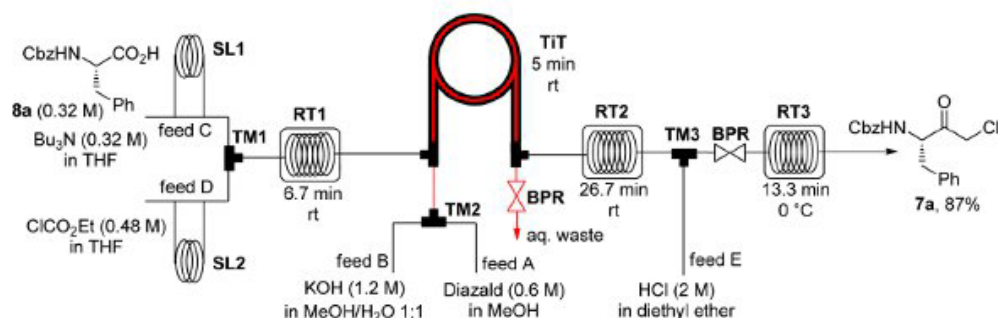


Publication 35: Continuous Flow Synthesis of alpha-Halo Ketones: Building Blocks for Anti-retroviral Agents



Chiral alpha-halo ketones derived from N-protected amino acids are key building blocks for the synthesis of HIV protease inhibitors such as atazanavir used in HAART combination therapy.

Kappe and De Souza have reported a continuous flow through route to these intermediates which utilises a tube-in-tube reactor to introduce diazomethane generated on demand into the reaction stream containing mixed anhydride derivatives of N-protected amino acids. The resulting alpha-diazo ketones are then decomposed with HCl or HBr to afford the corresponding alpha-halo ketones.

This process allows the safe generation, separation and use of diazomethane in a continuous integrated multi-step synthesis of important API intermediates.

[V. D. Pinho, B. Gutmann, L. S. M. Miranda, R. O. M. A. de Souza, C. O. Kappe, J. Org. Chem., 2014, 79, 4, 1555.](#)