A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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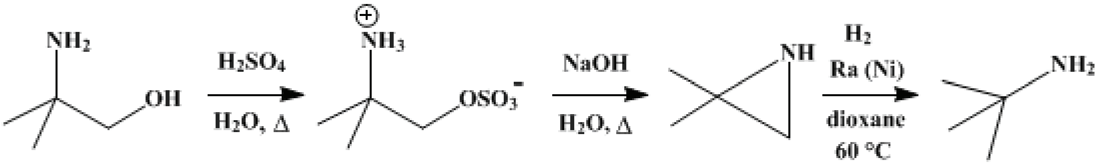
Organic Syntheses, Coll. Vol. 3, p.148 (1955); Vol. 27, p.12 (1947).

tert-BUTYLAMINE

[I. HYDROGENOLYSIS OF 2,2-DIMETHYLETHYLENIMINE]



Submitted by Kenneth N. Campbell, Armiger H. Sommers, and Barbara K. Campbell.
Checked by Nathan L. Drake and Sidney Melamed.

1. Procedure

A. *2,2-Dimethylethylenimine*. A cold mixture of 110 g. (60 ml., 1.06 moles) of concentrated sulfuric acid and 200 ml. of water is added in portions, with shaking, to a solution of 100 g. (107 ml., 1.12 moles) of 2-amino-2-methyl-1-propanol in 200 ml. of water contained in a 1-l. round-bottomed flask (Note 1). The flask is fitted with a thermometer extending into the liquid and a short still head carrying a downward condenser.

Water is distilled from the mixture at atmospheric pressure until the temperature of the solution reaches 115° (Note 2) and (Note 3), whereupon the liquid is transferred to a 500-ml. round-bottomed flask. This flask is connected to the distillation apparatus used previously except that the thermometer is replaced by a capillary tube. Distillation is then continued under the reduced pressure obtainable from a water aspirator. The bath temperature is raised to 175° over a period of about an hour and is held there until the mixture solidifies (usually 30–60 minutes longer), and for 1 hour thereafter. The flask is cooled and broken to remove the product.

The brown solid from the above operations is ground in a mortar and placed in a 500-ml. distilling flask equipped with a downward condenser and a receiver. A cold solution of 100 g. (2.5 moles) of technical sodium hydroxide in 150 ml. of water is added to the solid in the flask, and heat is applied by means of an oil bath whose temperature is slowly raised to 125° From 70 to 75 g. of distillate is collected; the head temperature ranges from about 70° to 101° (Note 2). The distillate is cooled in ice and saturated with technical potassium hydroxide; the organic layer that forms is separated and dried over potassium hydroxide pellets in a refrigerator for about 15 hours.

The organic layer is separated from the drying agent and distilled from a few fresh pellets of potassium hydroxide through a column of the Whitmore-Fenske type. After a 3- to 5-g. fore-run, the product distils at 71–72°; the yield is 36–41 g. (45–51%) (Note 4) and (Note 5).

B. *tert-Butylamine*. A hydrogenation bomb or bottle (Note 6) is charged with 100 ml. of purified dioxane,[1] 35.5 g. (0.5 mole) of freshly distilled 2,2-dimethylethylenimine, and about 9 g. (alcohol-wet weight) of Raney nickel.[2] The apparatus is filled with hydrogen, warmed to 60°, and shaken until hydrogenation is complete (Note 7). The contents of the bomb are removed and filtered to separate the catalyst, which is washed on the funnel with a little dioxane.

The filtrates from two such runs are combined and distilled through a Whitmore-Fenske column of 10–15 theoretical plates at a 5:1 reflux ratio. The yield of *tert*-butylamine is 55–60 g. (75–82%); the product boils at 44–44.5°, and its refractive index is n_D^{20} 1.3770 (Note 8).

2. Notes

1. The 2-amino-2-methyl-1-propanol used was the practical grade obtained from the Eastman Kodak Company. This aminoalcohol can also be secured from the Commercial Solvents Corporation.
2. An electric heating mantle may conveniently be substituted for the oil bath specified.

3. Approximately 285 ml. of water must be collected before the temperature of the reaction mixture reaches 115°.

4. 2,2-Dimethylethylenimine polymerizes on standing; the product should be hydrogenated within a few hours after preparation.

