SYNTHESIS AND BIOLOGICAL STUDIES OF A NEW CHROMOPHORE - STEROID CONJUGATE FOR THE PROGESTERONE RECEPTOR

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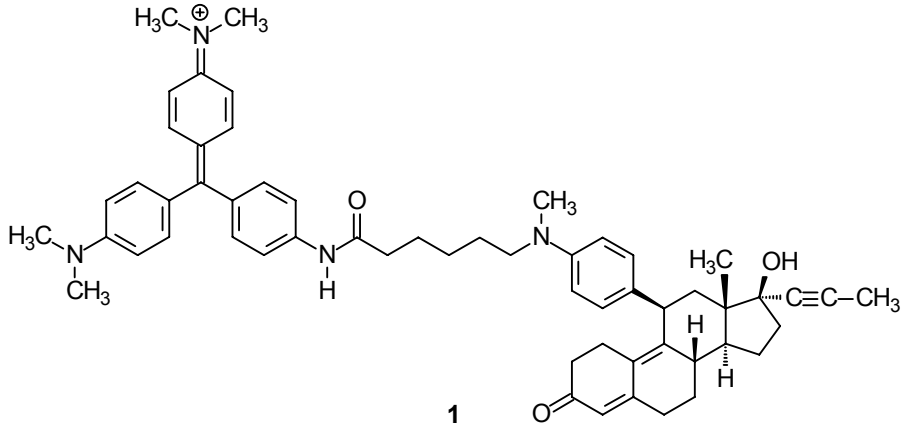
The progesterone receptor (PR) is a member of the nuclear receptor superfamily of ligand-dependent transcription factors. It mediates the effects of progesterone in various hormone-dependent tissues and plays a crucial role in normal breast development and in breast cancer. In some breast cancer cells PR overexpression was observed.
Chromophore-assisted laser inactivation (CALI) [1] is considered to be a powerful technology for acute protein inactivation in living cells. However, CALI has several limitations that restrict wider biological applications, mainly due to the use of antibodies for target recognition. To circumvent these limitations small molecule-based CALI (smCALI) was developed, where binding to the target protein is mediated by a synthetic molecule.
The PR was selected as target protein of interest, with reference to our previous work [2] demonstrating that functionalized mifepristone derivatives are shuttled into the nucleus of PR positive cancer cells.
The triphenylmethane-steroid-conjugate **1** was synthesized, using an activated carboxylate moiety on the steroid scaffold as linkage partner for the chromophore [3] and its biological activities, e.g. antiprogestagenic activity, was evaluated in appropriate cellular test systems.



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