

N,S-Diacetylcysteamine:

Cysteamine hydrochloride (15.0 g) is added to a 1-L 3-neck round bottom flask fitted with a magnetic stir bar, 2 addition funnels, and a pH electrode. Water (90 mL) is added and the stirred solution is cooled on ice. The pH is adjusted to 8.0 by addition of 8 N KOH. Acetic anhydride (37.5 mL) is placed in one addition funnel, and 8 N KOH is placed in the other addition funnel. The acetic anhydride is added dropwise to the cysteamine solution, with 8 N KOH being added so as to keep the reaction pH at 8+/-1. (Use about 2-4 mL of KOH per mL of AC₂O). After addition of acetic anhydride is complete, the pH was adjusted to 7.0 using 1 N HCl and the mixture is allowed to stir for 75 min on ice. Solid NaCl is added to saturation, and the solution is extracted 4 times using 400 mL portions of CH₂Cl₂. The organic extracts are combined, dried over Na₂SO₄, filtered, and concentrated under reduced pressure to yield 21.3 g of a colorless oil, which crystallizes upon standing at 4 °C. ¹H-NMR (CDCl₃, 400 MHz): δ 6.43 (brs, 1H) 3.42 (q, 2H, J=7) 3.03 (t, 2H, J=7), 2.36 (s, 3H), 1.98 (s, 3H), 1.98 (s, 3H). ¹³C-NMR (CDCl₃, 100 MHz): δ 196.09, 170.45, 39.42, 30.56, 28.71, 23.06.

For long term storage we recommend stopping at this step and hydrolyze to SNAc as needed.

N-Acylcysteamine (SNAc):

N,S-diacetylcysteamine (21.3g) is placed in a 2-L round bottom flask fitted with a magnetic stirrer, and dissolved in 1400 mL water previously sparged with N₂. The flask is purged with N₂, and the mixture is chilled in an ice bath. Sodium hydroxide (5.8 g, 1.1 eq) is added, and the mixture is stirred for 2 h on ice under inert atmosphere. The pH is adjusted to 7 using 6 N HCl, and solid NaCl is added to saturation. The mixture is extracted 7 times with 500 mL portions of CH₂Cl₂. The organic extracts are combined, dried over Na₂SO₄, filtered and concentrated under reduced pressure. This material may be distilled immediately prior to use (bp 138-140 °C / 7 mmHg) though this is typically not necessary. This material should be stored under N₂ and refrigerated, if solids are forming the material should be distilled or discarded.