

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



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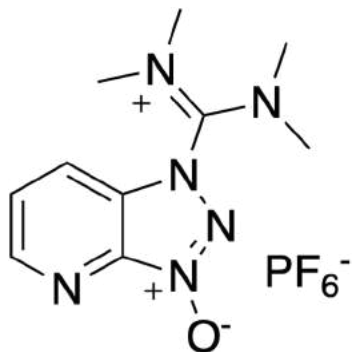


# The Safety Incident

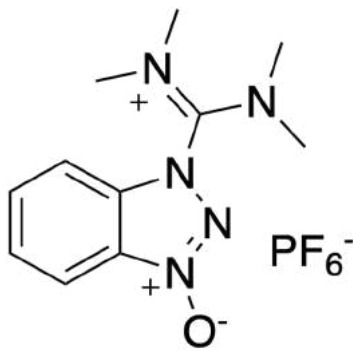
- I walked into lab and sat down at my desk.
- I started sneezing, coughing, and my throat began to feel constricted.
- After a couple minutes, I began to hear wheezing when I breathed.
- The wheezing got worse and worse until I could hear a whistling sound, even when breathing through my nose.
- **How could I and the lab have better prepared to handle an allergy-induced safety incident?**



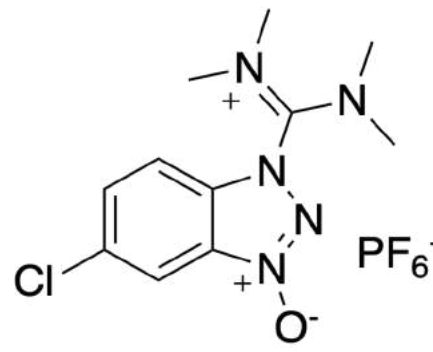
# Peptide Coupling Agents: HATU, HBTU, & HCTU



HATU



HBTU



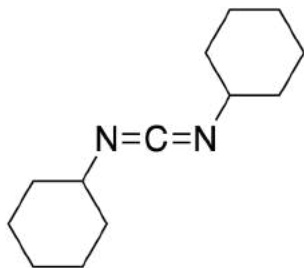
HCTU

## Uronium Coupling Agents

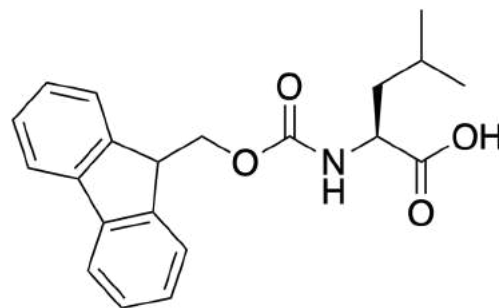
- The University of Leeds, where I did my MSc, treated coupling agents differently.
- I did not speak up.
- How could we empower younger students? How can we change safety culture into a proactive, rather than reactive culture?



