



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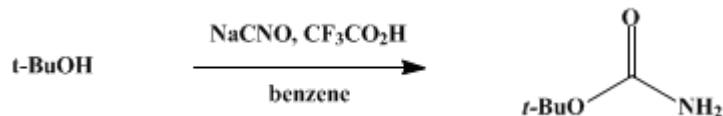
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## **t-BUTYL CARBAMATE**

### **[Carbamic acid, *tert*-butyl ester]**



Submitted by Bernard Loev, Minerva F. Kormendy, and Marjorie M. Goodman<sup>1</sup>.

Checked by David C. Armbruster and William D. Emmons.

### **1. Procedure**

*Caution! Because of the acrid nature of trifluoroacetic acid and the possibility of the evolution of toxic fumes the reaction should be carried out in a hood.*

A solution of 14.8 g. (0.20 mole) of *t*-butyl alcohol in 125 ml. of benzene (Note 1) is placed in a 500-ml. three-necked flask equipped with a stirrer, a thermometer, and an addition funnel, and 26.0 g. (0.40 mole) of sodium cyanate (Note 2) is added. The suspension is stirred as *slowly* as possible (*ca.* 120 r.p.m.; (Note 3)) while 48.0 g. (31.2 ml., 0.42 mole) of trifluoroacetic acid is added dropwise at a rapid rate. The temperature slowly rises to about 37° after three-quarters of the trifluoroacetic acid has been added (*ca.* 7 minutes). At this point (Note 4) the mixture is cooled to 33–35° by brief immersion in an ice-water bath, then the addition is continued. When the addition of the acid is completed (10–12 minutes total time), the temperature slowly rises to 40° and then gradually subsides. Slow stirring is continued overnight (Note 5) at room temperature.

The mixture is treated with 35 ml. of water (Note 6) and stirred vigorously for a few minutes. The benzene layer is decanted, and the aqueous slurry is rinsed with two 125-ml. portions of benzene (Note 7). The combined organic extracts are washed once with 100 ml. of aqueous 5% sodium hydroxide (Note 8) and with 100 ml. of water, dried over anhydrous magnesium sulfate, and filtered. The solvent is removed by distillation under reduced pressure, preferably on a rotary evaporator, from a water bath kept at 30° (Note 9) to give 17.7–22.0 g. (76–94%) of *t*-butyl carbamate as white needles, m.p. 104–109° (Note 10). The product may be recrystallized from hexane (Note 11); m.p. 107–109° (Note 12).

### **2. Notes**

1. The reagents should not be dried, as traces of moisture catalyze the reaction. The choice of solvent for this type of reaction markedly affects the yield; for most alcohols the use of benzene or methylene chloride gives yields superior to those obtained in other solvents.
2. Sodium cyanate cannot be replaced by other cyanates (potassium, ammonium, etc.), for the yields are then drastically lowered.
3. Vigorous agitation markedly lowers the yield; stirring rates of 40–120 r.p.m. are optimum.
4. The temperature may rise to 40°; within the range 20–50° the temperature has little effect on the yield.
5. A contact time of 3–4 hours is sufficient, but it is convenient to stir the reaction mixture overnight. The yield is slightly higher after this additional time.
6. Only a limited amount of water is added at this point because *t*-butyl carbamate has some solubility in the resulting aqueous slurry. With water-insoluble carbamates the amount of water added is immaterial.
7. The checkers found that quantitative recovery of the benzene layer by decantation was impossible, so that in the final benzene rinse the mixture was poured into a graduated cylinder, and the benzene layer was quantitatively removed by a syringe.
8. The alkaline wash serves to hydrolyze a small amount of *t*-butyl N-trifluoroacetylcarbamate which occasionally forms. It is not clear why this by-product forms on some occasions but not on others under

apparently identical conditions. The checkers found in every case that upon standing the alkaline wash deposited 1–2 g. (after drying) of white crystals which was shown to be identical with the *t*-butyl carbamate obtained as the main crop. This amount is included in the yield.

