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NIS-mediated ring-closure/opening cascade reactions of allylamides: an expedient route to oxazolines

Yancheng Hu, Xincheng Li, Boshun Wan *

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian 116023, China

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ABSTRACT

An unprecedented NIS-mediated ring-closure/opening cascade reaction of allylamides is developed. The substrates with various functionalities were well tolerated and the scope can be extended to allylic carboxylates. Notably, the resulting iodinated chain products are versatile building blocks for the synthesis of oxazolines and epoxides. Furthermore, propargylamides can also undergo this reaction smoothly, providing the corresponding diiodoketones in good yields. The protocol offers a value route to explore new reaction patterns of other functionalized alkenes or alkynes.

1. Introduction

Electrophilic cyclization of functionalized alkynes or alkenes represents an important strategy to directly construct complex heterocycles, which are ubiquitous core structures in abundant naturally occurring products.[1,6f] Among them, halonium-triggered cyclizations of allylamides and propargylamides have been well studied to synthesize oxazoles and their derivatives.[2–6] In 1998, Taguchi et al. reported a general I_2-induced cyclization of allylamide **I** into 5-iodomethyloxazoline **II** through the attack of the amide carbonyl oxygen (Scheme 1, a).[2] Later, the *t*-BuOCl/NaI system was also found to be effective for the same reaction (Scheme 1, a).[3] More recently, Han, Pan and co-workers described a facile NBS-mediated oxidative cyclization of allylamide **I** into 5-bromomethyloxazole **III** (Scheme 1, a).[4] Besides, the iodocyclization of propargylamide **IV** led to 5-iodomethyleneoxazoline **V**,[5] which can be further oxidized into oxazole-5-carbaldehyde **VI** (Scheme 1, b).[6e] Inspired by these results and our previous works,[6] we then reasoned that when *N*-substituted allylamide or propargylamide was submitted to the same conditions, iminium intermediate would be first generated via a 5-*exo*-*mode* cyclization pathway, followed by the attack of other nucleophiles such as H_2O to give the corresponding adducts, which possibly could undergo C–N/C–O bond cleavage to yield linear chain compounds (Scheme 1, c).[7] Just as anticipated, by employing H_2O as the nucleophile and NIS as the iodine source, the cyclization/ring-opening cascade reactions of *N*-tosyl allylamides furnished various iodinated chain tosylamides **2**, whereas that of *N*-tosyl propargylamides gave a series of diiodoketones **4** (Scheme 1, d). Here we report these preliminary results of our studies.

2. Results and discussion

Initially, *N*-tosyl allylamide **1a** was chosen as the model substrate to carry out our investigations. When the reaction was performed in DCM in the presence of NIS and H_2O at room temperature, iodinated chain tosylamide **2a** was obtained in 98% yield (Table 1, entry 1). The structure was unambiguously confirmed by X-ray crystallography.[8] Since this reaction had already given excellent results, we explored the scope of the substrates directly and the results are shown in Table 1. Both electron-withdrawing and electron-donating substituents on the phenyl ring of acyl units were well tolerated, giving the corresponding linear chain products **2b**–**2e** in 80–93% yield. Furyl substrate **1f** underwent this transformation as well, albeit with a slightly lower yield. To our delight, when aliphatic moiety such as methyl was employed in R, the desired product **2g** was obtained in 52% yield. NBS could also trigger the reaction and lead to the formation of **2h** in a nearly quantitative yield. Surprisingly, subjecting *N*-phenyl allylamide **1i** to a mixture of DCM, NIS, and H_2O at −20 °C delivered *para*-iodinated aniline derivative **2i** in a satisfactory yield, which possibly was attributed to the strong electron-donating character of the amino group.[9] *N*-(3-Trifluoromethylphenyl) allylamide **1j** and *N*-(4-methylphenyl) allylamide **1k** could also participate in the reaction to give the desired products **2j** and **2k** in 45% and 60%

* Corresponding author. E-mail address: bswan@dicp.ac.cn (B. Wan).