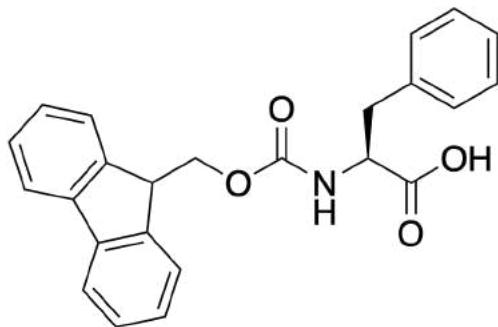
# Other Compounds Tested



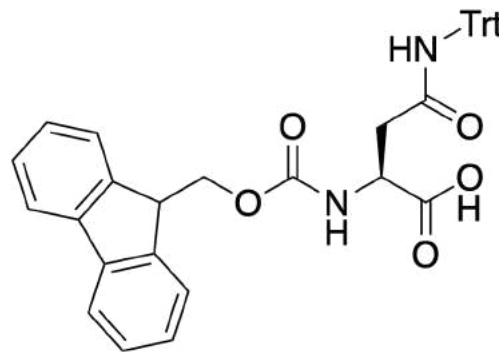
DCC



Fmoc-leucine-OH



Fmoc-phenylalanine-OH



Fmoc-asparagine(Trt)-OH



# Allergic Reactions



Histamine

HATU

HBTU

HCTU



Fmoc-leucine-OH

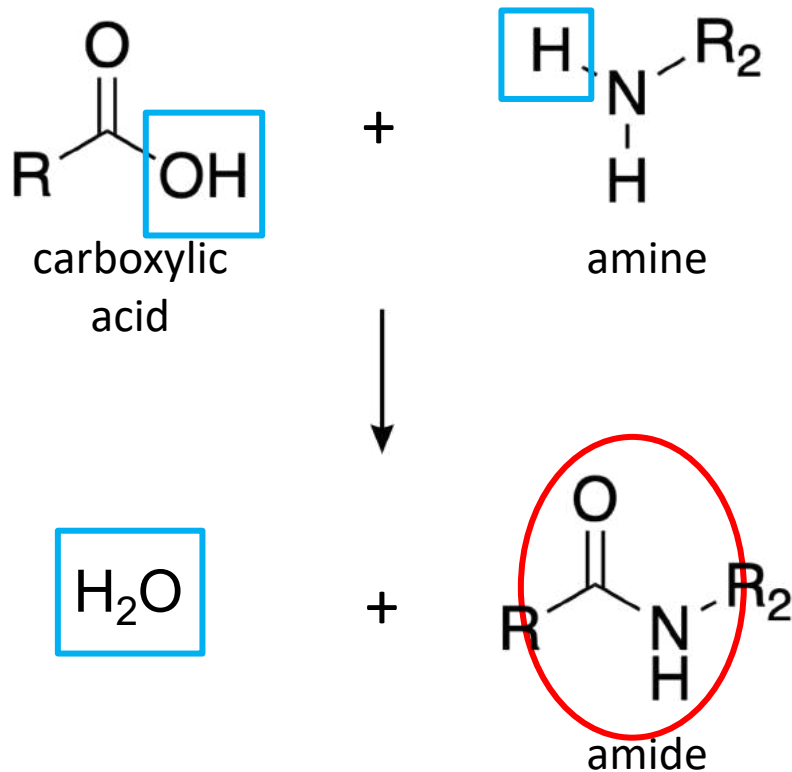
Fmoc-asparagine(Trt)-OH

Fmoc-phenylalanine-OH

DCC



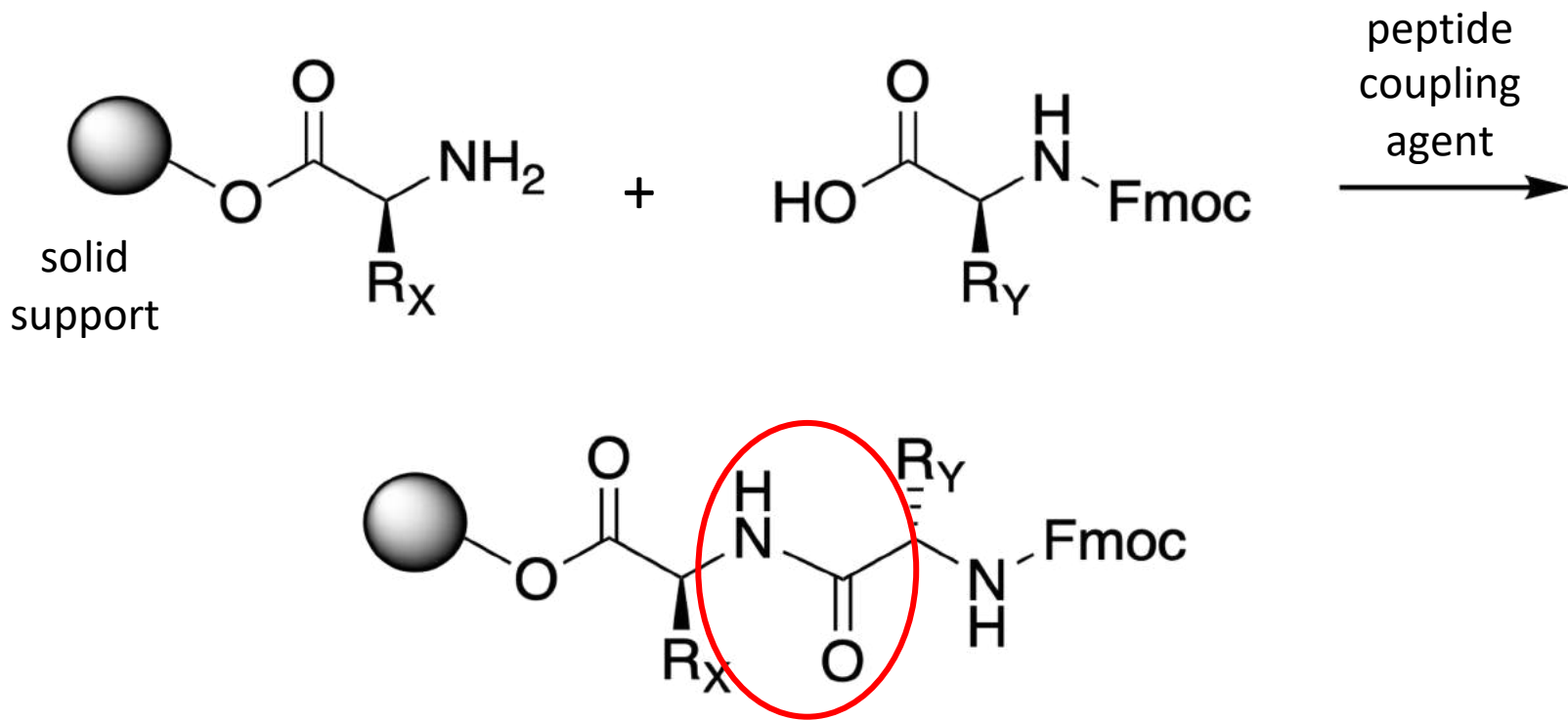
# Peptide Coupling Agents Facilitate Amide Bond Formation





