is refluxed with 500 cc. of carbon disulfide for about fifteen minutes in order to separate the soluble bromoethylphthalimide from the insoluble diphthalimidoethane (Note 8). The warm solution is filtered with suction. The carbon disulfide is distilled under diminished pressure (Note 9). The bromoethylphthalimide remains as light tan crystals which melt at 78-80°. The yield is 140-160 g. (69-79 per cent of the theoretical amount).

The product thus obtained is pure enough for most purposes. However, a purer product may be obtained by recrystallization from dilute alcohol in the presence of decolorizing carbon. When 50 g. of crude product is dissolved in 200 cc. of 75 per cent alcohol, boiled for about ten minutes with 5 g. of decolorizing carbon (Norite), filtered, and the solution cooled to 0°, 40 g. of white product is obtained. The recrystallized product melts at 80-81°. A second recrystallization raises the melting point to 82-83°.

2. Notes

1. The phthalimide used was the crude product obtained as described in Org. Syn. **2**, 75.

2. The crude product always contains a small amount of material insoluble in alcohol.

3. It is convenient to prepare enough potassium hydroxide solution for the two precipitations at one time. This solution is prepared by dissolving 61 g. of potassium hydroxide in 60 cc. of water. To this solution is then added 180 cc. of absolute alcohol. One-half of the resulting solution is used for each 80-g. portion of phthalimide:

4. After the first crop has filtered, most of it should be removed and the second crop should be filtered through the same paper. The alcoholic filtrate on distillation yields about 1500 cc. of 98 per cent alcohol.

5. The ethylene dibromide which was used, boiled at 129–131°.

6. The last 15 to 20 g. of this recovered product distils very slowly.

7. The alcohol recovered from the preparation of the potassium phthalimide may be used for this extraction.

8. About 10 g. of crude diphthalimidoethane is obtained.

9. If the carbon disulfide is distilled at ordinary pressures, the residue melts and turns very dark. The crude yield is not lowered, but the purification is made more difficult.

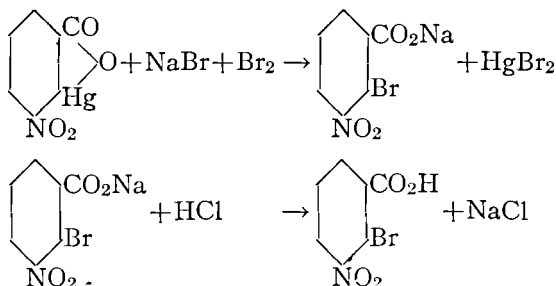
3. Other Methods of Preparation

The method described is based on that of Gabriel.¹

¹ Ber. **20**, 2224 (1887); **21**, 566 (1888); **22**, 1137 (1889)

V

2-BROMO-3-NITROBENZOIC ACID



Submitted by PAUL J. CULHANE.

Checked by HENRY GILMAN and C. C. VERNON.

1. Procedure

A SOLUTION of 50 g. (1.25 moles) of sodium hydroxide in 1.5 l of water is prepared in a 5-l. flask, and the solution is heated to gentle boiling. To the hot solution is added, in small quantities 330 g. (0.9 mole) of anhydro-2-hydroxymercuri-3-nitrobenzoic acid (p. 1) (Note 1). The mixture is stirred after the addition of each portion of about 50 g. until the material has gone into solution except for a small residue. The flask is then fitted with a stirrer and addition tube (Note 2) and with a connection to a reflux condenser. The material is heated to boiling and stirred vigorously. There is slowly added with continuous stirring 85 cc. (0.95 mole) (Note 3) of concentrated hydrochloric acid (sp. g. 1.19). Heating is discontinued at this point, and 30 cc (0.5 mole) of glacial acetic acid (sp. g. 1.05) (Note 3) is added slowly. A curdy precipitate forms.

A solution of bromine is prepared by dissolving 103 g

(1 mole) of sodium bromide and 160 g. (55 cc., 1 mole) of dry bromine in 150 cc. of water (Note 4). The mixture is stirred, and the bromine solution is added as rapidly as possible through the shaft of the stirrer. The precipitate dissolves. The solution is heated to boiling for five minutes after the last of the bromine has been added. The solution is then made slightly alkaline by the addition of 20 g. (0.5 mole) of solid sodium hydroxide and filtered through a fluted filter. The filtrate is then made acid to Congo Red, using about 150 cc. of concentrated hydrochloric acid. The precipitated 2-bromo-3-nitrobenzoic acid is filtered with suction and sucked as dry as possible. It is then crystallized from 1 l. of hot 30 per cent alcohol. The yield of product melting at 185–187° is 130–150 g. (53–61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used). About 25 g. of material melting at about 175° can be recovered from the mother liquor.

2. Notes

1. The reaction product from the mercuration of 3-nitrophthalic acid (1 mole) is used. The mercury compound can be used without drying if desired. If this is done, solution takes place much more readily.

2. A rapid distribution of the added material is necessary to prevent a local excess of the reagent added. This is very important when hydrochloric acid is added, as this tends to decompose the mercury compound. A convenient arrangement consists of a 3-way tube of about 15-mm. bore. The stirrer operates through the center tube. The other arms are used for the condenser and for the addition of material. A three-necked flask provided with a long-stemmed separatory funnel reaching below the stirrer may be used.

3. The addition of one mole of hydrochloric acid allows the formation of one mole of sodium chloride, which is of advantage in the subsequent addition of halogen, owing to the formation of a sodium salt of the chloromercuric acid, this being more soluble and hence more reactive than the anhydro compound. Acetic

acid is used for the final acidification because it does not decompose the mercury compound. The replacement by bromine takes place best in a slightly acid medium.

4. The mercury can be replaced by iodine in a similar manner. An iodine solution is made by dissolving 166 g. (1 mole) of potassium iodide and 255 g. (1 mole) of iodine in 250 cc. of water. This is used instead of the bromine solution. The mixture is filtered from the mercuric iodide and the filtrate acidified with 200 cc. of concentrated hydrochloric acid. The precipitate is filtered and then stirred with a solution of 10 g. of potassium iodide in 250 cc. of water to remove mercuric iodide. The mixture is filtered with suction and the precipitate crystallized from 1 liter of 50 per cent alcohol. The yield is 180 g. of 2-iodo-3-nitrobenzoic acid melting at 204–205.5° (61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used).

3. Other Methods of Preparation

2-Bromo-3-nitrobenzoic acid has been prepared by the nitration of 2-bromobenzoic acid, the 2,3 acid being separated from the 2,5 acid, which is the principal product of the nitration, by fractional crystallization of the potassium salts from water.¹

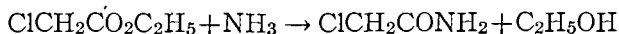
2-Iodo-3-nitrobenzoic acid has been prepared by the diazotization of 3-nitro-anthranilic acid.²

¹ Holleman and de Bruyn, *Rec. trav. chim.* **20**, 211 (1901).

² James, Kenner and Stubbings, *J. Chem. Soc.* **117**, 776 (1920).

VI

CHLOROACETAMIDE



Submitted by W. A. JACOBS and M. HEIDELBERGER.

Checked by C. S. MARVEL and D. D. COFFMAN.

1. Procedure

IN a 2-l. round-bottom flask fitted with a mechanical stirrer and surrounded by an ice-salt bath is placed 215 g. (1.75 moles) of ethyl chloroacetate (Note 1). Vigorous stirring is started and to the cold ester (Note 2) 200 cc. of chilled aqueous ammonia (sp. g. 0.9) is added. The solution is stirred in the cold for about fifteen minutes; then another 200-cc. portion of aqueous ammonia is added, and the stirring continued for about fifteen minutes. The mixture is then allowed to stand for thirty minutes, filtered with suction, and washed with two 25-cc. portions of cold water to remove ammonium chloride. The yield of air-dried material melting at 118–119° (Note 3) is 128–138 g. (78–84 per cent of the theoretical amount).

This product contains traces of ammonium chloride which may be removed by crystallization from water. When 100 g. of crude product is recrystallized from 400 cc. of water, about 80 g. of product is obtained. The recrystallized product melts at 119–120°.

2. Notes

1. The ethyl chloroacetate used may be a commercial grade which boils at 141–146°. The ethyl chloroacetate and the chloroacetamide have the usual irritating effect of chloroacetyl compounds.

2. The temperature is best maintained at 0-5°. At higher temperatures there is more replacement of the chlorine and the yields are considerably lower.
3. Traces of moisture lower the melting point considerably.

3. Other Methods of Preparation

Chloroacetamide has been prepared from chloroacetyl chloride and dry ammonia gas,¹ and by the treatment of ethyl chloroacetate² or methyl chloroacetate³ with cold aqueous ammonia solutions. The directions given above were developed from the methods of Scholl² and Tröger and Hille.²

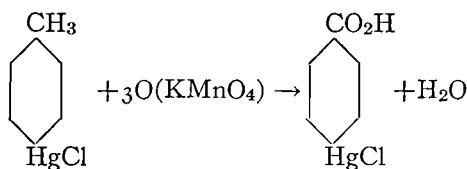
¹ Willm, Ann. **102**, 110 (1857).

² Willm, Ann. **102**, 110 (1857); Menschutkin and Jermoljew, Z. Chem. **1871**, 5; Bauer, Ann. **229**, 165 (1885); Scholl, Ber. **29**, 2417 (1896); Tröger and Hille, J. prakt. Chem. (2) **71**, 204, (1905).

³ Henry, Rec. trav. chim. **24**, 165 (footnote 3) (1905).

VII

p-CHLOROMERCURIBENZOIC ACID



Submitted by FRANK C. WHITMORE and GLADYS E. WOODWARD.
 Checked by HENRY GILMAN and J. D. ROBINSON.

1. Procedure

FIVE hundred grams (1.6 moles) of crude *p*-tolylmercuric chloride (Org. Syn. **3**, 99) and 720 g. (4.5 moles) of potassium permanganate are added to a solution of 1200 g. (30 moles) of sodium hydroxide in 18 l. of water contained in a large enamelled pail (or similar vessel) placed on a 15-cm. (6-in.) Fletcher burner and provided with a mechanical stirrer. The mixture is stirred and heated as near boiling as possible for fifteen minutes. The highest temperature conveniently obtainable is 95°. The tolylmercuric chloride dissolves (Note 1), forming the sodium salt of *p*-hydroxymercuribenzoic acid. The solution is cooled somewhat and alcohol is added to react with the excess of potassium permanganate (250 cc. is generally required to completely decolorize the solution). The manganese dioxide thus precipitated is removed by filtering with suction (Note 2). The filtrate should be clear and colorless. (If it is green, not enough alcohol has been added.) After the filtrate has become thoroughly cool, (Note 3), it is acidified with hydrochloric acid, about 1700 cc. of technical concentrated acid being necessary. The precipitated *p*-chloromercuribenzoic acid is difficult to filter because of its

flocculent character. It is best to allow it to stand at least over night and then filter by suction after siphoning most of the clear supernatant liquid. The acid retains much water and should be dried at 110° (Note 4). The yield is 350-420 g. (61-74 per cent of the theoretical amount). The crude acid may be purified by reprecipitation with hydrochloric acid from a solution in sodium hydroxide. The crude acid is sufficiently pure for the preparation of *p*-iodobenzoic acid (p. 58). It can be used for this purpose without drying.

2. Notes

1. The chief impurity in the tolylmercuric chloride is mercurous chloride, which is converted to the oxide and remains in the manganese dioxide precipitate.

2. In filtering the manganese dioxide from the strongly alkaline solution, it is best to support the filter paper by means of a cloth which is cut to fit the funnel and placed under the filter paper.

3. It is necessary that the filtrate be cooled at least to 20° before acidifying to avoid the splitting of the C-Hg linkage.

4. The caked acid loses water very slowly, even at 110° . Since the chief use of the acid is in preparing the *p*-halogen compounds, it need not be dried, but can be mixed with water while still wet.

3. Other Methods of Preparation

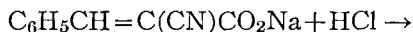
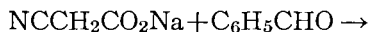
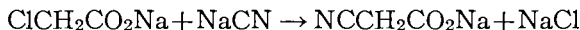
p-Chloromercuribenzoic acid has been prepared by the present process¹ and by heating the corresponding boric acid,² $(\text{HO})_2\text{BC}_6\text{H}_4\text{CO}_2\text{H}$, with mercuric chloride.

¹ Whitmore and Woodward, J. Am. Chem. Soc. **48**, 534 (1926).

² Michaelis, Ann. **315**, 35 (1901).

