Organic and Medicinal Chemistry
International Journal
ISSN 2474-7610

Short Communication
Volume 7 Issue 3 - August 2018
DOI: 10.19080/OMCIJ.2018.07.555718

Organic & Medicinal Chem IJ

Synthesis Of 2-Styryl Derivatives of N, N-Bis-Substituted Quinazolines

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Submission:July 28, 2018; **Published:** August 03, 2018

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Interest in the heterocyclic quinazoline system is largely due to the high biological activity that they exhibit, including anti protozoic, anti-inflammatory, sedative, antibacterial, as well as the ability to inhibit kinases, the aurora-serine/threonine kinase involved in the regulation of cell division [1]. In recent works, attention has been drawn to the substituted 2-styrylquinazolines, showing antibacterial, fungicidal and cytotoxic properties [2] and bis-quinazolines - inhibitors of the epidermal growth factor receptor (EGFR) [3]. In connection with this, in the continuation of our investigations [4], we synthesized substituted quinazolines, combining the above structural fragments - 2-(2-arylvinyl)-3,3'-(ethane-1,2-, butane-1,4-, hexane-1,6-diyl-bis [2-[(E)-2-arylvinyl]quinazolin-4(3H)-ones] and 3,3'-[imino-bis(ethane-2,1-diyl)]bis[2-[(E)-2-arylvinyl]-quinazoline-4(3H)-ones], according to the scheme: 2: n = 0; 3,6a,b: n = 1; 4,7a-e: n = 2; 6a,b: R= 4-ClC_6H_4 (a), 2,4-$Cl_2C_6H_3$ (b); 7a-e: R= Ph (a), 4-FC_6H_4 (b), 2,4-$Cl_2C_6H_3$ (c), pyridin-3-yl (d), thiophen-2-yl (e); 8a,b: R = Ph (a), 4-$NO_2C^6H_4$ (b).

The reaction of 2-methyl-4H-3,1-benzoxazin-4-one 1 with the corresponding diamines in the ratio 2/1 under heating conditions in poly phosphoric acid yielded 3,3'-bis [(2-methylquinazolin) -4 (3H) -ones] 2-5. The latter are condensed with aromatic and heterocyclic aldehydes by co-heating or by boiling in acetic anhydride to give the desired compounds 6a, b,7a-e and 8a, b. The structure of the synthesized compounds was proved by IR and NMR ^{1}H-spectroscopy. Some of the bis-quinazolines studied showed a weak, and bis-4-nitro derivative 8b is a moderate antibacterial action against four strains of Gram-positive and Gram-negative microorganisms, and some compounds also detected a noticeable anti mono amino oxidase activity.

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