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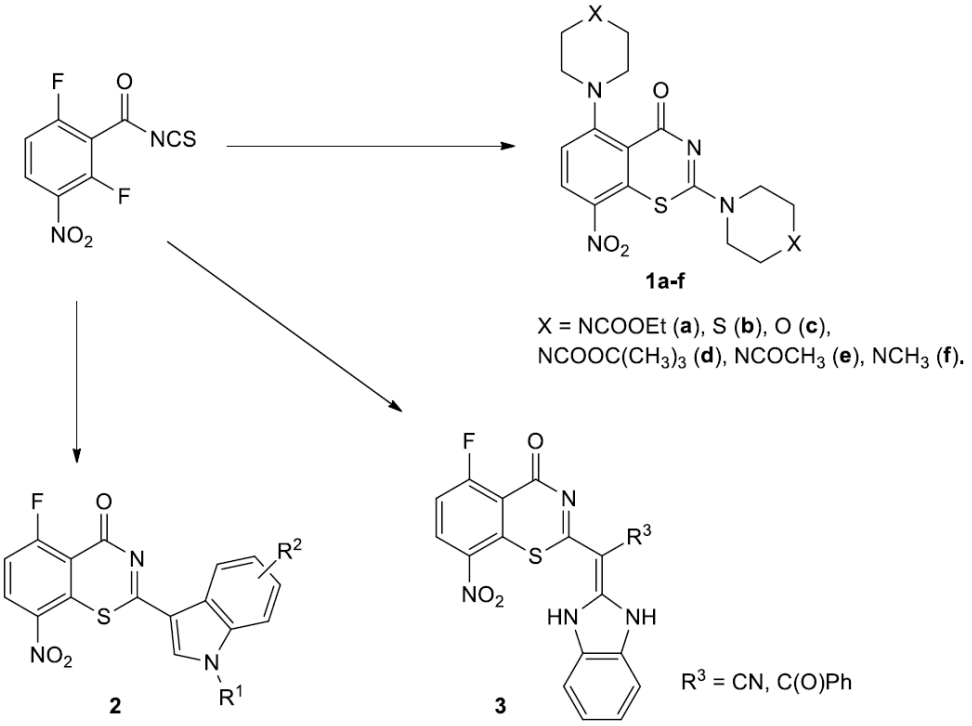
NOVEL 8-NITROSUBSTITUTED 1,3-BENZOTHIAZIN-4-ONES

E. V. Nosova*, O. A. Batanova

Chemical Technology Institute, UrFU, 620002 Ekaterinburg, 19 Mira St.
*E-mail: emilia.nosova@yandex.ru

Abstract. Many synthetic benzothiazines play an important role in the treatment of various diseases. Some 2-amino substituted 1,3-benzothiazin-4-ones (2-amino-1,3-benzothiazinones) represent a promising new class of antitubercular agents.[1] Recently we have reported the synthesis of novel fluorinated 2-cycloalkylaminosubstituted 1,3-benzothiazin-4-ones through the addition of N-nucleophiles to *ortho*-fluorobenzoylisothiocyanates and subsequent cyclization of fluorobenzoyl-thioureas, and 5-fluoro-2-(4-ethoxycarbonylpiperazin-1-yl)-1,3-benzothiazin-4-one was chosen as leading compound.[2]

The synthesis of novel 2,5-bis(cycloalkylamino)-8-nitro-1,3-benzthiazin-4-ones **1** was performed based on 2,6-difluorobenzoic acid. It was shown that ethoxycarbonylpiperazino derivative **1a** surpasses in tuberculostatic activity its 5-fluoro-8H-counterpart. We demonstrated the difference in the behavior of C-nucleophiles and N-nucleophiles under the reaction with 2,6-difluoro-3-nitrobenzoylisothiocyanate: application of C-nucleophiles allows to obtain derivatives of 5-fluoro-8-nitrobenzothiazinone **2, 3**, whereas the reaction with cycloalkylimines fails to avoid the nucleophilic substitution of fluorine at position 5.



The proposed strategy opens wide opportunities for varying the substituent at position 2 of 8-nitrobenzothiazin-4-ones.

References

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