VIII

α -CYANO- β -PHENYLACRYLIC ACID



Submitted by ARTHUR LAPWORTH and WILSON BAKER.

Checked by J. B. CONANT and W. C. BOYD.

1. Procedure

A. Preparation of Sodium Cyanoacetate Solution.—In a 3-l. round-bottom flask is placed 250 g. (2.65 moles) of monochloroacetic acid. To this are added 100 cc. of water and 375 g. (1.3 moles) of crystalline sodium carbonate (decahydrate), (Note 1), the mixture being gently warmed. The neutralization is completed by adding sodium carbonate solution with litmus paper as an indicator. The flask is transferred to the hood, and a solution of 130 g. (2.65 moles) of sodium cyanide in 250 cc. of warm water is added in two approximately equal portions, waiting after the first addition until no further evolution of heat occurs, or the mixture ceases to boil. The cooled solution is neutralized with hydrochloric acid, using methyl orange as an outside indicator. The solution is then diluted with water to 1000 cc. and filtered; it should be of a light straw color. It can be kept for long periods of time in a stoppered bottle, although the color deepens somewhat.

B. Condensation with Benzaldehyde.—To 400 cc. (1.06 moles) of the sodium cyanoacetate solution is added a solution of 5 g. (0.13 mole) of sodium hydroxide in 400 cc. of water. The resulting alkaline solution is warmed to 40° and treated with 100 g. (0.94 mole) of benzaldehyde which has been shaken with sodium carbonate solution and distilled under reduced pressure. The benzaldehyde dissolves after vigorous shaking for a few minutes. After standing one hour, during which time some of the sodium cyanophenylacrylate crystallizes, the mixture is acidified with concentrated hydrochloric acid until acid to litmus and 40 cc. additional concentrated acid added, and the whole is shaken vigorously. After another hour, the crystalline cyanophenylacrylic acid is filtered on a Büchner funnel, washed thoroughly with cold water, and dried in a steam oven. It is then shaken with 100 cc. of benzene, filtered on a Büchner funnel, and further washed with 50 cc. of benzene and dried. The yield of product melting at 178–179° is 105–115 g. (65–70 per cent of the theoretical amount). This product may have a slight pinkish color, which can be removed by recrystallization from 740 cc. of alcohol or 10 l. of hot water. The recovery is about 57 per cent for alcohol and 92 per cent for water (Note 2). The melting point remains unchanged.

2. Notes

1. In place of the crystallized sodium carbonate, the equivalent amount of dehydrated material (138 g.) and water (240 cc.) may be used.

2. Owing to hydrolysis in alkaline or neutral solutions, it is very difficult to free the acid from a slight odor of benzaldehyde if it is recrystallized from water, but a final washing with benzene removes this odor.

3. Other Methods of Preparation

α -Cyanophenylacrylic acid has been prepared by the hydrolysis of the corresponding ester obtained by the condensation of benzaldehyde with cyanoacetic ester in the presence of sodium

alcoholate or acetic anhydride.¹ The direct condensation of benzaldehyde and cyanoacetic acid or its sodium salt takes place when the substances are heated² for some time at 180°. The most convenient method for the preparation of the acid (as the sodium or potassium salt) is by the action of benzaldehyde on an alkaline aqueous solution of sodium or potassium cyanoacetate prepared by the interaction of salts of bromoacetic³ or chloroacetic acids⁴ with potassium or sodium cyanide in aqueous solution.

¹ Carrick, J. prakt. Chem. (2) **45**, 501 (1892).

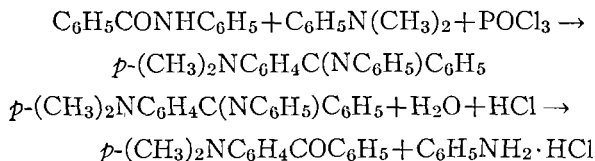
² Fiquet, Ann. chim. (6) **29**, 442 (1893); Bull. soc. chim. (3) **7**, 11 (1892).

³ Clarke and Francis, Ber. **44**, 273 (1911).

⁴ Lapworth and McRae, J. Chem. Soc. **121**, 1699 (1922).

IX

p-DIMETHYLAMINOBENZOPHENONE



Submitted by CHARLES D. HURD and CARL N. WEBB.

Checked by C. S. MARVEL and P. L. SALZBERG.

1. Procedure

FIVE hundred grams (2.5 moles) of dry, powdered benzanilide (p. 6), 1025 g. (8.4 moles) of technical dimethylaniline, and 525 g. (3.4 moles) of phosphorus oxychloride are mixed (Note 1) in a 3-l. round-bottom Pyrex flask (Note 2). The flask is fitted with a two-holed cork stopper which carries a reflux condenser and a thermometer. The top of the condenser is provided with a calcium chloride tube; the bulb of the thermometer reaches beneath the surface of the liquid.

The flask is warmed in a water bath until the appearance of a sudden exothermic reaction (Note 3), at which point the flask must be cooled at once by rotating it underneath the surface of cold water. The cooling is continued until the thermometer indicates a temperature of 125° or less. The flask is then immersed in a bath of boiling water for about three hours, after which the mixture is cooled to about 50°, and poured slowly into 2.5 l. of warm (Note 4) dilute hydrochloric acid, made from 325 cc. (about 4 moles) of concentrated acid, contained in a large crock of about 15 l. (4 gal.) capacity. The mixture is left for about three hours until hydrolysis is complete (Note 5).

About 8 l. of water is added to precipitate the *p*-dimethylaminobenzophenone. The solution, milky at first, soon deposits sandy crystals of light green color, which are collected on a 20-cm. Büchner funnel. They are transferred to a beaker and washed with 1.5 l. of water, after which they are again collected on the filter, washed, pressed as dry as possible, and air dried. With no further purification the melting point is 88–90°. The yield is 350–390 g. An additional 85–100 g. of inferior product, m.p. 70–80°, is obtained by treating the combined filtrates with a solution of 250 g. (6.2 moles) of sodium hydroxide. This product, air-dried as before, is dissolved in 300–400 cc. of hot alcohol from which, by partial evaporation and cooling, more than half separates in good crystalline form, m.p. 88–90.5°. This material may be combined with the first product of similar melting point. The total yield is 410–440 g. (72–77 per cent of the theoretical amount) (Note 6).

The crude product melts fairly sharply, but it is colored light green. The color may be almost completely removed by recrystallization from hot alcohol. The best result is obtained by dissolving 100 g. of the crude product in 600 cc. of boiling alcohol, heating with 5 g. of decolorizing carbon (Norite), filtering, and cooling the solution in an ice-salt bath. The crystals are then separated from the mother liquor by centrifuging (Note 7). The yield of almost colorless crystals melting at 89.5–90.5° is 80 g.

2. Notes

1. This causes an elevation in temperature to about 50°.
2. Pyrex is essential to avoid breakage when the hot flask is cooled rapidly.
3. This exothermic reaction usually begins at 90–110°, and the temperature rises in a few seconds to about 180°. In smaller runs, e.g., with 100 g. of benzanilide, it is not advisable to cool the flask before the temperature has reached about 180°, as some benzanilide may remain unchanged. The flask and the attached condenser should be readily detachable from the sup-

porting ringstand so that the whole can be lifted and cooled quickly. A pail of cold water should be at hand for this purpose.

4. The temperature of the acid is 50° at the start and about 80° during the addition.

5. This should give a homogeneous solution. Should there be unused benzanilide, it will appear at this point and should be removed by filtration.

6. It is impracticable to obtain a further yield of ketone by the addition of more sodium hydroxide to the filtrate. Nor does it seem practical to recover the aniline and the excess of dimethylaniline.

7. If the crystals are separated by suction filtration, it is very hard to remove all of the mother liquor. When such crystals are air-dried, the alcohol evaporates and leaves the outer layer of material colored deep green.

3. Other Methods of Preparation

p-Dimethylaminobenzophenone is best prepared from benzanilide, dimethylaniline, and phosphorus oxychloride.¹ It has also been obtained by treatment of malachite green² with concentrated hydrochloric acid at 180° , and by the methylation of *p*-aminobenzophenone³ with methyl iodide at 180° . Dimethyl sulfate⁴ has also been used as a methylating agent. It is noteworthy that the ketone has not been prepared by the Friedel-Crafts method, nor by condensation methods using zinc chloride. These methods give vigorous reactions, but no ketone has been isolated from the complex mixtures which are formed.

¹ Ger. pat. 41,751; Frdl. 1, 44 [1887]. Meisenheimer, Budkewicz and Kananow, Ann. 423, 84 (1921).

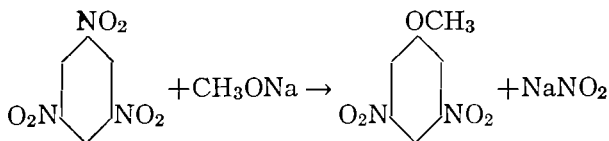
² Doebner, Ann. 217, 257 (1883); Ber. 13, 2225 (1880).

³ Doebner, Ann. 210, 269 (1881). Doebner and Weiss, Ber. 14, 1837 (1881).

⁴ Baeyer, Ann. 354, 190 (1907).

X

3, 5-DINITROANISOLE



Submitted by FREDERIC REVERDIN.

Checked by C. S. MARVEL and DOROTHY E. BATEMAN.

1. Procedure

A SOLUTION of sodium methylate is prepared by dissolving 6.3 g. (0.27 mole) of sodium in 150 cc. of absolute methyl alcohol (Note 1) in a 1-l. flask provided with a reflux condenser. To this is added a solution of 50 g. (0.23 mole) of 1,3,5-trinitrobenzene (Org. Syn. **2**, 93) in 550 cc. of absolute methyl alcohol. The mixture is boiled for about twenty minutes. The reflux condenser is then replaced by a still head and condenser, and about 300–350 cc. of alcohol is distilled. The residue in the flask is cooled to 20° and filtered. The crude product is purified by recrystallization from hot ordinary methyl alcohol. On account of the low solubility of the dinitroanisole in hot methyl alcohol, the best results are obtained by boiling the crude product with a few grams of decolorizing carbon (Norite) in about 500 cc. of methyl alcohol, filtering the hot solution through a hot funnel, cooling the solution, filtering, and using the mother liquors for another extraction. After five extractions no more of the product is dissolved. The yield of pure product melting at 105° is 29–35 g. (63–77 per cent of the theoretical amount).

2. Note

1. One liter of ordinary absolute methyl alcohol was treated with 5 g. of magnesium turnings and 0.1 g. of mercuric chloride, refluxed for ten hours, and then distilled.

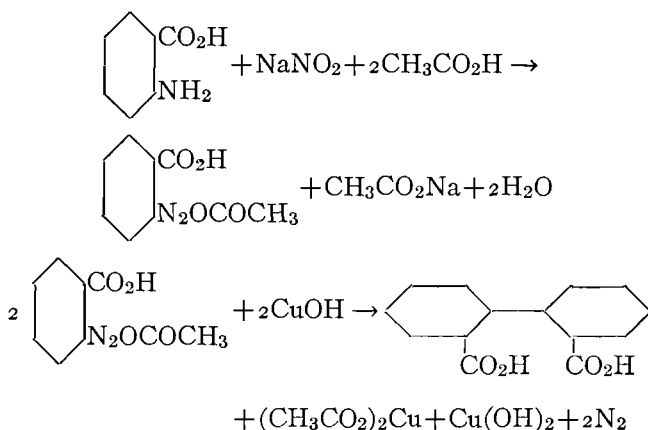
3. Other Methods of Preparation

3,5-Dinitroanisole has been made only by this method.¹

¹ Lobry de Bruyn, Rec. trav. chim. **9**, 208 (1890).

XI

DIPHENIC ACID



Submitted by E. H. HUNTRESS.

Checked by H. T. CLARKE and ROSS PHILLIPS.

1. Procedure

A. Preparation of Cuprous Hydroxide.—Cuprous chloride is prepared from a solution of 500 g. (2 moles) of crystallized copper sulfate and 150 g. (2.55 moles) of sodium chloride in 2.5 l. of water (Org. Syn. 3, 33) by the gradual addition of sodium sulfite (from 110 g. of sodium bisulfite). After decanting the supernatant solution, the precipitate of cuprous chloride is added to a solution of 350 cc. of 6 N sodium hydroxide in 1 l. of water contained in the 4-l. beaker in which the main synthesis is to be performed, the last portion of solid cuprous chloride being washed in with 1 l. of water. After vigorously stirring for a few minutes, the heavy precipitate of deep orange-colored cuprous hydroxide is permitted to settle and the supernatant

liquid siphoned off. The cuprous hydroxide is washed free from salt by another 2 l. of water which is not removed until the cuprous hydroxide is to be used.

