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NOMENCLATURE

Preparations appear in the alphabetical order of common names of the compounds. For convenience in surveying the literature concerning any preparation through *Chemical Abstracts* subject indexes, the *Chemical Abstracts* indexing name for each compound is given as a subtitle if it differs from the common name used as the title.

SUBMISSION OF PREPARATIONS

Chemists are invited to submit for publication in *Organic Syntheses* procedures for the preparation of compounds which are of general interest or which illustrate useful synthetic methods. The procedures submitted should represent, as nearly as possible, optimum conditions for the preparations, and should have been checked carefully by the submitter. Full details of all steps in the procedure should be included, and the range of yields should be reported rather than the maximum yield obtainable. The melting point of each solid product should be given, and the boiling-point range and refractive index (at 25°) of each liquid product. The method of preparation or source of the reactants and the criteria for the purity of the products should be stated.

Procedures submitted should be written in the style employed in the latest volume of *Organic Syntheses*. Copies of the current style sheet may be obtained upon request from the Secretary of the Editorial Board. Two copies of procedures which are submitted should be sent to the Secretary. Additions, corrections, and improvements to preparations previously published are welcomed and should be sent to the Secretary.

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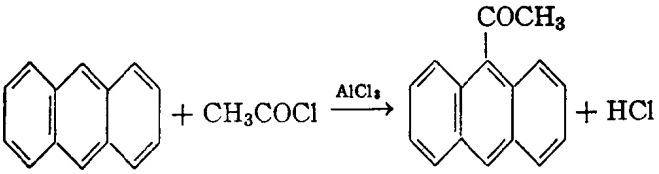
9-ACETYLANTHRACENE

(Ketone, 9-anthryl methyl)



Submitted by CHARLES MERRITT, JR., and CHARLES E. BRAUN.
Checked by WILLIAM S. JOHNSON and RALPH F. HIRSCHMANN.

1. Procedure

Fifty grams (0.28 mole) of purified anthracene (Note 1) is suspended in 320 ml. of anhydrous benzene and 120 ml. (1.68 moles) of reagent grade acetyl chloride contained in a 1-l. three-necked flask. The flask is fitted with a thermometer which is immersed in the suspension, a calcium chloride drying tube, an efficient motor-driven sealed stirrer, and a rubber addition tube to which a 125-ml. Erlenmeyer flask containing 75 g. (0.56 mole) of anhydrous aluminum chloride is attached.[1]

The flask is surrounded by an ice-calcium chloride cooling mixture, and the aluminum chloride is added in small portions from the Erlenmeyer flask at such a rate that the temperature is maintained between $-5°$ and $0°$. After the addition is complete, the mixture is stirred for an additional 30 minutes, and the temperature is then allowed to rise slowly to $10°$. The red complex which forms is collected with suction on a sintered-glass funnel and washed thoroughly with dry benzene (Note 2). The complex is added in small portions by means of a spatula with stirring to a 600-ml. beaker nearly filled with a mixture of ice and concentrated hydrochloric acid. The mixture is then allowed to come to room temperature, and the crude ketone is collected on a suction filter.

The product is digested under reflux for about 20 minutes with 100–150 ml. of boiling 95% ethanol. The suspension (Note 3) is then cooled quickly almost to room temperature and filtered rapidly with suction to remove any anthracene. The 9-acetylanthracene, which separates in the filtrate, is redissolved by heating and allowed to crystallize by slowly cooling the solution (finally to 0–5° in an icebox) (Note 4). A second recrystallization from 95% ethanol yields 35–37 g. (57–60%) of light-tan granules of 9-acetylanthracene melting at 75–76° (Note 5).

2. Notes

1. The Eastman Kodak Company grade melting at 214–215° is satisfactory. Technical anthracene can be purified by codistillation with ethylene glycol (ref. 1, p. 345, footnote 13).

2. A regular Büchner funnel fitted with a mat of glass wool can be employed successfully. The filtration should be carried out as rapidly as possible, and the hydrolysis should be performed immediately thereafter if the humidity is high to minimize reaction on the funnel.

3. Most of the unreacted anthracene remains undissolved as a brown fluffy residue.

4. If the product has a tendency to separate as an oil, the addition of more solvent followed by heating to redissolve the material and subsequent cooling will usually yield a crystalline product.