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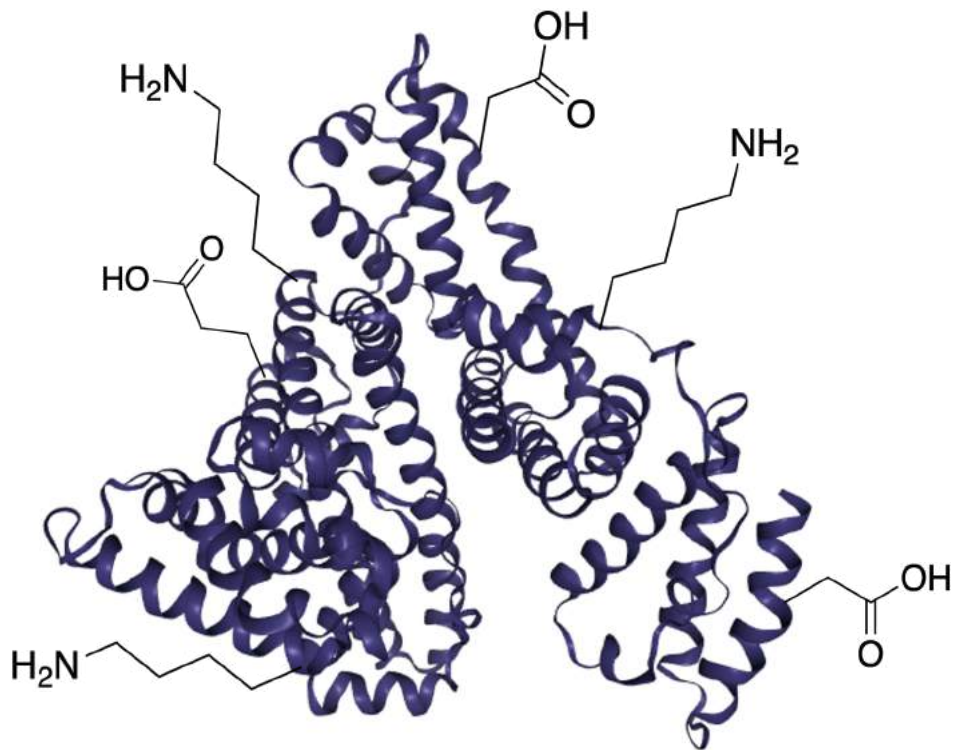
# Peptide Coupling Agents Facilitate Amide Bond Formation





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# How Can Peptide Coupling Agents Affect Biological Systems?



