

Synthesis of New Near-infrared Fluorescent Dyes

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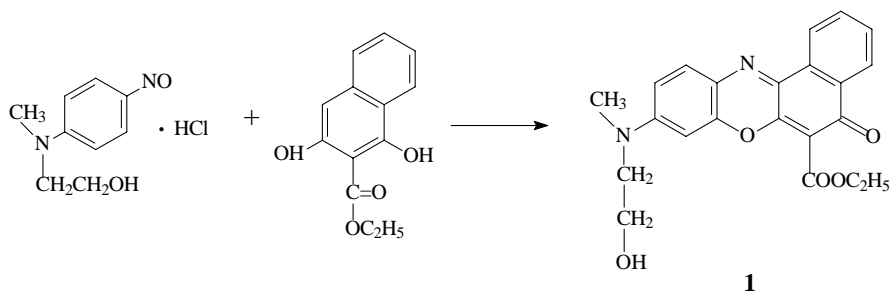
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Abstract: A new near-infrared fluorescent dye, 9-N-(2-hydroxyethyl)-N-methylamino-6-carbethoxy-5H-benzo[a]phenoxazin-5-one **1**, was prepared from the reaction of N-(2-hydroxy-ethyl)-N-methyl-4-nitrosoaniline hydrochloride and ethyl 1,3-dihydroxynaphthoate. Five more fluorescent compounds were synthesized by the reaction of the resulting dye **1** with appropriate amino acid or carboxylic acids.

Keywords: Fluorescent dyes, benzo[a]phenoxazinone, fluorogenic labels.

In recent years, a growing number of scientists are looking for procedures to label biologically important molecules (such as DNA, Proteins, *etc.*)¹⁻³. One efficient way currently exploited is the use of near-infrared fluorescent dyes as fluorogenic labels. Although there are many fluorescent dyes commercially available, only several classes of molecules can be operated in the far-visible or near-infrared region (600-1000nm) which are the areas of low interference. In an attempt to look for new near-infrared fluorescent molecules, our group synthesized a series of benzo[a]phenoxazinone derivatives with strong fluorescence in the near-infrared region.

Scheme 1

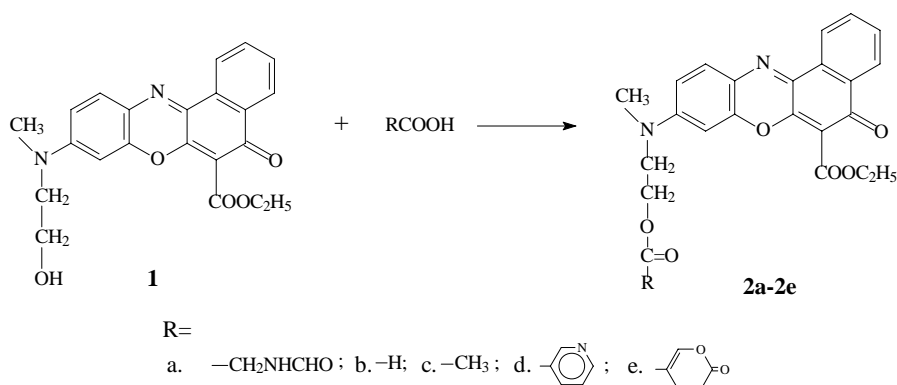


First, a functionalised fluorescent dye, 9-N-(2-hydroxyethyl)-N-methylamino-6-carbethoxy-5H-benzo[a]phenoxazin-5-one **1**, was prepared from the condensation reaction between

N-(2-hydroxyethyl)-N-methyl-4-nitrosoaniline hydrochloride and ethyl 1,3-dihydroxy-2-naphthoate in boiling absolute ethanol for 5 hours (**Scheme 1**). The resulting dye **1** was obtained in 30% yield and has excitation maximum around 580 nm and emission maximum around 630 nm.

Second, five fluorescent compounds **2a-2e**, were synthesized by the reaction of the resulting dye **1**, dicyclohexylcarbodiimide (DCC), a catalytic amount of 4-dimethylaminopyridine (DMAP) and appropriate amino acid or carboxylic acids (**Scheme 2**). This reaction gave **2a-2e** in quantitative yields after being stirred in dry dichloromethane at room temperature for 24 hours. The results implied that this series of compounds may be utilized as fluorogenic labels for biomolecules by covalent bond formation. The fluorescent properties of **2a-2e** were similar to that of **1**. All compounds have been determined by ^1H NMR, MS, and elemental analysis.

Scheme 2



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References

1. G. Patonay and M. D. Antoine, *Anal. Chem.*, **1991**, *63*, 321A.
2. M. S. J. Briggs, I. Bruce, J. N. Miller, C. J. Moody, A. C. Simmonds and E. Swann, *J. Chem. Soc., Perkin Trans.*, **1997**, *1*, 1051.
3. F. V. Bright, *Anal. Chem.*, **1988**, *60*, 1031A.

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