



Short communication

A mild acid-free one-pot reaction for synthesis of new phenanthridine dyes



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ABSTRACT

A series of new phenylphenanthridin dyes have been synthesized in the yields of 52–75% by a mild strategy in one-pot reaction. This is the first successful attempt to perform efficient soft acid-free reaction for phenanthridine ring construction. A large substrate scope was well demonstrated.

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1. Introduction

The phenanthridine family is widely found in medicinal chemistry and material science because of the biological activity and the presence in a variety of significant natural products and synthetic dye-stuffs [1]. So far, various synthetic strategies have been developed such as Bischler–Napieralski cyclization and Heck cyclization for the robust synthesis of phenanthridines [2]. However, the reported approaches remain the extreme difficulties including the multi-step routes, the limited substrate scopes, the use of metal catalysts or the weak generalities/limited diversities [3–5]. Therefore, there is a great demand to develop a simple, convenient protocol for expeditious synthesis of phenanthridine derivatives.

Phenanthridine could be accessed by Pictet–Spengler reaction

under various reaction conditions such as Lewis acids [6], Bronsted acids [7], tandem threefold reaction condition [8]. In 2009, Youn and the coworker found the trifluoroacetic acid (TFA)-mediated coupling reaction of 2-arylanilines with arylaldehydes for the synthesis of phenanthridines [9]. Some efforts were devoted to improve the reaction conditions [10], however, strong acid catalysis was still required.

In this letter, we describe a new entry for the efficient synthesis of phenylphenanthridine dyes by an acid-free one-pot reaction at room temperature under air atmosphere. In this way, 2'-amino-1,1'-biphenyl-3-ol reacts with different benzaldehydes to yield the target phenylphenanthridine dyes. To the best of our knowledge, this is the first successful attempt to perform one-pot reaction at mild acid-free conditions for synthesis of phenanthridine dyes.

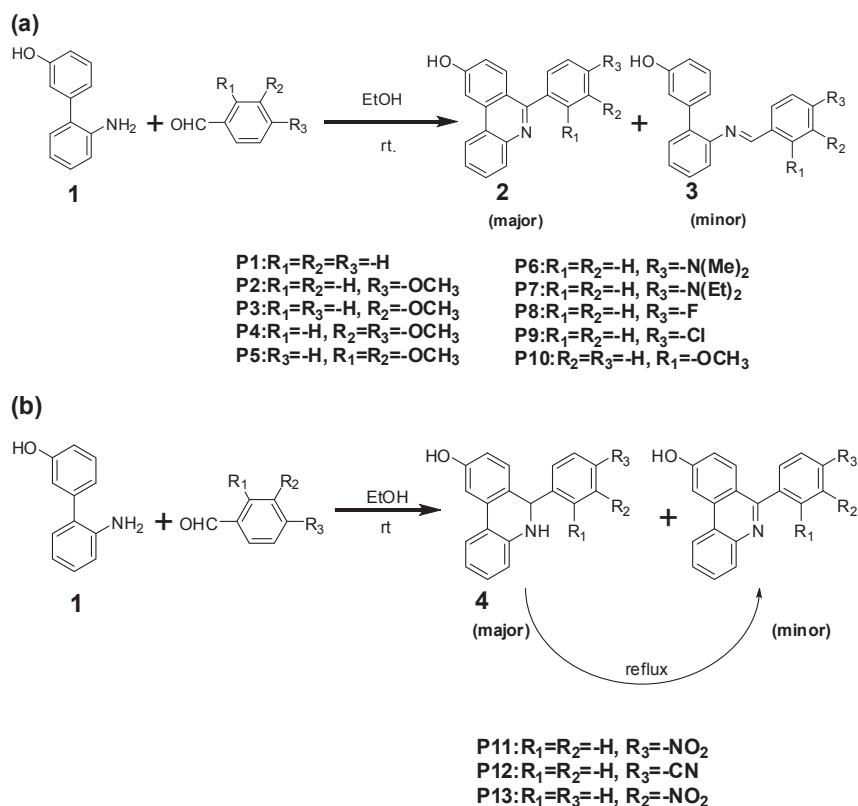
2. Results and discussion

The substrate **1** (shown in Scheme 1) was obtained by directly condensing 3-hydroxyphenylboronic acid and 2-bromo aniline via Suzuki reaction without protecting amino group in 90% isolated yield, which was used to undergo the reaction with benzaldehydes at room temperature under air atmosphere. The isolated major products and the yields of the above reactions are listed in Table 1. It

