

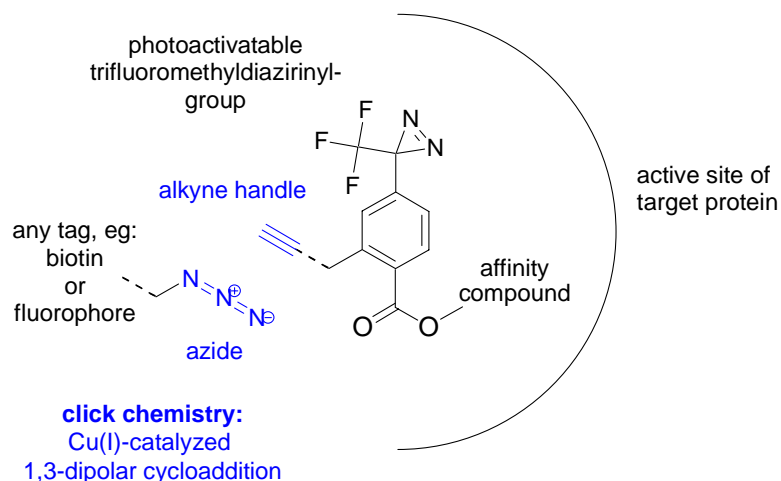
Design and synthesis of a “tag-free“ chemical probe for photoaffinity labeling

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Photoaffinity labeling (PAL) is a frequently used, powerful biochemical method to investigate structural and functional properties of biological systems.^[1] The method is based on the affinity of ligands to receptors, and is especially useful where the application of crystallography or NMR is difficult.

Conventional PAL probes are labeled with radioisotopes, which have certain disadvantages like the special care needed to avoid radiation exposure and the difficult biochemical purification of photolabeled proteins. Hence, novel radioisotope-free probes, which carry a biotin unit or a fluorophore have been developed recently. However, the presence of such bulky tags in an affinity compound might unfavorably affect the ligand-receptor interactions. To overcome these drawbacks, it is required to make use of a strategy, which allows the attachment of virtually any tag after the PAL experiment.^[2] Therefore we designed a trifluoromethyldiaziriny-based chemical probe, equipped with an alkyne group as sterically inconspicuous substitute for large tags. This alkyne handle can be used to conjugate optional tags chemoselectively through Cu(I)-catalyzed azide-alkyne cycloaddition reaction (click-chemistry) after photo-cross-linking.^[3] In model studies, we have confirmed the full functionality of this universally applicable probe under typical click chemistry and photoirradiation conditions.



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