Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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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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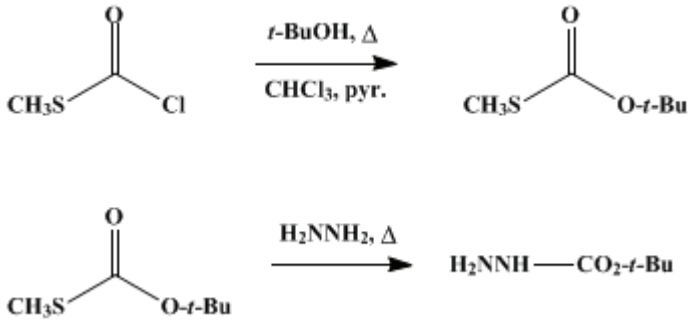
t-BUTYL CARBAZATE

[Carbazic acid, *tert*-butyl ester]

[Method I]



Submitted by Louis A. Carpino, David Collins, Siegfried Göwecke, Joe Mayo, S. D. Thatte, and Fred Tibbetts[1].
Checked by Fred G. H. Lee and Virgil Boekelheide.

1. Procedure

Caution! Methyl chlorothiolformate has an obnoxious odor. All operations should be conducted in a well-ventilated hood.

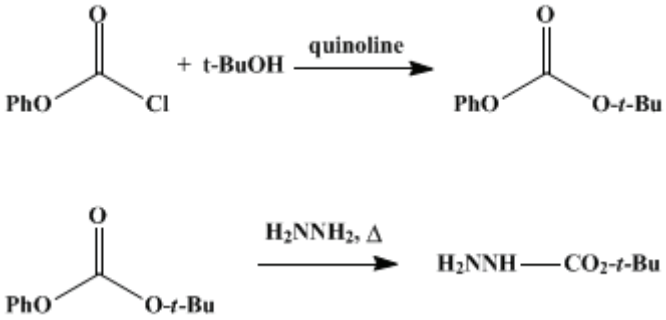
A. *t-Butyl S-methylthiolcarbonate*. In a 5-l. round-bottomed flask, fitted with mechanical stirrer, reflux condenser, and dropping funnel are placed 430 ml. (422 g., 5.33 moles) of pyridine, 508 ml. (395 g., 5.33 moles) of *t*-butyl alcohol, and 1.6 l. of chloroform (Note 1). The solution is stirred while 536 g. (4.85 moles) of methyl chlorothiolformate (Note 2) is added dropwise over a period of 30–40 minutes, and the solution is then stirred and heated at the reflux temperature for 24 hours. The resulting solution is divided into three equal portions of about 1 l., and each portion is washed in a 2-l. separatory funnel with two 500-ml. portions of water, three 275-ml. portions of 5% hydrochloric acid, and finally with 350 ml. of 1*M* sodium bicarbonate solution. The combined chloroform solutions are dried over anhydrous magnesium sulfate for 5 hours, and the solvent is removed by distillation from a water bath at atmospheric pressure followed by the use of a water aspirator. Distillation (Note 3) of the residue from a 1-l. Claisen flask by means of a water or oil bath gives 419–497 g. (58–69%) of a colorless liquid, b.p. 62–65° (24 mm.), n^{25}D 1.4525. This product is sufficiently pure for use in the preparation below but may be purified by distillation through a 30-cm. helices-packed column which gives 375–447 g. (52–62%) of the ester, b.p. 60–63° (24 mm.).

B. *t-Butyl carbazate*. In a 2-l. round-bottomed flask set up in a hood and fitted with an efficient mechanical stirrer and a reflux condenser are placed 500 g. (3.47 moles) of *t*-butyl S-methylthiolcarbonate and 186 g. (3.71 moles) of 64% hydrazine solution (Note 4). The contents of the flask are heated in an oil bath at 105–110° (external temperature) with mechanical stirring for 24 hours under a reflux condenser. The resulting mixture is diluted with 650 ml. of methylene dichloride, and anhydrous magnesium sulfate is added until the aqueous layer becomes nearly solid and nonflowing. The upper layer is decanted and dried over fresh anhydrous magnesium sulfate and the solvent removed by distillation from a water bath, the last portions being removed with the aid of a water aspirator. The residual liquid solidifies on cooling and stirring to give 322–385 g. (72–86%) of a snow-white solid, m.p. 37–40°. This product is pure enough for most purposes but can be purified by distillation, a 1-l. Claisen flask with a water or oil bath at 80° being used. After 1 or 2 drops of fore-run the carbazate is collected at 55–57° (0.4 mm.). The oil solidifies on cooling to give 312–358 g. (70–80%) of snow-white crystalline solid, m.p. 40–42° (Note 5).

