Synthesis of a 5HT\textsubscript{7}/5HT\textsubscript{2} Dual Antagonist

Significance: The target pyrazolo[3,4-d]azepane is a 5HT\textsubscript{7}/5HT\textsubscript{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\textsubscript{3}N (1.2 equiv) in refluxing i-PrOH. The reaction of C and D was conducted in Et\textsubscript{3}N as solvent in order to efficiently capture the HNO\textsubscript{2} eliminated during the pyrazole annulation.