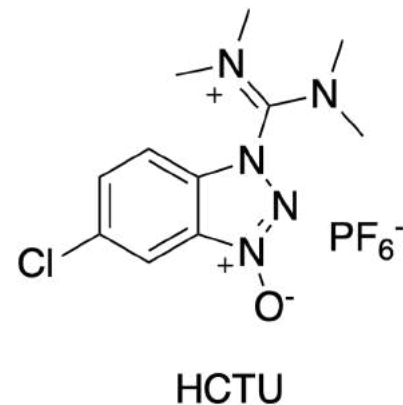
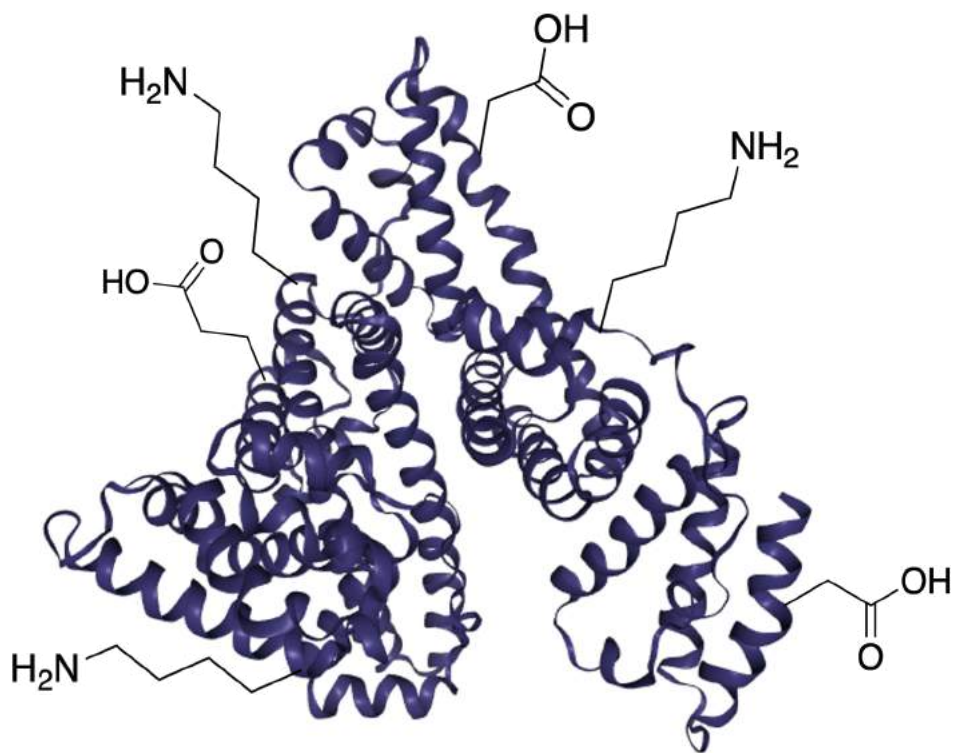
Human Serum Albumin, PDB ID: 1AO6





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# How Can Peptide Coupling Agents Affect Biological Systems?



