



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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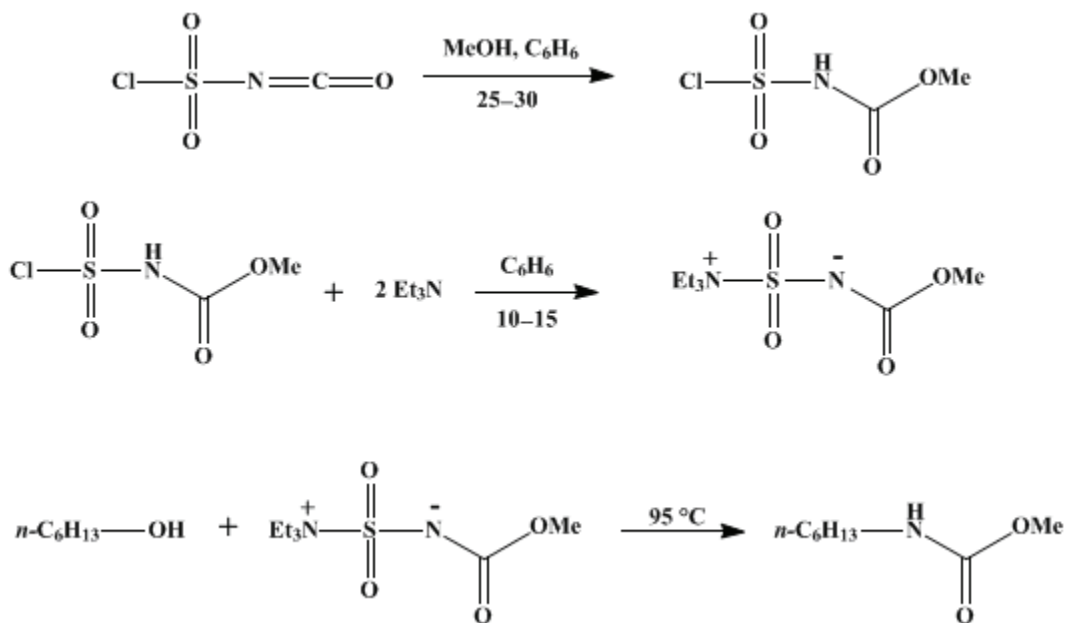
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.788 (1988); Vol. 56, p.40 (1977).

**CONVERSION OF PRIMARY ALCOHOLS TO URETHANES *via*
THE INNER SALT OF METHYL (CARBOXYSULFAMOYL)
TRIETHYLAMMONIUM HYDROXIDE: METHYL *n*-
HEXYLCARBAMATE**

[Carbamic acid, hexyl-, methyl ester]



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1. Procedure

Caution! Chlorosulfonyl isocyanate is highly corrosive. This preparation should be carried out in an efficient hood, and rubber gloves should be worn during the first step.

Benzene has been identified as a carcinogen; OSHA has issued emergency standards on its use. All procedures involving benzene should be carried out in a well-ventilated hood, and glove protection is required.

A. *Methyl (chlorosulfonyl)carbamate*. A dry, two-necked, 500-ml., round-bottomed flask fitted with a magnetic stirring bar, a 125-ml., pressure-equalizing dropping funnel, and a reflux condenser to which is attached a calcium chloride drying tube is charged with a solution of 70.8 g. (43.6 ml., 0.580 mole) of chlorosulfonyl isocyanate (Note 1) in 150 ml. of anhydrous benzene (Note 2). A solution of 16.0 g. (20.2 ml., 0.500 mole) of anhydrous methanol (Note 3) in 25 ml. of anhydrous benzene (Note 2) is placed in the dropping funnel. The flask is immersed in a water bath (Note 4), stirring is begun, and the methanol–benzene solution is added dropwise over 0.5 hour. Cold water is added to the bath as required to maintain a temperature of 25–30°. The reaction mixture is stirred for an additional 0.5 hour before 125 ml. of olefin-free hexane (Note 5) is added from the addition funnel over a 5-minute period while cooling the flask to 0–5° with an ice bath. The moisture-sensitive product is removed by filtration, washed twice with 40 ml. of hexane, and dried under reduced pressure, giving 76–80 g. (88–92%) of

methyl (chlorosulfonyl)carbamate as white crystals, m.p. 72–74° (Note 6). This material should be stored in a brown bottle protected from light (Note 7).

B. *Inner salt of methyl (carboxysulfamoyl)triethylammonium hydroxide*. A two-necked, 500-ml., round-bottomed flask is fitted with a magnetic stirring bar, a 500-ml., pressure-equalizing dropping funnel, and a condenser to which a calcium chloride drying tube is attached. A solution of 23.0 g. (31.8 ml., 0.225 mole) of anhydrous **triethylamine** (Note 8) in 50 ml. of anhydrous **benzene** (Note 2) is placed in the flask, stirring is begun, and a solution of 17.4 g. (0.100 mole) of **methyl (chlorosulfonyl)carbamate** in 225 ml. of dried **benzene** (Note 9) is added dropwise over 1 hour. During addition the flask is cooled with a water bath maintained at 10–15°. The resulting mixture is stirred at 25–30° for an additional 0.5 hour then filtered to remove **triethylamine hydrochloride** (13.8 g.). Evaporation of the filtrate under reduced pressure leaves 22–23 g. of light tan needles, m.p. 70–72° (dec.), which is dissolved in 160 ml. of anhydrous **tetrahydrofuran** (Note 10) at 30°. On cooling, 20.0–20.6 g. (84–86%) of the inner salt of **methyl (carboxysulfamoyl)triethylammonium hydroxide** precipitates as colorless needles, m.p. 70–72° (dec.) (Note 11).

