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Sulfuric acid immobilized on silica: A versatile and reusable heterogeneous catalyst for the synthesis of phenanthrimidazole derivatives

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Abstract

A new, convenient, efficient, and cost-effective one-pot synthesis of 1*H*-phenanthro[9,10]imidazol-2-yl from phenanthraquinone and aldehydes, using sulfuric acid immobilized on silica as catalyst is described. The present methodology offers several advantages such as excellent yields, simple procedure, shorter reaction times, the use of inexpensive reagents, easy recovery and eco-friendly. In addition to these, 2-alkyl phenanthrimidazole is obtained from triethyl orthoesters in good yields.

Keywords: 1H-phenanthro[9,10]imidazol-2-yl; Phenanthraquinone; Triethyl orthoesters; Sulfuric acid.

1. Introduction

Imidazoles are important heterocycles in medicinal chemistry. Imidazoles display a broad spectrum of biological activity which has made them privileged structures in combinational drug discovery libraries. The biological roles of imidazole such as antivirial, antiulcer, antihypertension, and anticancer properties are well documented [1]. They have also found application as a chromophore with high extinction coefficient, readily tuneable absorption wavelength, and fluorophoric properties and is desirable as a large planar synthetic building block in supramolecular chemistry [2].

In literature, there have been many solution-phase and solid-phase condensation of benzil and aldehydes in the presence of ammonia source to generate 2,4,5-trisubstituted imidazole [3,4]. In most cases, however, such reactions are carried out in AcOH or H_2SO_4 medium by refluxing for several hours. Obviously, such reaction conditions bring heavy burden to environment and equipments as well as dangerous operation. Besides, an additional acidic catalyst was indispensable for condensation in solvent-free pattern [5].

Recently, efficient synthesis of imidazoles from aldehydes, 1,2-diketones, and ammonium acetate in acetic acid have been reported [6]. The synthesis of 2,4,5-triaryl imidazole from aryl aldehydes and 1,2-diketones or α-hydroxy ketone in the presence of ionic liquid and silica

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sulfuric acid have also been described [7]. A variety of solid supports such as alumina, KSF, silica gel, bentonite, montmorilonite K10 and KSF were tested for the synthesis of 2,4,5-triaryl imidazoles under microwave irradiation [5].

Aside from the early reports, the synthesis of phenanthrimidazoles [8] from phenanthraquinone and an aromatic aldehyde, has received little interest. The formation of 2-substituted phenanthrimidazole from phenantharaquinone (1), certain aromatic aldehyde and aqueous ammonia was first noted by Japp and Streatfield [9-13]. It must be noted, however, that Japp's method is not a general one, since oxazole formation is favored rather than imidazole formation. It was found that when phenanthraquinone and an aldehyde were refluxed in glacial acetic acid solution containing ammonium acetate, excellent yields of 2-substituted phenanthrimidazoles resulted.

Recently some methods for synthesis of imidazoles are reported [14-17]. However, some of these methods have suffered from one or more drawbacks like high temperature requirement, highly acidic conditions, poor yields, prolonged reaction time period, use of hazardous and often expensive acid catalyst. Thus, simple efficient and flexible protocol for the synthesis of imidazoles are still in need as there is a scope for further improvement towards milder reaction conditions, development of simple and inexpensive reagents, convenient procedures and higher product yields.

During the recent years, the use of reusable heterogeneous catalysts has received considerable importance in organic synthesis because of their environmental, economical and industrial aspects [18]. The development of efficient methods using recoverable and reusable catalysts is an important goal in organic chemistry especially in asymmetric synthesis. Up to now, several reusable and heterogeneous catalysts have been designed and used. Metal colloids, mineral clays and supported reagents on silica gel, alumina and other solid supports are some common examples of heterogeneous catalysts that have extensive applications in organic transformations. These catalysts have attracted a great deal of attention due to their ease of handling, enhanced reaction rates, greater selectivity and simple work up in most cases [19].

Recent reports on the utilization of H_2SO_4–silica in various organic reactions [20], including the acetylation of aliphatic and aromatic alcohols [21], acetalation-acetylation of sugar derivatives [22], selective hydrolysis of the terminal *O*-isopropylidene group of sugar derivatives [23], synthesis of [1,2,4] triazine-4-on derivatives [24], Fischer type glycosylation [25], solvent free regioselective cyclization of 3-Allylmercapto-1,2,4-Triazoles to Thiazolo[3,2-b]1,2,4-Triazoles [26], vapor phase nitration of benzene [27], prompted us to investigate its use as an alternative promoter to synthesize phenanthrimidazole derivatives.

