Protein Binding Sites as Microvessels for Photochemical Reactions

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Transport proteins, such as serum albumins (SAs) or α-1-acid glycoproteins (AAGs) are carriers of endogenous and exogenous agents in the bloodstream and play a crucial role in relevant processes of living organisms. Hence, binding of ligands to transport proteins is an important issue, which has been addressed by different methodologies. In this context, the triplet excited states of different ligands, generated by laser flash photolysis, have been used as reporters for the microenvironments experienced within the protein binding sites.[1],[2] Analysis of triplet decays provides valuable information on the distribution of the ligand between the binding sites and its presence as the noncomplexed form in the bulk solution. Interestingly, encapsulation within transport proteins protects the ligand from attack by oxygen.[3],[4] For instance, the photooxidation rate of protein-bound anthracenes is strongly reduced and, in the case of chiral compounds, it is markedly configuration-dependent.[5],[6] The reaction mechanism involves energy transfer to molecular oxygen, followed by [4 + 2] cycloaddition of the resulting singlet oxygen to the central anthracene ring, rearrangement of the resulting endoperoxide, with cleavage of the ring substituent and formation of 9,10-anthraquinone as final product. The photoreactivity is markedly compartmentalized, with higher reaction rates in the bulk solution than within the protein microenvironments.[5],[6] Likewise, the photo-Fries rearrangement of naphthyl esters and the Norrish type II photoreaction of 2-alkyl substituted 1,3-diketones are markedly retarded upon complexation with proteins.[7],[8] Conversely, the photoreduction of chlorocarbazoles and the photocyclization of diphenylamines are remarkably enhanced within the protein binding sites.[2],[9] These results point to interesting chemical and biological implications.

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