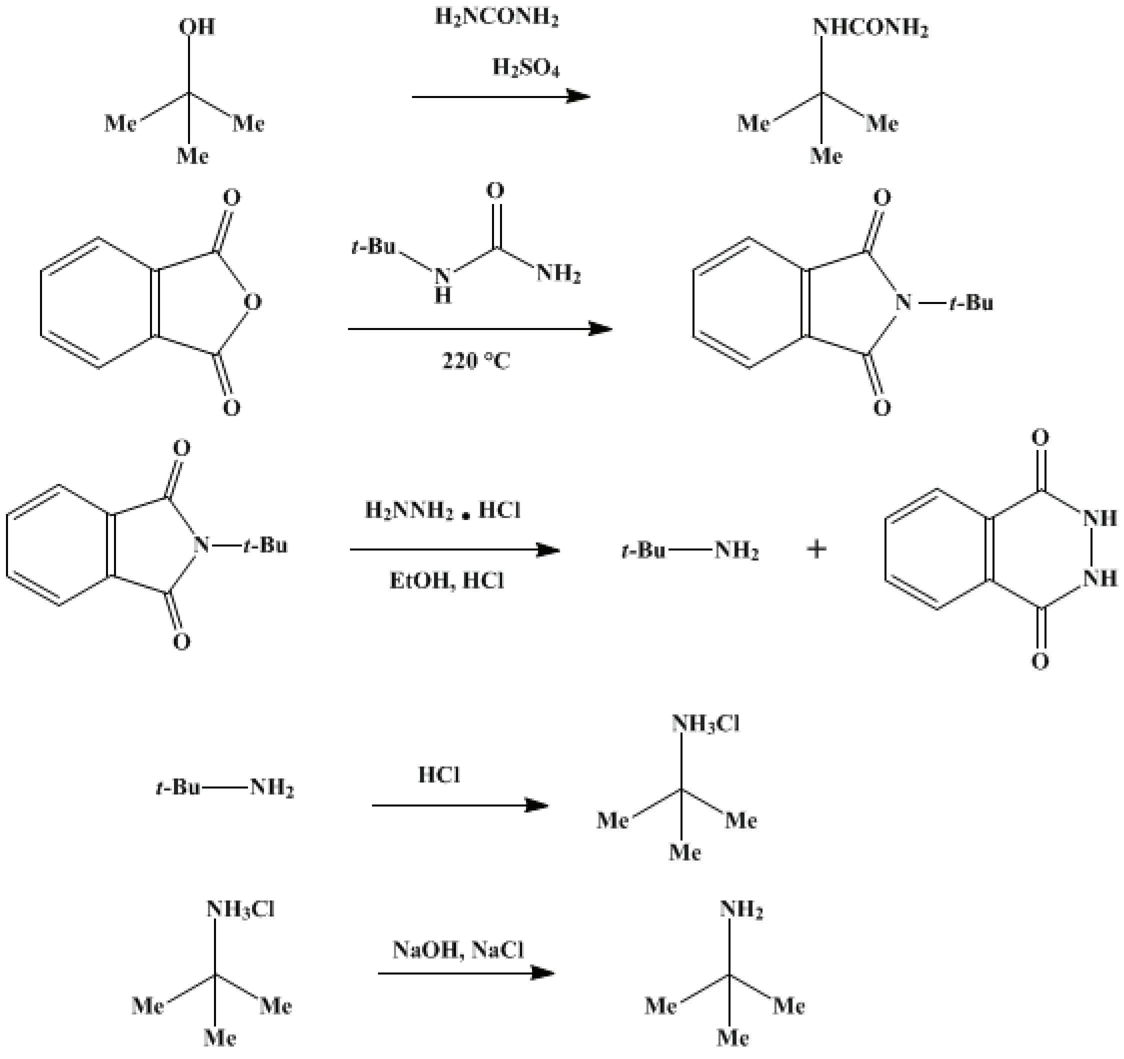
5. The checkers have followed the same procedure successfully using tenfold quantities; the yield of the imine was 42%.

6. The hydrogenation can be carried out equally well in metal or glass equipment. If a hydrogenator of the Parr low-pressure type is used, the bottle can be wound for electrical heating. Five turns of 24-gauge asbestos-covered Nichrome or Chromel A wire is satisfactory for the heating element. In use, current is supplied from a variable transformer, and the voltage necessary to heat the contents of the bottle to 60° is determined by experiment. The checkers used hydrogenation equipment supplied by the American Instrument Company.

7. If the hydrogenation is carried out in a Parr hydrogenation apparatus at 40–60 lb. pressure, about 2 hours is required to complete the hydrogenation as described. The low boiling point of the ethylenimine makes it impossible to remove the air from the bottle by evacuation in the usual way before hydrogenation. Instead the bottle is filled with hydrogen to 15–20 lb. pressure, the pressure is released, and the process repeated.

