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3-(1*H*-Imidazol-1-yl)propan-1-amine as synton for synthesis of novel biological active aminophosphonates

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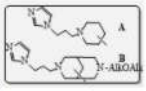
ABSTRACT

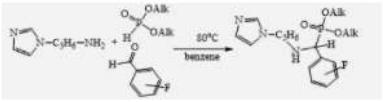
Introduction: A known approach is the synthetic assembly of pharmacophore fragments into new molecular systems, leading to an increase in the bioeffect of the initial substrates, but more interestingly, to the appearance of new types of activity. Previously, we synthesized derivatives (**A** and **B**) of 3-(1H-imidazol-1-yl)propan-1-amine containing imidazole [1-3] and piperidine or diazabicyclononane moieties, which are synthetic analogues of natural alkaloids. Among them, myelostimulants and plant growth stimulants were found [4,5].



The main *purpose* of Research is the synthetic assembly of novel molecules, containing imidazole and phosphonate fragments, as well as potential plant growth and development stimulants. In addition, a fluorine atom is introduced into the molecule as a "booster" of biological action.

Methods: Targeted aminophosphonates are synthesized by Kabachnik-Fields reactions. Plant growth action was evaluated on wheat *Triticum aestivum* of three Kazakh varieties. Myelostimulatory activity was carried out in rats with artificially induced myelosuppression by cytostatic - sodium cyclophosphamide.

Results and discussion: Reaction of 3-(1*H*-imidazol-1-yl)propan-1-amine with (*o*-, *m*- or *p*-) fluorobenzaldehyde and di(methyl- or ethyl-)phosphonate by refluxing in benzene for 37-61 h with simultaneous distillation of an azeotropic mixture of the obtained water with benzene leads to the target imidazole-containing aminophosphonates with 38-61% yields:



The reaction products are crystalline compounds that are poorly soluble in water. The bioactivity of aminophosphonates was evaluated in the form of their complexes with β-cyclodexrin.

It turned out that the synthesized substances stimulate the growth of the steam of wheat to 10% compared with the control experiment (water). One of the derivatives - dimethyl[(3-(1*H*-imidazol-1-yl) propylamino)(3-fluorophenyl)methyl]phosphonate, is slightly inferior in myelostimulating activity to the methyluracil used as comparison drug.

Thus, synthesized aminophosphonates on the basis of 3-(1*H*-imidazol-1-yl)propan-1-amine during pre-sowing treatment of wheat seeds stimulated stem growth and only one sample slightly improved the hematopoiesis of rats with pre-artificially induced myelosuppression.

References:

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