3-ARYLIDENE-2-OXINDOLES AS QUINONE REDUCTASE II INHIBITORS

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Quinone reductase II (QR2) is an enzyme which exhibits antioxidant, neuroprotective and chronobiotic properties. Previously we reported that 3-substituted-2-oxindoles possess an affinity towards this molecular target and act as potential anti-glaucoma agents [1,2]. A number of novel compounds with 3-aryliden-2-oxindole scaffold were synthesized [3].

R₁ = H, CH₃

R₅ = H, NO₂, Br, AcNH, CH₃OC(O)NH, (2-furoyl)NH, BzNH

Aryl = 2-pyridyl, 2-thienyl, 2-furyl, 3-pyridyl, 3-OH-Ph, 4-pyridyl, 4-OH-Ph, 4-OMe-Ph, 4-OEt-Ph, 4-NO₂-Ph, 4-Br-Ph, 4-F-Ph, 3,4,5-tri-OMe-Ph, 3,5-di-OMe-4-OH-Ph, 1-Me-1H-pyrazol-4-yl, 3,5-di-Me-pyrazol-4-yl, 1-Ph-1H-3,5-di-Me-pyrazol-4-yl, 3-ethoxycarbonyl-pyrazol-4-yl

Configuration of novel compounds was determined by ¹H NMR spectrometry. E-configuration was found to be predominant in 4-substituted benzylidene and 2-pyridinylmethylene derivatives, while in case of several pyrazole derivatives the stereoselectivity towards Z-configuration was observed. Obtained substances were tested as ligands of QR2 and displayed prominent activity.

Inhibitory activity of selected compounds

Nº	R1	R5	Aryl	% NQO2 Inhibition (10µM)	IC ₅₀ (NQO2)
1	H	(2-furoyl)NH	3,4,5-tri-OMe-Ph	90,98	0,660
2	H	AcNH	3,4,5-tri-OMe-Ph	92,78	0,368
3	H	(2-furoyl)NH	4-OH-Ph	96,4	0,37
4	H	CH ₃ OC(O)NH	4-OH-Ph	93,63	0,44
5	CH ₃	H	4-OH-Ph	98,87	0,62
6	H	H		37,67	0,68

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References

- [1] M. S. Volkova, K. C. Jensen, N. A. Lozinskaya, S.E. Sosonyuk, M.V. Proskurnina, A. D. Mesecar, N. S. Zefirov, *Bioorganic Med. Chem. Lett.* 2012, 22(24), 7578–7581
- [2] E. V. Zaryanova, N. A. Lozinskaya, O.V. Beznos, M. S. Volkova, N. B. Chesnokova, N.S. Zefirov, *Bioorganic and Medicinal Chemistry Letters*, 2017, 27, 3787–3793.
- [3] N. A. Lozinskaya, D. A. Babkov, E.V. Zaryanova, E. N. Bezsonova, M. Efremov, M.D. Tsymlyakov, L. Vanikina, O. Yu. V. Borisov, V.N. Perfilova, I.N. Tyurenkov, M. V. Proskurnina, *Bioorg. Med. Chem.* 2019, 27, 1804–1817.