



Photochemical functionalization of diazines: metal-free vinylation and phosphorylation



Guillaume Erbland, Jonas Ruch, Jean-Philippe Goddard*

Laboratoire de Chimie Organique et Bioorganique EA 4566, Université de Haute-Alsace, Ecole Nationale Supérieure de Chimie de Mulhouse, 3 bis rue Alfred Werner, 68093 Mulhouse Cedex, France

ARTICLE INFO

Article history:

Received 3 May 2016

Received in revised form 19 July 2016

Accepted 29 July 2016

Available online 3 August 2016

Keywords:

Photochemistry

Diazines

Radical chemistry

Photo-Arbuzov reaction

Diazinyl phosphonate

ABSTRACT

Under mild UVA irradiation, the C–Br bond of bromodiazines can be activated to generate the corresponding radical intermediate. In the presence of alkynes, alkenylation reactions occurred to afford vinyl pyrimidine in moderate yields. Csp²-phosphorous bond can also be easily created in a photochemical version of the Arbuzov reaction. With UVA and a stoichiometric amount of trimethyl phosphite, the corresponding phosphonates were isolated in good to high yields. Very interesting selectivities were observed under these mild irradiation conditions. Functionalized substrates can be engaged and the resulting products could be further derivatized.

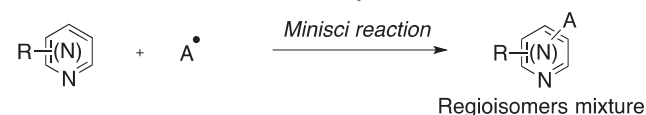
© 2016 Elsevier Ltd. All rights reserved.

1. Introduction

Diazines are π -deficient heteroaromatic compounds having a huge scope of applications.¹ In the fields of medicinal chemistry, material science, organic electronics and optoelectronics or agrochemistry, these valuable scaffolds are well recognized for their abilities to promote, for example, molecular recognition, metal coordination or chromophore polarizability.² Thus, the fast and efficient access to molecules containing diazinyl moiety is of primary importance. Chemical alterations of diazines have been reported by using ionic, organometallic and radical transformations.³ Metalations of such electro-deficient heterocycles generally involved over-stoichiometric amount of strong organometallic bases such as organolithium or Grignard reagents with low functional group tolerance.⁴ Transition metal catalysis allowed the C–H and C–X bond activations (X=halogen, triflate, ...) in cross-coupling reactions (arylation, vinylation, ...).⁵ However, some limitations appeared with electron-poor heteroarenes containing coordinating atoms like nitrogen or sulfur. Radical processes proved to be very powerful alternatives.⁶ For example, the Minisci reaction consists in the addition of a nucleophilic radical onto an electron-poor heteroarene.⁷ Because radical reactions are highly tolerant with number of organic functions, they are suitable for selective functionalization

of complex compounds. Thus, late derivatization of high value molecules would be possible through radical process that could be problematic through direct metalation. Radical additions onto an aromatic system as acceptor suffer from a lack of regioselectivity, which is highly dependent to the substitution pattern (Scheme 1). The location of the reactive radical center is a way to solve this selectivity issue. Then, the heteroarene becomes the donor, which is able to react with a radical acceptor.

The valuable substrate is the acceptor



The valuable substrate is the donor



Scheme 1. Strategies for aromatic functionalization through radical reaction.

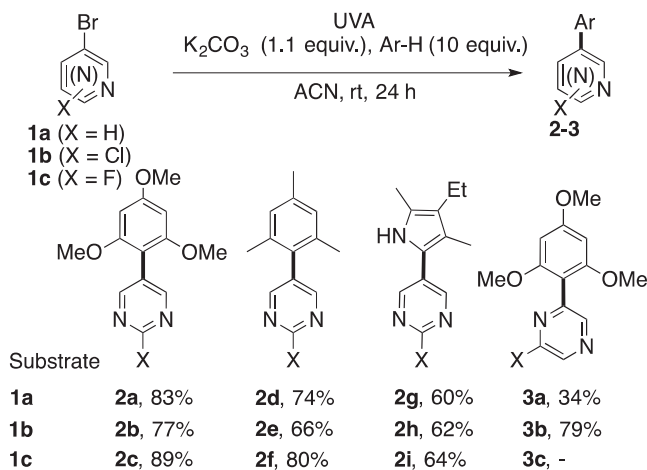
As an alternative to toxic radical chain mediators or over-stoichiometric amount of reagent, photochemistry is an appealing pathway to promote radical reactions. By selecting the right irradiation system, very selective transformations can be designed.⁸

* Corresponding author. E-mail address: jean-philippe.goddard@uha.fr (J.-P. Goddard).

Moreover, high functional group tolerance could also be obtained by using long wavelengths such as UVA and visible light irradiations.⁹ In some cases, it might need a photosensitizer, especially with visible light, that can also generate byproduct and waste. As a part of a research program dedicated to the functionalization of heteroaromatic compounds, we focused on methodologies with low environmental impact and high synthetic potential. Thus, we decided to investigate the behavior of diazines under photochemical conditions.¹⁰ We focused on C–C and C–P bond formation by using light as the only ‘promoter’ of the reaction.

