

# N, N-Disubstituted bispidines, a new class of compounds with actoprotective effects

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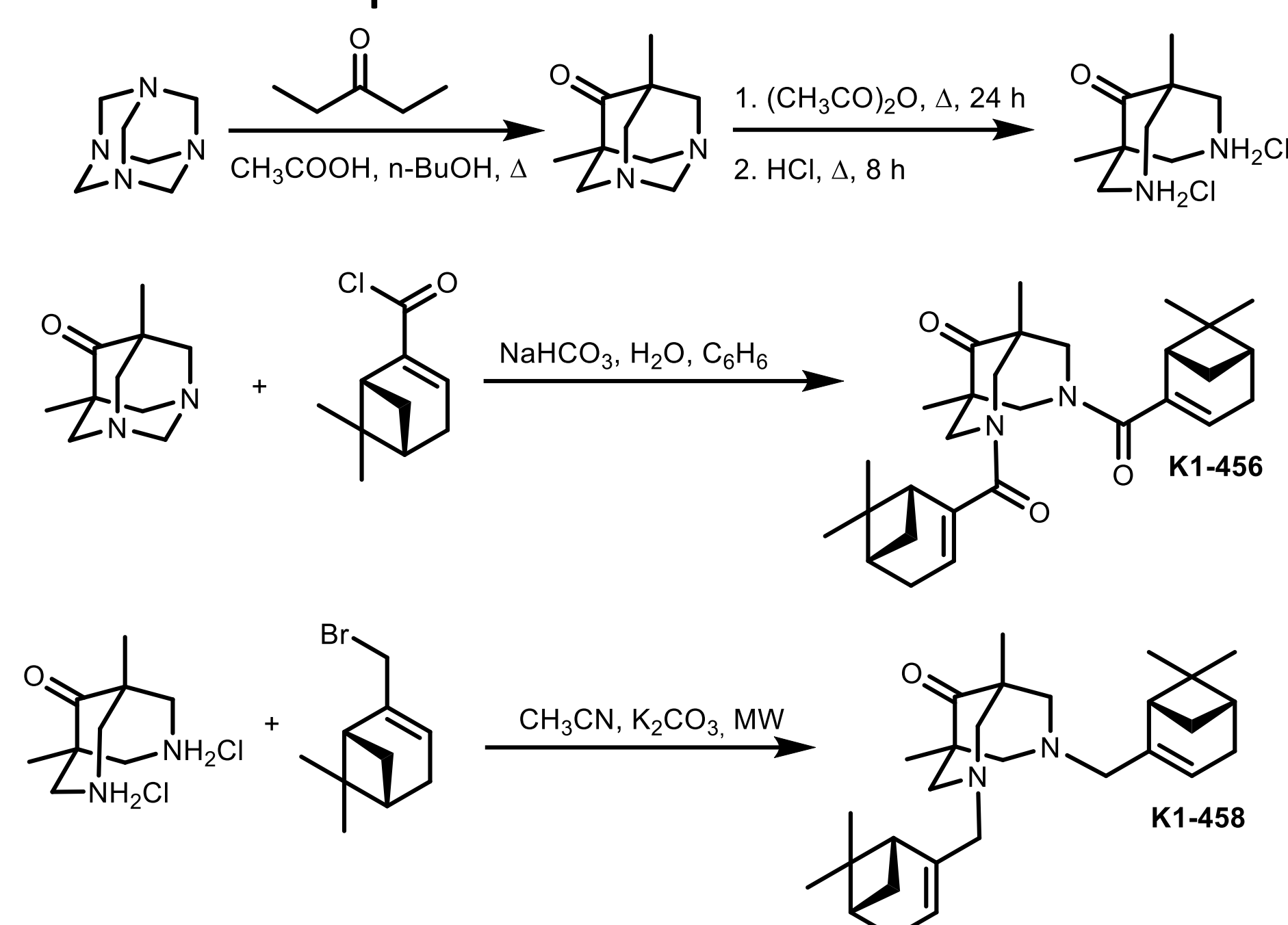
**Abstract:** One of the strategies for creating new pharmacologically active compounds is the use of a central scaffold and the addition of various substituents to it. The diazabicyclic molecule bispidine represents a promising basis for chemical modifications and synthesis of compounds with diverse biological activities. In this work, the actoprotective effect of N, N-disubstituted bispidine derivatives containing monoterpene substituents is shown for the first time.

