CHIMIA 1999, 53, No. 5

Chimia 53 (1999) 217

ISSN 0009-4293

Fluorescent Probes for Antioxidants and Host-Guest-Complexation: Fluorazophores

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Abstract. Fluorazophores are novel fluorescent probes based on the azo chromophore in diazabicyclooctene. They are useful for monitoring the kinetics of supramolecular association phenomena like host-guest complexation and antioxidant activity in biological systems.

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Our general area of research is physical organic chemistry, with a specialization in the use of spectroscopic techniques in photochemistry and radical chemistry [1][2]. One timely challenge in our group comprises the development of novel fluorescent probes. Such fluorescent probes are invaluable for sensing supramolecular [3] and biological [4] events. Their advantages include a high sensitivity of detection down to the single-molecule level, excellent temporal and spatial resolution, ease of application, and a wide variety of readily accessible experimental techniques.

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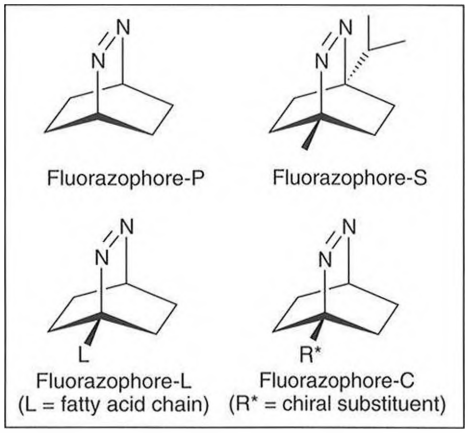
The fluorescent probes are based on diazabicyclooctene, a fluorescent azo chromophore, for which we have coined the name *fluorazophore*. Fluorazophores have the advantage of an exceedingly long lifetime (up to 1 μs) allowing us to monitor processes which are otherwise inaccessible to fluorescent probes due to their short lifetimes (typically < 10 ns). In particular, fluorazophores cannot only be employed to detect and measure naturally relevant concentrations of antioxidants (μM–mM) [4] but also to monitor the absolute kinetics of association with supramolecular host structures [3]. For the latter purpose, we make use of time-resolved spectroscopic techniques in the laboratory of Prof. *J. Wirz* (see this issue).

Fluorazophore-P, the parent compound, is useful for the direct determination of the reactivity and concentration of water-soluble antioxidants such as vitamin C, uric acid, and glutathione [4]. The same compound can also be employed to monitor the kinetics of host-guest complexation in aqueous solution, for example, inclusion into cyclodextrins [3]. Such absolute rate data for entry or association rates are crucial for the development of structure-activity relationships in supramolecular chemistry and are usually more difficult to obtain than conventional thermodynamic quantities like binding constants.

The unique spherical shape of the parent compound is lost in the sterically elaborated Fluorazophore-S [5] which displays the longest fluorescence lifetime. Fluorazophore-P and -S differ in their shape from established fluorescent probes, which are usually based on 'flat' aromatic chromophores. Variations in the complexation characteristics of the different fluorescent probes allow one to obtain valuable structural information regarding the cavity shape and diameter of the host.



Fluorazophore-L, which bears a lipophilic substituent at the bridgehead position, is being developed as a membrane-bound probe for lipophilic antioxidants such as vitamin E and may allow spatial resolution of antioxidant activity by means of fluorescent microscopes [6]. Fluorazophore-C, with a chiral substituent at the same position, is being explored for chiral-recognition purposes [7]. As a rule, fluorescent probes are usually too short-lived to sense the relatively subtle chiral interactions in supramolecular host systems, but the exceedingly long lifetime of fluorazophores provides an improved dynamic range to study such effects.

Received: February 26, 1999

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