

Title: **Bioconjugation. 1,3-Dipolar cycloaddition reactions not catalyzed by Cu(I)**

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Bioconjugation is a chemical technique in expansion that is increasingly arousing more interest in different fields such as medicine, nanotechnology or materials. This technique is based on the covalent binding between a biomolecule and one or more molecules. The most applied technique is the copper-catalyzed azide-alkyne cycloaddition ("CuAAC"), also known as the Huisgen's reaction, which follows the procedure of a "1,3 dipolar cycloaddition". The drawback of this technique is that, as the name suggests, it uses "copper (I)" in the reaction, and it has a significant toxicity to living cells. For this reason, alternatives to this method have been searched in recent years. In this work we talk about three copper free alternatives which are relatively new and are known as strain-promoted azide-alkyne cycloaddition ("SPAAC"), strain-promoted alkyne-nitrone cycloaddition ("SPANC") and strain-promoted alkyne-nitrile oxide cycloaddition ("SPANOC").

Keywords: CuAAC; 1,3 dipolar cycloaddition; copper (I); SPAAC; SPANC; SPANOC.