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CHEMBIOMOL-01: Chem. Biol. & Med. Chem. Workshop, Galveston, Texas-Harvard, Boston, USA, 2020
MOL2NET, International Conference Series on Multidisciplinary Sciences

PTML Computational Study, Synthesis, and Pharmacological Assay of MIF-1 Peptidomimetics

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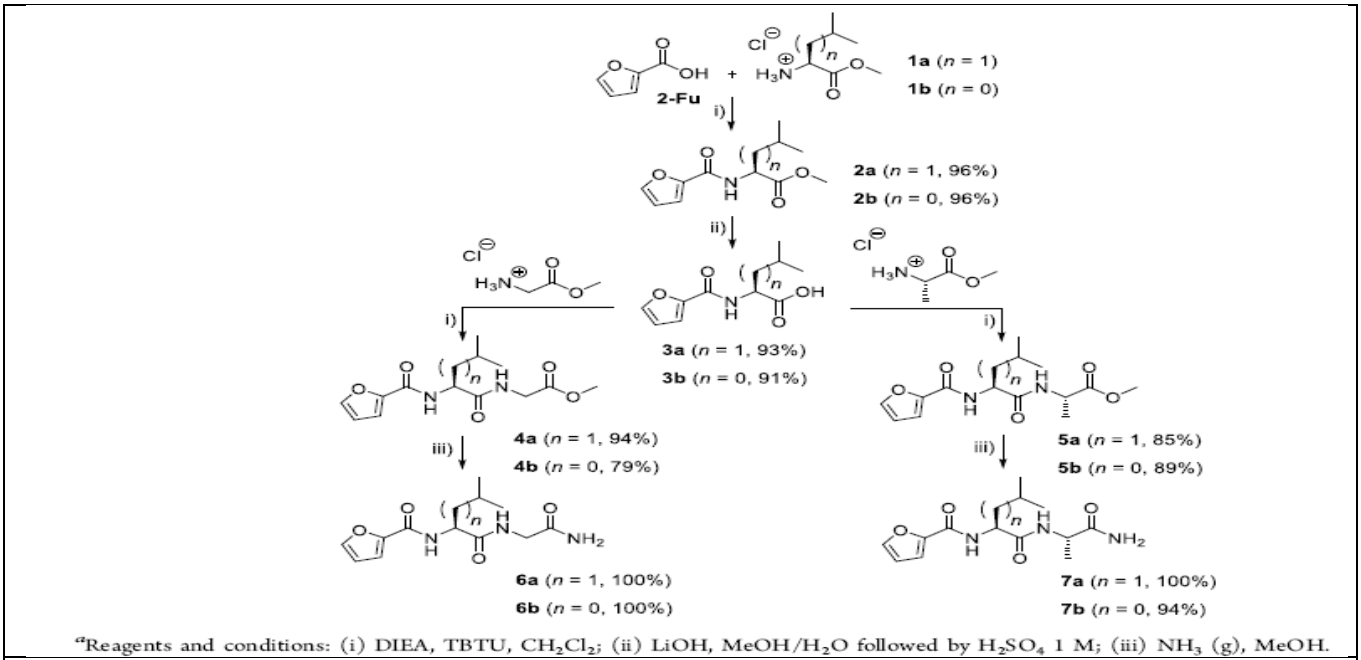

[a]Reagents and conditions: (i) DIEA, TBTU, CH_2Cl_2; (ii) LiOH, MeOH/H_2O followed by H_2SO_4 1 M; (iii) NH_3 (g), MeOH.

Abstract: In a recent work we described the organic synthesis and experimental pharmacological assay of MIF-1 peptidomimetics modulators of D_2 receptors (D_2R). We measured their ability to enhance the maximal effect of tritiated N-propylapomorphine ([^{3}H]-NPA) at D_2R. The 2-furoyl-l-leucylglycinamide (6a) showed increase maximal [^{3}H]-NPA response at 10 pM (11 ± 1%) compared to MIF-1. Neurotoxicity assays of MIF-1 derivative 6a with cortex neurons of Wistar-Kyoto rat embryos suggest low neurotoxicity. Additionally, we reported a predictive model >20 000 outcomes of preclinical assays reported in ChEMBL for this kind of modulators. The model shows high specificity Sp = 89.2/89.4%, sensitivity Sn = 71.3/72.2%, and accuracy Ac = 86.1%/86.4% in training/validation series, respectively. The model is useful to predict this and similar compounds.

References

ACS Chem Neurosci. 2021 Jan 6;12(1):203-215. doi: 10.1021/acschemneuro.0c00687.