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Vinyl Sulfone Bifunctional Tag Reagents for Single-Point Modification of Proteins

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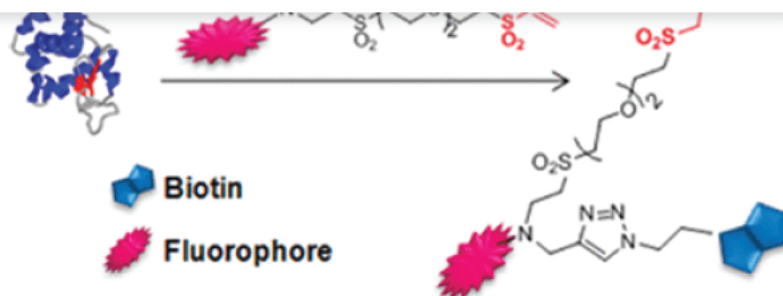
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The introduction of multiple labels onto biomolecules is a challenge. We report herein the synthesis of vinyl sulfone derivatized bifunctional tag single-attachment-point reagents (BTSAP) bearing biotin and a fluorescent tag and their applications in proteins for the introduction of multiple labels by means of the Michael-type addition of the electrophilic vinyl sulfone group. These BTSAP reagents were easily synthesized by a two-step chemical strategy involving the preparation of alkyne vinyl sulfone derivatized tags (AVST) and subsequent click CuAAC attachment of a second azide functionalized tag. The direct coupling of BTSAP reagents with the low reactive protein horseradish peroxidase (HRP) turned it into a dual reporter group (i.e., fluorescence and peroxidase activity) that may be coupled to any recognition system via biotin-avidin affinity. The AVST compounds are not mere synthetic intermediates for the preparation of BTSAP reagents but valuable *clickable self reporting* compounds that allow the simultaneous introduction in proteins of an alkyne function and labeling when conjugated via the vinyl sulfone group. The implementation of these clickable AVST compounds in a CuAAC-based sequential approach also allows attainment of the dual labeling of HRP. This approach yields equivalent results in terms of fluorescent labeling, specific activity, and functionality of the biotin tag when compared with the direct bifunctional labeling by the BTSAP reagent. However, for life science this direct approach is more convenient since it avoids the use of copper catalysis, overcoming the toxicity drawback of this metal in biological systems.

Supporting Information

Solvent accessibility of the residues comprising HRP, enzymatic activity of the labeled-HRP, and

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Supplementary Information

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