Abstract

Herein is reported the synthesis of molecular probes for action of neuroactive steroids *in vitro* and in living organisms. In the first part, preparation of enantiomeric pregnane steroids is investigated, ultimately resulting into the total synthesis of *ent*-progesterone. The chirality of the target molecule is introduced by a highly effective organocatalytic asymmetric Robinson annulation. A new method for the sequential construction of five-membered carbocyclic ring is introduced as the key step. This is composed of substrate-controlled copper-catalyzed conjugate addition followed by radical oxygenation and subsequent thermal cyclization employing the persistent radical effect. The synthesis of truncated neurosteroid analogs is described and their biological activity at the NMDA receptor is compared with the native hormone.

In the second part, methodology for specific deuterium labeling of both angular methyls of the 5β-pregnane steroid core is explored. Special attention was paid to the Barton-McCombie deoxygenation as the tool for introduction of the last deuterium atom into the methyl group. Both positions were labelled with total of three deuterium atoms in high isotopic purity.