

A GREEN, FLUORESCENT LABELING OF ESTROGENS

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Abstract

Novel 2- or 3-labeled 13 β - and 13 α -estrone derivatives were synthesized via Cu(I)-catalyzed azide-alkyne click reaction (CuAAC). The steroidal alkynes or azides were reacted with the appropriate BODIPY-based fluorescent dyes bearing the complementary functions. The newly synthesized fluorescent estrone derivatives may serve as good candidates for the development of “green” biological assays.

Introduction

Estrogens belong to a class of natural steroids, which possess estrogenic activity. Certain synthetic estrone-derived compounds are described as antitumoral compounds, but the mechanism of their action is mostly unknown [1]. In order to investigate and monitor their mechanism, their labeling is essential. Estrone-based enzymatic or receptorial assays use radioisotope labeling. It would be of particular interest to replace the harmful radioactive methods for greener fluorescent ones. The biological behavior of the fluorescent labeled biomolecules depends on the chemical structure of the conjugate. The size of the fluorescent dye, the linker between the two moieties and the nature of the coupling group may be crucial [2-4].

Results and discussion

Steroids bearing azide or terminal alkyne function and two BODIPY dyes have been synthesized. Estrone was provided with ethynyl function at C-2 via Sonogashira coupling of the steroidal aryl iodide with trimethylsilylacetylene. The steroidal azide was synthesized in a two-step procedure: by alkylation of the phenolic OH group with α,ω -dibromoalkanes and the subsequent nucleophilic substitution of the bromide with azide. Fluorescent dyes based on BODIPY-core were provided with azide or alkyne functional groups. Fluorescent labeling of estrone was efficiently achieved at the C-2 or C-3 position (Fig. 1). The *in vitro* testing of the newly synthesized labeled estrones is under progress.

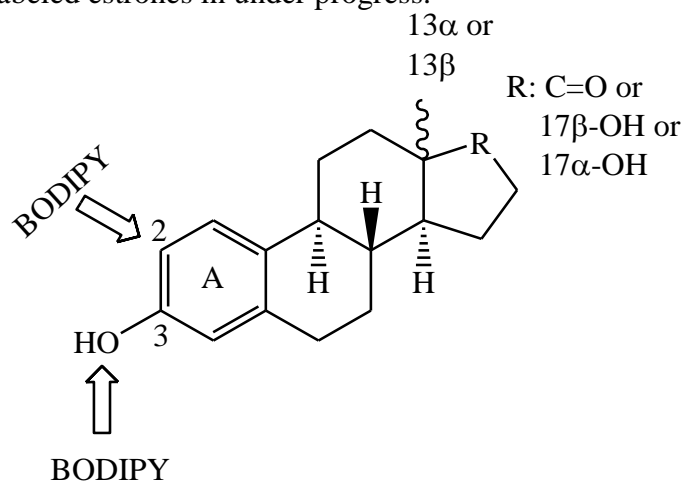


Figure 1. Fluorescent labeling of estrone at positions C-2 or C-3

Conclusion

We have developed an efficient “green” fluorescent labeling procedure for estrone derivatives using Sonogashira and/or CuAAC reactions as key steps.

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