B. Diazotization of Anthranilic Acid.—To 100 g. (0.73 mole) of anthranilic acid (m.p. 143–144°) in a 1.5-l. beaker arranged for vigorous mechanical stirring and efficient external cooling are added 300 cc. of distilled water and 133 cc. of glacial acetic acid (2.3 moles) (Note 1). A solution of 51 g. of sodium nitrite (0.74 mole) in 200 cc. of distilled water is slowly added from a separatory funnel during about forty minutes (Note 2).

C. Synthesis of Diphenic Acid.—When the diazonium solution is ready for use, the last wash water is siphoned from the cuprous hydroxide and the 4-l. beaker containing the latter is clamped in a 12-l. enamelled pail. The space between the beaker and the container is gradually filled with ice water as the level of the reaction mixture rises in the beaker. Provision is made for vigorous stirring of the reaction mixture, and by means of a long tube a separatory funnel is arranged to deliver the diazonium solution (Note 3) below the surface of the liquid in the beaker. Then 300 cc. of distilled water and 270 cc. (4 moles) of concentrated aqueous ammonia (sp. g. 0.90) are added (Note 4). Addition of the diazonium solution is begun at once and so regulated that all has been run in within about one hour. The thick foam is broken from time to time by adding a few drops of ether (Note 5). After the diazonium solution is added, the ice-bath is removed while stirring is continued at room temperature for half an hour.

The solution is then heated to boiling and carefully acidified to Congo Red with concentrated hydrochloric acid (sp. g. 1.19, about 600 cc.), which is added very slowly with constant stirring and scratching of the walls of the beaker. As the mixture becomes acid, the foam disappears and the thick precipitate of copper hydroxide is replaced by a granular one of crude diphenic acid. The beaker is then placed in running water until thoroughly cold; the crude diphenic acid is filtered by suction and washed with faintly acid, saturated ammonium chloride solution until free from copper salts, and then with water. If dried

at this point, the crude gray acid melts at $210-225^{\circ}$ and weighs 65-83 g.

The crude diphenic acid is next transferred to a 1.5-l. flask and dissolved in 400-450 cc. of glacial acetic acid. Then 100 cc. of hot water is added and the dark solution boiled not more than ten minutes with 15-20 g. of zinc dust (Note 6). Towards the end of this treatment, 4 g. of decolorizing carbon (Norite) is added, and the solution is filtered hot through a large preheated Büchner funnel. The clear deep-red filtrate is heated to boiling in a 2-l. flask and 700-800 cc. of hot water added slowly with stirring so that no permanent precipitation occurs. The flask is then allowed to cool somewhat and crystallization started by vigorously scratching the inside of the vessel (Note 7). The mixture is allowed to stand at room temperature for at least four hours. The diphenic acid is then filtered with suction and washed with 100-200 cc. of water. The yield of acid melting at $226-228^{\circ}$ is 40-50 g. (46-57 per cent of the theoretical amount).

2. Notes

1. The substitution of acetic for hydrochloric acid in the diazotization avoids the formation of *o*-chlorobenzoic acid and gives a crude product melting in some cases as high as $218-225^{\circ}$, as compared with $190-210^{\circ}$ when hydrochloric acid is employed.

2. In almost all samples of commercial anthranilic acid, even though showing the correct melting point, a small amount of insoluble material remains on diazotization. The clear liquor should be removed from this by decantation.

3. Only a portion of the diazotized solution is placed in the separatory funnel, the remainder being kept in an ice-bath supplied as required.

4. The use of more than this quantity of ammonia leads to its reaction with the diazonium salt and the formation of a brown tar, in the presence of which the diphenic acid fails to precipitate in the acetic acid purification. Less than this amount leads to low yields. The quantity employed suffices to

neutralize the excess acetic acid in the diazonium solution and the diphenic acid formed and still have 2.5 moles in excess.

5. When commercial anthranilic acid is employed the foam is extremely troublesome. *n*-Butyl alcohol sometimes gives more satisfactory results than ether as an anti-foam agent.

6. The zinc-dust treatment serves to reduce and remove small amounts of azo compounds (notably *o*-azobenzoic acid) which always discolor the crude product. Attempts to purify the crude product by crystallization from 33 per cent alcohol invariably led to a darker colored product with the same melting point as the crude. The decolorizing carbon is not intended to decolorize the solution but to clarify the filtrate before the precipitation of the diphenic acid.

7. Diphenic acid solutions show a strong tendency to become supersaturated. Crystallization begins at once, however, on scratching the wall of the container and, when allowed to proceed slowly, leaves most of the colored impurities in the solution. If suddenly chilled out of the acetic acid, however, or if rapidly thrown out by reckless addition of acid in the initial precipitation, large amounts of tar and coloring matter will be carried down. The final product varies from very light gray to pure white.

3. Other Methods of Preparation

Diphenic acid was first prepared by oxidizing phenanthrenequinone with chromic acid.¹ Many later workers² have modified this process in minor details. Vorländer and Meyer³ were the first to prepare diphenic acid from diazotized anthranilic acid and cuprous oxide, but their process is not well adapted to large scale preparation. Inasmuch as pure phenanthrene is now very difficult to obtain in quantity, the present process was devised for relatively large scale operation.

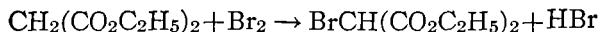
¹ Fittig and Ostermayer, *Ann.* **166**, 367 (1873).

² Fittig and Schmitz, *ibid.*, **193**, 116, (1878); Graebe and Aubin, *ibid.*, **247**, 263 (1888); Oyster and Adkins, *J. Am. Chem. Soc.* **43**, 209 (1921); Bischoff and Adkins, *ibid.*, **45**, 1031 (1923); Roberts and Johnson, *ibid.*, **47**, 1399 (1925).

³ *Ann.* **320**, 138 (1902).

XII

ETHYL BROMOMALONATE



Submitted by C. S. PALMER and P. W. McWHERTER.

Checked by ROGER ADAMS and M. M. BRUBAKER.

1. Procedure

A 1-l. three-necked flask is fitted with a stirrer, a reflux condenser with a tube leading to a flask of water for absorption of hydrogen bromide, and a separatory funnel with a stem drawn to a fine tip which reaches almost to the blades of the stirrer. In the flask are placed 160 g. (1 mole) of ethyl malonate (Note 1) and 150 cc. of carbon tetrachloride. In the separatory funnel is placed 165 g. (1.03 moles) of dry bromine (Note 2). The stirrer is started, and a few cc. of bromine is run into the solution. A large electric bulb is held under the flask until the reaction starts. Then the rest of the bromine is added gradually at such a rate as to keep the liquid boiling gently. It is then refluxed until no more hydrogen bromide is evolved (about one hour). The mixture is cooled and washed five times with 50-cc. portions of 5 per cent sodium carbonate solution. It is then distilled under reduced pressure, fractions being taken up to 130°/40 mm. and at 130-150°/40 mm. The residue amounts to about 20 g. The lower boiling fraction is redistilled. The combined fractions boiling at 130-150°/40 mm. are redistilled under reduced pressure. The product boiling at 132-136°/33 mm. (121-125°/16 mm.) amounts to 175-180 g. (73-75 per cent of the theoretical amount). Redistillation of the low fractions gives about 15 g. more of the product.

2. Notes

1. Commercial ethyl malonate distilled under reduced pressure and collected over a 3° range was used.
2. Commercial bromine was dried by shaking with an equal volume of concentrated sulfuric acid. A slight excess of bromine is used to insure complete bromination.

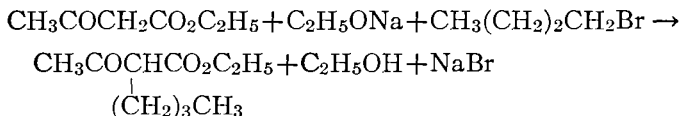
3. Other Methods of Preparation

Ethyl bromomalonate is usually prepared without the use of a solvent.¹

¹ Knoevenagel, Ber. **21**, 1356 (1888).

XIII

ETHYL *n*-BUTYLACETOACETATE



Submitted by C. S. MARVEL and F. D. HAGER.

Checked by FRANK C. WHITMORE and W. F. SINGLETON.

1. Procedure

A 5-l. round-bottom flask, fitted with an efficient mechanical stirrer (Note 1), a reflux condenser, the upper end of which is protected by a calcium chloride tube, and a separatory funnel, is arranged for heating on a steam bath.

In the flask is placed 2.5 l. of absolute alcohol (Note 2), and then there is added gradually 115 g. (5 moles) of metallic sodium cut into pieces. This requires three to four hours. After all the sodium has dissolved, 650 g. (5 moles) of ethyl acetoacetate (Note 3) is added. The stirrer is started and the solution heated to gentle boiling. To the boiling solution 750 g. (5.47 moles) of *n*-butyl bromide (Note 4) is added over a period of about two hours. The refluxing and stirring are continued until a sample of the solution is neutral to moist litmus paper. The time varies from six to ten hours.

When the reaction is complete, the mixture is cooled, and the solution is decanted from the sodium bromide. The salt is washed with 100 cc. of absolute alcohol, and the washings are added to the main solution. The alcohol (Note 5) is separated from the substituted acetoacetic ester by distilling through a short column from a steam bath. The crude residue after removal

of the alcohol weighs about 925 g. It is satisfactory for hydrolysis to give the corresponding ketone (p. 60). If the pure ester is desired, the crude product is distilled under reduced pressure. The yield of product boiling at 112–117°/16 mm. is 642–672 g. (69–72 per cent of the theoretical amount) (Note 6).

2. Notes

1. The stirrer should be efficient in order to prevent bumping due to the settling of the sodium bromide which is formed during the reaction.

2. The grade of absolute alcohol is important. Alcohol dried with sodium ethylate (Org. Syn. 5, 56) is satisfactory. It is more effective to dry alcohol with magnesium methylate if the presence of methyl alcohol in the absolute alcohol is permissible. This may be done by dissolving 24 g. of magnesium turnings in 200 cc. of absolute methyl alcohol (the reaction is very vigorous) and then adding three liters of the ordinary grade of absolute alcohol (about 99.5 per cent). The mixture is refluxed for about five hours and distilled into the flask in which the absolute alcohol is to be used.

3. The ethyl acetoacetate used in these experiments boiled over a range of five degrees under reduced pressure. The product prepared as described in Org. Syn. 6, 36, is satisfactory.

4. The *n*-butyl bromide (Org. Syn. 1, 5) boiled over a range of three degrees. The excess was used in order to decrease the time necessary to complete the reaction.

5. The alcoholic solution should be protected from moisture and the alcohol which is recovered by the distillation treated with sodium and boiled under a reflux condenser to remove the excess of alkyl halide. After distillation the alcohol may then be used in a subsequent preparation.

6. This reaction is very general and other substituted acetoacetic esters may be obtained in approximately the same yields if this procedure is followed.

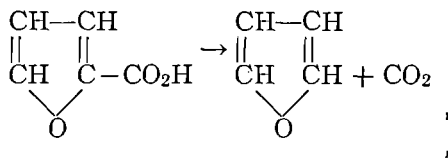
3. Other Methods of Preparation

Ethyl *n*-butylacetoacetate has always been prepared by the action of *n*-butyl bromide on the sodium salt of ethyl acetoacetate.¹ The procedure given above is the usual one for alkylating ethyl acetoacetate.

¹ Tafel and Jürgens, Ber. **42**, 2555 (1909); Shannon, Proc. Roy. Irish Acad. **36B**, 322 (1924) (C. A. **19**, 470 (1925)); Hess and Bappert, Ann. **411**, 153 (1925).

XIV

FURAN



Submitted by W. C. WILSON.

Checked by ROGER ADAMS and C. G. GAUERKE.

1. Procedure

IN a 200-cc. round-bottom flask is placed 80 g. (0.71 mole) of crude 2-furancarboxylic acid (Org. Syn. **6**, 44) (usually about 95 per cent pure). To the neck of the flask is fitted an upright tube 2.5 cm. in diameter and 15 cm. long, with a side arm of the same diameter leading out about 2 cm. from the top of the tube. This side arm is extended into the bottom of an efficient (25-cm.) soda-lime tower (Note 1) immersed in a water bath held at 40° to prevent condensation of the furan. From the top of the soda-lime tower an outlet tube (0.5 cm. in diameter) is extended to the top of an upright water condenser, to the lower end of which is attached a receiving flask surrounded by ice and salt (Note 2).