8. The checkers used high-pressure equipment and found that the hydrogenation of 336 g. of 2,2-dimethylethylenimine in 250 ml. of purified dioxane in the presence of 3 teaspoonfuls of Raney nickel under 3000 lb. hydrogen pressure was complete in 10–15 minutes; the temperature rise during the hydrogenation was about 50°. The yield of product was 283 g. (82%).

[II. VIA *tert*-BUTYLPHTHALIMIDE]



Submitted by Lee Irvin Smith and Oliver H. Emerson[3].
Checked by R. L. Shriner and Arne Langsjoen.

1. Procedure

A. *tert-Butylurea* (Note 1). In a 500-ml. three-necked flask equipped with a fast mechanical stirrer, a 200-ml. dropping funnel, and a thermometer is placed 193 g. (105 ml., 1.98 moles) of concentrated sulfuric acid (sp. gr. 1.84). The flask is surrounded by an ice bath, and 60 g. (1 mole) of finely powdered urea is added slowly at such a rate that the temperature remains between 20° and 25°. Then 148 g. (188 ml., 2 moles) of *tert*-butyl alcohol is added dropwise from the funnel at such a rate that the temperature is maintained between 20° and 25° (Note 2). After the addition is completed the mixture is stirred for an additional 30 minutes, allowed to stand at room temperature overnight (about 16 hours) (Note 3), and then poured with stirring on 1.5 kg. of cracked ice and water in a 4-l. beaker. Without removal of the precipitate, the mixture is made alkaline to Congo red indicator by adding slowly with stirring a solution of sodium hydroxide (160 g. in 750 ml. of water). The mixture is cooled with an ice bath to keep the temperature below 25°. The mixture is stirred in the ice bath until the temperature falls to about 15° (Note 4), at which point the precipitate is collected on a 15-cm. Büchner funnel, washed with two 100-ml. portions of cold water, and pressed and sucked as dry as possible. The cake is transferred to a 2-l. beaker, and 500 ml. of water is added. The mixture is heated to boiling and quickly filtered while hot through an 8-cm. steam-heated Büchner funnel (Note 5) with the aid of suction. The filtrate is cooled to 0–5° with occasional stirring, and the white precipitate of *tert*-butylurea is collected on a 15-cm. Büchner funnel with suction and pressed as dry as possible. After the product has been spread out on absorbent paper and air-dried overnight (Note 6) there is obtained 36–39 g. (31–33%) of *tert*-butylurea melting at 180–182° (Note 7).

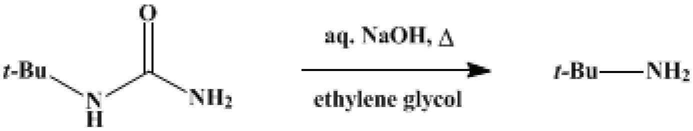
B. *tert-Butylphthalimide*. Thirty-five grams (0.3 mole) of *tert*-butylurea and 100 g. (0.675 mole) of phthalic anhydride are ground together in a mortar. The mixture is placed in a 1-l. Erlenmeyer flask which is then immersed in a metal bath previously heated to 200°. The mixture melts and effervesces vigorously; after 10 minutes the temperature of the bath is raised to 240° (internal temperature 200°) and held there for 5 minutes (Note 8). The flask is removed and cooled to 60–70°, and 100 ml. of 95% ethanol is added to dissolve the contents partially. A 20% solution of sodium carbonate is added until the solution is alkaline to litmus paper, and the mixture is diluted with water to 1 l. The solid is collected on a Büchner funnel with the aid of suction and pressed as dry as possible. The filter cake is warmed on a steam bath with 500 ml. of petroleum ether (b.p. 60–70°) in a 1 l. flask, and the hot mixture is filtered. Any water layer that may separate from the filtrate is removed, and the filtrate is cooled to 25° and again filtered. The clear filtrate is concentrated by distillation to about one-third of its original volume and placed in a refrigerator overnight. The crystalline material is collected on a filter, and as much as possible of the solvent is removed by suction. After air drying, this first crop weighs 40–43 g. and melts at 58–59°. By concentration of the filtrate an additional 2–4 g. may be obtained. The total yield of *tert*-butylphthalimide is 43–46.5 g. (72–76%).

