SYNTHESIS OF BOTH ENANTIOMERS OF 1-{2-HYDROXY-3-[4-(2-ISOPROPOXY-PHENYL)-PIPERAZIN-1-YL]-PROPYL}-PYRROLIDIN-2-ONE

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Chirality is a fundamental property of biological systems and reflects the underlying asymmetry of matter. Interactions of drugs with target site (receptor or enzymes) have been known to be stereoselective. It is possible that the pharmacological activity of chiral compound may reside in one enantiomer, while the second may be inactive or even toxic [1].

In search for a new $\alpha$-adrenoceptors ($\alpha$-AR) antagonist a series of racemic 1-{2-hydroxy-3-[4-(phenyl substituted piperazin-1-yl)-propyl}-pyrrolidin-2-one derivatives was synthesized. The obtained compounds displayed affinity for both $\alpha_1$ ($pK_i = 4.07 – 6.71$) and $\alpha_2$ ($pK_i = 4.31 – 6.68$) adrenoceptors. Taking into consideration that interaction between compound and receptor site is stereoselective an affords to synthesized enantiomers of the most active in vitro investigations compounds, thus were and 1-{2-hydroxy-3-[4-(2-hydroxyphenyl)-piperazin-1-yl]-propyl}-pyrrolidin-2-one, and its 2-isoproxyphenyl- analogues were undertaken.

The crucial point of our studied was the synthesis of both enantiomers of 1-(2, 3-epoxy-propyl)-pyrrolidin-2-one. This compounds were obtained via hydrolytic kinetic resolution (HKR) of racemic 1-(2, 3-epoxy-propyl)-pyrrolidin-2-one using relevant free or polymer supported (salen)Co(III)(OAc) complexes [2, 3]. Finally, the aminolysis of epoxy- derivatives with relevant substituted phenylpiperazine gave enantiomers of 1-{2-hydroxy-3-[4-(phenyl substituted piperazin-1-yl)-propyl}-pyrrolidin-2-one.

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