The top of the upright tube in the reaction flask is closed by a cork stopper holding a glass plunger which may be used for pushing back into the flask any sublimed 2-furancarboxylic acid.

The acid is heated just to its boiling point (200–205°) (Note 3), when it decomposes with the evolution of furan and carbon dioxide. The small amounts of 2-furan-carboxylic acid

that sublime are pushed back from time to time. The distillate is finally redistilled, when it is found to boil at $31-34^{\circ}$ at 745 mm. The yield is 33-36 g. (72-78 per cent of the theoretical amount).

2. Notes

1. The drying column removes carbon dioxide, moisture, and some of the other by-products which are formed. The product which is collected is nearly pure, and the redistillation completes the purification.

2. In a number of experiments a second receiver was used in addition to the first one, but it was found that practically all of the furan condensed in the first receiver.

3. Care should be taken in heating 2-furancarboxylic acid. If the temperature is too low, decomposition takes place too slowly; if too high, much 2-furancarboxylic acid sublimes and causes difficulty. In one run a thermometer was placed in the melted acid. It read $200-205^{\circ}$ during the evolution of the furan.

3. Other Methods of Preparation

Limpricht,¹ in 1873, prepared furan by heating barium 2-furancarboxylate with soda lime. It has since been prepared by the dry distillation of barium 2-furancarboxylate;² in small amounts by distillation of calcium succinate;³ by the destructive distillation of resinous pine wood;⁴ by heating succinaldehyde with water at 180° ;⁵ and by heating 2-furancarboxylic acid in a sealed tube.²

¹ Limpricht, *Ann.* **165**, 281 (1873).

² Freundler, *Compt. rend.* **124**, 1157 (1897); *Bull. soc. chim.* (3) **17**, 613 (1897).

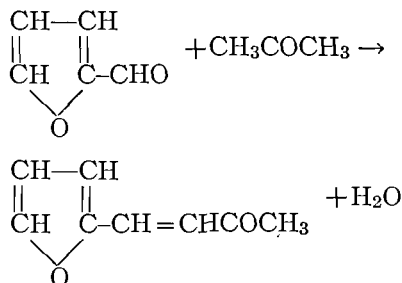
³ Metzner and Vorländer, *Ber.* **31**, 1886 (1898).

⁴ Atterberg, *Ber.* **13**, 879 (1880).

⁵ Harries, *Ber.* **34**, 1496 (1901).

XV

FURFURALACETONE



Submitted by G. J. LEUCK and L. CEJKA.

Checked by FRANK C. WHITMORE and H. H. ROWLEY.

1. Procedure

In a 5-l. round-bottom flask equipped with a mechanical stirrer are mixed 385 g. (335 cc.) (3.8 moles) of 95 per cent furfural (Org. Syn. **1**, 49) (Note 1) and 3 l. of water. Then 500 g. (630 cc.) (8.6 moles) of acetone is added. The mixture is stirred and cooled to 10° and to it is added 75 cc. of 33 per cent sodium hydroxide solution (Note 1), whereupon some heat is generated. Without cooling, the stirring is continued for four hours. At the end of this time 10 per cent sulfuric acid is added until the mixture is acid to litmus (about 350 cc.) (Note 2). The two layers which have formed are separated and the upper aqueous layer is distilled (Note 3) under ordinary pressure until the distillate no longer forms two layers. The bottom layer of this distillate is added to the original lower layer and distilled under reduced pressure from a 1-l. modified Claisen flask (Org. Syn. **1**, 40) provided with an air condenser and heated in an oil bath. The

receiving flask is placed in a large funnel connected with the drain. A stream of cold water is run over the receiver. When a solid appears in the receiver, distillation is interrupted, the liquid distillate is discarded, and the distillation is continued. The product which distils at $114-118^{\circ}/10$ mm. ($135-145^{\circ}/50$ mm.) Note 4) weighs 310-340 g. (60-66 per cent of the theoretical amount, based on the furfural used). The yellow crystals melt at $37-39^{\circ}$ and when melted show a sharp freezing point of 37° (Note 5).

2. Notes

1. Commercial chemicals were used. The use of purer chemicals, including furfural distilled over a 2° range under diminished pressure, gives no higher yield, but the product is lighter colored, although the boiling point and melting point are the same as with the crude materials.

2. When the alkali is neutralized, the mixture loses its milky appearance and forms definite layers.

3. The distillation of the water layer may be omitted, since it yields only 10-20 g. of the product.

4. A large residue of higher boiling material remains in the flask. This residue contains much difurfuralacetone, the formation of which takes place to a considerable extent in spite of the large excess of acetone used.

5. The highest melting point recorded in the literature is $39-40^{\circ}$. The crystals gradually become reddish on standing even in the dark. This change is much slower when freshly distilled furfural is used.

3. Other Methods of Preparation

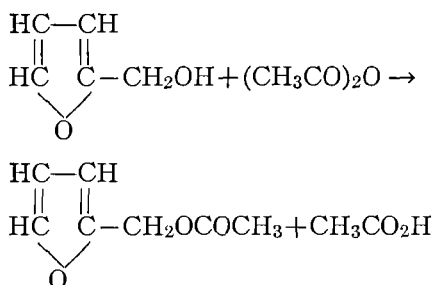
The method ¹ of condensation of furfural with acetone in the presence of bases is the only one reported as giving furfuralacetone.

¹ Schmidt, Ber. **14**, 574, 1459 (1881); Claisen, Ber. **14**, 2468 (1881); Ann. **223**, 137 (1884).

XVI

2-FURYLMETHYL ACETATE

(Furfuryl Acetate)



Submitted by THE MINER LABORATORIES.
Checked by ROGER ADAMS and C. G. GAUERKE.

1. Procedure

A MIXTURE of 1 l. of benzene, 600 g. (6.1 moles) of 2-furyl-carbinol (Org. Syn. **6**, 44) (Note 1), 225 g. of fused and powdered sodium acetate, and 650 g. (6.4 moles) of a good grade of acetic anhydride are placed in a 5-l. round-bottom flask (Note 2) fitted with a mechanical stirrer (Org. Syn. **1**, 4, Fig. 1*b*) and a reflux condenser provided with a calcium chloride tube. The flask is heated on a steam bath (Note 1) for four hours with stirring to prevent caking of the sodium acetate.

The reaction mixture is allowed to cool and is poured into 4 l. of cold water (Note 3). The upper layer is separated and allowed to stand for two hours over about 500 cc. of 5 per cent sodium carbonate solution with frequent shaking or mechanical stirring. This decomposes any excess of acetic anhydride. It

is finally washed with about 3 l. of water. The benzene solution is distilled under ordinary pressure to remove the benzene (800-900 cc. is recovered). The 2-furylmethyl acetate is distilled under diminished pressure, b.p. $69-70^{\circ}/7$ mm. The yield is 750-800 g. (87-93 per cent of the theoretical amount) (Note 4).

2. Notes

1. If the water-insoluble form of the alcohol (Org. Syn. **6**, 46) is used, the mixture should be allowed to stand under a reflux condenser for about two hours before it is heated. During this period a certain amount of heat is evolved, and sometimes it is sufficient to cause the benzene to boil vigorously, thus making cooling necessary. After it has stood the required time, the mixture is refluxed as described above.

2. If a two- or three-necked flask is available it can be used to advantage.

3. The washing can best be done in a large separatory apparatus prepared by cutting the bottom out of an 18-l. (5-gal.) glass carboy and wiring into its neck a piece of glass tubing carrying a rubber tube and pinch clamp. The inverted carboy forms a useful separatory funnel of large capacity.

4. Saponification of the product with standard potassium hydroxide shows 93-94 per cent ester. It contains some furfuryl alcohol, the removal of which by fractional distillation is difficult, because the boiling points of the alcohol ($169^{\circ}/752$ mm.) and the ester ($175^{\circ}/764$ mm.) are so close together. Furfuryl acetate darkens on standing. It may be redistilled with little loss to give an almost colorless product.

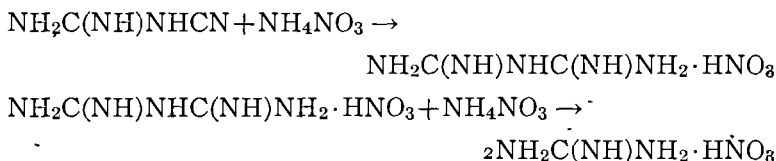
3. Other Methods of Preparation

2-Furylmethyl acetate has been prepared by heating 2-furylcarbinol with acetic anhydride alone, or with acetic anhydride and sodium acetate.¹

¹ Wissell and Tollens, *Ann.* **272**, 303 (1892); Zanetti, *J. Am. Chem. Soc.* **47**, 535 (1925).

XVII

GUANIDINE NITRATE



Submitted by TENNEY L. DAVIS.

Checked by H. T. CLARKE and ROSS PHILLIPS.

1. Procedure

IN a 1-l. round-bottom flask is placed an intimate mixture of 210 g. of dicyanodiamide (2.5 moles) and 440 g. of ammonium nitrate (5.5 moles) (Note 1). The flask is introduced into an oil bath at 110–120° and the temperature of the oil is raised during about half an hour to 160°. The bath is then held at this temperature (Note 2) for three hours. During the first hour the mass melts to a clear liquid which begins to deposit crystals and finally sets to a solid cake (Note 3). At the end of three hours the flask is removed from the bath; the product is allowed to cool and is extracted on the steam bath with successive quantities of water (about 2 l. is necessary to bring all soluble material into solution) (Note 4). The solution is filtered to remove white amorphous insoluble material (ammeline and ammeline) (Note 5).

The filtrate contains guanidine nitrate along with a small amount of ammonium nitrate and very small amounts of dicyanodiamide and biguanide nitrate (Note 6). The solution is concentrated to about 1 l. and the guanidine nitrate which crystallizes on cooling is filtered off. A second crop is obtained by

concentrating to 250 cc. (Note 7). The combined yield of crude guanidine nitrate is 520–560 g. (85–92 per cent of the theoretical amount). The product may be purified by recrystallization from 1 l. of water (Note 8), taking a second crop after concentrating the mother liquor to 250 cc. The yield of recrystallized guanidine nitrate melting at $213\text{--}214^\circ$ amounts to 500–520 g. (Note 9).

2. Notes

1. A 10 per cent excess of ammonium nitrate is used because the biguanide mononitrate which is formed as an intermediate is strongly basic and tends to attack the unreacted ammonium nitrate, as is evidenced by the liberation of ammonia during the heating. The excess of ammonium nitrate can be easily separated from the guanidine nitrate by the crystallization from water, and it does not interfere with the conversion of guanidine nitrate into nitroguanidine by the action of strong sulfuric acid.

2. When the molten mass reaches 150° its temperature begins to rise above that of the bath, generally reaching 200° during the course of five or six minutes. The mass should not be stirred at any time, especially before the mixture has completely melted; otherwise, the temperature may run somewhat higher.

3. The guanidine nitrate begins to crystallize soon after the temperature of the mixture begins to fall.

4. The hard cake goes into solution slowly and time must be given for each portion to become saturated before it is decanted.

5. When the hot filtrate cools, it will deposit flocks of ammelide along with the crystals of guanidine nitrate. Water may conveniently be added until the crystals dissolve, and the cold solution again filtered for the removal of ammelide.

6. This filtrate on evaporation to dryness and baking at 100° leaves a residue of 650 g., which is suitable for the preparation of nitroguanidine (p. 68).

7. At this point the mother liquor (about 200 cc.) may be discarded as it contains mainly ammonium nitrate.

8. Alcohol is a satisfactory solvent for guanidine nitrate but appears to have no advantage over water. A saturated solution of guanidine nitrate in water contains about 10 per cent at 15°.

9. The second mother liquor may advantageously be worked up with a subsequent run.

3. Other Methods of Preparation

Guanidine salts have been prepared by heating ammonium thiocyanate,¹ by hydrolysis of dicyanodiamide by acids,² (whereby one molecule of the guanidine salt is produced), and by the action of ammonium salts on dicyanodiamide,³ from which two molecules of guanidine salt result. The nitrate has been prepared from the thiocyanate by the action of nitric acid.⁴

¹ Delitsch, J. prakt. Chem. (2) **8**, 240 (1873); (2) **9**, 2 (1874); Volhard, *ibid.* (2) **9**, 15 (1874).

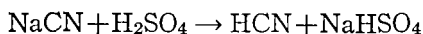
² Baumann, Ber. **7**, 1766 (1874); Davis, J. Am. Chem. Soc. **43**, 669 (1921).

³ Rathke, Ber. **18**, 3107 (1885); Davis, J. Am. Chem. Soc. **43**, 2234 (1921).

