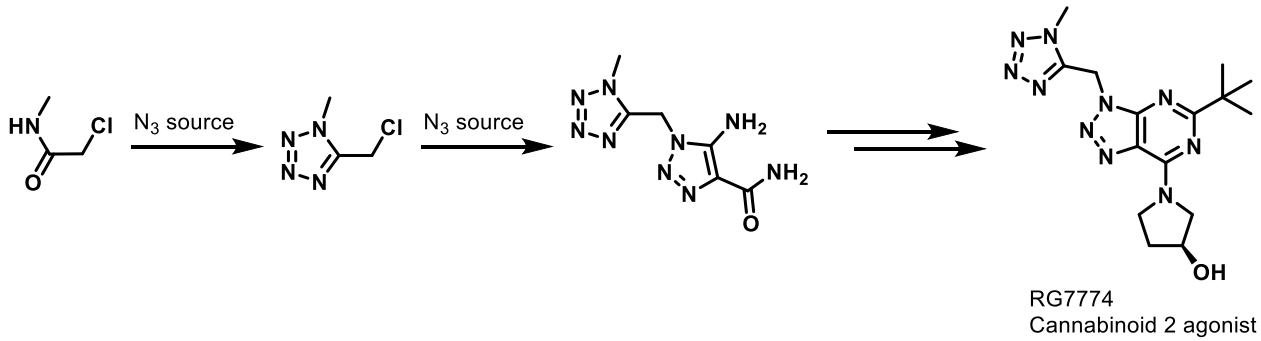
Taming highly energetic materials with flow technologies to enable API supplies for clinics and beyond

J. Sedelmeier, D. Kaldre, S. Trokowski, C. Moessner, E. Santandrea, R. Agra

F. Hoffmann-La Roche Ltd.
Pharmaceutical Division
Synthetic Molecules Technical Development
Process Chemistry & Catalysis
Basel, Switzerland

Cannabinoid 2 (CB2) agonist RG7774 is currently in phase II trials for the treatment of diabetic retinopathy.[1,2] Thus far, the clinical supply has been produced using a linear 8-step route, hindered by a final *N*-alkylation step with poor regioselectivity, which is detrimental to the overall API yield. We report the use of continuous flow and batch processing to enable a new route toward CB2 agonist, RG7774.[3] Flow processing allows the handling of nitrogen-rich, highly energetic intermediates in a safe and rapid manner, which would not be feasible in a classic batch environment. The new synthetic route contains 7 chemical transformations of which four key transformations are executed in continuous flow mode.



RG7774
Cannabinoid 2 agonist

[1] https://clinicaltrials.gov/ct2/show/NCT04265261
[2] Grether, U. EFMC-ISMC Meeting, September 4-8 2022, Nice, France
[3] WO 2022/106669; *Org. Process Res. Dev*. **2021**, *25*, 1206–1214.