

N,S-Diacetylcysteamine:

Cysteamine hydrochloride (15.0 g) was 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) was added and the stirred solution was cooled on ice. The pH was adjusted to 8.0 by addition of 8 N KOH. Acetic anhydride (37.5 mL) was placed in one addition funnel, and 8 N KOH in the other. The acetic anhydride was added dropwise to the cysteamine solution, with 8 N KOH being added so as to keep the reaction at $\text{pH } 8 \pm 1$. (Use about 2-4 mL of KOH per mL of Ac_2O). After addition of acetic anhydride was complete, the pH was adjusted to 7.0 using 1 N HCL and the mixture allowed to stir for 75 min on ice. Solid NaCl was added to saturation, and the solution was extracted 4 times using 400 mL portions of CH_2Cl_2 . The organic extracts were combined, dried over Na_2SO_4 , filtered, and concentrated under reduced pressure to yield 21.3 g of a colorless oil, which crystallizes upon standing at 4 °C. $^1\text{H-NMR}$ (CDCl_3 , 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). $^{13}\text{C-NMR}$ (CDCl_3 , 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) was placed in a 2-L round bottom flask fitted with a magnetic stirrer, and dissolved in 1400 mL water previously sparged with N_2 . The flask was purged with N_2 , and the mixture chilled in an ice bath. Sodium hydroxide (5.8 g, 1.1 eq) was added, and the mixture stirred for 2 h on ice under inert atmosphere. At completion 6 N HCl was added to reach pH 7, and solid NaCl was added to saturation. The mixture was extracted 7 times with 500 mL portions of CH_2Cl_2 . The organic extracts were combined, dried over Na_2SO_4 , filtered and concentrated under reduced pressure to yield a colorless oil. 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 N_2 and refrigerated, if solids form the material should be distilled or discarded.