C. *tert-Butylamine hydrochloride*. In a 2-l. flask fitted with an efficient bulb-type reflux condenser are placed 203 g. (1 mole) of *tert*-butylphthalimide, 1 l. of 95% ethanol, and 59 g. (1 mole) of 85% hydrazine hydrate. The solution is refluxed for 2 hours and cooled, and concentrated hydrochloric acid (about 100 ml.) is added until the solution is strongly acid to Congo red paper, though a large excess of acid is avoided. The voluminous precipitate of phthalhydrazide is collected on a 15-cm. Büchner funnel with the aid of suction and washed with four 100-ml. portions of 95% ethanol. The combined filtrate and washings are concentrated under reduced pressure to a volume of 200 ml. About 1 l. of water is added, any insoluble material is removed by filtration, and the filtrate is concentrated to about 300–350 ml. If any additional insoluble material separates it is removed by filtration, and the solvent is completely removed by evaporation under reduced pressure. This crude amine hydrochloride may be converted to the free amine as described below, or it may be purified by solution in 500 ml. of absolute ethanol, the solution being filtered and 500 ml. of dry ether being added to the filtrate. The crude amine hydrochloride is collected on a filter; the solvent is removed by suction, and the residue is dissolved in hot absolute ethanol using 5 ml. per gram of material; absolute ether (50% of the volume of ethanol) is added, and the solution is cooled in a refrigerator for several hours. All the *tert*-butylamine hydrochloride is collected on a Büchner funnel and dried in a vacuum desiccator. It weighs 79–97 g.

(72–88%) and melts with sublimation at 270–290°.

D. *tert-Butylamine*. To 150 ml. of cold 40% solution of sodium hydroxide is added 109.5 g. (1 mole) of *tert*-butylamine hydrochloride with stirring. The solution is saturated with potassium carbonate (about 100–150 g.); the layer of amine is separated and dried over 20 g. of sodium hydroxide pellets. The product is distilled using an ice-cooled receiver, and the fraction boiling at 44–46° is collected. If the purified amine hydrochloride is the starting material for this step the yield ranges from 65 g. to 69 g. (89–94%). When the crude amine salt is employed, the yield is 46–60 g. (64–83%) (Note 9).

[III. HYDROLYSIS OF *tert*-BUTYLUREA]



Submitted by D. E. Pearson, J. F. Baxter, and K. N. Carter.
Checked by R. L. Shriner and Calvin N. Wolf.

1. Procedure

A 1-l. round-bottomed flask is charged with 60 g. (1.5 moles) of sodium hydroxide pellets dissolved in 75 ml. of water, 70 g. (0.6 mole) of *tert*-butylurea, and 225 ml. of commercial ethylene glycol. The flask is fitted with an efficient reflux condenser, and a glass tube is led from the top of the condenser to a small flask immersed in ice water (Note 10).

The mixture is refluxed gently for 4 hours (Note 11). The flask is cooled and equipped for distillation, and the fraction boiling at 40–60° is collected in an ice-cooled receiver. The crude amine, including any collected in the trap, weighs 37–39 g. It is dried overnight with 5–7 g. of sodium hydroxide pellets (Note 12) and then distilled, a 12- to 15-cm. fractionating column (Note 13) and an ice-cooled receiver equipped with a soda-lime tube being used. The fraction boiling at 44–46° amounts to 31–34 g. (71–78%) of *tert*-butylamine; d_4^{20} 0.699; n_D^{20} 1.3800.

2. Notes

1. This step may be omitted if a practical grade of *tert*-butylurea is purchased from the Eastman Kodak Company. Since the commercial product may contain sodium sulfate and di-*tert*-butylurea it should be recrystallized from hot water, about 1 l. of solvent being used for 100 g. of the urea.
2. The temperature of the mixture should be kept in the range 20–25°. Higher temperatures lead to the formation of diisobutylene, and at lower temperatures (15°) the urea does not dissolve readily. Even at 25° the urea is usually not completely in solution. It has been found convenient to warm the *tert*-butyl alcohol to about 30–35° before placing it in the dropping funnel. This avoids solidification in the stem (the melting point of *tert*-butyl alcohol is 25.5°).
3. Longer standing does not improve the yield.
4. If the temperature is allowed to fall below 15°, large amounts of sodium sulfate decahydrate crystallize with the product. If this happens it may be necessary to recrystallize the *tert*-butylurea several times.
5. The insoluble residue weighs 10–22 g. and consists of di-*tert*-butylurea, which sublimes above 200° but melts in a sealed tube at 243°. If several runs are being made, the di-*tert*-butylurea should be saved and dried. It may be converted to *tert*-butylphthalimide in 63% yields by heating with four equivalents of phthalic anhydride under the same conditions as specified for mono-*tert*-butylurea.
6. The product should not be dried in an oven at elevated temperatures, as it sublimes.
7. This material is pure enough for the next step. Melting points of 172° (dec.) and 183° are given in the literature.[4,5] Recrystallization from dilute ethanol gives long, white needles melting at 182° (cor.), whereas use of 95% ethanol gives plates melting at the same temperature. The temperature of the melting-point bath should be raised more rapidly than usual since the product sublimes slowly above 100°.