2. Notes

1. The pyridine was a pure product, b.p. 113–115°, obtained from the Mallinckrodt Chemical Company. *t*-Butyl alcohol, m.p. 24.5–25.5°, and chloroform (U.S.P. or reagent grade) were obtained from the Matheson Company. All reagents were used as supplied.
2. The methyl chlorothiolformate, b.p. 110–111°, was used as supplied by the Stauffer Chemical Company.
3. This distillation is accompanied by foaming which is very difficult to prevent. The checkers recommend carrying out the distillation in two separate batches to allow greater free space in the distillation flask.
4. Hydrazine hydrate (64% hydrazine) was used as supplied by the Fairmount Chemical Company.
5. Further purification can be effected by recrystallization with 90% recovery from a 50-50 mixture of low- (b.p. 30–60°) and high-boiling (b.p. 60–70°) ligroin. This procedure gives white needles, m.p. 41–42°.

[Method II]



Submitted by Louis A. Carpino, Barbara A. Carpino, Chester A. Giza, Robert W. Murray, Arthur A. Santilli, and Paul H. Terry[1].
Checked by Virgil Boekelheide and S. J. Cross.

1. Procedure

A. *t-Butyl phenyl carbonate*. In a 2-l. round-bottomed flask fitted with thermometer, dropping funnel, and mechanical stirrer are placed 248 g. (3.35 moles) of *t*-butyl alcohol, 430 g. (3.33 moles) of quinoline, and 500 ml. of methylene dichloride (Note 1). The solution is stirred while 520 g. (3.32 moles) of phenyl chloroformate (Note 2) is added dropwise over a period of 4 hours. During the addition the temperature is maintained at 28–31° (Note 3) by cooling the flask, as needed, by a stream of tap water. The solution is allowed to stand overnight and is then treated with 800 ml. of water to dissolve the precipitated quinoline hydrochloride (Note 4). The mixture is shaken well in a separatory funnel; the organic layer is separated and washed with two 200-ml. portions of water and three or four 200-ml. portions of 5% hydrochloric acid. After the extract has dried over anhydrous magnesium sulfate for 5 hours, the solvent is removed by distillation, a water aspirator being used to remove the last portions of the methylene dichloride. Distillation of the residue from a 1-l. Claisen flask by means of an air bath maintained at 125–135° gives 460–495 g. (71–76%) (Note 5) of a colorless oil, b.p. 74–78° (0.5 mm.), n^{24}D 1.4832. This product is sufficiently pure for use in the preparation below.

B. *t-Butyl carbazate*. In a 1-l. Erlenmeyer flask are placed 388.4 g. (2.0 moles) of phenyl *t*-butyl carbonate and 120.2 g. (2.4 moles) of a 64% hydrazine solution (Note 6). The mixture is swirled by hand and heated on a hot plate. When the internal temperature reaches 75–80°, it then rises rapidly and spontaneously to 104–110°, the two layers forming a clear solution. The solution is allowed to cool overnight. The mixture is then diluted with 500 ml. of ether and transferred to a separatory funnel in which it is shaken vigorously for about 10 minutes with a solution prepared from 160 g. (4.0 moles) of sodium hydroxide and 1.2 l. of water. The resulting two layers are placed in a 2-l. continuous extractor and extracted for 48 hours with ether. The ether solution is dried over magnesium sulfate, and the ether

is removed by distillation from a water bath. The last portions of ether are removed with the aid of a water aspirator. The residual oil is then distilled using a Claisen flask with an air bath maintained at 115–125°. After 1 or 2 drops of fore-run the carbazate is collected at 61–65° (1.2 mm.), n^{24}D 1.4518. The yield is 235–256 g. (89–97%) (Note 7).

