Optochemical Control of Therapeutic Agents through Photocatalyzed Isomerization

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DOI: 10.1002/anie.202203390

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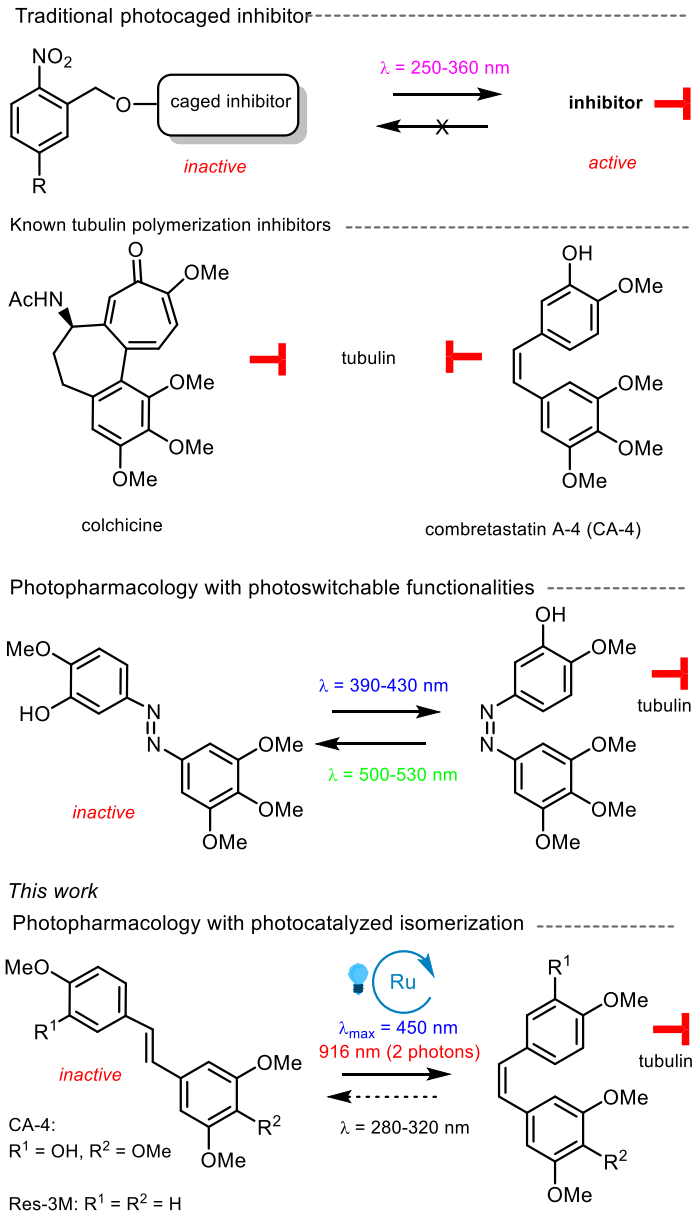
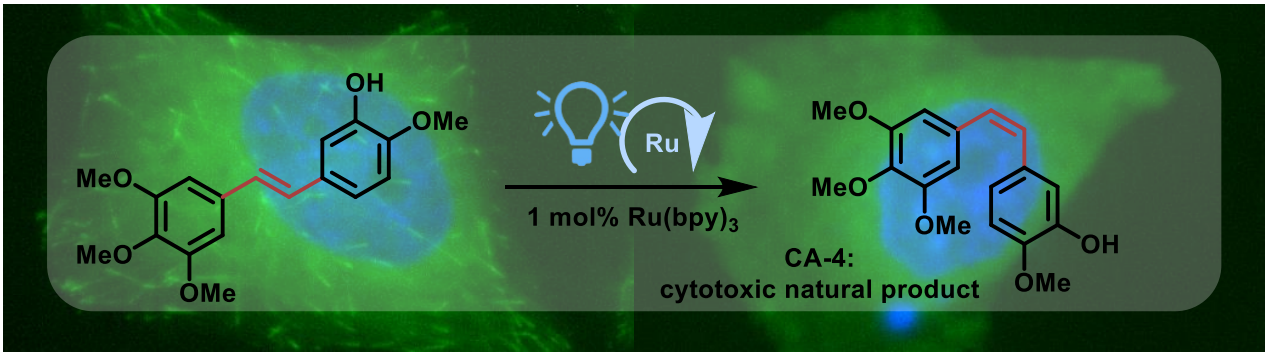


In this work, a $Ru(bpy)_3Cl_2$ photocatalyst enables the rapid trans to cis isomerization of a range of alkene-containing pharmacological agents. Amongst them, trans-combretastatin (CA-4), a clinical candidate in oncology, and trans-trimethoxy resveratrol (Res-3M) derivatives were selected to show efficient photoactivation in cells. The ability to disrupt microtubular infrastructure is hundreds to thousands of folds higher for cis Res-3M and CA-4 compared to the trans isomers[1,2]. Therefore, we used our system to show efficient tubulin depolymerization by photo-isomerizing the compounds *in vitro* or in cells using a 450 nm LED light. Encouraged by this result, we investigated the possibility to use microscopy settings to trigger photoisomerization and visualize tubulin depolymerization in real-time which we were able to achieve within 60 seconds. The isomerization is carried out at 450 nm which shows poor tissue penetration, hence hampering its clinical application. To expand the scope of our system we decided to capitalize on a two-photon irradiation system that enables deeper tissue penetration due to the longer wavelengths deployed (916 nm). Thus, we have shown a simple and efficient way to access novel drug-like compounds by late-stage modification of a carbon-carbon double bond, demonstrated the robustness of the system in cells, and expanded its scope to a possible application *in vivo*.



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