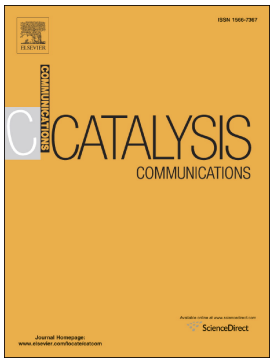

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Jingmiao Yu, Chun Cai

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Photocatalytic oxidative cyclization of α-halo hydrazones with tetrahydroisoquinoline for construction of isoquino[3,4-a][1,2,4]-triazines

Jingmiao Yu, Chun Cai* c.cai@njust.edu.cn
Chemical Engineering College, Nanjing University of Science & Technology, 200 Xiaolingwei, Nanjing 210094, P. R. China

*Corresponding author.

ABSTRACT
A mild and efficient method for the photocatalytic oxidative cyclization of α-halo hydrazones with tetrahydroisoquinoline has been described. This strategy provides a potential protocol for the construction of functionalized isoquino[3,4-a][1,2,4]-triazines in moderate to good yields.
Keywords:
Photocatalysis
Oxidative cyclization
α-Halogeno hydrazine
Tetrahydroisoquinoline
Isoquino[3,4-a][1,2,4]-triazine

1. Introduction

The construction of nitrogen-containing heterocycles is of particular importance due to their prevalence in natural products, agrochemicals, pharmaceuticals, and materials. Among them, 1,2,4-triazines represent a class of privileged heterocycles that frequently encountered in biologically active natural products and pharmaceuticals [1-3]. For example, as illustrated in Fig.1, well-known antiviral drug Azaribine® is structurally based on the 1,2,4-triazine scaffold and various 1,2,4-triazine skeletons have been investigated due to their potential drug application. Driven by their rich biological activities, a plethora of synthetic approaches toward this structures have received considerable attention in synthetic organic chemistry [4]. These unique structures are typically constructed by means of hetero Diels-Alder reactions and 1,3-dipolar cycloadditions [5-7], which suffer from the need of significant amounts of precious metals or harsh reaction conditions.

Recently, α-halogeno hydrazones have been widely explored in building various ring products via cyclization reactions, such as [4 + 1] [8,9], [4 + 2] [10-16], [4 + 3] [17-19] cycloadditions, which can generate electron-deficient dienes (1,2-diaza-1,3-dienes) in situ in the presence of base. For instance, in 2014, Bolm and co-workers [8] realized the first copper-catalyzed formal [4+1] cycloadditions of α-halogeno hydrazones to sulfur ylides for the synthesis of dihydropyrazoles in an

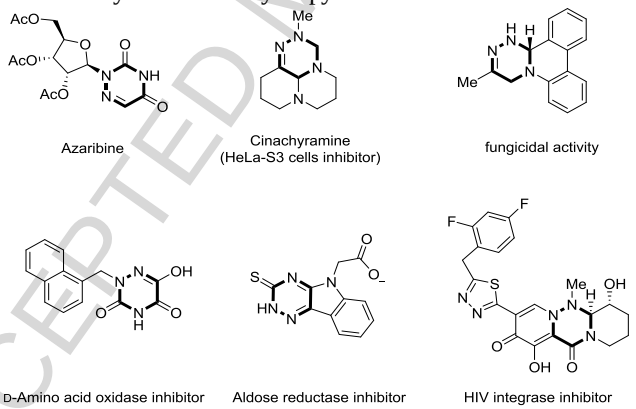

Fig. 1 Selected examples of bioactive 1,2,4-triazine motif in pharmaceuticals

enantioselective manner. Soon after, the Wang group [10] reported the [4+2] cycloaddition of α- halogeno hydrazones to indoles for the preparation of enantiopure [2,3]-fused indoline heterocycles. Besides these, the Xiao group [17] successfully designed a catalyst free [4+3] cycloaddition of α-halogeno hydrazones with C,N-cyclic azomethine imines providing highly functionalized 1,2,4,5-tetrazepine derivatives. Apart from these, our laboratory [20] reported the first photocatalytic radical cyclization of α-halo hydrazones with β-ketocarbonyls for selective synthesis of functionalized 4, 5-dihydropyrazoles (scheme 1a).