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BOOK OF ABSTRACTS

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The SF_5 moiety as promising substituent for the design of novel D_2 and D_3 receptors ligands

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Dopamine receptors are divided into two subclasses: D_1 like receptors (D_1 and D_5 subtypes) and D_2 like receptors (D_2, D_3 and D_4) [1]. Based on a general pharmacophore [2] we introduced the pentafluorosulfanyl moiety (SF_5-) group as an interesting pharmacological tool to investigate D_2 like receptors. This moiety displays high electronegativity and lipophilicity, while being thermally stable [3] and more resistant to hydrolysis in comparison to that of other polyfuorinated moieties (e.g. CF_3 or OCF_3). Four novel compounds with SF_5 substituent have been synthesized, *in silico* and *in vitro* tested in order to examine their affinity and selectivity towards human dopamine D_2 and D_3 receptor subtypes. All compounds showed high affinity in the nanomolar concentration ranges at both receptors with ST 2200 expressing highest selectivity. *In silico* examination determined high values of coefficient of determination (R^2) and Spearman correlation coefficient revealed good correlation between *in silico* parameters and experimentally obtained Ki values. These results show that pentafluorosulfanyl substituent is a highly suitable moiety for structural variations that has to be further investigated and could serve as novel substituent in numerous compound classes.

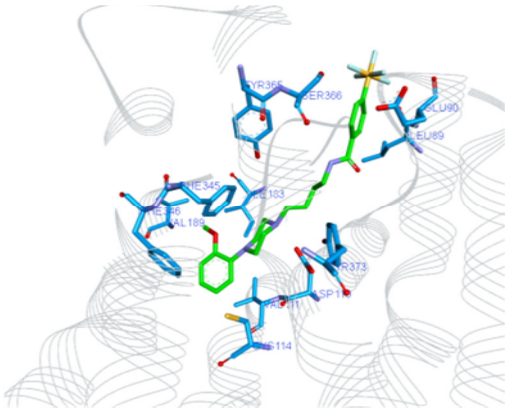

Figure 1: Binding mode of ST 2200 (green sticks) with pKi value of 8.42 at hD3 receptor

[1] Beaulieu, J.M.; Gainetdinov, R.R.,. *Pharmacological Reviews* **2011**, *63* (1), 182-217.

[2] Hackling, A.E., Stark, H., *ChemBioChem.* **2002,** *3* (10):946-6*58* (52), 4803-4815.

[3] Vida, N., Václavík, J., Beier, P., Beilstein Journal of Organic Chemistry, **2016,** *12* (1), 110-111.