The present work evaluated the actoprotective activity, locomotor and anxiety-like behavior in mice, and the effect on the cholinergic system in the central nervous system. Bromantane was used as a reference drug.

**Keywords:** actoprotectors; treadmill; bromantane; monoterpenoids; 3,7-diazabicyclo[3.3.1]nonane (bispidine) scaffold

## 1. Materials and Methods

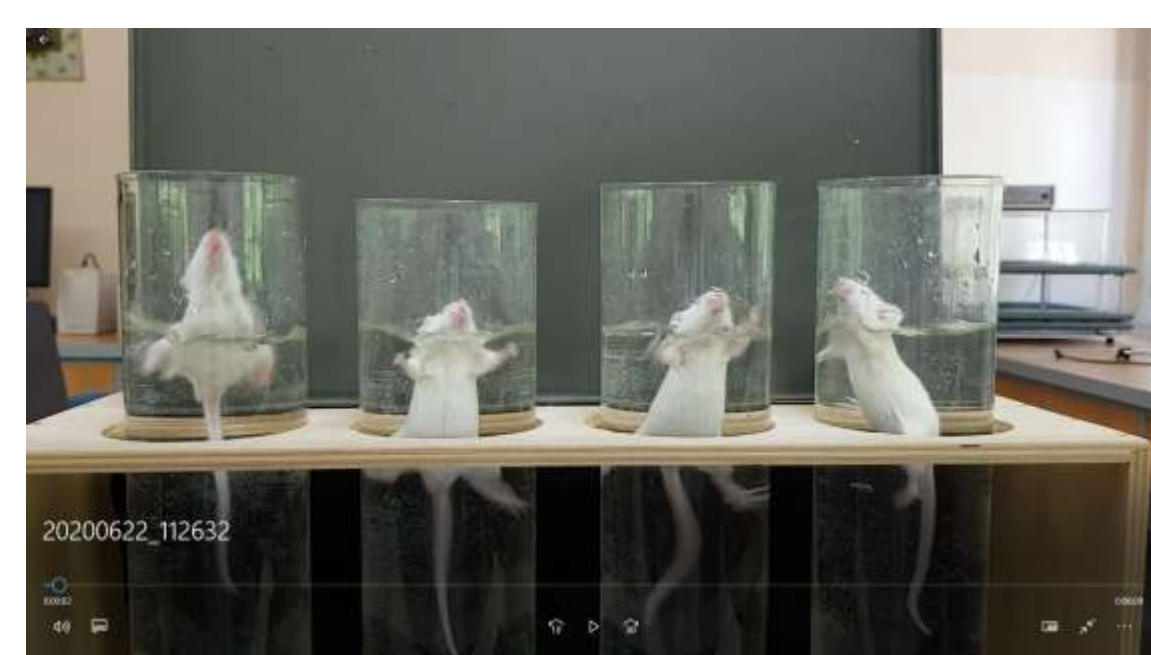
### 1.1. Synthesis of bispidine derivatives



### 1.2. Determination of physical performance [1]



Treadmill running



Swimming with a load of 10% of body weight

### 1.3. Elevated locomotor and anxiety-like behavior [2]

The "Open field" test was used.