9. Most carbamates, including those of high molecular weight, are volatile. They are generally thermally unstable until they are purified.

10. The melting range varies markedly with the rate of heating, the temperature at which the sample is put into the bath, the solvent used, and the crystal form of the product. The compound at this stage is analytically pure and gives a single spot on thin-layer chromatography.

11. The carbamate may also be recrystallized from water in somewhat lower recovery. With either solvent, extensive heating should be avoided since a considerable amount of product is lost by volatilization. The checkers found that a relatively large volume of hexane was required for recrystallization and therefore used a 1:1 benzene-hexane or 1:1 benzene-ligroin solvent system for the recrystallization.

12. The reported melting points range from 108° to 110°.<sup>2,3,4,5</sup>

### 3. Discussion

Although numerous methods are known for the synthesis of carbamates of primary and secondary alcohols,<sup>6</sup> they are not satisfactory for the preparation of carbamates of tertiary alcohols.<sup>7,8</sup> *t*-Butyl carbamate was first obtained by reaction of sodium *t*-butoxide with phosgene and thionyl chloride at –60°, followed by reaction with concentrated aqueous ammonia; the overall yield was less than 20%.<sup>2</sup> This procedure, however, was found to be unsuitable for the preparation of carbamates of other tertiary alcohols.<sup>8</sup> Carbamates have been prepared by the reaction of phenyl chloroformate (prepared from phenol and phosgene at –60°) with a tertiary alcohol in pyridine, followed by treatment with liquid ammonia.<sup>8</sup> A variation of this procedure involves hydrazinolysis of phenyl *t*-butyl carbonate, prepared as described above, conversion to the azide, and ammonolysis.<sup>3,4</sup> *t*-Butyl carbamate has also been prepared by a four-step procedure that starts with the preparation of *t*-butyl ethyl oxalate from ethoxalyl chloride. This mixed ester was converted to *t*-butyl oxamate, which was dehydrated to *t*-butyl cyanoformate, and this was treated with ammonia.<sup>4</sup>

The carbamates of tertiary acetylenic alcohols have also been made by reaction of these alcohols with sodium cyanate in trifluoroacetic acid.<sup>9</sup> The yields by this procedure are significantly lower than those obtained by the present modification, which is essentially that described by Loev and Kormendy.<sup>5</sup>

### 4. Merits of the Preparation

This one-step procedure is a convenient and general method for the preparation of carbamates. It is substantially simpler, quicker, and safer than the multistep methods hitherto used for the preparation of carbamates of tertiary alcohols. This procedure is applicable to the preparation of carbamates of primary, secondary, and tertiary alcohols and mercaptans, polyhydric alcohols, acetylenic alcohols, phenols, and oximes. It has also been extended to the preparation of carbamyl derivatives (*i.e.*, ureas) of inert (non-basic) amines.<sup>10</sup>

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### References and Notes

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

benzene-ligroin  
ethoxalyl chloride  
ammonia (7664-41-7)  
Benzene (71-43-2)  
sodium hydroxide (1310-73-2)  
thionyl chloride (7719-09-7)  
phenol (108-95-2)  
pyridine (110-86-1)  
phosgene (75-44-5)  
methylene chloride (75-09-2)  
magnesium sulfate (7487-88-9)  
benzene-hexane (1077-16-3)  
hexane (110-54-3)  
sodium cyanate (917-61-3)  
t-butyl alcohol (75-65-0)  
trifluoroacetic acid (76-05-1)  
phenyl chloroformate (1885-14-9)  
phenyl t-butyl carbonate (6627-89-0)  
t-butyl cyanoformate  
t-BUTYL CARBAMATE,  
Carbamic acid, tert-butyl ester (4248-19-5)  
t-butyl N-trifluoroacetylcarbamate

t-butyl ethyl oxalate

t-butyl oxamate

sodium t-butoxide (865-48-5)

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