

Experimental Procedure Preparation of Methyl N-*tert*-Butoxycarbonyl L-Alanyl-L-Phenylalaninate

1. Place 0.63 g of methyl L-phenylalaninate hydrochloride in a 150-mL Erlenmeyer flask.
2. Add 10 mL of dimethylformamide and 0.3 mL of N-methylmorpholine to the flask, swirl the flask to mix the contents, and place the flask in an ice-water bath. Label the flask as Solution A.
3. Add 0.50 g of N-*tert*-butoxycarbonyl-L-alanine in a 100-mL round-bottom flask containing a one inch stirbar. Add 10 mL of dimethylformamide, and then using a 1-mL syringe transfer 0.3 mL of N-methylmorpholine to the flask. Place the flask in an ice-water bath and stir the solution for 5 min.
4. Using a 1-mL syringe add 0.4 mL of isobutyl chloroformate dropwise to the cooled solution in the round-bottom flask and continue stirring the mixture in the ice-water bath for 5–10 min.
5. Transfer Solution A into the round-bottom flask and continue to stir the reaction with cooling in the ice-water bath for 45 min.
6. Add 20 mL of water to the reaction mixture and transfer it to a separatory funnel. Rinse the round-bottom flask with a 30-mL portion of diethyl ether and transfer the rinse to the separatory funnel.
7. Shake the funnel gently, venting as necessary. Separate the layers and wash the organic layer with two 25-mL portions of 1 M HCl, a 25-mL portion of saturated sodium bicarbonate, and a 25-mL portion of brine.
8. Transfer the organic layer to a 125-mL Erlenmeyer flask and add several spatula-tips full of anhydrous sodium sulfate.
9. Decant the solution into a 150 mL beaker and air dry the sample until the ether is almost gone. Add 2-3 mL ether back into the beaker and swirl until the solid has dissolved.
10. Add approximately 15 mL of hexanes to the flask and place the flask in an ice-water bath for about 15 minutes. Use a spatula to scrape all the solid from the bottom of the flask.
11. Isolate the crystals by vacuum filtration and air-dry them.
12. Weigh the recrystallized product, determine its melting point, and obtain an IR spectrum.