### 1.4. Influence on the cholinergic and adrenergic neurotransmitter systems of the brain.

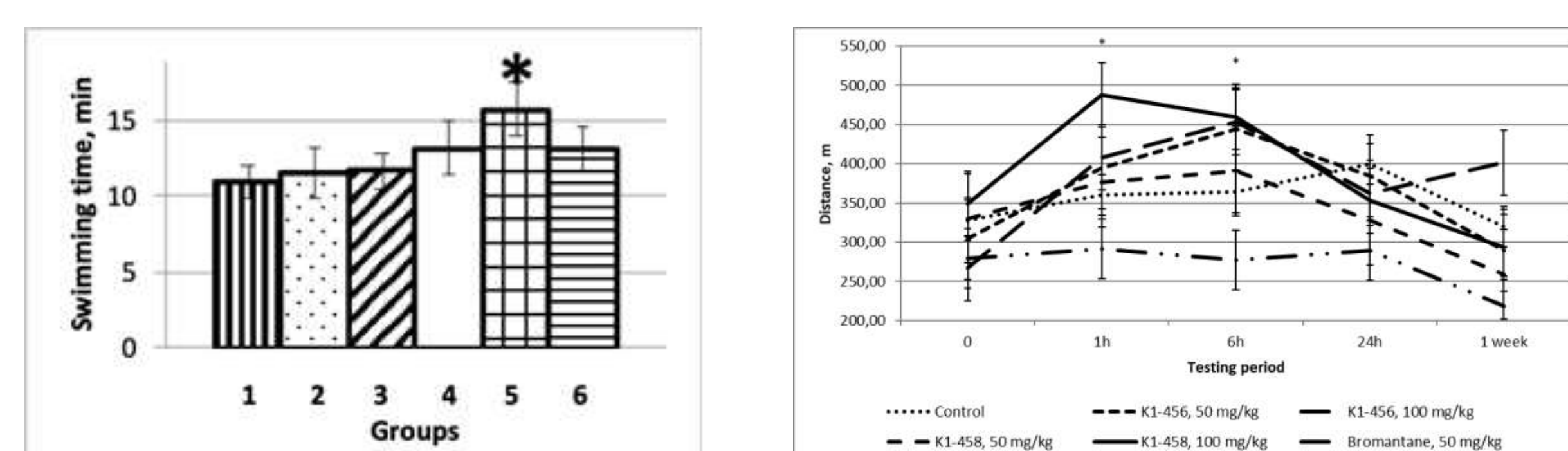
The influence of the studied compounds on the manifestation of toxicity of nicotine and yohimbine was estimated.

## Acknowledgements

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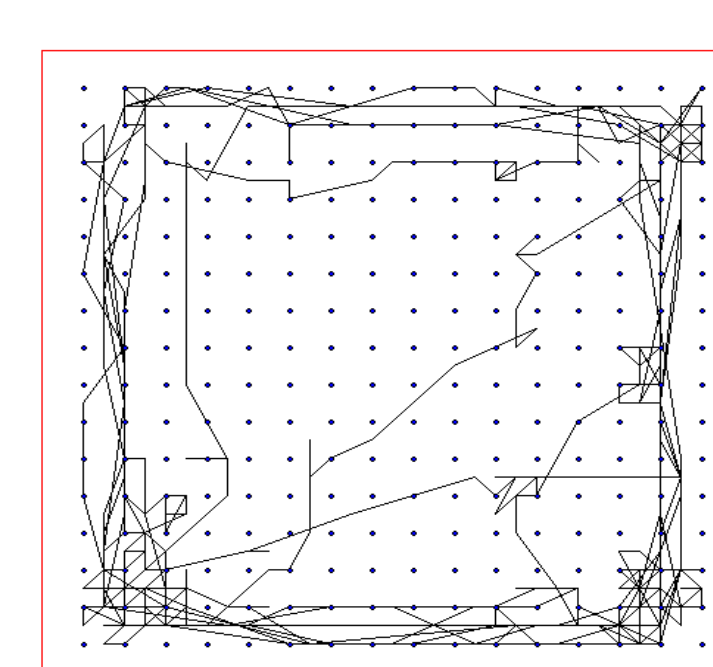
## 2. Results

The results showed that compounds combining bispidine scaffold and monoterpene fragments exhibit **actoprotective effect** in tests on a treadmill and swim with a load of 10% of body mass, increasing the duration of physical work.