5. Lüttringhaus and Kacer [2] reported the melting point as ca. 80°, but May and Mosettig [3] have found it to be 74–76°.

3. Methods of Preparation

The procedure described is essentially that of Lüttringhaus and Kacer [2] except for the method of isolation of the product, which is due to May.[4]

[1] Fieser, *Experiments in Organic Chemistry*, 2nd ed., p. 311, Fig. 39, D. C. Heath and Company, 1941.

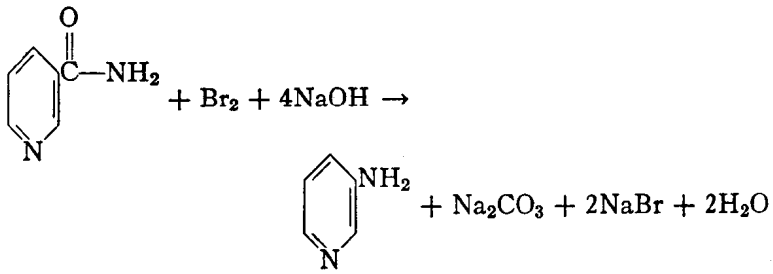
[2] Lüttringhaus and Kacer, Ger. pat. 493,688 [*C. A.*, **24**, 2757 (1930)].

[3] May and Mosettig, *J. Am. Chem. Soc.*, **70**, 686 (1948).

[4] May, private communication.

3-AMINOPYRIDINE

(Pyridine, 3-amino-)



Submitted by C. F. H. ALLEN and CALVIN N. WOLF.
Checked by CLIFF S. HAMILTON and MARJORIE DEBRUNNER.

1. Procedure

In a 2-l. beaker equipped with a mechanical stirrer and immersed in an ice-salt bath is placed a solution of 75 g. (1.87 moles) of sodium hydroxide in 800 ml. of water. To the solution is added, with stirring, 95.8 g. (30.2 ml., 0.6 mole) of bromine. When the temperature of the solution reaches 0°, 60 g. (0.49 mole) of nicotinamide (Note 1) is added all at once with vigorous stirring. After being stirred for 15 minutes, the solution is clear. The ice-salt bath is replaced by a bath containing water at 75°, and the solution is stirred and heated at 70–75° for 45 minutes.

The solution is cooled to room temperature, saturated with sodium chloride (about 170 g. is required), and extracted with ether in a continuous extractor (Note 2). The extraction time is 15–20 hours. The ether extract is adjusted to a volume of 1 l., dried over 4–5 g. of sodium hydroxide pellets, and filtered, and the ether is removed by distillation from a steam bath. The residue crystallizes on cooling. The yield of dark red crystals melting at 61–63° is 39–41 g. (83–89%).

The crude product is dissolved in a mixture of 320 ml. of benzene and 80 ml. of ligroin (b.p. 60–90°) and heated on a steam bath with 5 g. of Norit and 2 g. of sodium hydrosulfite for 20

minutes. The hot solution is filtered by gravity, allowed to cool slowly to room temperature, and then chilled overnight in a refrigerator. The product is isolated by gravity filtration (Note 3), washed on the filter with 25 ml. of ligroin, and dried in a vacuum desiccator. The yield of white crystals melting at 63–64° amounts to 28–30 g. (61–65%). By concentrating the combined filtrate and washings to a volume of 150 ml., an additional 2–3 g. of pale yellow crystals melting at 62–64° can be obtained. The total yield of 3-aminopyridine is 30–33 g. (65–71%).

2. Notes

1. The nicotinamide should be finely powdered to facilitate rapid solution.

2. The continuous extractor described by Pearl [1] was used. If the material is extracted in a separatory funnel, four 800-ml. portions and ten 500-ml. portions of ether are required to give the above yield.

