

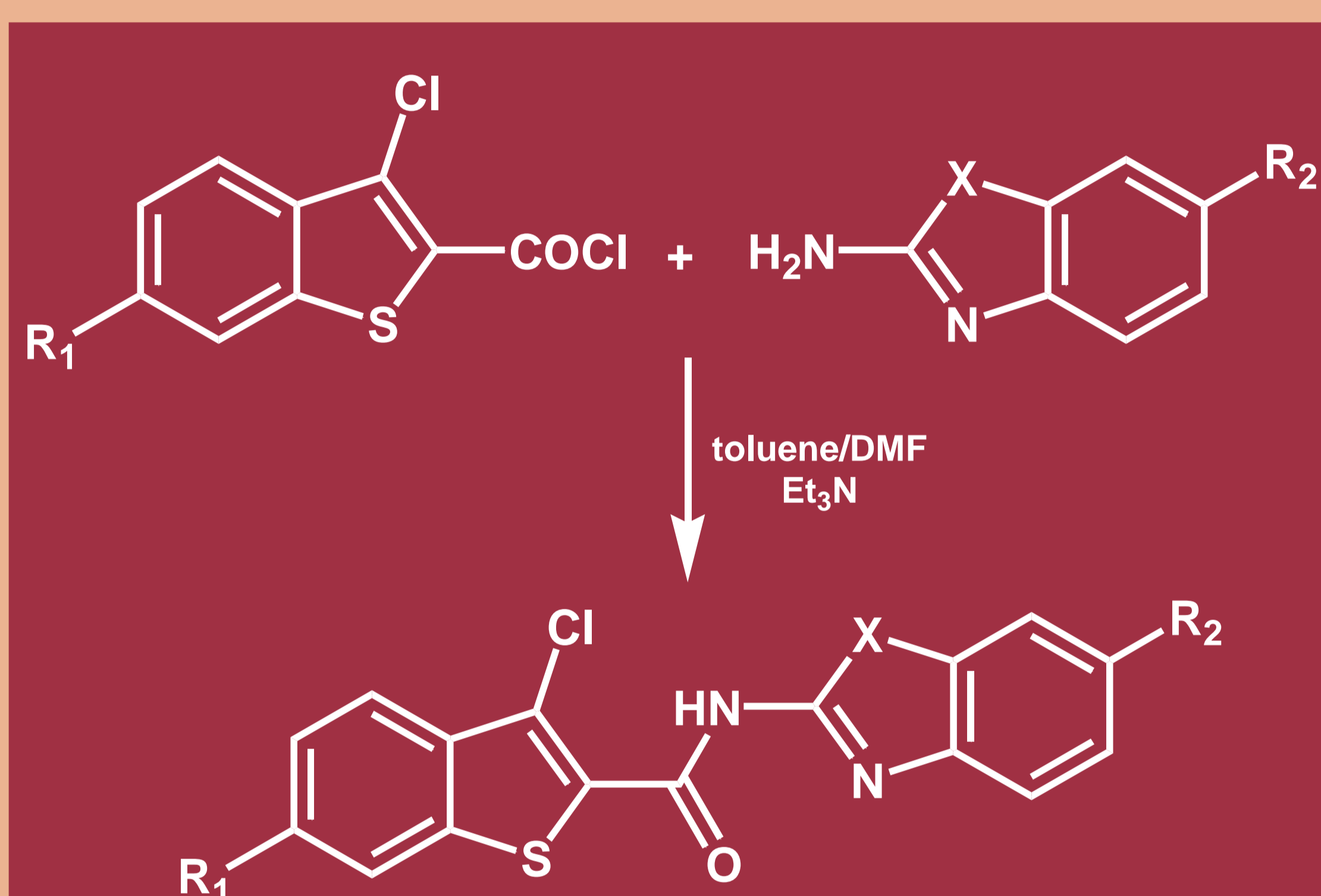
NOVI BIOLOŠKI AKTIVNI AMIDNI DERIVATI BENZIMIDAZOLA I BENZOTIAZOLA

NOVEL BIOLOGICALLY ACTIVE BENZIMIDAZOLE AND BENZOTHIAZOLE AMIDES

Maja Aleksić, Irena Sović, Grace Karminski-Zamola, Jurica Bunjevac, Maja Šuš, Valentina Rep and Marijana Hranjec

