

Supporting Information for

Anaphylaxis Induced by Peptide Coupling Agents: Lessons Learned from Repeated Exposure to HATU, HBTU, & HCTU

Kate J. McKnelly, William Sokol, and James S. Nowick*

*Department of Chemistry & Department of Pharmaceutical Sciences,
University of California, Irvine, Irvine, CA 92697, United States*

*To whom correspondence should be addressed: jsnowick@uci.edu

Standard Operating Procedure (SOP): How to Safely Handle Peptide Coupling Agents

Hazards: Peptide coupling agents are potent immune sensitizers. They have caused cases of both skin and respiratory sensitization in the form of rashes and lesions (dermatitis) and coughing, sneezing, and throat-closing (anaphylaxis) reactions. Peptide coupling agents can modify human proteins, which is the most likely mechanism through which they cause immune sensitization. Researchers should take care to avoid exposure to them as much as possible. As with other standard operating procedures for handling hazardous chemicals, personal protective equipment (PPE) in the form of a lab coat, eye protection, and disposable gloves should be worn at all times when handling coupling agents.

Engineering Precautions: Every research laboratory using peptide coupling agents should have a fume hood with a balance dedicated to weighing out peptide coupling agents and other sensitizing agents. The fume hood and balance should be free of debris and clutter, and any spilled reagents should be promptly cleaned up and removed. The fume hood should also be equipped with a waste container dedicated to contaminated weighing paper.

Procedure

1. Obtain a closed bottle of peptide coupling agent and a sealable container (such as a glass flask with a screw-on lid) and transport both to a fume hood equipped with a balance.
2. Open the bottle of peptide coupling agent completely inside the fume hood. Do not open the bottle outside the fume hood or you will risk exposure to the peptide coupling agent.
3. Weigh out the desired amount of peptide coupling agent on weighing paper and transfer it to the sealable container, or weigh it directly into the sealable container.
4. While still working in the fume hood, seal the sealable container with the coupling agent inside the container.
5. Dispose of the contaminated weighing paper in the waste container within the fume hood. Do not dispose the weighing paper in a trash can outside of the fume hood, as this will cause exposure to peptide coupling agents. (Note: If you spill peptide coupling agents on the balance, fume hood floor, your gloves, etc., make sure to clean up your spill and place your contaminated gloves in the waste container in the fume hood before removing your hands from the fume hood.)
6. Transport your sealable container with coupling agent to your own fume hood or to the automated peptide synthesizer.
7. Continue performing your reactions as normal, always inside a fume hood if possible. If using an automated peptide synthesizer that is not in a fume hood, open all reagent containers as little as possible outside of a fume hood.