3. Since 3-aminopyridine is somewhat hygroscopic, it tends to liquefy if collected on a suction filter.

3. Methods of Preparation

3-Aminopyridine has been prepared by heating nicotinamide in an alkaline potassium hypobromite solution at 70°; [2,3] by hydrolysis of β-pyridylurethan with oleum; [4] by heating 3-aminopyridine-2-carboxylic acid at 250°; [5] by reduction of 3-nitropyridine with zinc and hydrochloric acid; [6] and by heating 3-bromopyridine with ammonia and copper sulfate in a sealed tube. [7,8]

[1] Pearl, *Ind. Eng. Chem., Anal. Ed.*, **16**, 62 (1944).
[2] Camps, *Arch. Pharm.*, **240**, 354 (1902).
[3] Philips, *Ann.*, **288**, 263 (1895).
[4] Curtius and Mohr, *Ber.*, **31**, 2494 (1898).
[5] Gabriel and Colman, *Ber.*, **35**, 2833 (1902).
[6] Binz and Räth, *Ann.*, **486**, 95 (1931).
[7] Maier-Bode, *Ber.*, **69**, 1534 (1936).
[8] Gitsels and Wibaut, *Rec. trav. chim.*, **60**, 176 (1941).

p-AMINOTETRAPHENYLMETHANE

(*p*-Toluidine, α,α,α-triphenyl-)

$$C_6H_5NH_2 \cdot HCl + (C_6H_5)_3COH \rightarrow p\text{-}NH_2C_6H_4C(C_6H_5)_3 \cdot HCl + H_2O$$

$$p\text{-}NH_2C_6H_4C(C_6H_5)_3 \cdot HCl + NaOH \rightarrow p\text{-}NH_2C_6H_4C(C_6H_5)_3 + NaCl + H_2O$$

Submitted by BENJAMIN WITTEN and E. EMMET REID.
Checked by RICHARD T. ARNOLD and JEROME J. ROSENBAUM.

1. Procedure

Into a 1-l. round-bottomed flask equipped with a reflux condenser are introduced 100 g. (0.385 mole) of technical grade triphenylcarbinol (Note 1), 105 g. (0.81 mole) of dry aniline hydrochloride (Note 2), and 250 ml. of glacial acetic acid. The mixture is heated at the reflux temperature for 3 hours. During the period of reflux a clear brown homogeneous solution is formed. The solution while still hot is poured with stirring into a 4-l. beaker containing 2 l. of water. *p*-Aminotetraphenylmethane hydrochloride, which is not very soluble in water, separates as a light-brown solid. It is collected on a Büchner funnel and washed with 1 l. of water. The solid is then put back into the beaker, and a solution of 40 g. of sodium hydroxide in 2 l. of water is added. The mixture is heated to boiling for 1 hour to convert the hydrochloride to the free base (Note 3), which likewise is not very soluble in water. The mixture is allowed to cool to room temperature and is filtered with suction through a Büchner funnel. The solid material is washed with 500 ml. of water and is dried in an oven at 110–120°. The crude substance melts at 243–247°. It is purified by crystallization from 1.7 l. of toluene. The purified product (90–95 g., 70–74%) melts at 249–250° (Note 4).

2. Notes

1. Technical grade triphenylcarbinol is satisfactory, provided it is dry. The checkers obtained a final product having a higher melting point by starting with Eastman Kodak Company purest grade triphenylcarbinol.

2. The aniline hydrochloride must be dry if a good yield of product is to be obtained. Aniline hydrochloride can be prepared conveniently by mixing 75 g. of aniline and 80 ml. of concentrated hydrochloric acid in an evaporating dish and evaporating to dryness. The aniline hydrochloride should be dried in an oven at 110–120° before use. Aniline hydrochloride (Merck) which has been washed with ether and dried at 110–120° can be employed satisfactorily.

3. The mixture tends to bump during the period of heating. This bumping can be overcome by stirring the solution mechanically.

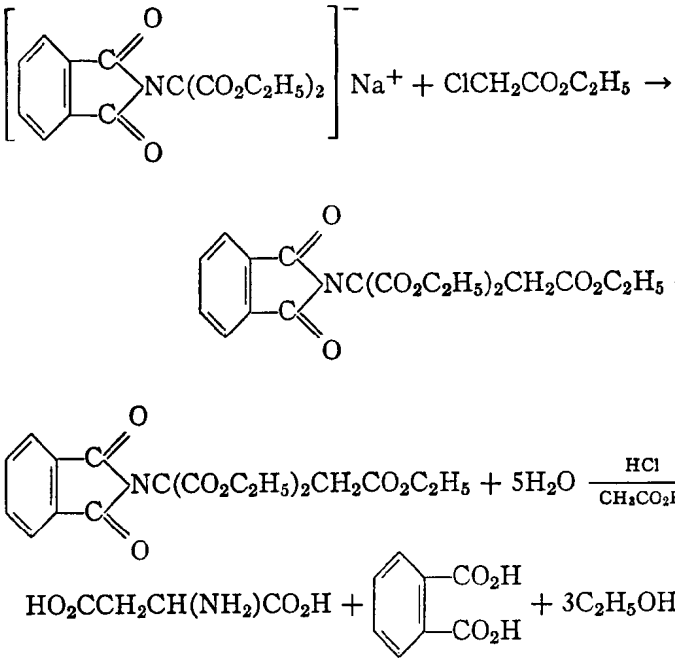
4. A product melting at 256–257° (uncor.) [1] was obtained by the checkers (Note 1).