2. Experimental

2.1. Materials and apparatus

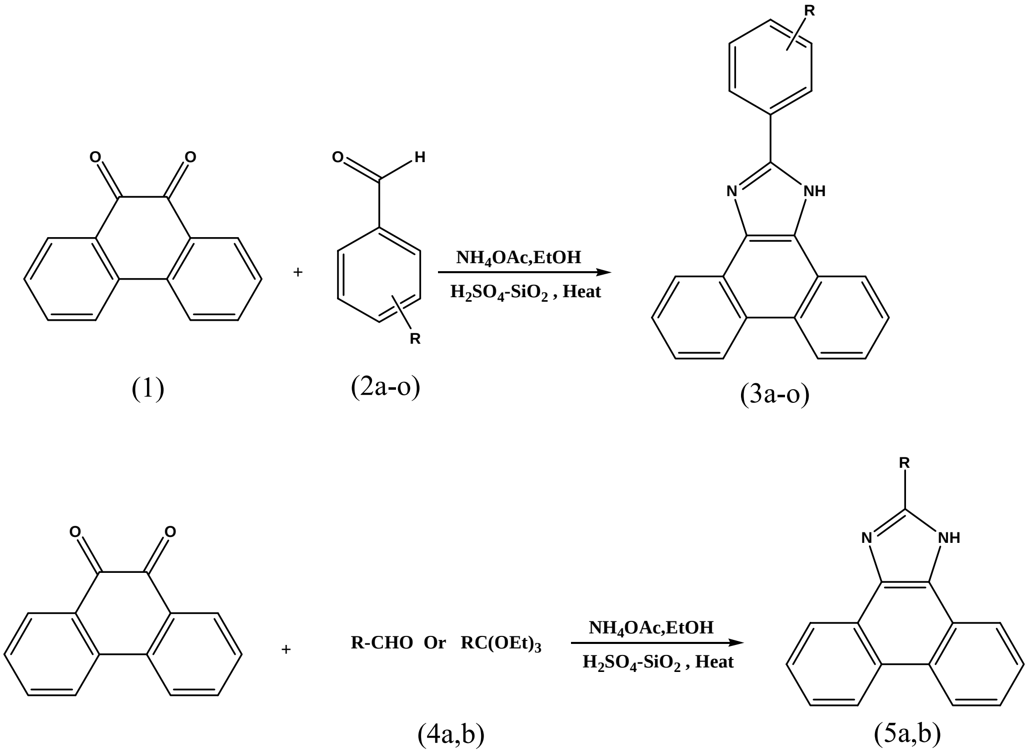
All yields refer to isolated products and all of products were known and characterized by comparison of their physical and spectral data with those of already reported [8,28]. Melting points were measured on an electrothermal Stuart SMP3. Infrared spectra were recorded as KBr pellets on a Bruker Tensor 27 spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker AC 100 spectrometer at 100 MHz with d_6-DMSO as the solvent and TMS as the internal standard. The mass spectra were scanned on a Varian Mat CH-7 instrument at 70 ev. The other materials were purchased from Fluka.

2.2. General procedure

To a solution of the starting materials (1 mmol) and NH_4OAc (3 mmol) in ethanol (10 mL), H_2SO_4-silica [22] (100 mg) was added and the mixture was stirred at reflux temperature for 20 min. Completion of reaction was indicated by TLC. After complete conversion, the mixture was filtered to remove catalyst. On cooling, the desired product was obtained. The structures of products were deduced by comparison with authentic samples.

3. Results and discussion

In continuation of our efforts towards developing new reagent systems for synthesis of phenanthrimidazoles [28], we found that H_2SO_4–silica could act as a good protic acid source under milder and safer conditions than other catalysts such as molecular iodine.



(1) (2a-o) (3a-o)

(4a,b) (5a,b)

Scheme 1

In a model condensation reaction, phenanthraquinone (1) and benzaldehyde (2a) were stirred in different solvents at reflux temperature. Among different solvents (EtOH, THF, CH_3CN, toluene) screened, EtOH was demonstrated as the best solvent. In addition to the simplicity of the product isolation, the catalyst can be recycled several times. Over three cycles, the catalyst did not show any significant change in reactivity.

Beside, we used triethyl orthoesters instead of aliphatic aldehydes. There is no any report in the literature using triethyl orthoester as the starting material for the synthesis of phenanthrimidazoles. We found that our methodology works very well for triethyl orthoesters. Consequently, the use of triethyl orthoester in our methodology constitutes a significant improvement in the synthesis of 2-alkyl phenanthrimidazoles.

4. Conclusion

In conclusion, a very simple, efficient and eco-friendly synthesis of 1*H*-phenanthro[9,10]imidazol-2-yl has been devised. Several derivatives of the title compounds with different substituents were synthesized to show the diversity of the method. This method offers several advantages including high yield of products, short reaction time, recyclability of the catalyst and easy experimental work-up procedure.

Table 1

H_2SO_4-Silica catalyzed synthesis of phenanthrimidazole derivatives.

Product	R	Yield (%)	m.p. (ºC) [lit.]	Ref.
3a	H	90	316 [314-315]	8
3b	4-Me	95	285-286[287-288]	28
3c	3-Me	95	259-260 [260-260.5]	28
3d	4-OH	90	> 350 [>360]	8
3e	3-OH	95	344-345 [343-344]	8
3f	2-OH	85	287-288 [287-287.5]	8
3g	4-OMe	90	259-260 [254-255]	8
3h	2-OMe	85	215-216 [214-215]	8
3i	4-NO_2	90	338-340 [341]	8
3j	3-NO_2	88	272-273[271.5-272]	8
3k	2- NO_2	85	268-269 [267]	8
3l	2-Cl	88	236-237 [235-235.5]	8
3m	3-Cl	90	157-158 [155-156]	8
3n	4-Cl	92	348-349 [349-350]	8
3o	4-NMe_2	95	258-259 [259-260]	8
5a	H	90	290-291 [292]	8
5b	Me	92	223-224 [222-225]	28

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