Prodigiosin derivatives and their Cu(II)-dependent antimicrobial and photoinduced anticancer activity

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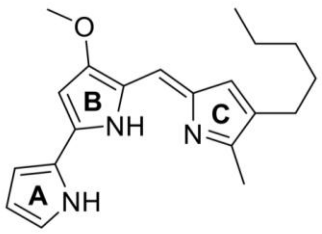
Prodigiosenes are derivatives of prodigiosin, a natural red pigment (**1**) occurring in *Serratia marcescens* bacteria. Prodigiosenes like undecylprodigiosin (**C11**), also naturally occurring, have shown diverse biological activity (antimalerial, immunosuppressive, anticancer and antibacterial), based on, *inter alia*, their interaction with Cu(II). In order to study and modify the mechanism behind this activity, several modifications have been carried out at the **A**, **B** and **C** ring of the tripyrrolic molecule. It has been concluded that the structural integrity of the pyrrolylpyrromethene scaffold is decisive.[1]

We have thus carried out a simple and yet impactful modification: changes of the length of the alkyl chain of the **C** ring (**C0**, **C6**, **C16**) resulted in different properties regarding DNA binding, DNA cleavage, (photoinduced) cytotoxicity and antimicrobial activity of their Cu(II) complexes. Two complexes demonstrated high antibacterial activity against *S. aureus* strains. The complex of a prodigiosene without an alkyl chain (**C0**) showed the most promising photoinduced anticancer activity suggesting its potential as an PDT (photodynamic therapy) agent.[2]



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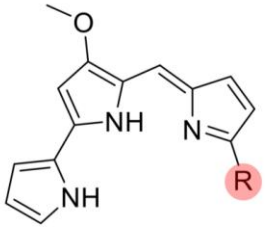

C0: R=H **C11**: R=$C_{11}H_{23}$
C6: R=C_6H_{13} **C16**: R=$C_{16}H_{33}$

[1] R. D'Alessio, A. Bargiotti, O. Carlini, F. Colotta, M. Ferrari, P. Gnocchi, A. Isetta, N. Mongelli, P. Motta, A. Rossi, M. Rossi, M. Tibolla, E. Vanotti *J. Med. Chem.*, **2000**, *43*, 2557–2565. D. L. Boger, M. Pate *J. Org. Chem.*, **1988**, *53*, 1405–1415. V. Rizzo, A. Morelli, V. Pinciroli, D. Sciangula, R. D'Alessio *J. Pharm. Sci.* **1999**, *88*, 73–78. R. I. S. Díaz, J. Regourd, P. V. Santacroce, J. T. Davis, D. L. Jakeman, A. Thompson *Chem. Commun.*, **2007**, 2701–2703.
[2] S. Doniz Kettenmann, M. White, J. Colard-Thomas, M. Kraft, A. T. Feßler, K. Danz, G. Wieland, S. Wagner, S. Schwarz, A. Wiehe, N. Kulak *ChemMedChem*, **2022**, *17*, e202100702.