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ATTI DEL CONGRESSO

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Synthesis and biological evaluation of pyrrolo[3',2':6,7]cyclohepta[1,2-*d*]pyrimidin-2-amines

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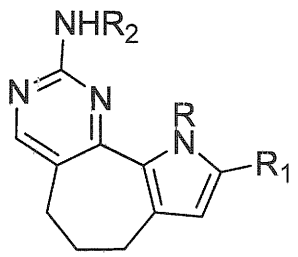
The photodynamic therapy (PDT) is an interesting therapeutic option for the treatment of tumors. [1] It requires systemic administration of a photosensitizing agent (PS), followed by irradiation of the tumor with light of the proper wavelength. Up to date studies are focused on the development of powerful photosensitizers that more specifically target cancer cells. [2] In consideration of the great interest in the pyrimidine nucleus, being the scaffold of many antitumor drugs, we studied in the last years pyrrolopyrimidine systems which showed promising antitumor properties either in the dark and under light irradiation. [3,4] Here we present, the synthesis of pyrrolo[3',2':6,7]cyclohepta[1,2-*d*]pyrimidin-2-amines of type **1** which were conveniently prepared by us using a versatile synthetic pathway.



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The biological effect of these compounds was evaluated in tumoral cells, where the compounds displayed cytotoxicity in the micromolar range and photocytotoxicity in the nanomolar range, with an overall selectivity index for the best molecules higher than 2600. Since compounds exhibited low or no significant effect on DNA, their activity was evaluated in terms of cellular cycle perturbation and induction of apoptosis/necrosis, in order to define the mechanism of action involved in the photoinduced cell death.

[1] see for example: R. Allison et al. *Photodiagnosis and Photodynamic Therapy*, 2010, **7**, 61 – 75.
[2] see for example: D. E. Dolmans et al. *Nt. Rev. Cancer*, 2003, **3**, 380 – 387.
[3] V. Spanò et al. *Eur. J. Med. Chem.*, 2014, **74**, 340 – 357.