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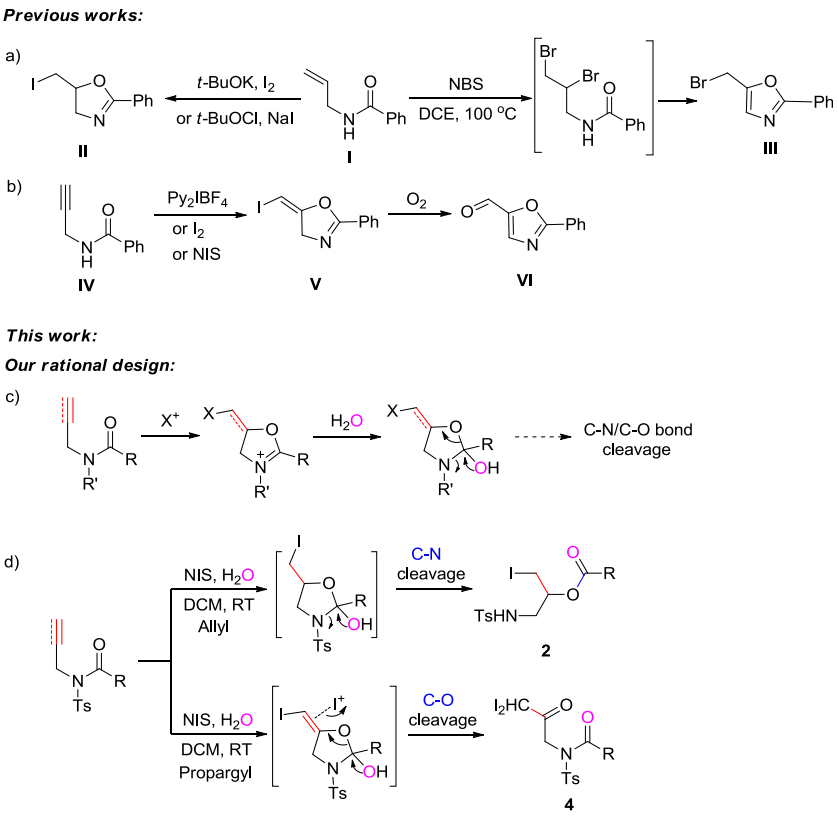
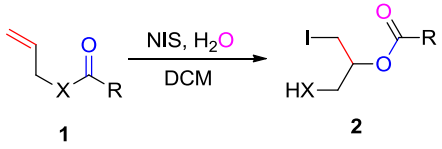
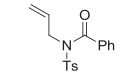
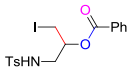
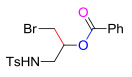
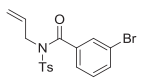
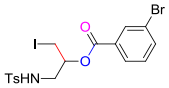
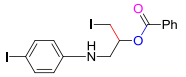
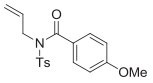
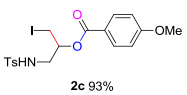
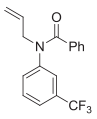
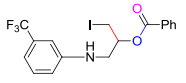
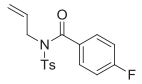
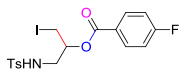
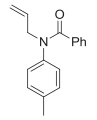
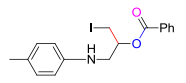
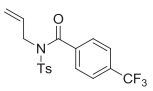
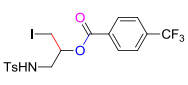
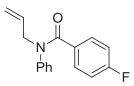
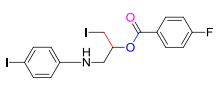


Scheme 1. NIS-mediated ring-closure/opening cascade reactions of allylamides and propargylamides.

Table 1
NIS-mediated ring-closure/opening cascade reactions of allylic substrates[a]



Entry	Substrate **1**	Product **2**	Entry	Substrate **1**	Product **2**
1	 **1a**	 **2a** 98%	8[b]	 **1a**	 **2h** 98%
2	 **1b**	 **2b** 88%	9[c]	 **1i**	 **2i** 80%
3	 **1c**	 **2c** 93%	10[c]	 **1j**	 **2j** 45%
4	 **1d**	 **2d** 88%	11[c]	 **1k**	 **2k** 60%
5	 **1e**	 **2e** 80%	12[c]	 **1l**	 **2l** 81%