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(54) Title: HYDROPHILIC TRANS-CYCLOOCTENE (HYTCO) COMPOUNDS, CONSTRUCTS AND CONJUGATES CONTAINING THE SAME

(57) Abstract: The invention relates to the field of bioconjugation of functional entities, such as payloads and targeting agents, mediated by novel trans-cyclooctene (TCO) compounds. More particularly the present invention relates to novel trans-cyclooctene compounds, unnatural amino acids comprising such trans-cyclooctene compounds and preparation thereof. Said novel trans-cyclooctene compounds and unnatural amino acids comprising such trans-cyclooctene compounds are characterized by high structural stability and hydrophilicity and thus instrumental to ease the conjugation of said functional entities. The invention further relates to respective trans-cyclooctene-functionalized construct obtainable by, in particular covalently, binding said novel trans-cyclooctene compounds to a targeting agent or payload molecule, said functionalized construct containing at least one functionalizing residue comprising a mono-unsaturated trans-cyclooctene entity. The invention further relates to conjugates obtainable by covalently linking, in particular, via biorthogonal bioconjugation via a Diels-Alder-type cycloaddition, a first functionalized molecule, particularly selected from said trans-cyclooctene-functionalized constructs with a second functionalized molecule comprising a docking group (DG) capable of reacting with the trans-cyclooctene-type functional group of the first functionalized molecule. The present invention further relates to preparation methods of said constructs and conjugates. The invention also relates to the use of such conjugates of the present invention for use in medicine, to corresponding pharmaceutical compositions as well as to corresponding diagnostic and analytical kits.

WO 2025/021929 A1