⁴ Jousselin, Bull. soc. chim. (2) **34**, 497 (1880).

XVIII

HYDROGEN CYANIDE (ANHYDROUS)



Submitted by K. ZIEGLER.

Checked by HENRY GILMAN and L. C. HECKERT.

1. Procedure

A 5-l. round-bottom flask, set up in a good hood (Note 1), is fitted with a three-holed rubber stopper that holds two 250-cc, separatory funnels, *A* and *B* (Fig. 1). A small funnel, *F*, (about 3-4 cm. in diameter) is suspended directly under the outlets of the two separatory funnels and is attached to the

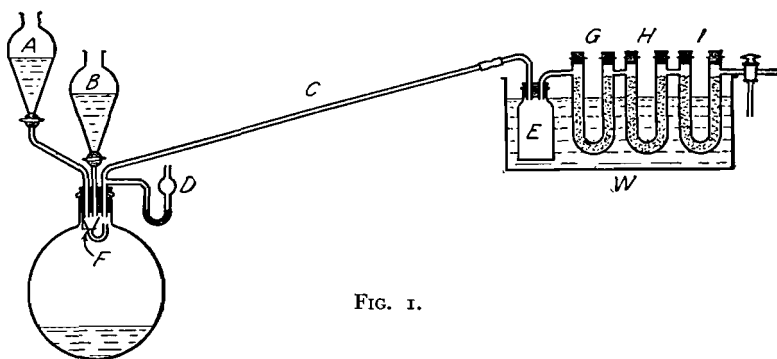


FIG. 1.

rubber stopper by a loop of stiff copper wire. The discharge tube of the funnel is bent in the shape of a U so that its end is about one cm. below the top of the funnel. In the third hole of the rubber stopper is inserted an inclined glass tube, *C*, of about 10 mm. internal bore and approximately 50 cm.

long. A mercury safety vent, *D*, is sealed in the side of this tube. *C* acts as an air condenser and leads to an empty gas bottle, *E*, of about 250 cc. capacity and then to three large U tubes, *G*, *H*, and *I*, filled with anhydrous calcium chloride. The gas bottle and the U tubes are contained in a water bath, *W*, warmed to 30–40°. The last calcium chloride tube is fitted with a three-way glass stopcock so that the gaseous anhydrous hydrogen cyanide may be used directly or diverted to an efficient condenser for liquefaction. The condenser is a glass coil of 4–5 mm. bore and about 50 cm. long that is surrounded by ice (Note 2) contained in a percolator arrangement like that described in Org. Syn. 6, 13.

One of the separatory funnels is filled with 1 l. of sulfuric acid prepared by the careful addition of 302 g. (4 moles) (213 cc.) of concentrated sulfuric acid to 213 cc. of water. The other separatory funnel is filled with a solution of 203 g. of commercial sodium cyanide (about 96 per cent) (4 moles) dissolved in sufficient water to make 500 cc. of solution. Evolution of hydrogen cyanide takes place on the simultaneous addition of the two solutions. Practically all of the reaction occurs in the funnel, *F*, and the sodium bisulfate solution continuously drains into the flask so that fresh solutions are always present. The solution in the funnel remains clear as long as sufficient sulfuric acid is present. An excess of sodium cyanide colors the solution yellow and leads to the formation of a muddy brown precipitate. By adjusting the flow of solutions the rate of evolution is easily controlled, and the preparation requires no attention beyond that involved in the occasional replenishment of the solutions in the separatory funnels. The last part of the hydrogen cyanide can be driven from the apparatus by boiling the bisulfate solution for a few minutes. The yield of acid melting at -15° to -14.5° is 100–105 g. (93–97 per cent of the theoretical amount) (Notes 3 and 4).

2. Notes

1. Gattermann¹ recommends that the operator smoke during the preparation, for he found that a trace of hydrogen cyanide is

sufficient to give the tobacco smoke a highly characteristic flavor. This preliminary warning is useful in case of leaky apparatus or a faulty hood.

2. It is essential that the coil be cooled with ice only. A freezing mixture causes solidification of the hydrogen cyanide with consequent clogging of the apparatus.

3. The hydrogen cyanide is best kept over anhydrous calcium chloride. In this way it remains clear and water-white for months; otherwise, it soon becomes yellow, owing to the formation of azulmic acid.

4. If larger quantities of hydrogen cyanide are desired, the apparatus may be modified as suggested by Lindemann³ by using a four-hole rubber stopper in the generating flask and fitting it with a siphon tube by means of which the sodium bisulfate solution can be removed from time to time. With this modification the generating flask need be of only 2- to 3-l. capacity.

3. Other Methods of Preparation

The only other method of preparative value for the generation of hydrogen cyanide is the reaction between potassium ferrocyanide and sulfuric acid.¹ It is convenient for the preparation of small amounts of hydrogen cyanide; however, it is too expensive in larger runs. The present method is based on the work of Ziegler² and Lindemann.³

¹ Gattermann, *Ann.* **357**, 318 (1907).

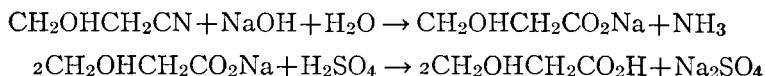
² Ziegler, *Ber.* **54**, 110 (1921).

³ Lindemann, *Ann.* **431**, 291 (1923).

XIX

β -HYDROXYPROPIONIC ACID

(Hydracrylic Acid)



Submitted by R. R. READ.

Checked by H. T. CLARKE and C. R. NOLLER.

1. Procedure

To a cold solution of 160 g. (4 moles) of sodium hydroxide in 500 cc. of water in a 2-l. round-bottom flask provided with a mechanical stirrer is added slowly 250 g. (3.5 moles) of ethylene cyanohydrin (Org. Syn. **3**, 57), the temperature being kept below 30° (Note 1) by means of a cold water bath. The mixture is allowed to stand over night in the bath, when the flask is fitted with a two-holed rubber stopper bearing a capillary tube reaching almost to the bottom and a delivery tube bent slightly downward for attachment to a suction pump. The flask is then heated slowly to 80° during four hours by raising the temperature of the surrounding water. A rapid current of air is drawn through the mixture during the heating. The mixture is now evaporated to dryness under reduced pressure by heating in an oil bath, the temperature of which is raised as rapidly as the boiling of the material will permit. The oil bath is finally held at 125° until the product becomes pasty. The flask is allowed to cool, and 50 cc. of water is poured down one side of the flask, and the solid material at that point worked carefully into a paste with a stout stirring rod.

A cooled mixture of 200 g. (109 cc.) of concentrated sulfuric acid (2 moles) and 300 cc. of water is now added slowly with careful cooling (Note 2), the pasty mixture being stirred with a thermometer and the temperature not being allowed to rise above 35°. Sodium sulfate crystallizes during this addition. The mass is now shaken vigorously with 400 cc. of ether and allowed to stand for some minutes. The ether is then decanted as completely as possible and the residue filtered with suction. The sodium sulfate is now shaken with six successive 300-cc. portions of ether, the ether solutions being subsequently employed for extraction of the filtrate. This latter requires 10-14 such extractions (each with 300-400 cc. of ether) for the satisfactory extraction of the β -hydroxypropionic acid. The combined ethereal solution is dried over 50 g. of anhydrous sodium sulfate and the ether distilled from a water bath, the temperature of which is not allowed to rise above 50°. The product is then concentrated under reduced pressure from a water bath maintained at 55-60°. The residue should have attained constant weight after four to six hours of this treatment; it consists of a sirupy liquid of pale straw color which contains 75-80 per cent of β -hydroxypropionic acid (by titration) (Note 3). The yield is 120-125 g. (28-31 per cent of the theoretical amount).

2. Notes

1. If the temperature of the mixture of nitrile and sodium hydroxide is allowed to rise too soon or too rapidly, the evolution of ammonia may become almost explosive, as the reaction is exothermic.

2. The temperature during the addition of the sulfuric acid must be carefully controlled, as the heat of neutralization is sufficient to decompose the product. The use of a minimum amount of water is desirable in order to decrease the number of extractions.

3. β -Hydroxypropionic acid is an uncrystallizable and hygroscopic sirup. The 20-25 per cent of impurity remaining in the final product is largely water.

3. Other Methods of Preparation

β -Hydroxypropionic acid has generally been prepared by the hydrolysis of β -iodopropionic acid¹ or the corresponding bromo compound.² Owing to the readiness with which ethylene cyanohydrin may now be prepared, this was considered to be the most suitable starting product, alkali³ being regarded as a more suitable hydrolytic agent than acid.⁴ β -Hydroxypropionic acid has also been prepared by the action of alkali upon acrylic acid.⁵

¹ Beilstein, Ann. **122**, 369 (1862); Socoloff, Ann. **150**, 168 (1869); Heintz, Ann. **157**, 298 (1871); Wislicenus, Ann. **166**, 10 (1873).

² Lossen, Ann. **342**, 128 (1905).

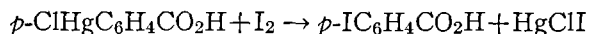
³ Wislicenus, Ann. **128**, 6 (1863).

⁴ Erlenmeyer, Ann. **191**, 269 (1878).

⁵ Erlenmeyer, Ann. **191**, 281 (1878); Linnemann, Ber. **8**, 1095 (1875).

XX

p-IODOBENZOIC ACID



Submitted by FRANK C. WHITMORE and GLADYS E. WOODWARD.

Checked by HENRY GILMAN and C. C. VERNON.

1. Procedure

ONE hundred fifty grams (0.6 mole) of iodine is dissolved in 2.5 l. of 95 per cent ethyl alcohol in a 5-l. round-bottom flask set on a tripod and provided with a mechanical stirrer and a reflux condenser. To this solution is added 300 g. (0.84 mole) of powdered dry crude *p*-chloromercuribenzoic acid (Note 1) (p. 18). The mixture is stirred and heated. The acid gradually goes into solution and the color of iodine disappears. The hot stirred mixture is treated with iodine until a yellow color persists for at least ten minutes. This is conveniently done by weighing out iodine in 10-g. portions, dissolving in a little alcohol and adding through the condenser. The total amount of iodine required depends on the purity of the mercurated acid. It should not exceed 210 g. (0.83 mole). If there is any insoluble material left after an excess of iodine has been added, it is removed by rapid filtration through a pre-heated suction filter. On cooling, the filtrate yields about 175 g. of *p*-iodobenzoic acid. Concentration of the mother liquor yields crystals which are contaminated with mercuric iodide. The latter may be removed by grinding the crystals in a mortar with water and enough sodium iodide or potassium iodide to destroy the red color of the mercuric iodide (Note 2). The mixture is filtered and the crystals are washed with a little sodium iodide solution and

then with water. The washed *p*-iodobenzoic acid melts at 266–267°. The total yield is 150–170 g. (72–81 per cent of the theoretical amount).

2. Notes

1. The crude *p*-chloromercuribenzoic acid may be sucked as dry as possible and transferred in this pasty form to the iodine solution. If, however, it has caked at all, it must be thoroughly dried and powdered. A respirator should be worn as the dust is rather irritating.

2. Another method of removing most of the mercuric iodide is to grind the crystals, suspend them in a little water, and pour off the lighter suspension of iodobenzoic acid, leaving the heavy mercuric iodide behind. Washing with iodide solution is necessary to remove the last of the mercuric iodide.

3. Other Methods of Preparation

p-Iodobenzoic acid has been prepared by the oxidation of *p*-iodotoluene with chromic acid mixture¹ and with nitric acid;² from the nitrile obtained from *p*-iodonitrobenzene and potassium cyanide;³ and from *p*-aminobenzoic acid by diazotization.⁴

¹ Körner, Z. Chem. 1868, 327.

² Cohen and Raper, J. Chem. Soc. 85, 1273 (1904).

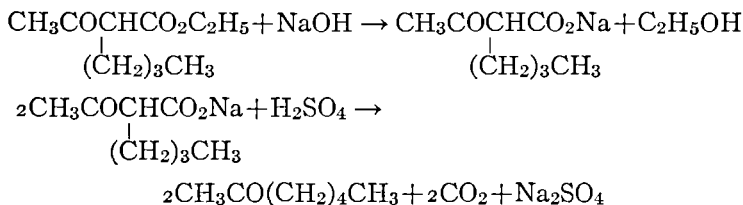
³ Richter, Ber. 4, 553 (1871).

⁴ Marshall, Ber. 28, 338 (1895).

XXI

METHYL *n*-AMYL KETONE

(Heptanone-2)



Submitted by JOHN R. JOHNSON and F. D. HAGER.

Checked by FRANK C. WHITMORE and W. F. SINGLETON.