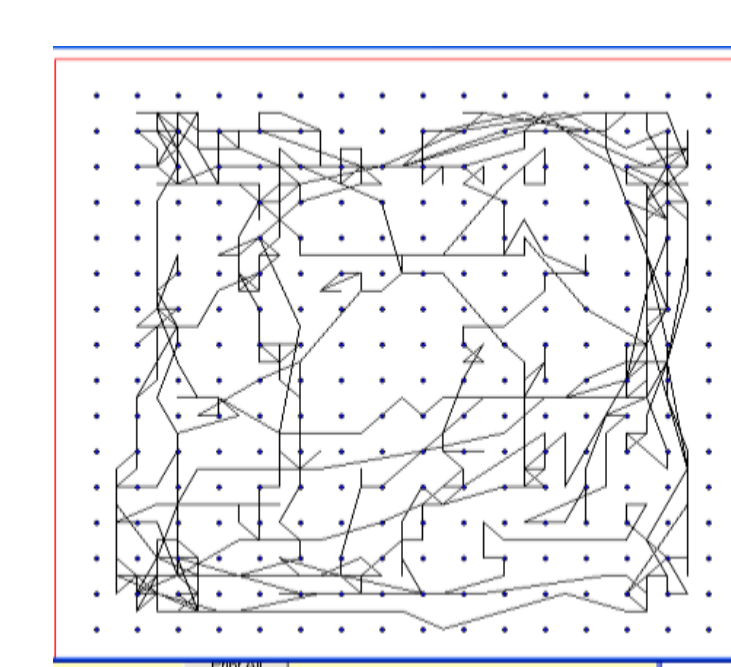


Designation of groups: 1- Control, 2 - K1-456, 50 mg/kg, 3 - K1-456, 100 mg/kg, 4 - K1-458, 50 mg/kg, 5 - K1-458, 100 mg/kg, 6 - Bromantane, 50 mg/kg.

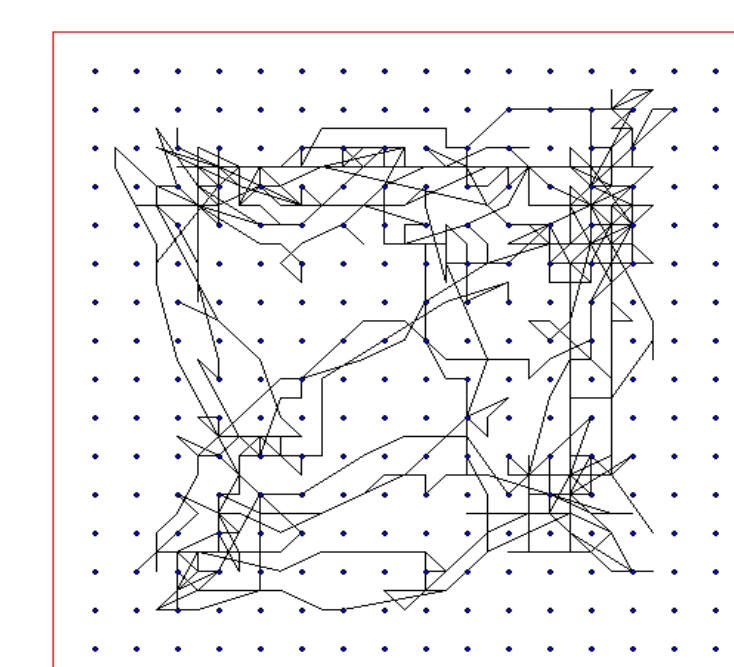
In the "Open field" test, which determines the locomotor and anxiety-like behavior in mice, it was found that some disubstituted derivatives significantly increased the distance and residence time of animals in the center of the open field compared to intact controls.



Track plot Control



Track plot Bromantane



Track plot K1-458 100 mg/kg

As a result of in vivo experiments, it was shown that the studied compounds exhibit an **anticholinergic effect** (reduce mortality from the administration of nicotine) without affecting the **adrenergic system** of the brain.

## Conclusion

For the first time it was shown that compounds combining fragments of a monoterpene and 3,7-diazabicyclo[3.3.1]nonane (bispidine) core exhibit actoprotective activity, acting on various neurotransmitter systems.

[1] A. A. Kotlyarova, et al. The effect of 3,7-diazabicyclo[3.3.1]nonanes containing monoterpene moieties on the physical activity of mice. J.Res.Pharm. 2020; 24(2): 196-204. <http://dx.doi.org/10.35333/jrp.2020.136>

[2] A. A. Kotlyarova et al. Effect of bispidine containing monoterpene moieties on physical performance in mice. 2020 Cognitive Sciences, Genomics and Bioinformatics (CSGB), Novosibirsk, Russia, 2020, pp. 114-117, doi: 10.1109/CSGB51356.2020.9214697