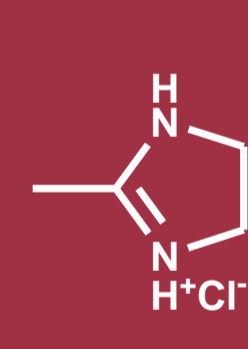
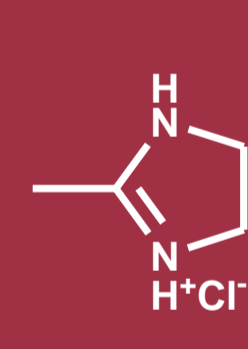
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The development of effective antineoplastic drugs has become one of the most intensively studied aspects of contemporary medicinal chemistry and therefore has been tremendous growth in the number and types of new anticancer agents. Substituted heterocyclic amides exhibit wide range of pharmacological activities and have therefore attracted considerable attention from medicinal and synthetic organic chemists. The amide functional moiety is considered to be an important building block present in the structure of many natural and synthetic medical and biochemical agents.

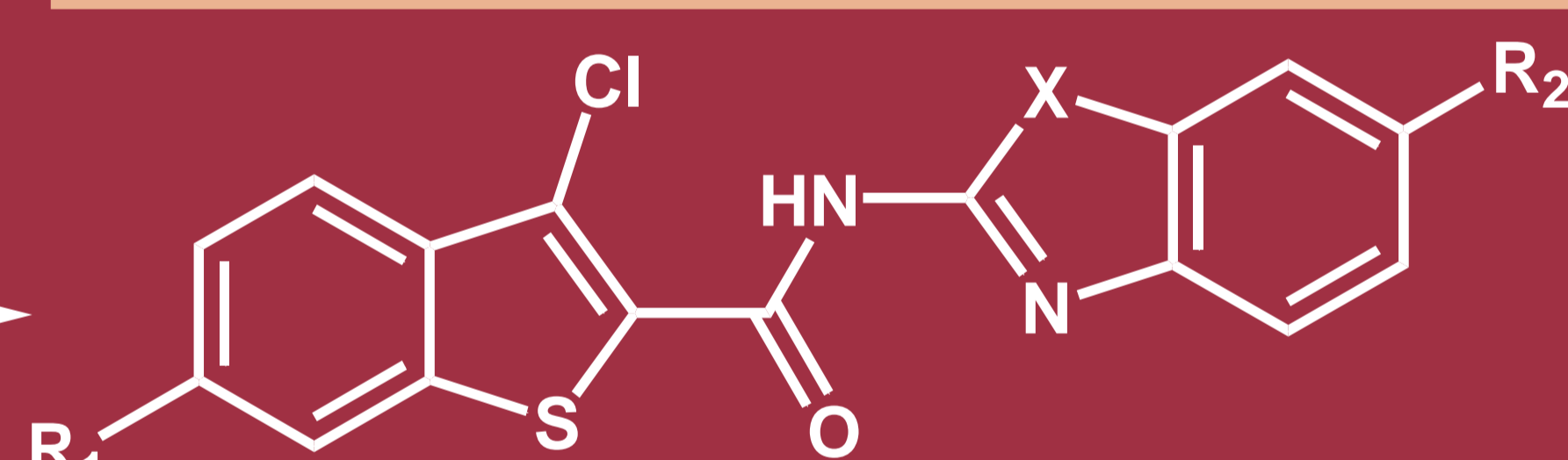


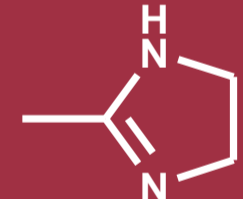
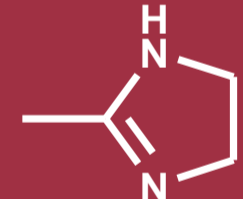
1 X = NH, R₁ = R₂ = H
2 X = S, R₁ = R₂ = H

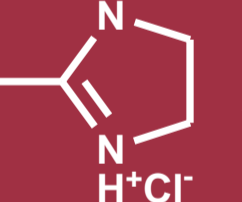
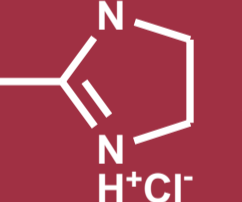
3 X = NH, R₁ = H, R₂ = CN,
4 X = S, R₁ = H, R₂ = CN
5 X = NH, R₁ = CN, R₂ = H
6 X = S, R₁ = CN, R₂ = H
7 X = NH, R₁ = R₂ = CN
8 X = S, R₁ = R₂ = CN

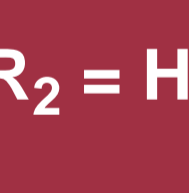
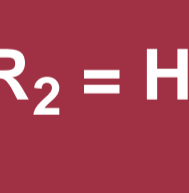
9 X = NH, R₁ = H, R₂ = 
10 X = S, R₁ = H, R₂ = 

This work presents, as a part of our continuing research in the field of medicinal chemistry, the synthesis of novel benzimidazole and benzothiazole amides. For the preparation of targeted compounds classical linear and convergent methods of organic synthesis were used. The synthesis of imidazolyl substituted amides 9-14 starts from benzo[*b*]thiophene-2-carbonyl chlorides which gave in the reaction with cyano substituted 2-aminobenzimidazoles and 2-aminobenzothiazoles amides 3-8. Cyano group was then transformed into imidazolyl group using Pinner reaction followed by protonation with HCl (g) (Scheme 1).



