Laboratory and practical synthesis of Suvorexant, a selective dual orexin receptor antagonist

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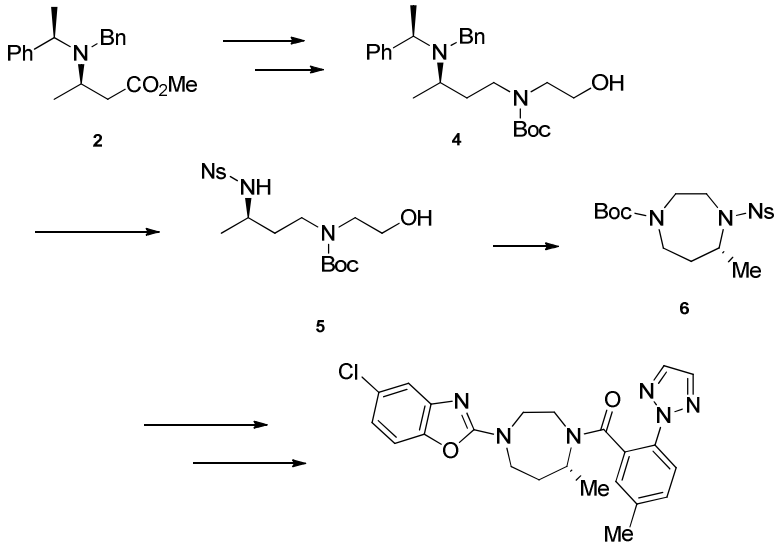
The development of a laboratory and practical synthesis of Suvorexant 1, using intramolecular Mitsunobu cyclization reaction of intermediate 5 as the key reaction, has been reported. Compound 5 was obtained from known chiral ester 2 in three steps, and the key cyclization proceeded smoothly to provide the core seven-membered ring compound 6, which was transformed into 1 by an additional four-step sequence.



The procedure described here needs no chiral-HPLC separation, no classical resolution, and no unique enzyme reactions, and offers an alternative practical synthesis of 1.

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