

Synthesis and characterization of BODIPY- α -tocopherol: A fluorescent form of vitamin E. R.

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Fluorescent nitrobenzoxadiazole analogues of α -tocopherol (NBD- α -Tocs; $\lambda_{\text{ex}} = 468 \text{ nm}$, $\lambda_{\text{em}} = 527 \text{ nm}$) have been made previously to aid study of the intracellular location and transfer of vitamin E. However, these analogues are susceptible to photobleaching while under illumination for confocal microscopy as well as in in vitro FRET transfer assays. Here we report the synthesis of three fluorescent analogues of α -tocopherol incorporating the more robust dipyrrometheneboron difluoride (BODIPY) fluorophore. A BODIPY-linked chromanol should have no intervening polar functional groups that might interfere with binding to the hydrophobic binding site of the tocopherol transfer protein (α -TTP). A key step in bringing the two ring systems together was a metathesis reaction of vinyl chromanol and an alkenyl BODIPY. An *o*-tolyl containing second generation Grubbs catalyst was identified as the best catalyst for effecting the metathesis without detectable alkene isomerization, which when it occurred produced a mixture of chain lengths in the alkyl linker.

C8-BODIPY- α -Toc **10c** ($\lambda_{\text{ex}} = 507 \text{ nm}$, $\lambda_{\text{em}} = 511 \text{ nm}$, $\epsilon_{507} = 83,000 \text{ M}^{-1} \text{ cm}^{-1}$) having an eight-carbon chain between the chromanol and fluorophore, had the highest affinity for α -TTP ($K_{\text{d}} = 94 \pm 3 \text{ nM}$) and bound specifically as it could not be displaced with cholesterol.