1. Procedure

In a 12-l. round-bottom flask, fitted with an efficient mechanical stirrer, is placed 5 l. of a 5 per cent solution of sodium hydroxide (6.25 moles). To this is added the crude ethyl *n*-butylacetoacetate (about 925 g.) (p. 36) obtained from 5 moles of ethyl acetoacetate. The mixture is stirred at room temperature for four hours, during which time the mono-substituted acetoacetic ester is completely saponified and passes into solution. The mixture is then allowed to stand until the unsaponified material separates completely as an oily layer. The aqueous layer is separated (Note 1) and transferred to a flask provided with a stopper fitted with a separatory funnel and a large bent glass tube leading to a condenser set for distillation.

Through the separatory funnel is added slowly 500 cc. of 50 per cent (sp. gr. 1.40) sulfuric acid (3.6 moles), which is somewhat more than the amount required to neutralize the alkali (6.25 moles) used in the saponification of the ester. When the evolution of carbon dioxide ceases to be vigorous, the reaction mixture is heated slowly to boiling, and from one-third

to one-half of the total volume is distilled. The distillate is made alkaline with solid sodium hydroxide (Note 2) and redistilled until 80-90 per cent has been collected.

In the distillate the ketone layer is separated from the water, and the latter is distilled until one-third has been collected. The ketone layer in this distillate is separated, and the water layer is again distilled. This procedure is repeated as long as any considerable amount of ketone is obtained in the distillate (Note 3). The combined ketone fraction is washed four times with one-third its volume of a concentrated solution of calcium chloride (sp. gr. 1.3 or greater) to remove alcohol (Note 4), then dried over 50 g. of solid calcium chloride, filtered and distilled. The yield of methyl *n*-amyl ketone boiling at 148-151° at 750 mm. is 300-350 g. (52-61 per cent of the theoretical amount, based upon the original ethyl acetoacetate) (Note 5).

2. Notes

1. The insoluble layer is usually quite small in amount and may be discarded. On distillation it yields but a small amount of ketone and monosubstituted ester, along with considerable high-boiling material, presumably the disubstituted ester, which was present in the crude ethyl *n*-butylacetoacetate.

2. The distillate is rendered alkaline to remove any acids formed by the acid decomposition of the substituted acetoacetic ester or unreacted ethyl acetoacetate.

3. With methyl *n*-amyl ketone this process was repeated three times after the first separation. In the case of higher ketones a fewer number of separations is required, while with the simpler ketones a greater number is advisable, on account of their solubility in water.

4. With the lower molecular weight ketones it is advantageous to distil the calcium chloride solution to recover the dissolved ketone. This is carried out exactly as described for the separation from the water. With methyl *n*-amyl ketone the loss is slight if a sufficiently concentrated solution of calcium chloride is employed.

5. Other ketones may be prepared by the same general procedure. Based upon the ethyl acetoacetate used, the following yields were obtained:

Methyl *n*-butyl ketone (hexanone-2) b.p. 126–128°, 50 per cent.

Methyl *iso*-butyl ketone (4-methylpentanone-2) b.p. 115–119°,
20 per cent.

Methyl *sec*-butylmethyl ketone (4-methylhexanone-2) b.p. 139–
142°, 30 per cent.

The lower yields are due in some cases to the difficulty of isolating the products, and, in the last two, to the less complete reaction between the secondary alkyl bromide and the sodium derivative of ethyl acetoacetate.

3. Other Methods of Preparation

Methyl *n*-amyl ketone has been prepared by the hydration of heptene-1 and of heptene-2 under various conditions,¹ and by heating *n*-amyl propiolic acid with potassium hydroxide.² It has also been obtained by the oxidation of methyl *n*-amyl carbinol with chromic acid.³

The procedure used in the ketone decomposition of ethyl *n*-butylacetoacetate is adapted from that used by Michael and Wolgast⁴ for ethyl ethylacetoacetate.

¹ Behal, Ann. chim. phys. (6) 15, 270 (1888); Desgrez, *ibid.* (7) 3, 228, 234 (1894).

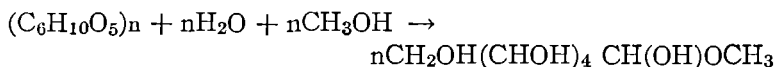
² Moureu and Delange, Bull. soc. chim. (3) 23, 674 (1903).

³ Schorlemmer, Ann. 161, 279 (1872).

⁴ Ber. 42, 3177 (1909).

XXII

α -METHYL MANNOSIDE



Submitted by C. S. HUDSON.

Checked by FRANK C. WHITMORE and R. D. GREENE.

1. Procedure

ONE kilogram of dry finely ground vegetable ivory waste (Note 1) is added gradually to 1250 g. of 85 per cent sulfuric acid in an 8-l. (2-gal.) enamelled vessel (Note 2) at such a rate as to keep the temperature at 30–35° (one to two hours). The mass is well kneaded (Note 3) and then kept at about 25° for fifteen hours (Note 4). A mixture of 1 l. of acetone-free methyl alcohol and 250 cc. of pure concentrated hydrochloric acid (sp. gr. 1.19) (Note 8) is kneaded into the soft mass, which is then transferred to a 12-l. flask. The flask is adjusted on a large steam bath (Note 5), 6 l. of absolute methyl alcohol is added, and the mixture is refluxed eight hours. At the end of this time the mixture is cooled somewhat, and 100 g. of decolorizing carbon and 150 g. of infusorial earth or fuller's earth are added, and refluxing is resumed for half an hour. The solution is filtered hot with suction through a Büchner funnel previously heated by blowing steam into the side neck of the suction flask (Note 6). The cake is washed with 500 cc. of hot absolute methyl alcohol. The filtration is likely to be slow unless a large funnel (30 cm.) is used. The light yellow filtrate soon begins to deposit crystals (Note 7). It is kept in an ice box twenty

to fifty hours. The crystals are filtered off by suction, washed with 50 cc. of absolute methyl alcohol, then with 50 cc. of dry acetone, and dried on porous plates at room temperature. The yield is 480-520 g. The mannoside is pure enough for most chemical purposes. It melts at about 170° and has a rotation in water of $+78.6^{\circ}$. If a purer product is desired, the mannoside may be crystallized from four parts of 80 per cent ethyl alcohol with 80-90 per cent recovery if the mother liquors are worked up. Slight acidity in the solutions used in recrystallization should be carefully neutralized with ammonia. The recrystallized mannoside melts at $188-189^{\circ}$ and has a rotation of $[\alpha]_D^{20}$, $+80.8^{\circ}$.

2. Notes

1. The ivory nut waste was obtained from the Rochester Button Company, Rochester, N. Y. It was ground in a mill, dried to constant weight at 100° , and sifted through a 20-mesh screen (8 per cm.).

2. The bottom of an Elyria enamelled kettle was used. A crock can be used almost as conveniently. On smaller runs a large porcelain mortar was used.

3. The kneading can conveniently be done by means of a heavy stick, the end of which has been thoroughly charred in a fire and then polished to remove loose carbon. Stirring is not practical.

4. A convenient method of heating is to suspend a 60-watt electric light about 20 cm. above the mixture.

5. The flask may be immersed half way in a large kettle of water heated on a large radial burner.

6. Another convenient device for rapid filtration is to use a large Witt plate in a steam funnel attached to a suction flask.

7. In some runs spontaneous crystallization is slow to start. It is advantageous to inoculate the solution with a crystal of the mannoside.

8. Later experiments indicate that the addition of hydrochloric acid is not essential since the sulfuric acid is sufficient to cause the formation of the mannoside. (C. S. Hudson.)

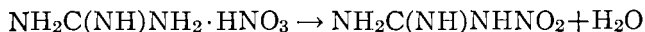
3. Other Methods of Preparation

α -Methyl mannoside has been prepared from mannose and methyl alcohol in the presence of hydrochloric acid.¹ The present method of preparing it directly from vegetable ivory has obvious advantages over any method for preparing it from isolated mannose.

¹ Fischer and Beensch, Ber. **29**, 2928 (1896).

XXIII

NITROGUANIDINE



Submitted by TENNEY L. DAVIS.

Checked by H. T. CLARKE and ROSS PHILLIPS.

1. Procedure

To 500 cc. (Note 1) of concentrated sulfuric acid (sp. g. 1.84), previously cooled in a freezing mixture, is added in small portions and with hand stirring 560 g. of crude (Note 2) guanidine nitrate (obtained from 210 g. of dicyanodiamide as described on p. 46). The temperature is not allowed to rise above 20° during the addition. When all has been added, the milky mixture is allowed to stand at room temperature with occasional stirring until it is homogeneous and free from crystals (Note 3). It is then poured with stirring into 6 l. of a mixture of cracked ice and water. The precipitated nitroguanidine is filtered, washed free from acid, and recrystallized from the least possible amount (4-5 l.) of boiling water (Note 4). The yield (Note 5) is 380-390 g. (73-75 per cent of the theoretical amount, based on the dicyanodiamide used). The product melts with decomposition at about 232° (Note 6).

2. Notes

1. It has been found in checking that the use of 800 cc. of acid, while not necessary, gives a much less viscous solution, which becomes homogeneous more rapidly.

2. This contains ammonium nitrate, which, however, does not interfere with the reaction.

3. The mixture has to stand fifteen to twenty hours before solution is complete.

4. The solution should be allowed to cool slowly, preferably over night, when the nitroguanidine separates in long needles which resemble sublimed phthalic anhydride. The mother liquor contains only 3-4 g. per liter, and may be discarded.

5. In checking, yields amounting to 85-90 per cent of the theoretical quantity were obtained from pure guanidine nitrate.

6. Melting points varying between 220° and 250° have been obtained on the same sample, according to the rate of heating.

3. Other Methods of Preparation

Nitroguanidine may be prepared by the nitration of guanidine salts by means of nitric acid,¹ or by the action of concentrated sulfuric acid upon guanidine nitrate.² The nitration of guanidine thiocyanate yields a product which retains a small proportion of sulfur compounds, and the nitration of the sulfate requires vigorous treatment and gives poor yields. The present procedure, which yields the *alpha* form,³ is simple and economical, and furnishes a good yield.

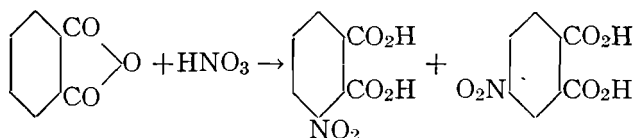
¹ Thiele, Ann. **270**, 16 (1892).

² Jousselin, Compt. rend. **88**, 1087 (1879); Pellizzari, Gazz. chim. ital. **21** (II), 406 (1891).

³ Davis, J. Am. Chem. Soc. **47**, 1063 (1925).

XXIV

3-NITROPHTHALIC ACID



Submitted by P. J. CULHANE and GLADYS E. WOODWARD.
 Checked by HENRY GILMAN and C. C. VERNON.

1. Procedure

A 2-l. beaker placed on a piece of board in the bottom of a 4-l. (1-gal.) crock is fitted with a mechanical stirrer (Note 1). In the beaker are placed 650 cc. of commercial sulfuric acid (sp.g. 1.84) and 500 g. (3.4 moles) of technical phthalic anhydride. The mixture is stirred and steam is passed into the crock. When the mixture reaches 80°, the steam is shut off and 210 cc. of fuming nitric acid (sp.g. 1.51) is added slowly from a separatory funnel at such a rate as to maintain the temperature of the stirred mixture at 100–110°. The addition requires one to two hours. After the fuming acid has been added, 900 cc. of concentrated nitric acid (sp.g. 1.42) is added as rapidly as possible without causing the temperature to rise above 110° (Note 2). The mixture is then stirred and heated by passing steam into the crock for two hours longer. The mixture is allowed to stand over night and then poured into 1.5 l. of water in a 4-l. (1-gal.) crock. After cooling, the solid mixture of 3- and 4-nitrophthalic acids is filtered by suction through a Büchner funnel without a filter paper (Note 3) or through a filtros plate (Org. Syn, 5, 7). The wet cake is returned to the

crook and stirred thoroughly with 200 cc. of water, which dissolves a large amount of the 4-nitrophthalic acid. The mixture is again filtered by suction (Note 4) and the wet cake is dissolved by boiling with 200-300 cc. of water (Note 5). The solution is filtered hot and stirred mechanically until crystallization starts. It is then allowed to stand over night, as the crystallization is slow. The crystals are filtered by suction and air-dried. The product melts at $205-210^{\circ}$ in a sealed tube. The yield is 200-220 g. (28-31 per cent of the theoretical amount) (Note 6). Recrystallization of 200 g. of the crude acid from 300 cc. of water gives 170 g. of acid melting at $215-218^{\circ}$ (capillary tube sealed 2 cm. from bottom). The washings and mother liquor from the crystallization may be saved for the recovery of 4-nitrophthalic acid (Note 7).

