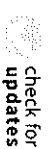


Reaction Products of β -Aminopropioamidoximes Nitrobenzenesulfochlorination: Linear and Rearranged to Spiropyrazolinium Salts with Antidiabetic Activity

Lyudmila Kayukova ^{1,*}, Anna Vologzhanina ^{2,*}, Pavel Dorovatovskii ³, Gulnur Baitursynova ¹, Elmira Yergaliyeva ¹, Ayazhan Kurmangaliyeva ¹, Zarina Shulgau ⁴, Sergazy Adekenov ⁵, Zhanar Shaimerdenova ⁵ and Kydymolla Akatan ⁶



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1. JSC A. B. Bekturov Institute of Chemical Sciences, 106 Shokan Ualikhanov St., Almaty 050010, Kazakhstan; guni-27@mail.ru (G.B.); erg_el@mail.ru (E.V.); ayazhanb98@mail.ru (A.K.)
2. A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28 Vavilova St., B-334, 119991 Moscow, Russia
3. NRC "Kurchatov Institute", 1, Akademika Kurchatova pl., 123182 Moscow, Russia; paulgemini@mail.ru
4. RSE National Center for Biotechnology, Science Committee of ME&S RK, 13/5 Kurgalzhinskoe highway, Nur-Sultan 010000, Kazakhstan; shulgau@biocenter.kz
5. JSC International Research and Production Holding Phytochemistry, 4 M. Gazalieva St., Karaganda 100009, Kazakhstan; info@phyto.kz (S.A.); zh.shaimerdenova@phyto.kz (Z.S.)
6. National Scientific Laboratory, S. Amanzholov East Kazakhstan State University, 18/1 Annurskaya St., Ust-Kamenogorsk 070002, Kazakhstan; ahnurh@mail.ru

* Correspondence: lkayukova@mail.ru (L.K.); vologzhanina@mail.ru (A.V.); Tel.: +7-(705)-166-81-53 (L.K.)

Abstract: Nitrobenzenesulfochlorination of β -aminopropioamidoximes leads to a set of products depending on the structure of the initial interacting substances and reaction conditions. Amidoximes, functionalized at the terminal C atom with six-membered *N*-heterocycles (piperidine, morpholine, thiomorpholine and phenylpiperazine), as a result of the spontaneous intramolecular heterocyclization of the intermediate reaction product of an S_N2 substitution of a hydrogen atom in the oxime group of the amidoxime fragment by a nitrobenzenesulfonyl group, produce spiropyrazolinium *ortho*- or *para*-nitrobenzenesulfonates. An exception is *ortho*-nitrobenzenesulfochlorination of β -(thiomorpholin-1-yl)propioamidoxime, which is regioselective at room temperature, producing two spiropyrazolinium salts (*ortho*-nitrobenzenesulfonate and chloride), and regioselective at the boiling point of the solvent, when only chloride is formed. The *para*-Nitrobenzenesulfochlorination of β -(benzimidazol-1-yl)propioamidoxime, due to the reduced nucleophilicity of the aromatic β -amine nitrogen atom, is regioselective at both temperatures, and produces the *O*-*para*-nitrobenzenesulfochlorination product. The antidiabetic screening of the new nitrobenzenesulfochlorination amidoximes found promising samples with in vitro α -glucosidase activity higher than the reference drug acarbose. ¹H-NMR spectroscopy and X-ray analysis revealed the slow inversion of six-membered heterocycles, and experimentally confirmed the presence of an unfavorable stereoisomer with an axial N–N bond in the pyrazolinium heterocycle.

Keywords: β -aminopropioamidoximes; nitrobenzenesulfochlorination; spiropyrazolinium salts; X-ray diffraction

1. Introduction

Heterocycles with potential bioactive properties are of great interest, first of all, for medical chemists working in the field of heterocyclic compounds synthesis. Among the new drugs approved by the FDA in 2021, almost 50% are substances with nitrogen-containing heterocycles [1]. Pyrazoline derivatives, as prominent representatives of nitrogen-containing heterocycles, became the subject of a report on the world market of diphenylpyrazolines from Market Strides (global aggregator and publisher of market intelligence research

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Data Availability Statement: The data presented in this study are available in this article.

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Conflicts of Interest: The authors declare no conflict of interest.

Sample Availability: Samples of the compounds 6–14 are available from the authors.

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