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Convergent Synthesis of a $5HT_7/5HT_2$ Dual Antagonist
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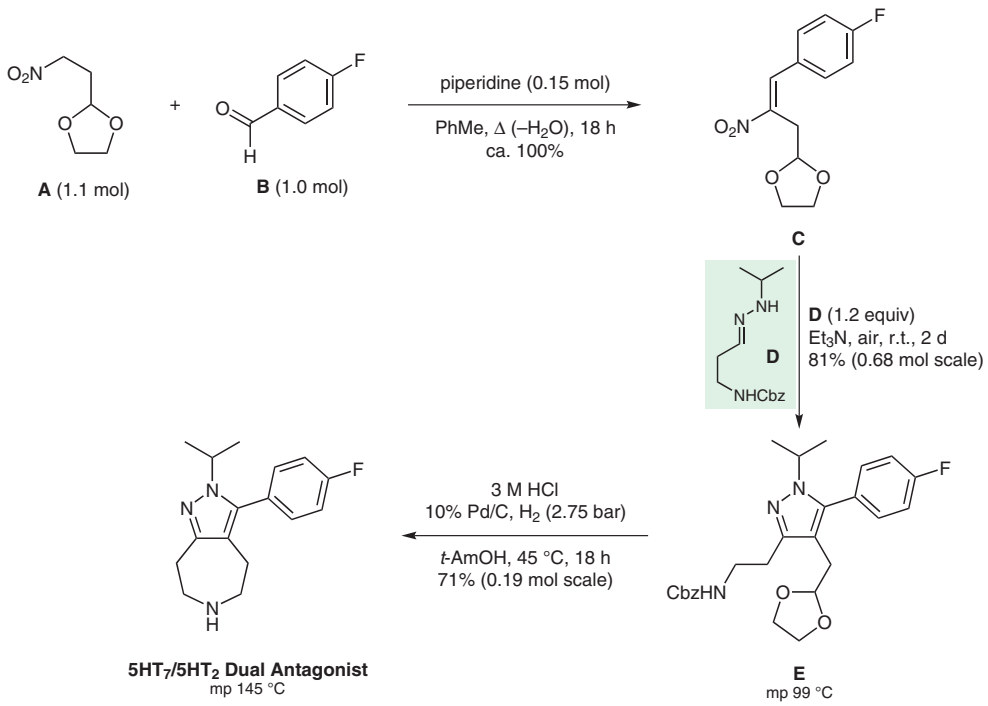
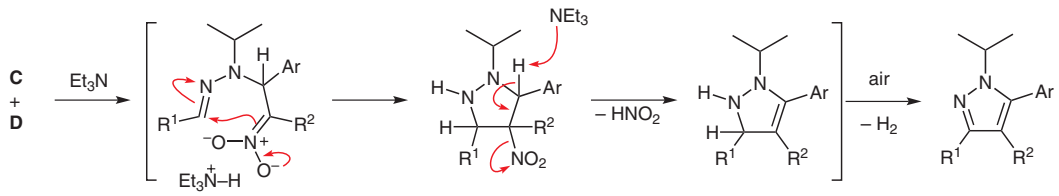
Synthesis of a $5HT_7/5HT_2$ Dual Antagonist



Mechanism of pyrazole ring formation:



Significance: The target pyrazolo[3,4-*d*]azepane is a $5HT_7/5HT_2$ dual antagonist that was of interest for the treatment of depression, psychosis, anxiety and sleep disorders. This notably short synthesis features (1) the regioselective construction of pyrazole **E** by reaction of hydrazone **D** with nitroalkene **C** and (2) the four-step, one-pot reductive annulation sequence converting **E** into the target azepane.

Comment: Hydrazone **D** was prepared in 98% yield (crude) by the reaction of benzyl-*N*-(3-oxopropyl)carbamate with isopropylhydrazine in the presence of Et_3N (1.2 equiv) in refluxing *i*-PrOH. The reaction of **C** and **D** was conducted in Et_3N as solvent in order to efficiently capture the HNO_2 eliminated during the pyrazole annulation.

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nitroaldol reaction
pyrazole ring formation