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A Convenient Large Scale Synthesis of N-BOC-Ethylenediamine

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A CONVENIENT LARGE SCALE SYNTHESIS OF *N*-BOC-ETHYLENEDIAMINE

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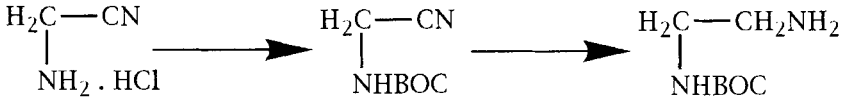
Abstract: A simple, convenient large scale synthesis of *N*-BOC-ethylenediamine is described.

The *tert*-butoxycarbonyl (BOC) group is an important protective group[1] for amines and is extensively used in the synthesis of peptides. This group can be readily removed using anhydrous hydrogen chloride gas to afford the amines as hydrochloride salts. Recently, the BOC group has been removed using TMSCl/Phenol.[2,3] There are several reports[4-10] on the synthesis of *N*-BOC-ethylenediamine and it is also commercially available from Fluka.[11] During the course of our study on the synthesis of analogs of DNA for use as antisense theraputic

drugs,[12-25] we had a need for a large quantity of *N*-BOC-ethylenediamine.

We report here an easy and convenient method for the large scale synthesis of the title compound. Treatment of 2-aminoacetonitrile with 1.1 equivalents of di-*tert*-butyl dicarbonate and 3.5 equivalents of triethylamine in anhydrous dichloromethane at room temperature gave *N*-BOC-2-amino-acetonitrile in 95% yield. Reduction of the cyano group was achieved under Parr hydrogenation conditions using Raney nickel in ethanol saturated with ammonia to afford *N*-BOC-ethylenediamine in almost quanitative yield.



(1) (2)

EXPERIMENTAL

2-Aminoacetonitrile hydrochloride, triethylamine, di-tert-butyl dicarbonate, Raney nickel and anhydrous dichloromethane were obtained from Aldrich Chemical Company, Milwaukee, Wisconsin and used as received. ^{1}H NMR spectra were obtained on a Varian Gemini 200 MHz spectrometer. Chemical shifts are reported in parts per million

(ppm) using tetramethylsilane as an internal standard with $CDCl_3$ as solvent. Infrared spectrum, obtained as thin film between sodium chloride plates on an IBM IR/32 FT-IR spectrometer, is reported in wave numbers (cm^{-1}) and is uncalibrated.

N-tert-Butoxycarbonyl-2-aminoacetonitrile (1):

A solution of di-*tert*-butyl dicarbonate (60 g, 0.275 mol) in dichloromethane (200 mL) was added over a period of 1 h to a mixture of 2-aminoacetonitrile hydrochloride (23.13 g, 0.25 mol) and triethylamine (88.55 g, 0.875 mol) in dichloro methane (300 mL) which was cooled in an ice bath. The mixture was allowed to stir at room temperature for 16 h, then filtered, and the solid residue washed thoroughly with dichloromethane (200 mL). The filtrate was concentrated under reduced pressure, redissolved in ethyl acetate (400 mL), washed with water (2X75 mL), brine (75 mL), and dried ($MgSO_4$). Concentration of the dried extract under vacuo afforded product (**1**) as a viscous oil which was sufficiently pure to be used in the next step. Yield : 37 g (95%); IR(cm^{-1}) 1710, 2240, 3360; ^1H NMR($CDCl_3$) δ : 1.42(s, 9H), 4.05 (bd, 2H), 5.58 (bs, 1H); m/z (CI/NH_3) 156.

N-tert-Butoxycarbonyl-1,2-ethanediamine (2):

A solution of *N-tert*-butoxycarbonyl-2-aminoacetonitrile (23.4 g, 0.15 mol) in ethanol (150 mL) saturated with ammonia and Raney nickel (20 g) was hydrogenated at 50 psi at room

temperature using Parr hydrogenation apparatus for 14 h. The reaction mixture was filtered, the catalyst washed thoroughly with ethanol (100 mL) and concentrated under reduced pressure. The product was passed through a pad of silica gel (70-230 mesh) (120 g) and eluted with dichloromethane. The eluant on concentration afforded the desired product (2) as a viscous oil (23.7 g, 99%); IR(cm^{-1}) 1670, 3340; ^1H NMR($CDCl_3$) δ : 1.4(s, 9H), 1.8 s, 2H), 2.8 (t, 2H), 3.0-3.2 (m, 2H), 5.6 (bs, 1H); m/z (CI/NH_3) 160 (100, M^+), 105 (40.9).

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