C. *Methyl n-hexylcarbamate*. In a dry, 100-ml., round-bottomed flask fitted with a reflux condenser, to which a calcium chloride drying tube is attached, are placed a boiling chip, 14.8 g. (0.0622 mole) of the inner salt of **methyl (carboxysulfamoyl)triethylammonium hydroxide**, and 6.0 g. (0.058 mole) of freshly distilled **1-hexanol** (Note 12). After a mildly exothermic reaction (occasionally there is a 5-minute induction period), the viscous, yellow reaction mixture is heated with an oil bath at 95° for 1 hour. The mixture is cooled to 30°, diluted with 50 ml. of water, and extracted with three 50-ml. portions of **dichloromethane**. The organic extracts are combined, washed successively with 100 ml. of 5% **hydrochloric acid** and 50 ml. of water, and dried over anhydrous **magnesium sulfate**. After filtration, **dichloromethane** is removed with a rotary evaporator. The residue is triturated with 50 ml. of anhydrous **diethyl ether** and filtered; the recovered solid is triturated with two further 50-ml. portions of **ether**. The three ethereal filtrates are combined and concentrated with a rotary evaporator, affording 8.0 g. of crude product. Fractionation of this oil through a short-path distillation apparatus gives 4.8–4.9 g. (51–52%) of **methyl n-hexylcarbamate** as a colorless oil, b.p. 59–60° (0.08 mm.); n_D^{20} 1.4361 (Note 13).

2. Notes

1. The preparation of **chlorosulfonyl isocyanate** is described in *Org. Synth., Coll. Vol. 5*, 226 (1973). This compound is highly corrosive, reacts explosively with water, and may be contaminated with **cyanogen chloride**.
2. Throughout this preparation the submitters used reagent grade materials distilled prior to use. The checkers used ACS reagent grade **benzene** available from Fisher Scientific Company.
3. The checkers used ACS reagent grade **methanol** available from Fisher Scientific Company.
4. The water bath should not be positioned around the flask until after the solution of **chlorosulfonyl isocyanate** has been added.
5. The checkers used spectro-grade reagent available from Phillips Petroleum Company.
6. $^1\text{H NMR}$ (CD_3CN) δ : 3.64 (s).
7. The checkers observed a violent decomposition when product stored in a clear glass container was inadvertently exposed to sunlight.
8. **Triethylamine** was dried by distillation from **phosphorus pentoxide** at atmospheric pressure. The checkers used reagent grade material available from Eastman Organic Chemicals.
9. The compound dissolves readily in **benzene** on warming to 40°.
10. The checkers used ACS reagent grade material available from Fisher Scientific Company, taken from a freshly opened bottle.
11. IR (CHCl_3) cm^{-1} : 1690 (C=O), 1345, 1110 (SO_2), 1260 (C-O); $^1\text{H NMR}$ (CDCl_3), δ (multiplicity, coupling constant J in Hz., number of protons): 1.15 (t, $J = 7$, 9H), 3.29 (q, $J = 7$, 6H), 3.66 (s, 3H).
12. The checkers used practical grade material (available from Eastman Organic Chemicals) distilled immediately prior to use.
13. IR (neat) cm^{-1} : 3400, 2950, 1700, 1520, 1255, 1190, 774; $^1\text{H NMR}$ (neat), δ (multiplicity, number of protons): 0.8–1.5 (m, 13H), 3.6 (s, 3H), 6.14 (broad t, 1H).

3. Discussion

The above procedure describes the only known preparation of the inner salt of methyl (carboxysulfamoyl)triethylammonium hydroxide and illustrates the use of this reagent to convert a primary alcohol to the corresponding urethane.² Hydrolysis of the urethane would provide the primary amine. The method is limited to primary alcohols; secondary and tertiary alcohols are dehydrated to olefins under these conditions, often in synthetically useful yields.²

Other sequences that transform primary alcohols to primary amines include: (a) conversion of the alcohol to a cyanate, rearrangement to an isocyanate, and hydrolysis,³ and (b) conversion of the alcohol to an *N*-alkylformamide *via* the Ritter reaction, followed by hydrolysis.⁴

References and Notes

1. School of Chemistry, Georgia Institute of Technology, Atlanta, Georgia 30332. This work was supported by a grant (GM-12672) from the National Institutes of Health.
 2. E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Org. Chem.*, **38**, 26 (1973).
 3. J. W. Timberlake and J. C. Martin, *J. Org. Chem.*, **33**, 4054 (1968).
 4. L. I. Krimen and D. J. Cota, *Org. React.*, **17**, 213 (1969).
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Appendix

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

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

methanol (67-56-1)

ether,
diethyl ether (60-29-7)

Triethylamine hydrochloride (554-68-7)

1-Hexanol (111-27-3)

dichloromethane (75-09-2)

magnesium sulfate (7487-88-9)

urethane (51-79-6)

cyanogen chloride (506-77-4)

Tetrahydrofuran (109-99-9)

hexane (110-54-3)

triethylamine (121-44-8)

CHLOROSULFONYL ISOCYANATE (1189-71-5)

METHYL (CARBOXYSULFAMOYL)TRIETHYLAMMONIUM HYDROXIDE (29684-56-8)

Carbamic acid, hexyl-, methyl ester (22139-32-8)

Methyl (chlorosulfonyl)carbamate (36914-92-8)

phosphorus pentoxide (1314-56-3)

METHYL n-HEXYLCARBAMATE