Nefopam

5-Methyl-1-phenyl-1,3,4,6-tetrahydro-5H-benz[f]-2,5-ozazocine

Acupan® - 3M Health Care
Nefopam Hydrochloride

Used clinically as the racemic mixture
The synthetic process outlined above is not ideal for a process synthesis due to the expense and risk of using LiAlH₄.

Alternative process, outlined below, uses NaBH₄, which is cheaper and safer to use on a large scale.

The overall synthesis is more economical than the synthesis outlined above, is more straightforward to perform on a large scale, and requires two steps from 2-chloromethyl benzophenone.
Alternative nefopam synthesis

\[ \text{bromobenzene} \xrightarrow{\text{Mg, Et}_2\text{O}} \text{MgBr} \]

\[ \text{THF, } <10^\circ\text{C} \text{ then rt, 3h post addition quench with ice/ aq. NH}_4\text{Cl} \]

\[ \text{PCl}_3 \]

\[ \text{2-chloromethyl benzophenone} \]

\[ \text{Na}_2\text{CO}_3, \text{EtOH reflux, 3h} \]

\[ \text{2-\{[N-(2-hydroxyethyl)-N-methyl]-amino\}-methylbenzophenone HCl salt m.p. 135-136^\circ\text{C}} \]

\[ \text{NaBH}_4, \text{H}_2\text{O/MeOH, NaOH 30min, rt} \]

\[ \text{nefopam} \]