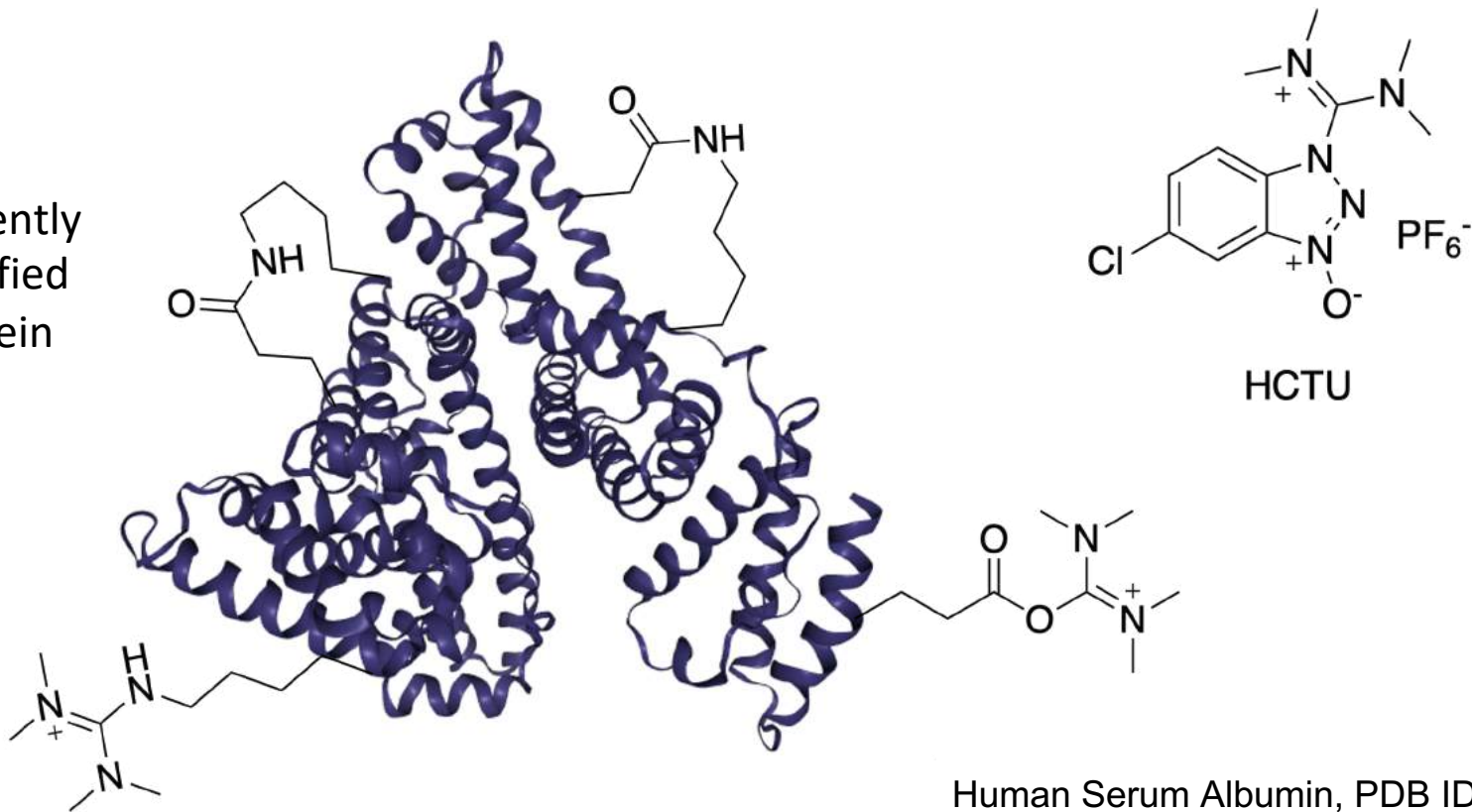
Human Serum Albumin, PDB ID: 1AO6



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# How Can Peptide Coupling Agents Affect Biological Systems?

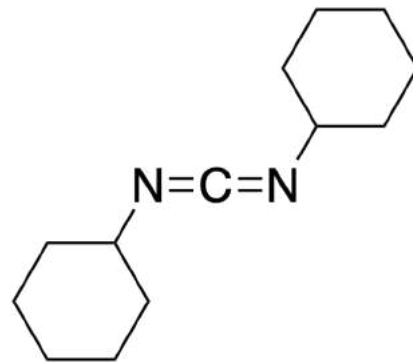
covalently  
modified  
protein





# DCC is a Notorious Chemical Sensitizer

- Since 1959, over 20 reported cases of sensitization
- Widely known sensitizer
- Handled carefully in labs



DCC



# Uronium Coupling Agents

- Compounds that perform peptide coupling chemistry have the potential to be sensitizers.
- My case of anaphylaxis from HATU, HBTU, and HCTU is the 9<sup>th</sup> case reported.
- Even if chemicals are not widely known as being hazardous does not mean that they are not hazardous.
- **Should researchers look out for odd symptoms or analyze a chemicals potential to react in a biological system, or both?**



# Conclusion

- When determining if a chemical is safe to use, whether in a research lab or undergraduate lab, think beyond the MSDS sheets.
- Think about what that chemical can do in a biological setting to predict how it can adversely affect someone who is exposed to that chemical.
- **How can we encourage reporting?** Where can there be a home for these case-studies? **Specifically, how can researchers who need this information easily access it without having to sift through “the literature?”**
- **Do many treat newer, unvetted, chemicals like they are harmless?** We should take extra precautions because we don't know the harm they may cause. **How do we help change safety culture to be more proactive rather than reactive?** I'm not saying to treat everything like it will kill you, but I think a healthy skepticism about a chemical's safety is valid. **Scientists have healthy skepticism about almost every other aspect of their research - the data, the interpretation, the conclusions we make.**