

SYNTHESIS AND ANTIOXIDATIVE ACTIVITY OF NOVEL *N*-SUBSTITUTED BENZIMIDAZOLE CARBOXAMIDES



FKITMCMXIX



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A variety of biochemical processes in the human body could produce oxygen free radicals and other reactive oxygen species (ROS) as by-products which may cause oxidative damage of most important biomolecules such as nucleic acids, lipids and proteins. There has been tremendous and constant growing interest for the searching of novel natural or synthetic organic molecules as potential antioxidants. [1,2]

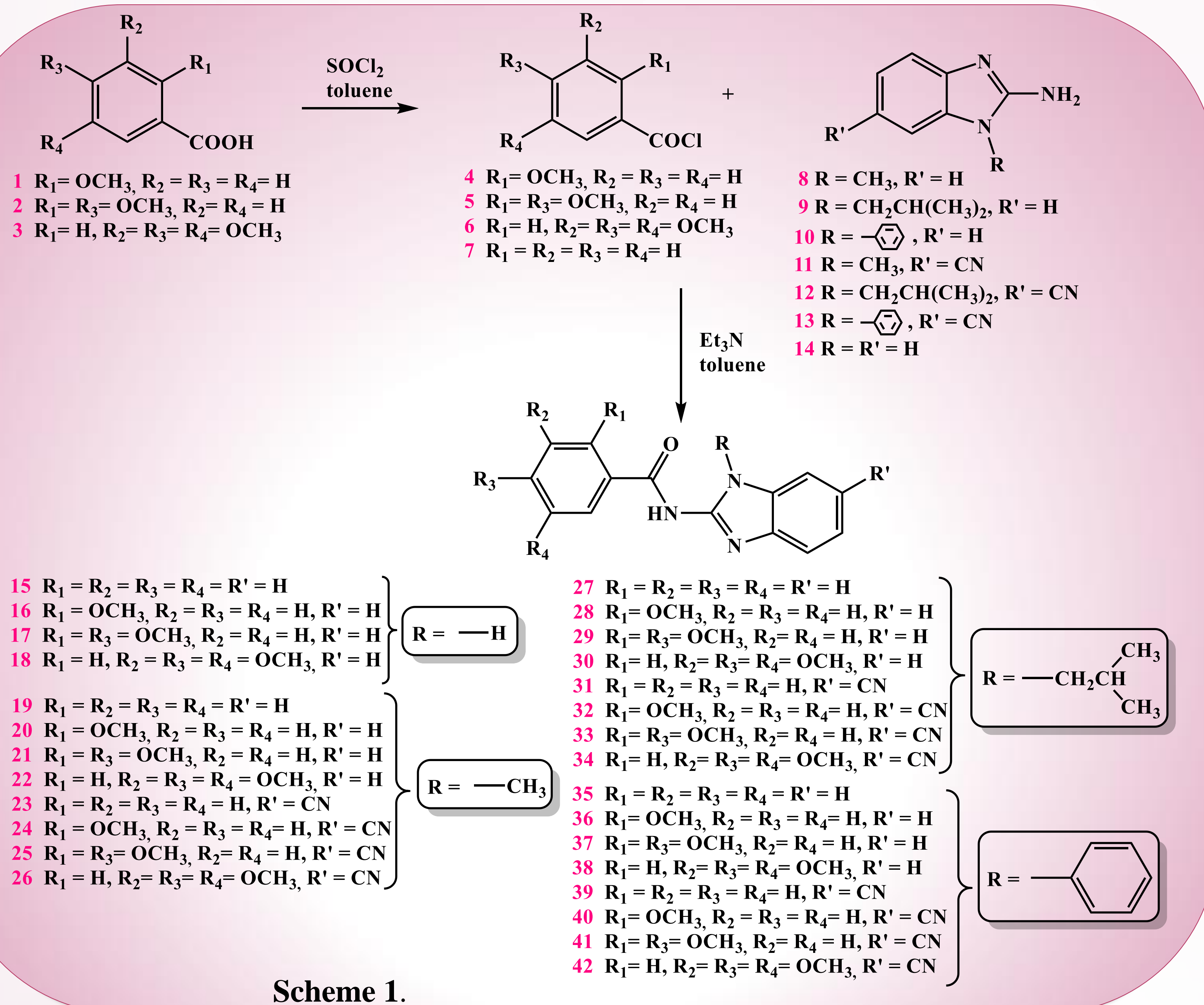
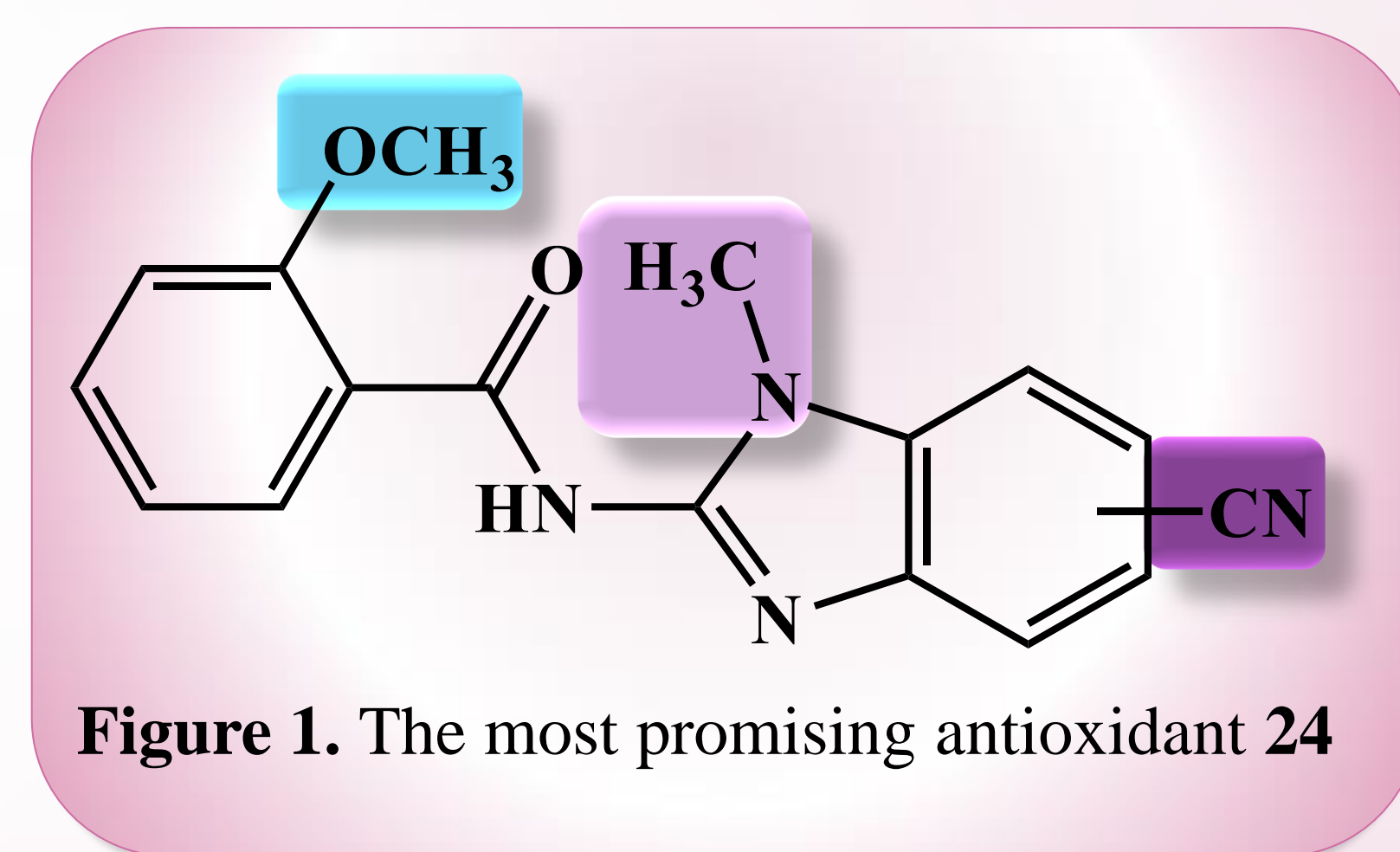


Table 1. Antioxidant activity of compounds 15-42 by DPPH and FRAP method.

