

## The synthesis of fused heterocyclic building blocks and their application as core structures of GPCR ligands

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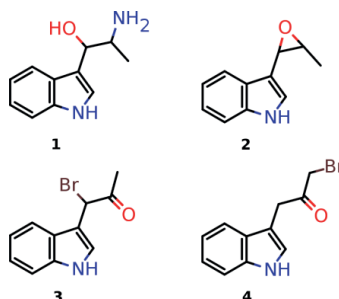
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Indole is an exceptionally electron rich fused ring heterocycle. It is among the most widely distributed scaffolds in nature as well as one of the most important building blocks in medicinal chemistry. The unusually high abundance of indole nucleus in ligands of different biological activity led to its classification as 'privileged structure'.<sup>1</sup>

Our search for selective aminergic GPCR ligands led us to the syntheses of heterocyclic molecules which can serve as substrates for derivatization, e.g. attachment of basic aminergic moiety, ring closure, reactions with various nucleophiles. Our efforts to obtain 2-amino-1-(1H-indol-3-yl)ethan-1-ol (**1**), yielded a straightforward method of synthesis of 3-(3-methyloxiran-2-yl)-1H-indole (**2**) - a very attractive building block for drug discovery which has not been mentioned in literature till date. This epoxide can be readily opened by numerous nucleophiles to yield potential GPCR ligands.

The synthesis of appropriate halocarbonyl compounds enables a very large chemical space to be covered. Herein we describe our way to concise method of preparation of 1-bromo-1-(1H-indol-3-yl)propan-2-one (**3**) and 1-bromo-3-(1H-indol-3-yl)propan-2-one (**4**). Despite the great versatility of **3** and **4** as starting materials for the total syntheses of alkaloids and potentially bioactive compounds, the synthesis of **3** has not been yet described, while the synthesis of **4** involves the use of extremely toxic reagent - diazomethane.<sup>2</sup>



[1] Evans B. E., Rittle K. E., Bock M. G. et al. *J. Med. Chem.* 31 (1988) 2235.

[2] Gaspari P., Banerjee T., Malachowski W. P. et al. *J. Med. Chem.* 49 (2006) 684.

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