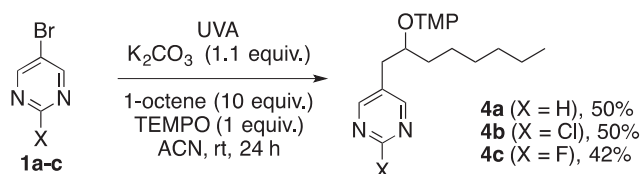
2. Results and discussion

Recently, we found very convenient conditions for the photoarylation of diazines.¹¹ After optimization we were able to conduct arylation of pyrazine and pyrimidine compounds from the corresponding bromides (Scheme 2).¹² Mild UVA irradiation was used in the presence of potassium carbonate (1.1 equiv) as the sole additive. Biaryl compounds were obtained in good to high yields with excellent selectivities. The irradiation system we used was a medium pressure mercury lamp (100 W) equipped with a hypercaloric filter, which cut wavelengths below 340 nm. The same photochemical system was used for the transformation reported in the present manuscript. Halogen substitution either on the diazine or on the aryl acceptor was tolerated as well as free pyrrole. Thus, this photoarylation reaction allowed to access compounds, which can be further derivatized by ionic or organometallic processes.



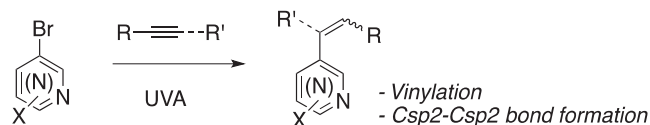
Scheme 2. Biaryl formation under photochemical conditions.

Our photochemical functionalization of diazines was extended to tandem reaction. Under the optimized conditions, aryl acceptors were changed to 1-octene (Scheme 3). Addition on the olefin occurred and the resulting secondary alkyl radical was trapped with TEMPO. Previously, we reported this oxoarylation of octene with pyrimidine in 50% yield. Similar yields were obtained with the 2-chloro and 2-fluoro pyrimidinyl radical and the corresponding products **4b** and **4c** were isolated in 50% and 42% yield, respectively.



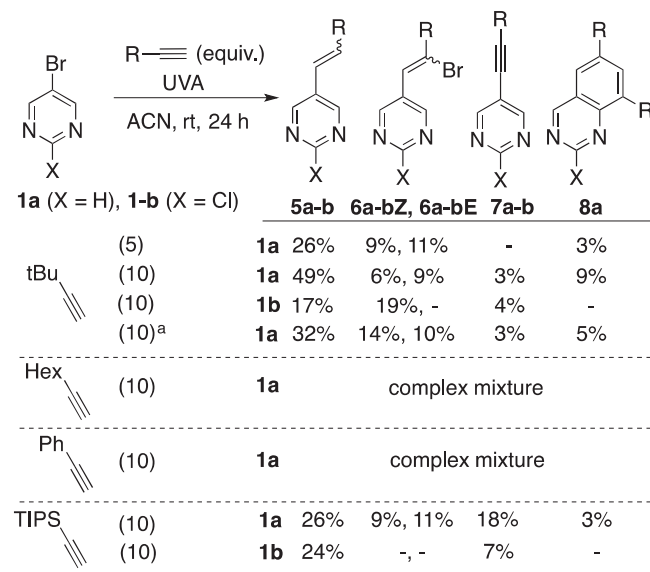
Scheme 3. Alkoxyarylation of 1-octene with pyrimidines derivatives.

While arylation and alkylation of diazine proceeded smoothly under mild photochemical conditions, we decided to investigate the alkenylation by radical addition onto alkynes (Scheme 4).



Scheme 4. Alkenylation of diazines.

In a first task, we irradiated 5-bromo pyrimidine with *t*-butyl acetylene (5 equiv) as acceptor in acetonitrile (Scheme 5). We were able to isolate the alkenylation product **5a(t-Bu)** in 26% yield and a 95:5 *E:Z* ratio. **6a(t-Bu)** and **6b(t-Bu)** were also obtained in 9% and 11% yields, respectively. They could originate from a bromine atom transfer reaction. A very low yield of 3% was obtained for quina-zoline **8a(t-Bu)**, resulting from the incorporation of two *t*-butyl acetylene moieties. By increasing the amount of radical acceptor to 10 equiv, the formation of **5a(t-Bu)** was improved to reach an encouraging 49% yield as well as the interesting quina-zoline **8a(t-Bu)** (9%) and the formal alkynylation compounds **7a(t-Bu)** (3%). Unfortunately, we were not able to promote the formation of **8a-b(t-Bu)** even by adding potassium carbonate or by changing the electronic properties of the pyrimidine moieties (with **1b**).



^a With 1.1 equivalent of K₂CO₃

Scheme 5. Additions of pyrimidinyl radicals onto alkynes.

Changing *t*-butyl acetylene by 1-octyne or phenyl acetylene resulted in the observation of unseparable mixtures. With triisopropylsilyl acetylene, comparable results were obtained than with *t*-butyl acetylene except a larger amount of alkynylation product **7a(TIPS)**, isolated in 18% yield. In spite of the low efficiency of the photoalkenylation, we proved that our method is attractive in the context of diazine functionalization and further investigation will be done in order to optimize the formation of Csp²-Csp² bond.

The formation of Csp²-heteroatom bond is a crucial transformation, especially on diazines. The classical way consists in aromatic nucleophilic substitution even if transition metal catalysis is used in recent developments. Concerning the formation of Csp²-P bond, secondary phosphonate have been used with aryl bromide or triflate in catalyzed cross coupling reactions.¹³ For very electro-

Download English Version:

<https://daneshyari.com/en/article/5212961>

Download Persian Version:

<https://daneshyari.com/article/5212961>

[Daneshyari.com](https://daneshyari.com)