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Scheme 1. Synthesis of phenanthridine dyes with different electron donating or accepting substrates by one-pot reaction.

is shown that phenanthridine dyes **2** are the major products with the yields from 52% to 75% produced by various benzaldehydes, while the condensed products **3** could be isolated as the minor products (~10%) only in some reactions, such as 2'-amino-1,1'-biphenyl-3-ol reacted with the 2-methoxybenzaldehyde (Scheme 1(a)).

Fig. 1(a) gives the representative 1H NMR spectra of the phenanthridine dye **P1**. There are two separated peaks at 8.615 ppm of 1H NMR chemical shift, suggesting the absence of imino group. The 1H NMR spectral integration area ratio of different hydrogen atoms is consistent with that of the numbers of hydrogen atoms.

The molecular structures of the yielded phenanthridine dyes were further confirmed by single crystals obtained by the vapor diffusion of *n*-hexane into the solution in dichloromethane. The typical X-ray single crystal diffraction of **P1** shows the presence of phenanthridine ring, which is defined by the small torsion angle of C6-C7-C8-C13 (1.06°). Hence, the fused three aromatic rings (A, B, C) are almost in a plane. In addition, we notice a dihedral angle of 58.95° between the fused three aromatic rings (A, B, C) and aromatic ring D (Fig. 2(a)).

Table 1 shows that the main target phenanthridine dyes and the yields are not greatly varied by different electron-rich or -deficient benzaldehydes. The unhydrogenated phenanthridines are the major products while the aromatic aldehydes are substituted by electron-donating groups. In addition, the substituted positions of the groups in the benzaldehydes caused negligible effects on the reaction (Table 1, **P2**, **P3**, **P10**).

It is noticed that the hydrogenated phenanthridines become the predominant products as the benzaldehydes carry the strong electron-withdrawing groups such as nitro and cyano groups, while

the unhydrogenated phenanthridines are the minor products (Scheme 1(b), Table 1). On the other hand, the hydrogenated phenanthridines can be converted into unhydrogenated phenanthridines as the temperature was raised (under reflux), which indicates the presence of a large reaction energy barrier.

The chemical structures of the hydrogenated phenanthridines were identified by 1H & ^{13}C NMR spectra. As shown in Fig. 1(b), the 1H NMR chemical shifts of 5.565 ppm and 6.712 ppm in **P11** can be assigned to $-NH-$ and its adjacent $-CH-$ groups, respectively. X-ray single crystal diffraction of **P11** further confirms the structures of hydrogenated phenanthridines (Fig. 2(b)).

It is found that the phenanthridine dyes could be produced by this reaction in a variety of organic solvents. However, a much longer reaction time (75 h) was required in aprotic solvents such as benzene, tetrahydrofuran and acetonitrile, which only produced a dramatic low yields of phenanthridines (<10%), and a higher yields of the main condensed products (60–75%).

As discussed, a shorter time (18 h) and a higher yield of the reaction were found in alcoholic solvents, particularly in methanol and ethanol solvents. However, the phenanthridine dyes were obtained in lower yields in *n*-propanol and *n*-butyl alcohol solvents (30–40%). Furthermore, the yields of phenanthridine dyes reached ~30% as the reaction was performed in mixed solvents of methanol or ethanol and tetrahydrofuran (1:1, v:v) with a longer time (46 h).

In addition, the reaction time could be reduced by the increase of the reaction temperature, while the yields of the phenanthridine dyes were not increased remarkably. It is further observed that the same reaction occurred under oxygen or argon atmosphere in ethanol or methanol. It is also found that the target phenanthridine

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