3. Method of Preparation

The procedure given is similar to one described by Ullmann and Münzhuber,[1] except that one-half as much aniline hydrochloride and two-thirds as much glacial acetic acid are used, and the time of reflux is reduced from 6 to 3 hours. *p*-Aminotetraphenylmethane also can be prepared from triphenylchloromethane and aniline hydrochloride, following the same procedure outlined for triphenylcarbinol and aniline hydrochloride, except that a reaction time of 1 hour is sufficient.

[1] Ullmann and Münzhuber, *Ber.*, **36**, 407 (1903).

DL-ASPARTIC ACID



Submitted by M. S. DUNN and B. W. SMART.
Checked by H. T. CLARKE and W. PEARLMAN.

1. Procedure

A. *Triethyl α-phthalimidoethane-α,α,β-tricarboxylate.* Three hundred and twenty-seven grams (1.0 mole) of diethyl sodium phthalimidomalonate [1] and 735 g. (6.0 moles) of ethyl chloroacetate (b.p. 144–145°) are placed in a 2-l. Claisen flask fitted with a reflux condenser and rubber stoppers. The mixture is heated under reflux in an oil bath at 150–160° for 2.25 hours. The excess ethyl chloroacetate is removed by distillation at 30 mm. until the heating bath temperature reaches 150° and no more distillate is obtained (Note 1). The brown residual mass is

cooled and then extracted with 1250 ml. of ether. The oil dissolves, leaving a solid residue which is separated by filtration and washed with 750 ml. of ether. The combined ether extracts are distilled to remove ether, and the residual oil is heated on a steam bath under reduced pressure (35 mm.) to remove traces of ethyl chloroacetate. The yield of triethyl α-phthalimidoethane-α,α,β-tricarboxylate, dried at 45° for 48 hours, is 373–389 g. (95–99%) (Note 2).

B. DL-*Aspartic acid.* A mixture of 383 g. of the above crude product, 1 l. of concentrated hydrochloric acid, 1 l. of glacial acetic acid, and 1 l. of water is boiled under reflux in a 5-l. round-bottomed flask for 2–3 hours. The reflux condenser is then replaced by a fractionating column, and the mixture is slowly distilled until the temperature at the head of the column has risen to 108°. This requires about 13 hours. The distillate amounts to 1.5 l. (Note 3).

The residual mixture is allowed to cool, and the phthalic acid which crystallizes is removed by filtration and washed with 350 ml. of 1% hydrochloric acid (Note 4). The combined filtrate and washings are distilled nearly to dryness on a steam bath under reduced pressure; the bulk of the hydrochloric and acetic acids remaining is removed by slowly adding 300 ml. of water through a dropping funnel while the distillation under reduced pressure is continued. The dark brown residue is warmed on a steam bath with 700 ml. of water, is allowed to cool, and is filtered to remove a small amount of black insoluble matter. The filtrate is decolorized with 2 g. of Norit, 200 ml. of hot water being used to wash the Norit. The volume of the combined filtrate and washings, amounting to about 1.2 l., is measured accurately, and a small aliquot portion is analyzed for chloride (Note 5). An amount of pyridine corresponding exactly to the chloride content is added, diluted with 500 ml. of 95% ethanol. The DL-aspartic acid, which crystallizes at once, is separated by filtration after the mixture has stood for 24 hours at room temperature and is washed with 50–100 ml. of cold water (Note 6).

The crude DL-aspartic acid, amounting to 58–60 g., is recrystallized from 600 ml. of hot water and yields 54 g. of pure DL-

aspartic acid. The mother liquors on evaporation to about 90 ml. yield an additional 2–3 g. (Note 7). The total yield of pure colorless DL-aspartic acid is 56–57 g. (42–43%) (Note 8).