2. Notes

1. The *t*-butyl alcohol and methylene dichloride were used directly as received from the Matheson Company. The quinoline was a practical grade material (Eastman Kodak Company) which was redistilled [b.p. 100–102° (25 mm.)].
2. Phenyl chloroformate was prepared by the method of Strain *et al.*,[2] except that methylene dichloride or chloroform was used in place of benzene as the solvent. The yield was 85–95% [b.p. 74–76° (15 mm.), n^{24}D 1.5125]. The checkers used commercial phenyl chloroformate (Eastman Kodak).
3. The reaction may be run without cooling by adding the acid chloride at a rate to maintain the temperature at 39–43°. On the scale indicated this requires about 5 hours. The yield is substantially the same, although more high-boiling material is formed.
4. Occasionally the quinoline hydrochloride does not separate; this does not affect the yield, however. If it is desired to recover the quinoline, the salt may be filtered at this point, dissolved in water, and converted to the free base.
5. The carbonate decomposes on attempted distillation of large amounts at water aspirator pressure (20–25 mm.).
6. Hydrazine hydrate (64% hydrazine) was used as supplied by the Olin-Mathieson Company.
7. The carbazate is sufficiently pure for most applications and is conveniently handled as a liquid. When the product is cooled in an ice box, it crystallizes as a waxy mass; such samples remain tacky after several recrystallizations from petroleum ether, however. A pure sample may be obtained by extracting an ether solution of the carbazate with dilute sodium hydroxide to remove any phenol, followed by distillation and recrystallization of the product from petroleum ether (b.p. 30–60°). White needles are obtained which melt at 41–42°.

3. Discussion

t-Butyl S-methylthiolcarbonate has been prepared from sodium *t*-butoxide, carbonyl sulfide, and methyl iodide[3] and from methyl chlorothiolformate and *t*-butyl alcohol.[4] *t*-Butyl phenyl carbonate has been prepared from phenyl chloroformate and *t*-butyl alcohol.[5,6]

t-Butyl carbazate has been prepared by reaction of hydrazine with *t*-butyl phenyl carbonate,[5,6] *t*-butyl S-methylthiolcarbonate,[3] *t*-butyl-*p*-nitrophenyl carbonate,[7] and N-*t*-butyloxycarbonylimidazole.[8]

4. Merits of the Preparation

Method I is easily adapted to larger-scale operation and provides a product which crystallizes readily. Method II provides a product which is difficult to crystallize; however, the procedure obviates the use of methyl chlorothiolformate and affords higher yields of product.

t-Butyl carbazate is a useful reagent for preparing 1,1-disubstituted hydrazines.[6] In turn, the 1,1-disubstituted hydrazines can undergo an elimination of nitrogen followed by radical coupling of the two substituent groups. This reaction is promoted either by direct oxidation of the 1,1-disubstituted hydrazine[9,10,11] or by base-catalyzed elimination of benzenesulfinic acid from the corresponding benzenesulfonhydrazide.[6] For example, 1,1-dibenzyl-2-benzenesulfonhydrazide is converted to bibenzyl in 85% yield.

t-Butyl carbazate is also a key intermediate in the synthesis of *t*-butyl azidoformate,[5,6,12] *t*-butyl hydrazodiformate,[6] *t*-butyl azodiformate,[13] and *t*-butyl N-hydroxycarbamate,[12,14] all of which are valuable synthetic intermediates.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 5, 157
- Org. Syn. Coll. Vol. 5, 160

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

petroleum ether

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

phenol (108-95-2)

nitrogen (7727-37-9)

pyridine (110-86-1)

Methyl iodide (74-88-4)

hydrazine hydrate (7803-57-8)

Quinoline (91-22-5)

hydrazine (302-01-2)

methylene dichloride (75-09-2)

magnesium sulfate (7487-88-9)

bibenzyl (103-29-7)

benzenesulfonhydrazide (80-17-1)

t-butyl alcohol (75-65-0)

phenyl chloroformate (1885-14-9)

Methyl chlorothiolformate (18369-83-0)

quinoline hydrochloride (530-64-3)

benzenesulfinic acid (618-41-7)

1,1-dibenzyl-2-benzenesulfonhydrazide

t-BUTYL AZIDOFORMATE (1070-19-5)

phenyl t-butyl carbonate,
t-Butyl phenyl carbonate (6627-89-0)

t-butyl carbazate,
Carbazic acid, tert-butyl ester (870-46-2)

t-BUTYL AZODIFORMATE (870-50-8)

t-butyl hydrazodiformate

t-Butyl S-methylthiolcarbonate (29518-83-0)

sodium t-butoxide, carbonyl sulfide

N-t-butyloxycarbonylimidazole (49761-82-2)

t-butyl N-hydroxycarbamate (36016-38-3)

t-butyl-p-nitrophenyl carbonate