8. Less rapid heating results in a diminished yield. The reaction is usually completed after a total time of 15 minutes, no further evolution of carbon dioxide or ammonia occurring. Prolonged heating causes the formation of a colored product and reduces the yield.
9. A similar series of reactions may be used to prepare *tert*-amylamine. The *tert*-amylurea is produced in yields of 50–58%, *tert*-amylphthalimide in yields of 63–72%, and *tert*-amylamine, b.p. 77–78°, in 87% yields (N. L. Drake and John Garman, private communication).
10. If the water in the condenser is cold enough to prevent loss of the amine the extra trap is unnecessary.
11. The *tert*-butylurea gradually dissolves, and a gelatinous mass of sodium carbonate forms.
12. If an aqueous layer forms it is separated and the amine is dried with a fresh portion of 5 g. of sodium hydroxide pellets.
13. The submitters and checkers used a Vigreux column.

3. Discussion

tert-Butylurea has been prepared by the action of *tert*-butyl bromide upon a mixture of urea and white lead;[4] by the action of *tert*-butylamine upon potassium cyanate;[5] in small amounts by heating N-*tert*-butylurethan with alcoholic ammonia.[4] The method given above is a modification of a general method for preparation of alkyl ureas, described by Harvey and Caplan in a patent.[6]

The direct hydrolysis of *tert*-butylurea is perhaps the simplest and most convenient method for preparing *tert*-butylamine.[7] In addition to the ethylene glycol method described here, it is possible to carry out the hydrolysis in a pressure vessel with aqueous sodium hydroxide (40%) at 130° (A. H. Sommers, private communication).

tert-Butylphthalimide is a new compound. The procedure given here is a modification[8] of a general procedure for the cleavage of alkylphthalimides, as developed by Ing and Manske[9] and Manske.[10]

2,2-Dimethylethylenimine has been prepared by the dehydration of 2-amino-2-methyl-1-propanol. The method described here is essentially that of Cairns.[11]

Methods for the hydrogenolysis of 2,2-dimethylethylenimine have been published.[12,13]

tert-Butylamine has also been obtained from trimethylacetamide by the Hofmann rearrangement,[14] from trimethylacetic acid by the Schmidt reaction,[15] from trimethylacetazide,[16] by the reduction of *tert*-butylhydrazide,[17] and by the reaction of *tert*-butylmagnesium chloride with O-methylhydroxylamine[18] or with monochloramine.[19]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 801

References and Notes

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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

petroleum ether

trimethylacetazide

ethanol (64-17-5)

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

ether (60-29-7)

hydrogen (1333-74-0)

sodium hydroxide (1310-73-2)

lead (7439-92-1)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

tert-Butyl bromide (507-19-7)

carbon dioxide (124-38-9)

phthalic anhydride (85-44-9)

nickel (7440-02-0)

potassium hydroxide (1310-58-3)

ethylene glycol (107-21-1)

urea (57-13-6)

hydrazine hydrate (7803-57-8)

potassium cyanate (590-28-3)

Trimethylacetic acid (75-98-9)

dioxane (123-91-1)

monochloramine (10599-90-3)

2,2-Dimethylethylenimine (2658-24-4)

2-amino-2-methyl-1-propanol (124-68-5)

Phthalhydrazide (1445-69-8)

sodium sulfate decahydrate (7727-73-3)

trimethylacetamide (758-96-3)

O-methylhydroxylamine (67-62-9)

tert-butyl alcohol (75-65-0)

tert-Butylamine (75-64-9)

tert-butylmagnesium chloride (677-22-5)

tert-Butylphthalimide (2141-99-3)

tert-Butylurea,
mono-tert-butylurea (1118-12-3)

tert-Butylamine hydrochloride (10017-37-5)

di-tert-butylurea

tert-amylamine (594-39-8)

tert-amylurea

tert-amylphthalimide

N-tert-butylurethan

tert-butylhydrazide (3619-17-8)