2. Notes

1. From 490 to 536 g. of ethyl chloroacetate (b.p. 144–145°) is recovered by the distillation.

2. Although this product cannot be purified by distillation, it contains almost the theoretical amount of nitrogen as shown by Kjeldahl analysis.

3. During the first few hours the distillate contains ethyl acetate; the distillate obtained during the first hour, amounting to 137 ml., distils below 99° and on saturation with sodium chloride yields 115 ml. of crude ethyl acetate.

4. The phthalic acid so obtained is brown and weighs 140–150 g.

5. The total amount of chloride found should be less than 1 mole.

6. The mother liquor contains too little DL-aspartic acid to justify its recovery. When the filtrate and washings are evaporated to a syrup and treated with 500 ml. of 95% ethanol, the pyridine hydrochloride dissolves completely, leaving 8–9 g. of crude glycine which yields little or no sparingly soluble DL-aspartic acid on treatment with a minimum quantity of cold water.

7. The final mother liquor from the recrystallization of DL-aspartic acid yields a small quantity (about 0.5 g.) of glycine.

8. The purity of the recrystallized DL-aspartic acid was established by nitrogen analysis by the Kjeldahl and Van Slyke methods. The decomposition point of this product is 325–348°.

3. Methods of Preparation

The above method for the preparation of DL-aspartic acid is a modification of one described by Dunn and Smart.[2] Other methods are: the decomposition of acid ammonium malate by

heat,[3] the racemization of active aspartic acid [4] and active asparagine; [5] the reaction of maleic and fumaric acids with ammonia in a closed tube; [6] the reduction of oxalacetic ester oxime; [7] the reduction of silver fumarate by hydroxylamine hydrochloride; [8] the reduction of nitrosuccinic ester; [9] the catalytic reduction and amination of oxalacetic acid; [10] and the hydrolysis of triethyl α-aminoethane-α,α,β-tricarboxylate.[11]

[1] *Org. Syntheses* Coll. Vol. 2, 384 (1943).
[2] Dunn and Smart, *J. Biol. Chem.*, **89**, 41 (1930).
[3] Dessaignes, *Compt. rend.*, **30**, 324 (1850); **31**, 432 (1850); Wolff, *Ann.*, **75**, 293 (1850).
[4] Michael and Wing, *Ber.*, **17**, 2984 (1884); *Am. Chem. J.*, **7**, 278 (1885).
[5] Piutti, *Ber.*, **19**, 1691 (1886).
[6] Engel, *Compt. rend.*, **104**, 1805 (1887); **106**, 1734 (1888); Stadnikoff, *Ber.*, **44**, 44 (1911).
[7] Piutti, *Gazz. chim. ital.*, **17**, 519 (1887).
[8] Tanatar, *Ber.*, **29**, 1477 (1896).
[9] Schmidt and Widmann, *Ber.*, **42**, 497 (1909).
[10] Knoop and Oesterlin, *Z. physiol. Chem.*, **148**, 294 (1925).
[11] Keimatsu and Kato, *J. Pharm. Soc. Japan*, **49**, 111 (1929) [*C. A.*, **24**, 70 (1930)].

BENZOYLCHOLINE IODIDE AND CHLORIDE

(Choline, chloride benzoate, and Choline, iodide benzoate)

$$C_6H_5COCl + HOCH_2CH_2Cl \rightarrow C_6H_5CO_2CH_2CH_2Cl + HCl$$

$$C_6H_5CO_2CH_2CH_2Cl + NaI \rightarrow C_6H_5CO_2CH_2CH_2I + NaCl$$

$$C_6H_5CO_2CH_2CH_2I + (CH_3)_3N \rightarrow C_6H_5CO_2CH_2CH_2\overset{+}{N}(CH_3)_3I^-$$

$$C_6H_5CO_2CH_2CH_2\overset{+}{N}(CH_3)_3I^- + AgCl \rightarrow C_6H_5CO_2CH_2CH_2\overset{+}{N}(CH_3)_3Cl^- + AgI$$

Submitted by A. H. FORD-MOORE.
Checked by R. L. SHRINER and CALVIN N. WOLF.