2. Notes

1. A large steam bath may be used instead of the crook. A motor should not be used directly above the nitration mixture because of the fumes evolved. The motor should be connected with the stirrer by a belt or, better still, a stirrer of the wind turbine type should be used. If a hood is not available, a 3-l. three-necked flask provided with a glass tube to conduct the fumes outside has been found satisfactory. When a beaker is used, it is recommended that two rectangular glass plates be placed across the top to reduce the danger of acid spattering.

2. The indicated proportions of fuming nitric acid and concentrated acid give as good results as fuming acid alone. The addition of the concentrated acid first does not work well.

3. The filtrate is repeatedly poured through the filter until clear. The mother liquor containing sulfuric acid and nitric acid cannot be worked up profitably for the recovery of the nitrophthalic acids.

4. The mother liquor is saved for the recovery of 4-nitrophthalic acid (Note 7). The product, if air-dried at this point, weighs about 500 g.

5. The amount of water needed depends on the dryness of the cake of crude acids.

6. By various refinements the yields may be increased, but the cost of the 3-nitrophthalic acid obtained is also increased. Because of the extreme cheapness of phthalic anhydride, it is inadvisable to increase the labor cost unduly in order to improve the yield. If a purer product is desired, crystallization from acetic acid will give 3-nitrophthalic acid melting at about 217° (closed tube).

7. The washings and mother liquors from crystallizations may be evaporated and esterified to separate the isomeric acids.³

About 370 g. of air-dried solid material may be recovered from the mother liquors and washings. Care must be exercised in concentrating these solutions, as the solid material chars readily when the solution becomes concentrated.

3. Other Methods of Preparation

3-Nitrophthalic acid has been prepared by the oxidation of nitronaphthalene,¹ and by the nitration of phthalic acid in a variety of ways by many different workers.² The present method is based on those of Bogert and Boroschek³ and of Lawrance.⁴

¹ Beilstein and Kurbatow, *Ann.* **202**, 217 (1880); de Aguiar, *Ber.* **5**, 899 (1872).

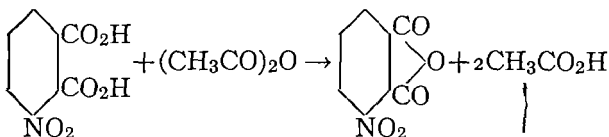
² Faust, *Ann.* **160**, 57 (1871); Miller, *Ann.* **208**, 223 (1881); Kenner and Mathews, *J. Chem. Soc.* **105**, 2476 (1914); Cohen, Woodroffe and Anderson, *J. Chem. Soc.* **109**, 232 (1916); Littmann, *J. Am. Chem. Soc.* **47**, 1980 (1925).

³ *J. Am. Chem. Soc.* **23**, 743 (1901).

⁴ *J. Am. Chem. Soc.* **42**, 1872 (1920).

XXV

3-NITROPHTHALIC ANHYDRIDE



Submitted by B. H. NICOLET and J. A. BENDER.

Checked by FRANK C. WHITMORE and W. F. SINGLETON.

1. Procedure

To 211 g. (1 mole) of 3-nitrophthalic acid (p. 70) in a 300-cc. round-bottom flask fitted with a reflux condenser is added 205 g. (2 moles) of acetic anhydride (99-100 per cent). The mixture is heated to gentle boiling until the acid is completely dissolved and then for about ten minutes longer. The hot mixture is poured (hood) into a 15-cm. porcelain dish and allowed to cool. The crystal mass is ground thoroughly in a mortar and filtered by suction. The crystals are returned to the mortar and the filtrate (about 140 cc.) is placed in a 300-cc. distilling flask. The crystals are ground with 150 cc. of alcohol-free ether (Note 1) and filtered. They are again returned to the mortar and similarly washed. After drying in the air for a short time, the product is dried to constant weight at 105°. The yield of product melting at 163-164° is 170-180 g. (88-93 per cent of the theoretical amount). The acetic acid filtrate is distilled with a thermometer in the liquid until the temperature is 150°. The distillate amounts to about 120 cc. The residue is poured into the mortar and, after cooling, is ground with some of the ether used in washing the original crystals. Thus about 10 g. of a product melting at 160-163° is obtained.

2. Note

1. Dry ether is recommended because ordinary ether contains alcohol, and the formation of some mono-ethyl ester may take place. Ordinary U.S.P. ether which has stood over calcium chloride for two days is satisfactory.

3. Other Methods of Preparation

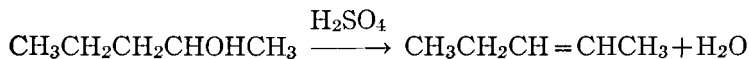
3-Nitrophthalic anhydride has been prepared by heating the acid under various conditions¹ and by the action of acetic anhydride,² essentially as in the present method.

¹ Kahn, Ber. **35**, 3859 (1902).

² McKenzie, J. Chem. Soc. **79**, 1137 (1901).

XXVI

PENTENE-2



Submitted by JAMES F. NORRIS.

Checked by FRANK C. WHITMORE.

1. Procedure

To a cooled mixture of 200 cc. of water and 200 cc. of concentrated sulphuric acid in a 1-l. round-bottom flask is added slowly 176 g. (2 moles, 214 cc.) of pentanol-2 (b.p. 118–120°) (Note 1). The flask is connected with a long efficient condenser for distillation (Note 2). The end of the condenser is provided with an adapter which passes well into a receiver surrounded by ice water (Note 2). The flask is heated on a boiling water bath as long as distillation takes place (two to three hours).

The distillate is shaken in the receiver with about 25 cc. of a 5 per cent solution of sodium hydroxide to remove any trace of sulfur dioxide that may be present. The hydrocarbon is separated and dried with 10 g. of anhydrous calcium chloride. It is then distilled, the fraction boiling at 35–41° (Note 3) being collected. The yield is 92–112 g. (65–80 per cent of the theoretical amount).

2. Notes

1. Pentanol-2 is now manufactured on a large scale from petroleum. As the quality of the commercial alcohol varies, the product should be distilled before use and the proper fraction

used. The material was kindly supplied by the Petroleum Chemical Corporation, Cambridge, Mass. (A. D. Little, Inc.).

2. Because of the volatility of the product, unusual precautions must be taken in its preparation to avoid loss.

3. Most of the product distils at $36-37^{\circ}$. The product may contain a small amount of the isomeric pentene-1. By redistilling it through a 25-cm. (10-in.) fractionating column containing small pieces of glass rod, the pure hydrocarbon can be readily obtained. Pentene-2 boils at $36.39^{\circ} \pm 0.04^{\circ}/760$ mm., melts at $-138^{\circ} \pm 2^{\circ}$ has the density d_{4}^{15} 0.6555, and n_D^{25} 1.3839.

3. Other Methods of Preparation

Pentene-2 has been prepared¹ by treating the iodide made from diethylcarbinol with alcoholic potash, by dehydrating active amyl alcohol by means of fused zinc chloride,² and from 3-bromopentane and alcoholic potash.³

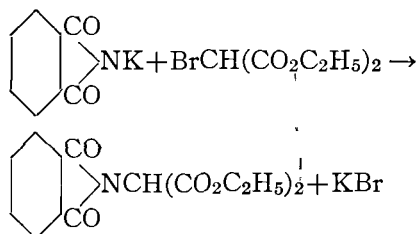
¹Wagner and Saytzeff, Ann. **175**, 373 (1875).

²Tissier, Bull. soc. chim. (3) **9**, 100 (1893).

³Lucas and Moyse, J. Am. Chem. Soc. **47**, 1461 (1925).

XXVII

PHTHALIMIDOMALONIC ESTER



Submitted by A. E. OSTERBERG.

Checked by FRANK C. WHITMORE and H. C. BENEDICT, Jr.

1. Procedure

IN a 600-cc. beaker 210 g. (0.87 mole) of ethyl bromomalonate (p. 34) (Note 1) and 165 g. (0.89 mole) of potassium phthalimide (p. 8) are intimately stirred together. The mixture is stirred approximately every ten minutes. If no spontaneous reaction starts in half an hour (Note 1), it is necessary to initiate the reaction by heating to 110–120°. The mixture then becomes liquid and can be stirred easily. It turns to a light brown color, especially near the top where it comes in contact with the air. When the temperature begins to drop, the mixture is heated in an oil bath at 110° for one hour to insure completion of the reaction. The mixture is then poured into a mortar where it solidifies to a solid mass (Note 2). When cold, the mixture is ground up with water and filtered to remove most of the potassium bromide. The precipitate is then reground with water and refiltered, finally washing the precipitate well with water. The solid material on the filter consists of some potassium bromide, some phthalimide, and the phthalimidomalononic ester.

Without drying, it is put into a 1-l. flask with 400 cc. of benzene and heated to boiling. After cooling, the insoluble bromide and phthalimide are removed by filtration. The filtrate contains some water, which is removed by means of a separatory funnel.

The benzene solution is dried with 20 g. of calcium chloride and the benzene removed by distillation under diminished pressure on a water bath. The residue is poured into a mortar where it solidifies. The crystalline mass is then ground with small amounts of ether (200 cc. in all), filtered, and washed with ether (about 100 cc.) until pure white. The yield of phthalimidomalon^tC ester melting at 73-74° is 155-162 g. From the ether filtrate after distilling the ether, there may be recovered a further amount by washing with a small amount of ether to remove the brown color. The total weight of ester obtained in the two crops is 180-190 g. (67-71 per cent of the theoretical amount),

2. Notes

1. When freshly prepared ethyl bromomalonate is used, the temperature of the mixture may rise spontaneously to 140°. In such event no heat should be applied until the temperature falls again.

2. If solidification does not take place as soon as the mixture is cold, about 100 cc. of water should be added. This accelerates the solidification.

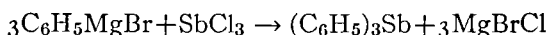
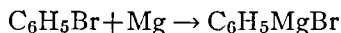
3. Other Methods of Preparation

The present method is adapted from that of Sörenson.¹

¹ Chem. Zentr. 1903, II, 33.

XXVIII

TRIPHENYL STIBINE



Submitted by G. S. HIERS.

Checked by HENRY GILMAN and F. SCHULZE.

1. Procedure

IN a 2-l. round-bottom three-necked flask fitted with a mercury-seal mechanical stirrer, a reflux condenser, and a separatory funnel is placed 40 g. (1.65 moles) of magnesium turnings (Note 1). This is covered with 200 cc. of dry ether, and there is then added 100 cc. of a mixture of 260 g. (1.65 moles) of dry bromobenzene and 800 cc. of dry ether. As soon as the reaction starts, 200 cc. more of dry ether is added and the remainder of the bromobenzene solution at such a rate as to cause gentle boiling (about two hours). With external cooling, the time may be shortened.

When all the bromobenzene has been added, there is added slowly through the separatory funnel a solution of 114 g. (0.5 mole) of freshly distilled antimony trichloride (m.p. 67–73°) in 300 cc. of dry ether. The reaction proceeds smoothly and even briskly with the freshly distilled chloride. However, if the latter has not been freshly prepared, gentle warming may be required to start the reaction. When all the antimony trichloride has been added (one to two hours), the mixture is heated on the steam bath for an hour longer.

When cool, the reaction mixture is poured slowly with stirring into 1 l. of ice and water (Note 2). If the stirring is thorough, most of the triphenyl stibine is to be found in the ether layer.

The hydrolysis mixture is filtered through a Büchner funnel and the residue on the filter extracted three times (Note 3) with 100-cc. portions of ether. The aqueous layer is separated and extracted twice with 200-cc. portions of ether. The combined ether portions are evaporated slowly on a steam bath to remove the ether, and there remains behind a yellow semi-solid which crystallizes to a white solid on cooling (Note 4). The yield of crude product melting at 49° is 145-160 g. (82-90 per cent of the theoretical amount). For purification from a small amount of diphenyl which is present in the crude product 90 g. of triphenyl stibine is dissolved in 200 cc. of petroleum ether (b.p. $40-50^{\circ}$) by warming on a steam bath. There is generally a small amount of insoluble residue which is filtered and the filtrate cooled in a freezing mixture. The triphenyl stibine separates as small prisms and weighs 58-65 g.; by further concentration of the filtrate to an approximate volume of 50 cc. and then cooling again, an additional 15-20 g. of product separates. Both portions melt at 50° .

