

J. T. LIANG,\* X. DENG, N. S. MANI (JANSSEN PHARMACEUTICAL COMPANIES OF JOHNSON & JOHNSON, SAN DIEGO, USA)  
Convergent Synthesis of a 5HT<sub>7</sub>/5HT<sub>2</sub> Dual Antagonist  
*Org. Process Res. Dev.* **2011**, *15*, 876-882.

## Synthesis of a 5HT<sub>7</sub>/5HT<sub>2</sub> Dual Antagonist

Category

Synthesis of Natural Products and Potential Drugs

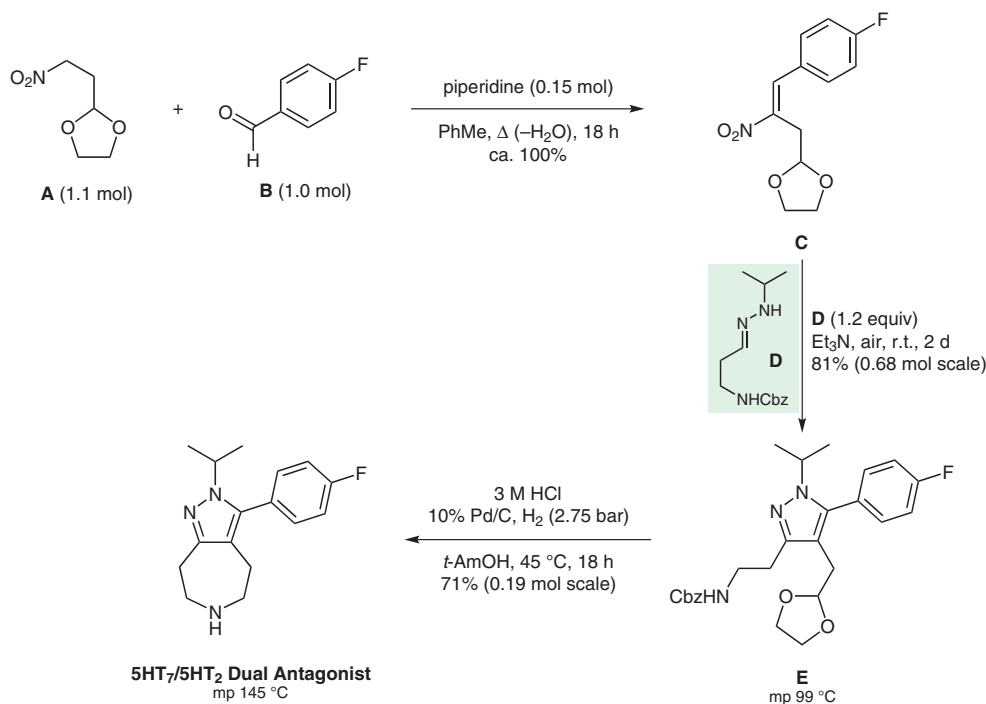
Key words

5HT<sub>7</sub>/5HT<sub>2</sub> dual antagonist

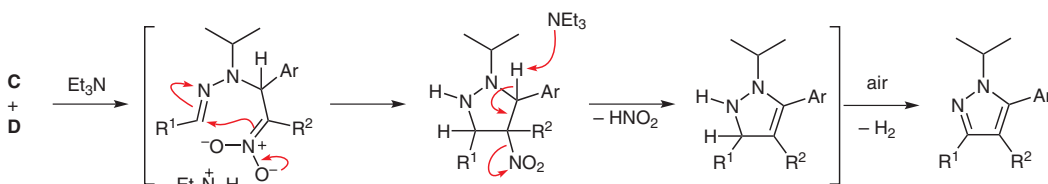
nitroaldol reaction

pyrazole ring formation

**SYNFACT**  
*of the month*



### Mechanism of pyrazole ring formation:



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

**SYNFACTS Contributors:** Philip Kocienski  
Synfacts 2011, 10, 1041-1041 Published online: 20.09.2011  
**DOI:** 10.1055/s-0030-1261043; **Reg-No.:** K04611SF