Compd	R ₁	R ₂	R ₃	R ₄	R'	R	% inhibition DPPH	FRAP mmolFe ²⁺ /mg _c
15	H	H	H	H	H	H	14,2	-
16	OCH ₃	H	H	H	H	H	19,9	166,61
17	OCH ₃	H	OCH ₃	H	H	H	18,6	5,59
18	H	OCH ₃	OCH ₃	OCH ₃	H	H	42,1	358,81
19	H	H	H	H	H	CH ₃	57,6	110,16
20	OCH ₃	H	H	H	H	CH ₃	42,6	-
21	OCH ₃	H	OCH ₃	H	H	CH ₃	25,6	124,28
22	H	OCH ₃	OCH ₃	OCH ₃	H	CH ₃	45,3	160,27
23	H	H	H	H	CN	CH ₃	-	124,28
24	OCH ₃	H	H	H	CN	CH ₃	50,5	429,60
25	OCH ₃	H	OCH ₃	H	CN	CH ₃	-	618,10
26	H	OCH ₃	OCH ₃	OCH ₃	CN	CH ₃	21,4	338,50
27	H	H	H	H	H	CH ₂ CH(CH ₃) ₂	53,0	179,70
28	OCH ₃	H	H	H	H	CH ₂ CH(CH ₃) ₂	21,9	-
29	OCH ₃	H	OCH ₃	H	H	CH ₂ CH(CH ₃) ₂	3,8	5,80
30	H	OCH ₃	OCH ₃	OCH ₃	H	CH ₂ CH(CH ₃) ₂	51,1	217,20
31	H	H	H	H	CN	CH ₂ CH(CH ₃) ₂	20,3	203,50
32	OCH ₃	H	H	H	CN	CH ₂ CH(CH ₃) ₂	53,2	154,30
33	OCH ₃	H	OCH ₃	H	CN	CH ₂ CH(CH ₃) ₂	47,7	-
34	H	OCH ₃	OCH ₃	OCH ₃	CN	CH ₂ CH(CH ₃) ₂	5,7	243,30
35	H	H	H	H	H	phenyl	4,9	184,70
36	OCH ₃	H	H	H	H	phenyl	36,7	-
37	OCH ₃	H	OCH ₃	H	H	phenyl	33,6	-
38	H	OCH ₃	OCH ₃	OCH ₃	H	phenyl	4,0	236,90
39	H	H	H	H	CN	phenyl	5,2	138,98
40	OCH ₃	H	H	H	CN	phenyl	26,8	221,31
41	OCH ₃	H	OCH ₃	H	CN	phenyl	15,6	506,70
42	H	OCH ₃	OCH ₃	OCH ₃	CN	phenyl	4,4	132,56
BHT	-	-	-	-	-	-	-	679,15

Methoxy substituted benzoyl-chlorides 15-42 were obtained by nucleophilic substitution reactions from corresponding carboxylic acids 1-3 using thionyl chloride in toluene. *N*-substituted benzimidazole-2-carboxamides with a variable number of methoxy groups were synthesized by condensation reactions of benzoyl-chlorides 4-7 with *N*-substituted derivatives of 2-aminobenzimidazole and 2-amino-5-cyanobenzimidazole 8-13 and 2-aminobenzimidazole 14.

Antioxidant activity determination of newly synthesized benzimidazole amide derivatives 15-42 was performed by DPPH and FRAP method. Comparing values of antioxidant activity in both methods, the most active compound is *N*-methyl-5(6)-cyanobenzimidazolyl substituted derivative 24 with one methoxy group. Isobutyl substituent at *N* atom of the benzimidazole core has the greatest impact on increasing activity of synthesized compounds.



međunarodni znanstveno-stručni skup
18 RUŽIČKINI DANI
 DANAS ZNANOST – SUTRA INDUSTRIJA
 16. – 18. rujna 2020. | Vukovar, Hrvatska



This work was funded by the
Croatian Science Foundation
 under the project 4379,
AntioxPot.

[1] M. Cindrić, I. Sović, I. Martin-Kleiner, M. Kralj, T. Mašek, M. Hranjec, K. Starčević, *Med. Chem. Res.* 26 (2017) 2024-2037.

[2] I. Sović, M. Cindrić, N. Perin, I. Boček, I. Novaković, A. Damjanović, T. Stanojković, M. Zlatović, M. Hranjec, B. Bertoša, *Chem. Res. Toxicol.* 32 (2019) 1880-1892.