9 X = NH, R₁ = H, R₂ = 
10 X = S, R₁ = H, R₂ = 

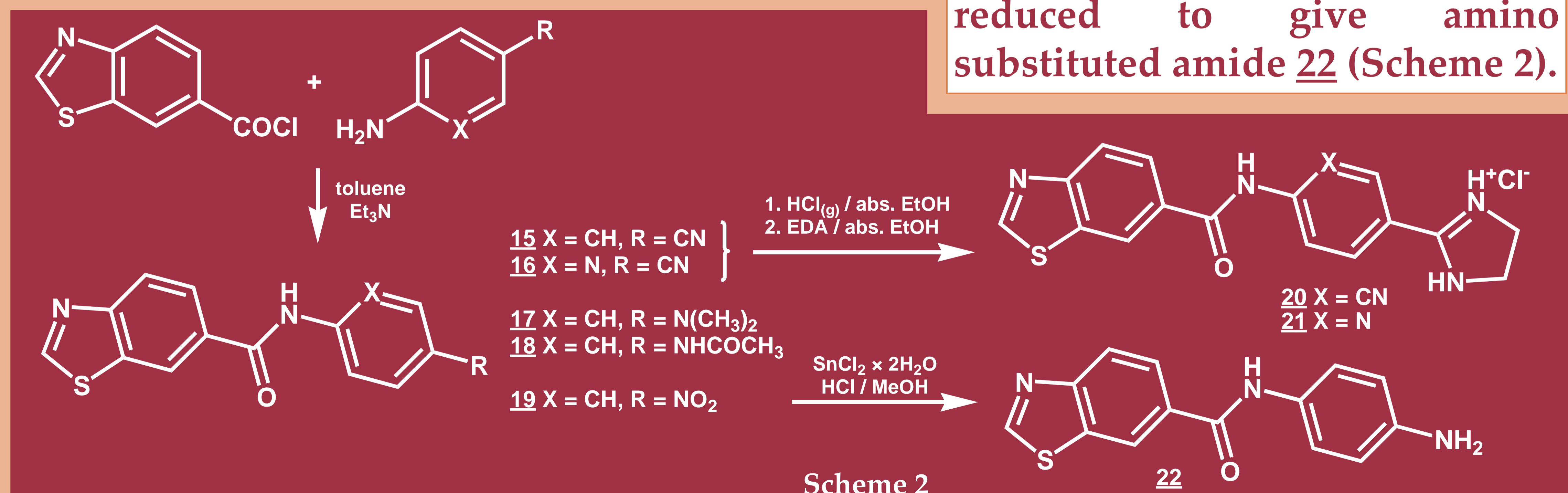
11 X = NH, R₁ = , R₂ = H
12 X = S, R₁ = , R₂ = H

13 X = NH, R₁ = R₂ = 
14 X = S, R₁ = R₂ = 

Scheme 1

Benzothiazole amides 15-19 were prepared starting from benzothiazole-6-carbonyl chloride in the reaction with corresponding amines. Cyano substituted amides 15 and 16 were then converted into targeted imidazolyl substituted amides 20 and 21 by Pinner reaction and nitro substituted amide 19 was reduced to give amino substituted amide 22 (Scheme 2).

Structures of prepared compounds were confirmed by ¹H and ¹³C NMR analysis based on the chemical shifts as well as the analysis of H-H coupling constants.



Scheme 2

LITERATURE:

1. M. Hranjec, I. Sović, I. Ratkaj, G. Pavlović, N. Ilić, L. Valjalo, K. Pavelić, S. Kraljević Pavelić, G. Karminski-Zamola, *Eur. J. Med. Chem.* 59 (2013) 111-119.
2. M. Aleksić, B. Bertoša, R. Nhili, L. Uzelac, I. Jarak, S. Depauw, M. H. David-Cordonnier, M. Kralj, S. Tomić, G. Karminski-Zamola, *J. Med. Chem.* 55 (2012) 5044-5060.