1. Procedure

A. *2-Chloroethyl benzoate.* In a 500-ml. round-bottomed flask attached to a 100-cm. air condenser by a ground-glass joint are placed 80.5 g. (65 ml., 1 mole) of redistilled ethylene chlorohydrin (b.p. 128–129°) and 140.5 g. (115.5 ml., 1 mole) of benzoyl chloride. The apparatus is set up in a good hood, and the mixture is warmed gently with a low flame until the reaction starts (Note 1). The source of heat is withdrawn until the reaction moderates and is then again applied for an additional 30 minutes, during which time the temperature rises to about 200–215°. The flask is fitted with a short column (about 20 cm.) and arranged for distillation. After volatile material has been removed by evacuation with a water pump at a bath temperature of 100–110° the residual liquid is fractionated under reduced pressure. The yield of 2-chloroethyl benzoate boiling at 101–104°/2 mm. is 165–168 g. (89–91%), n_D^{19} 1.5298.

B. *2-Iodoethyl benzoate.* A mixture of 170 g. of anhydrous sodium iodide and 1.2 l. of methyl ethyl ketone (Note 2) is heated on a steam bath for 1 hour with occasional shaking in a 3-l. round-bottomed flask fitted with a water-cooled reflux condenser. 2-Chloroethyl benzoate (162 g., 0.88 mole) is added to the mixture, and heating is maintained for an additional 22–24 hours with occasional shaking. The mixture is cooled to room temperature and filtered through a 15-cm. Büchner funnel with suction. The inorganic salts on the filter are washed with 200 ml. of methyl ethyl ketone, and the filtrate is concentrated by distillation of about 1 l. of the solvent. The residue is poured into 1 l. of water contained in a separatory funnel, which is shaken, and the lower layer is withdrawn. The latter is washed successively with 200 ml. of 10% sodium bisulfite solution, 200 ml. of 5% sodium bicarbonate solution, and 100 ml. of water. It is dried with anhydrous magnesium sulfate (5–7 g.) and fractionated under reduced pressure. The yield of material boiling at 133–136°/2.5 mm., n_D^{15} 1.5820, is 190–196 g. (78–81%).

C. *Benzoylcholine iodide.* A solution of 194 g. (0.70 mole) of 2-iodoethyl benzoate in 200 ml. of dry acetone is treated with

270 ml. of a 19.5% solution of trimethylamine in acetone (Note 3) in a 1-l. Pyrex reagent bottle which is closed with a tightly fitting rubber stopper wired in place. The solution is allowed to stand at room temperature for 24 hours (Note 4), and at the end of this time the quaternary salt is separated by filtration with suction, washed with 200 ml. of dry acetone, and air-dried (Note 5). The weight of the quaternary iodide melting with decomposition at 247° is 200–210 g. (85–90%) (Note 6).

D. *Benzoylcholine chloride.* Silver chloride is prepared by dissolving 160 g. (0.94 mole) of silver nitrate in 500 ml. of boiling distilled water and adding 120 ml. of analytical reagent hydrochloric acid (sp. gr. 1.18) from a dropping funnel in a period of 15 minutes, with continuous stirring. The silver chloride is washed by decantation with three 300-ml. portions of boiling distilled water. The moist silver chloride is suspended in 750 ml. of water warmed to 50–60° in a 2-l. beaker, and 210 g. (0.63 mole) of benzoylcholine iodide is added in a period of 1 hour, with good mechanical stirring. After the addition is completed, stirring is continued for an additional 30 minutes without the application of heat. The mixture is cooled and filtered with suction. The silver salts on the filter are washed with 200 ml. of hot water (Note 7), and the combined filtrates are evaporated to dryness under reduced pressure (water pump). The residue is dried by twice distilling to dryness with 250 ml. of absolute ethanol and then once with 250 ml. of dry acetone, the last of the acetone being removed under reduced pressure. The product is recrystallized by dissolving it in 240 ml. of isopropyl alcohol (Note 8) and allowing the solution to cool in a refrigerator. It is filtered and dried, first at 100° and then in a vacuum desiccator over silica gel. The yield of pure product, m.p. 207° (dec.), is 125–132 g. (82–87%) (Note 9).

2. Notes

1. Usually the reaction starts at a temperature of 55° to 60° as evidenced by liberation of hydrogen chloride. If the reaction becomes too vigorous it may be moderated by applying a wet towel to the flask.