2. Notes

1. The excess of the Grignard reagent insures the complete removal of all the halogen from the antimony.

2. During the hydrolysis the use of acids to dissolve the magnesium hydroxide must be avoided, for the presence of acid tends to decompose the antimony compound.

3. During the filtration some ether evaporates and the stibine compound is left on the filter with the magnesium hydroxide. Extraction is necessary to remove this product.

4. The same method may be used for the preparation of tri-*p*-tolyl-stibine. Starting with 282 g. of *p*-bromotoluene (Org. Syn. 5, 21) and proceeding in the same manner as described there was secured 150-157 g. (77-80 per cent of the theoretical amount) of crude tri-*p*-tolyl-stibine. This product purified by recrystallization from methyl alcohol or ether melts at $125-126^{\circ}$. The reaction is somewhat more vigorous in this case and sometimes cooling is necessary at first.

3. Other Methods of Preparation

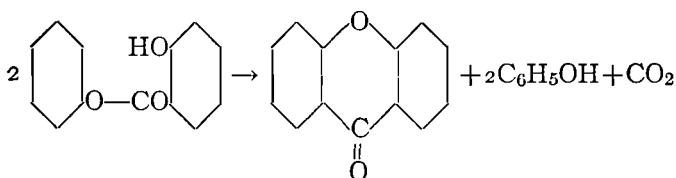
Triphenyl stibine has been prepared¹ from antimony trichloride and chlorobenzene dissolved in dry benzene in the presence of sodium. This yields triphenyl stibine dichloride, which on decomposition with hydrogen sulfide yields triphenyl stibine. Triphenyl stibine has also been prepared² by the action of phenyl magnesium bromide and antimony trichloride.

¹ Michaelis and Reese, *Ann.* **233**, 42 (1886).

² Pfeiffer and Heller, *Ber.* **37**, 4621 (1904).

XXIX

XANTHONE



Submitted by A. F. HOLLEMAN.
Checked by H. T. CLARKE.

1. Procedure

FIVE hundred grams (2.34 moles) of phenyl salicylate is heated in a 1-l. special distilling flask having a wide (Note 1) side-arm 20-25 cm. long, and fitted with two thermometers, one extending to the bottom of the flask, and the other just below the side-arm. When the temperature of the liquid reaches 275-285°, phenol begins to distil. The heating is so regulated that the temperature of the vapor never exceeds 175° and preferably remains below 170° (Note 2). In this way the phenol distils at the rate of 5-10 drops per minute. The temperature of the liquid rises gradually (Note 3), and after six to seven hours reaches 350-355°. At this point the distillation of the phenol practically ceases; the weight of the distillate is 220-225 g.

The receiver is now changed, the lower thermometer is raised from the liquid (Note 4), and the contents of the flask distilled as rapidly as possible (Note 5). Heating is continued until the tarry residue begins to foam; towards the end of the distillation the color of the vapor becomes deep yellow with a greenish fluorescence. The distillate weighs 165-170 g.; it is poured

while still molten into a cold dish and allowed to cool, ground in a mortar with 100 cc. of 5 per cent sodium hydroxide, and warmed on the steam bath for ten to fifteen minutes with 400 cc. of this solution. When cold, the xanthone is filtered off, washed free of alkali, and dried. A small amount of low-melting impurity is removed by boiling for ten to fifteen minutes with 250 cc. of methyl alcohol, cooling, filtering, and washing with the same solvent. A few grams can be recovered from the filtrate. The product melting at $170-172^{\circ}$, after softening slightly at $168-170^{\circ}$, weighs 141-145 g. (61-63 per cent of the theoretical amount). It is pure enough for the preparation of xanthydrol (p. 88). A purer product may be obtained by recrystallization from twenty parts of 95 per cent ethyl alcohol, from which it separates as pale yellow needles, melting at $173-174^{\circ}$.

2. Notes

1. The side-arm should have an internal diameter of at least 10 mm. in order to minimize the danger of stoppage by solidified distillate. This danger occurs particularly when the higher melting xanthone first begins to distil. No condenser is employed, the flask used as a receiver being cooled sufficiently by the air to condense all the vapors.

2. The regulation of temperature is difficult at first, but becomes easier after the first half-hour.

3. In consequence of this gradual rise in temperature, it is necessary to increase the size of the flame gradually.

4. Although the boiling point of xanthone is about 350° , the liquid in the flask reaches temperatures which would be dangerous to a mercury thermometer.

5. If a Pyrex flask is used, it is not only safe, but advisable, to remove the wire gauze and heat directly with the free flame. This permits the xanthone to be distilled rapidly and with a minimum loss.

3. Other Methods of Preparation

The procedure is based on the directions of Graebe,¹ which outline the most convenient method of preparing xanthone. Somewhat similar is that of Perkin,² in which salicylic acid is first converted by boiling with acetic anhydride into salicylide, which on distillation is partially converted into xanthone. A practically quantitative yield of xanthone is stated to be obtainable by warming *o*-phenoxybenzoic acid with concentrated sulfuric acid,³ but the preparation of this intermediate product is less satisfactory.

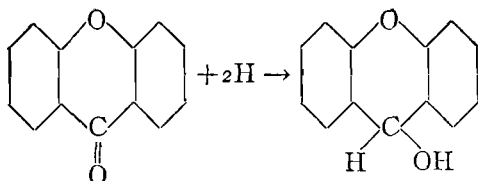
¹ Ann. **254**, 279 (1889).

² Ber. **16**, 339 (1883).

³ Graebe, Ber. **21**, 501 (1888).

XXX

XANTHYDROL



Submitted by A. F. HOLLEMAN,

Checked by H. T. CLARKE and C. R. NOLLER.

1. Procedure

AN amalgam prepared from 9.0 g. (0.39 mole) of sodium and 750 g. (55 cc.) of mercury (Note 1) is warmed to about 50° (Note 2) in a 500-cc. Pyrex round-bottom flask (Note 3). To it is then added a cold suspension of 25 g. (0.13 mole) of xanthone (p. 84) in 175 cc. of 95 per cent ethyl alcohol. The flask is at once stoppered, held in a cloth, and vigorously shaken, raising the stopper from time to time to release any pressure. The temperature rises rapidly to 60–70°. The solid xanthone rapidly goes into solution, a very faint and transient blue color being developed. At the end of about five minutes the alcoholic solution is clear and practically colorless. After shaking for ten minutes longer, the mercury is separated and washed with 10–15 cc. of alcohol. The alcoholic solution is filtered while warm and slowly poured with stirring into 2 l. of cold distilled water. The precipitated xanthydroxol is filtered with suction, washed with water until free of alkali, and dried at 40–50° to constant weight. The crystalline product, which weighs 23–24 g. (91–95 per cent of the theoretical amount), melts at 121–123° and is practically pure (Note 4).

2. Notes

1. The amalgam may be conveniently prepared by placing the sodium in the 500-cc. flask, covering it with 15-20 cc. of dry toluene and cautiously melting the metal over a free flame. The flame is then extinguished and the mercury added in drops, with occasional shaking. The reaction is extremely vigorous at first, but the rate of addition may be rapidly increased after the first 2-3 cc. of mercury has been added. The addition is so regulated that the toluene boils continuously, and it is finally allowed to volatilize completely. The toluene vapor remaining above the amalgam tends to protect it from the action of the air.

2. The amalgam is semi-solid at room temperature, but is completely melted at 50°. If made as in Note 1, it is merely allowed to cool to 50° before adding the alcoholic xanthone.

3. A thick-walled flask is necessary; although no great pressure is developed at any time, the impact of the mercury during shaking might break thin glass.

4. Xanthydrol is employed as a reagent for the determination of urea, with which it forms an insoluble condensation product. The material obtained is entirely satisfactory for this purpose; if desired, however, it may be recrystallized from alcohol, whereupon the melting point is raised by about 1°.

3. Other Methods of Preparation

Xanthydrol was first prepared by reducing xanthone by means of zinc dust in the presence of boiling alcoholic sodium hydroxide;¹ it was later shown by Fosse that it could be conveniently prepared by the action of a low percentage sodium amalgam upon xanthone in alcohol. The method is based upon the directions of Fosse.²

¹ Meyer and Saul, *Ber.* **26**, 1276 (1893); Adrian, *Rec. trav. chim.* **35**, 180 (1915).

² *Ann. chim.* (9) **6**, 58 (1916).

ADDITIONS AND CORRECTIONS FOR PRECEDING VOLUMES

(The numbers following the name of a compound refer to the volume and page of "Organic Syntheses.")

Allyl alcohol (1, 15), see 6, 103

Benzoin (1, 33), see 6, 103

n-Butyl *n*-butyrate (5, 23). If after the addition of the *n*-butyl alcohol, the oxidation mixture is heated on the steam bath to 90–100° until the supernatant liquid is practically colorless and then the reaction mixture is worked up as described, the yield of ester is increased to 147–149 g. (64–65 per cent of the theoretical amount).

If the ratios of the starting materials are changed slightly the yield of ester is further increased. Thus when 148 g. (2 moles) of *n*-butyl alcohol, 187 g. (0.62 mole) of crystallized sodium dichromate and 500 g. (5.1 moles) of sulfuric acid (sp. g. 1.84) are used and the reaction mixture heated after the addition of the butyl alcohol the yield of ester is 57–61 g. (70–75 per cent of the theoretical amount). (Private communication from W. J. Hickinbottom.) (Compare also Reilly and Hickinbottom, Scientific Proceedings of the Royal Dublin Society, 16, 246 (1921).)

Cyclohexyl carbinol (6, 22). The amount of cyclohexyl bromide indicated in line 6 should be 163 g. (1 mole).

9, 10-Dibromoanthracene (3, 41), see 6, 103

2-Furancarboxylic acid (6, 44) is most satisfactorily purified by recrystallizing from carbon tetrachloride. A few cc. of water should be added to coagulate and float the dark impurities. The clear subjacent liquid is separated and deposits colorless crystals of correct melting point.

Furfural (1, 49), see 6, 103.

Methylene iodide (1, 5;). The methylene iodide obtained after vacuum distillation melts at 6°.

Pinacol hydrate (5, 87). The mixture should be chilled and kept cold for several hours instead of a few minutes.

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(The numbers following the name of a compound refer to the volume and page of "Organic Syntheses.")

Allyl alcohol (1, 15), see 6, 103

Benzoin (1, 33), see 6, 103

n-Butyl *n*-butyrate (5, 23). If after the addition of the *n*-butyl alcohol, the oxidation mixture is heated on the steam bath to 90–100° until the supernatant liquid is practically colorless and then the reaction mixture is worked up as described, the yield of ester is increased to 147–149 g. (64–65 per cent of the theoretical amount).

If the ratios of the starting materials are changed slightly the yield of ester is further increased. Thus when 148 g. (2 moles) of *n*-butyl alcohol, 187 g. (0.62 mole) of crystallized sodium dichromate and 500 g. (5.1 moles) of sulfuric acid (sp. g. 1.84) are used and the reaction mixture heated after the addition of the butyl alcohol the yield of ester is 57–61 g. (70–75 per cent of the theoretical amount). (Private communication from W. J. Hickinbottom.) (Compare also Reilly and Hickinbottom, Scientific Proceedings of the Royal Dublin Society, 16, 246 (1921).)

Cyclohexyl carbinol (6, 22). The amount of cyclohexyl bromide indicated in line 6 should be 163 g. (1 mole).

9, 10-Dibromoanthracene (3, 41), see 6, 103

2-Furancarboxylic acid (6, 44) is most satisfactorily purified by recrystallizing from carbon tetrachloride. A few cc. of water should be added to coagulate and float the dark impurities. The clear subjacent liquid is separated and deposits colorless crystals of correct melting point.

Furfural (1, 49), see 6, 103.

Methylene iodide (1, 5;). The methylene iodide obtained after vacuum distillation melts at 6°.

Pinacol hydrate (5, 87). The mixture should be chilled and kept cold for several hours instead of a few minutes.

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(This Index Comprises Material from all Volumes of this Series.)

(Names of compounds in small capital letters indicate substances for which directions are given, the numbers in bold face type refer to volumes of Organic Syntheses, numbers in italics refer to pages in those volumes on which preparative directions are given, and numbers in Arabic refer to pages on which the compounds or subjects are mentioned in connection with other preparations. For example: ACETOACETIC ESTER, **4**, 45; **6**, 36 indicates that acetoacetic ester is mentioned in volume 4 on page 45 and that directions for its preparation are given in detail in volume 6 on page 36; Acetophenone, **2**, 1 indicates that this substance is mentioned in volume 2 on page 1 but that no directions for its preparation are given in this series.)

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