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

**Organic Process Research & Development**

**J. T. LIANG,* X. DENG, N. S. MANI (JANSSEN PHARMACEUTICAL COMPANIES OF JOHNSON & JOHNSON, SAN DIEGO, USA)**

**Abstract:** 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.

**Mechanism of pyrazole ring formation:**

Hydrazone \( D \) was prepared in 98% yield (crude) by the reaction of benzyl-\( N \)-(3-oxopropyl)carbamate with isopropylhydrazine in the presence of \( \text{Et}_3\text{N} \) (1.2 equiv) in refluxing \( \text{i-PrOH} \). The reaction of \( C \) and \( D \) was conducted in \( \text{Et}_3\text{N} \) as solvent in order to efficiently capture the HNO\textsubscript{2} eliminated during the pyrazole annulation.

**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 \( \text{Et}_3\text{N} \) (1.2 equiv) in refluxing \( \text{i-PrOH} \). The reaction of \( C \) and \( D \) was conducted in \( \text{Et}_3\text{N} \) as solvent in order to efficiently capture the HNO\textsubscript{2} eliminated during the pyrazole annulation.