Synthesis of Bioactive 2-(arylamino)thiazolo[5,4-f]-quinazolin-9-ones via the Hügershoff Reaction or Cu- Catalyzed Intramolecular C-S Bond Formation

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The occurrence and properties of the thiazole ring in various natural and synthetic products have been the interest of many research groups on account of its useful biological properties. In this context, our research group is mainly invested in the synthesis of C,N,S-containing bioactive molecules able to modulate the activity of deregulated kinases (CDK5, GSK-3, CLK1, CK1 and the dual-specificity kinase DYRK1A) involved to some extent in Alzheimer's disease (AD) studied (Logé, C., *et al. Eur. J. Med. Chem.* 2008, *43*, 1469; Testard A., *et al. Bioorg. Med. Chem. Lett.* 2006, *16*, 3419 ; Foucourt A., *et al*. *Molecules* 2014, *19*, 15546; Foucourt A., *et al*. *Molecules* 2014, *19*, 15411).

A library of thirty eight novel thiazolo[5,4-*f*]quinazolin-9(8*H*)-one derivatives (series **I**, **II**,**III** and **IV**) was prepared via the Hügershoff reaction and a Cu catalyzed intramolecular C-S bond formation, helped by microwave-assisted technology when required. The efficient multistep synthesis of the key 6-amino-3-cyclopropylquinazolin-4(3*H*)-one has been reinvestigated and performed on a multigram scale from the starting 5-nitroanthranilic acid. The inhibitory potency of the final products was evaluated against five kinases involved in Alzheimer's disease and showed that some molecules of the **IV** series described in this communication are particularly promising for the development of novel multi-target inhibitors of kinases, a new strategy for the development of powerful tools against neurodegenerative diseases.

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