

# Structurally optimized tetrazines for rapid biological labeling

## Introduction

Bioorthogonal chemical reactions are closely associated with the characteristics of “click” chemistry, occurring with high selectivity and fast reaction kinetics *in vivo*.<sup>1,2</sup> Consequently, these reactions found use as multipurpose tools for chemical biology. The Inverse-electron-Demand Diels–Alder (**iEDDA**) reaction between tetrazines and strained alkenes is fairly new ligation reaction, which displays **rates 3-7 orders of magnitude faster** than many bioorthogonal reactions.<sup>3</sup> High reaction rates, biocompatibility, together with the ability of tetrazines to quench fluorescence of some fluorophores, widely used for fluorescent labeling, and recover it after **iEDDA**

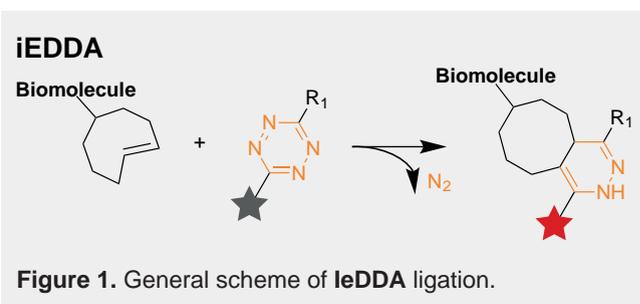


Figure 1. General scheme of **iEDDA** ligation.

reaction (**Figure 1**) make tetrazine derivatives unique and versatile tools for bioorthogonal chemistry. **Figure 2** is showcasing possible approach to modification of commonly used fluorophore as fluorescein (**A**) with tetrazines<sup>4</sup> and application of tetrazine derivatives in DNA encoded libraries technologies (DELT), as the core scaffolds (**B**).<sup>5</sup>

## Application

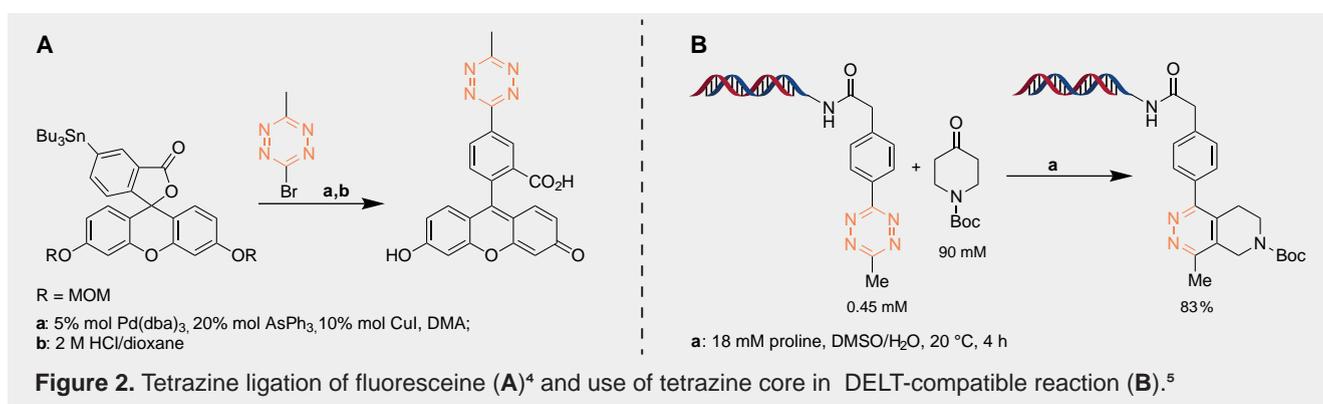
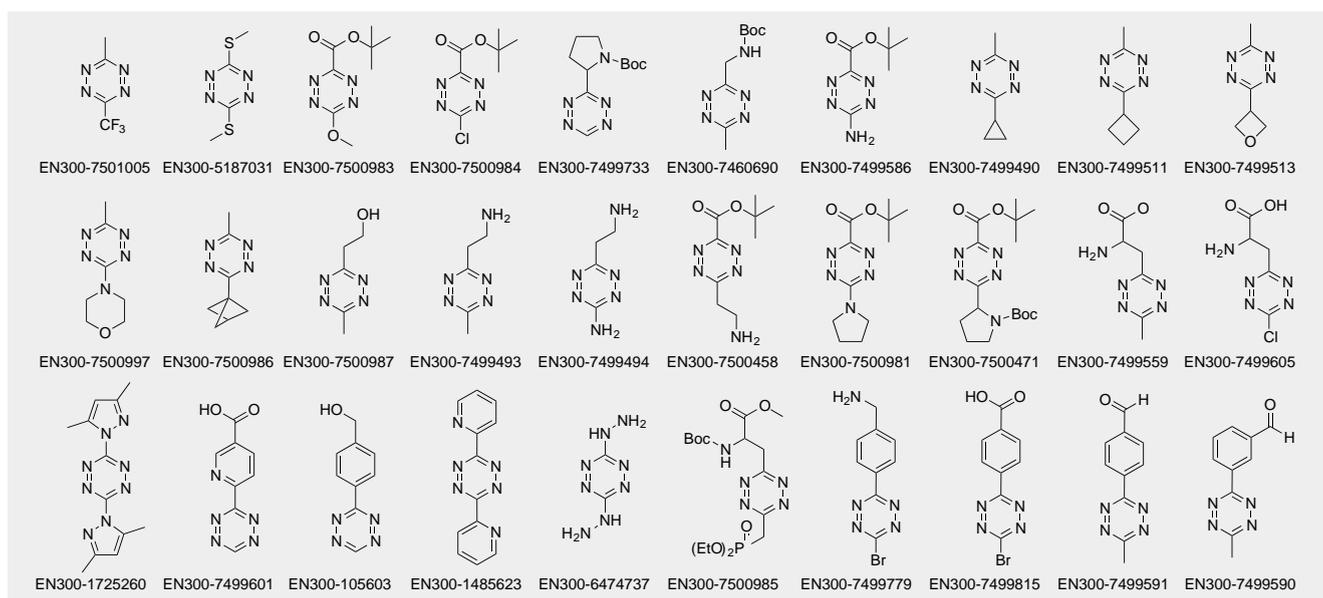


Figure 2. Tetrazine ligation of fluorescein (**A**)<sup>4</sup> and use of tetrazine core in DELT-compatible reaction (**B**).<sup>5</sup>

We offer herein, we propose a diverse library of tetrazine derivatives, carefully selected to match the widest scope of chemical biology challenges (> 30 compounds in stock). Moreover custom synthesis of tetrazine building blocks is available.



## References

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4. A. Wieczorek, *Chem. Sci.* **2017**, 8, 1506.

5. Li, H.; Sun, Z., *Org. Lett.* **2018**, 20 (22), 7186.