Click Chemistry for the Synthesis of Azides

Significance: Copper-catalyzed azide alkyne click chemistry (CuAAC) is a powerful bioorthogonal reaction that provides triazole products in very high yields. A significant limitation is the restricted access to the azide precursors because azide preparation with NaN₃ or TfN₃ suffers from long reaction times, toxicity, or risk of explosion. The authors present a new, highly reactive diazo transfer reagent that enables rapid and safe access to azides from amines.

Comment: Previously reported fluorosulfonyl imidazolium triflate salt (Guo et al. Angew. Chem. Int. Ed. 2018, 57, 2605) was treated with NaN₃ to generate fluorosulfonyl azide 1 in situ. In an optimized solvent system (DMF–MTBE–H₂O), 1 undergoes diazo transfer to a broad variety of amines in a click chemistry fashion.