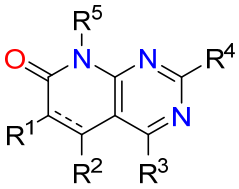
RESEARCH PROJECT

Covalent binding strategy: Synthesis of suitable linkers for pyrido[2,3-*d*]pyrimidines structures as a potential anticancer agents.

During the last years, our group has designed and developed many compounds with pyrido[2,3-*d*]pyrimidine as a main scaffold.[1]



Among several applications, some of these compounds showed good activity as tyrosine kinase inhibitors, which are one of the main targets to fight against cancer.[2] Until now, reversible interaction between drug and protein has been the most extended one (hydrogen bond, van der Waals, …). Recently, a new approach is emerging, focusing the research efforts on designing new entities with the ability to create an irreversible interaction with their therapeutic targets. The covalent inhibitors possess numerous advantages: increased biochemical efficacy, longer duration of action, the high potential for improved therapeutic index due to lower effective dose, and the potential to inhibit certain drug resistance mechanisms.[3] This project is focused on the introduction into the pyrido[2,3-*d*]pyrimidine scaffold suitable linkers allowing a covalent binding with tyrosine kinase FGFR1.

References

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[2] Puig de la Bellacasa, R.; Roué, G.; Balsas, P.; Pérez-Galán, P.; Teixidó, J.; Colomer, D.; Borrell, J. I.; *Eur. J. Med. Chem.* **2014**, *86*, 664-675.

[3] Wang, L.; Zhao, J.; Yao, Y.; Wang, C.; Zhang, J.; Shu, X.; Sun, X.; Li, Y.; Liu, K.; Yuan, H.; Ma, X.; *Eur. J. Med. Chem.* **2017**, *142*, 493-505.

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