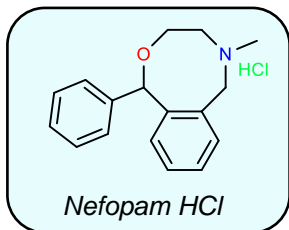


A Non-opioid and Non-steroidal Analgesic Drug:



*Nefopam, an orphenadrine derivative, is sold under numerous other names such as Acupan and Fenazoxine, is a non-opioid and non-steroidal analgesic. *Is thought to work as a non-narcotic SNDRI, meaning it inhibits the reuptake of serotonin, norepinephrine, and dopamine. It also plays a role in reducing glutamate signaling by modulating calcium and sodium ion channels. *Approved in the UK as a POM, meaning its available as a prescription-only medication and approve in the AU as an S4 drug, effectively giving it the same status.

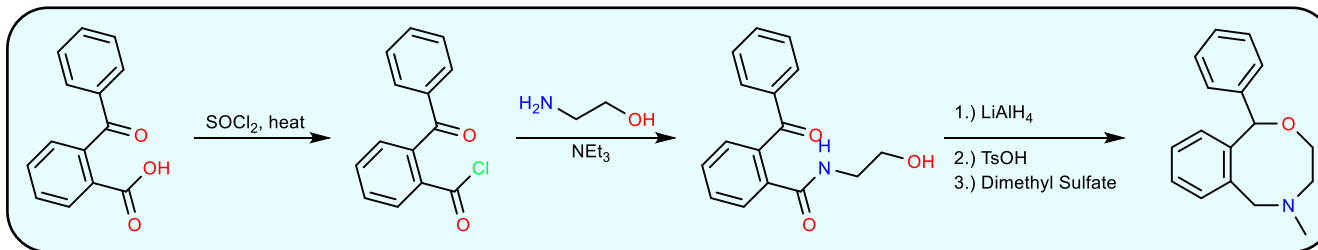
Common Problems With Process Routes:

*Industrial and commercially existing routes all suffer from at least one of the following drawbacks:

- 1.) Workup protocols can be laborious and cumbersome.
- 2.) Routes are impractical and unviable for industrial synthesis.
- 3.) Various solvents and undesirable solvents (chlorinated, low bp, etc.) often required.
- 4.) Often requires isolation, drying, analysis, and is multi-step. This requires extra time, effort, and labor.

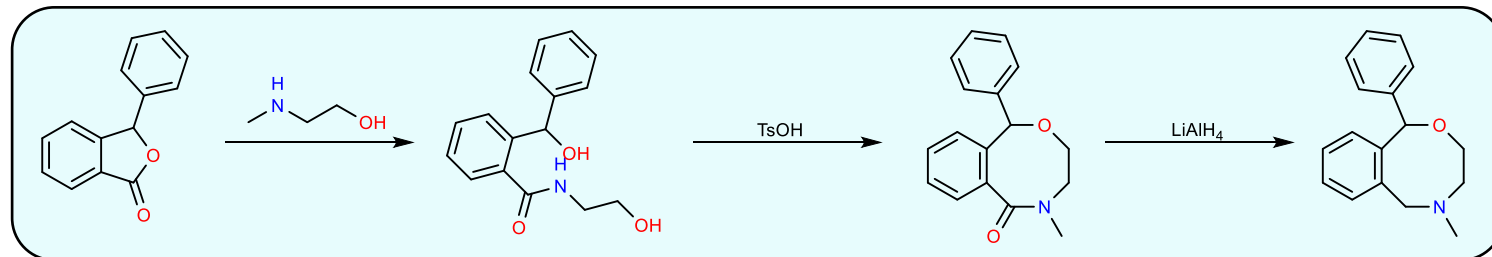
Kumar, P. *Org. Process Res. Dev.* **2017**, 21, 11, 1745–1751 <https://doi.org/10.1021/acs.oprd.7b00228>

A Few Previously Patented Synthesis:

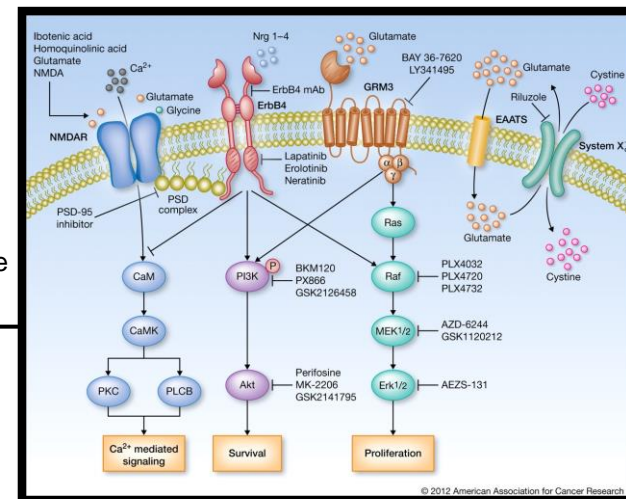


Patent: ES 8605495

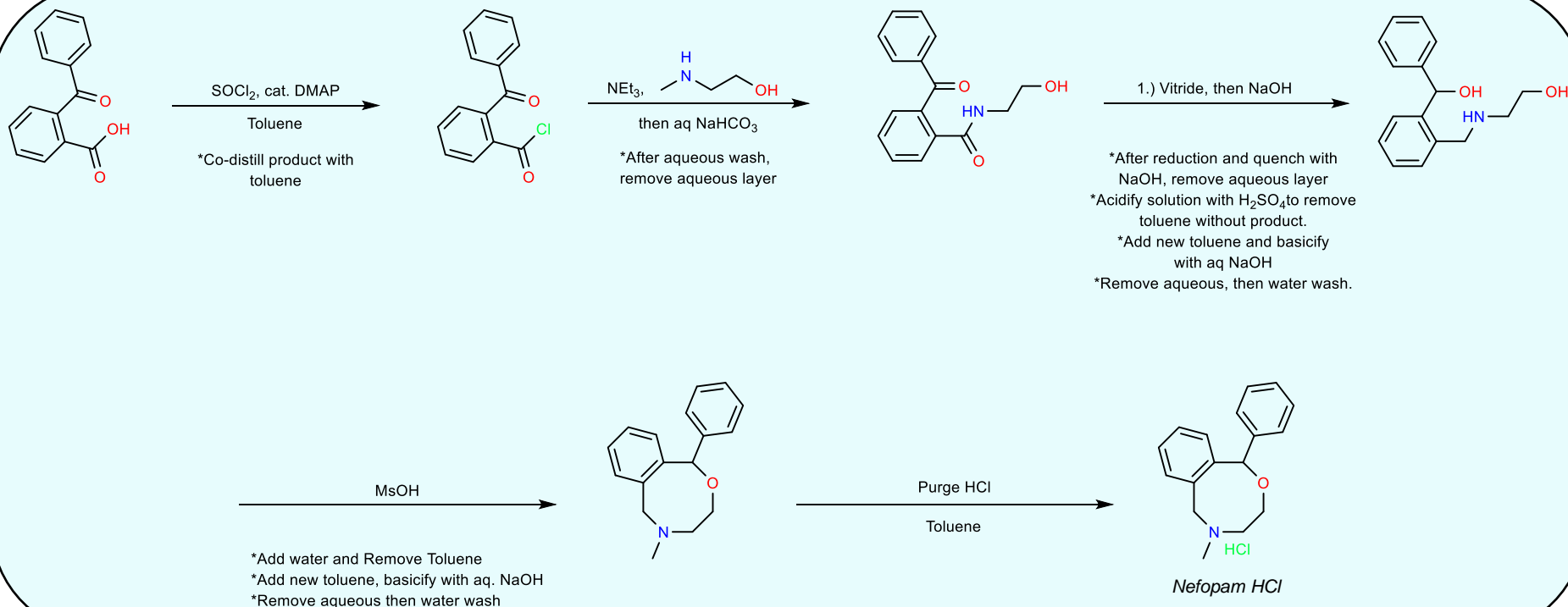
Patent: KE 8201564



Kumar, P. *Org. Process Res. Dev.* **2017**, 21, 11, 1745–1751 <https://doi.org/10.1021/acs.oprd.7b00228>



A One Pot Synthesis of Nefopam:



Analysis of the Synthesis:

- *Greater than 90% yield each step, overall yield above 79% over the whole synthesis, surpassing previous routes.
- *A single solvent is utilized throughout the entirety of the synthesis.
- *No genotoxic impurities are formed over the course of the synthesis.
- *Synthesis performed on the multiple kilogram scale.
- *Reaction conditions are mild, safe, and procedural steps are very user-friendly.
- *API collected and isolated with purity greater than 99.9%
- *Reaction sequence is very cost effective.

