Heterocycl. Commun., Vol. 17(5-6), pp. 223–226, 2011 • Copyright © by Walter de Gruyter • Berlin • Boston. DOI 10.1515/HC.2011.040

Sulfamic acid as an efficient and cost-effective catalyst for the synthesis of 2,4,5-triarylimidazoles and 2-arylphenanthrimidazoles

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Abstract

A simple and efficient synthesis of 2,4,5-triarylimidazoles and 2-arylphenanthrimidazoles was developed using the one-pot, three-component condensation reaction of an aromatic aldehyde, benzil or 9,10-phenanthroquinone and ammonium acetate in refluxing ethanol in the presence of the catalyst sulfamic acid.

Keywords: one-pot condensation; phenanthrimidazoles; sulfamic acid; 2,4,5-triarylimidazoles.

Introduction

Substituted imidazoles have gained remarkable importance as herbicidal (Viktor et al., 1975), fungicidal (Heeres et al., 1979), anti-inflammatory (Lombardino and Wiseman, 1974) and antibacterial agents (Sharma et al., 2009) and as inhibitors of P38 MAP kinase (Laufer et al., 2010). In addition, imidazole derivatives have been widely used as precursors to *N*-heterocyclic carbenes in organometallic catalysis and as ionic liquids in green chemistry (Kim et al., 2005; Jiménez et al., 2008). Several substituted imidazoles also show cardiovascular and antitrypanosomal activities (Malhotra et al., 2011; Samant and Sukhthankar, 2011). In light of these properties, the synthesis of substituted imidazole derivatives has received considerable attention in recent years.

2,4,5-Triphenylimidazole was first synthesized more than a century ago by the three-component condensation of a 1,2-dicarbonyl compound, aldehyde and ammonia (Japp and Robinson, 1882; Radziszewski, 1882). Recently, numerous synthetic methods for the preparation of analogous compounds have been developed using similar three-component condensation in the presence of different catalysts. These catalysts include molecular iodine (Kidwai et al., 2007; Behmadi et al., 2009), trifluoroacetic acid (Mohammadizadeha et al., 2009), scolecite (Gadekara et al., 2009), L-proline (Samai et al., 2009), ytterbium perfluorooctanesulfonate (Shen et al., 2008), tetrabutylammonium bromide (Chary et al., 2008), silica sulfuric acid (Shaabani et al., 2007), indium trichloride (Sharma et al., 2008), potassium dodecatungstocobaltate (Nagarapu et al., 2007) and silica perchloric acid (Kantevari et al., 2007). The reaction can also be performed in acetic acid under reflux conditions (Puratchikody and Doble, 2007), under microwave irradiation (Chauveau et al., 2010; Damavandi, 2011) and in ionic liquid (Zang et al., 2010).

In recent years, sulfamic acid (NH_2SO_3H) has successfully been used as a solid acid catalyst for various organic synthetic transformations (An et al., 2007; Heravi et al., 2007; Heydari et al., 2007; Kamal et al., 2007; Li et al., 2007; Upadhyaya et al., 2007; Mitragotri et al., 2008). The benefits of its use include low cost, eco-friendliness, ease of handling, low toxicity, excellent product yields and high reactivity. These features prompted us to explore the three-component condensation reactions of aldehydes, benzil or 9,10-phenantherenquinone and ammonium acetate in the presence of a catalytic amount of NH_2SO_3H to synthesize the corresponding 2,4,5-triarylimidazoles and 2-arylphenanthrimidazoles.

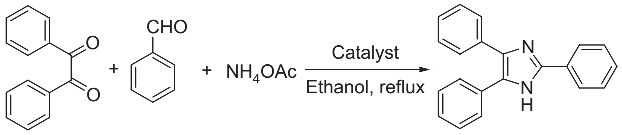
Results and discussion

Different acidic catalysts in the reaction of benzaldehyde (2 mmol), benzil (2 mmol) and ammonium acetate (6 mmol) were compared (Table 1). The catalysts included F_3CCOOH, H_3BO_3, CH_3SO_3H, p-$CH_3C_6H_5SO_3H$, NH_2SO_3H and p-$NH_2C_6H_5SO_3H$, each at an amount equal to 10 mmol%. As can be seen from entries 1–6, NH_2SO_3H is the most effective catalyst in terms of product **4a** yield (85%). Next, the amount of NH_2SO_3H was varied and it was found that 10 mmol% of the catalyst was the optimal quantity for catalysis. The yield was further improved by increasing the amount of NH_4OAc from 6 mmol to 10 mmol (entry 11).

Next, a wide range of substituted benzaldehydes were tested under the optimized conditions. The results are given in Table 2. Interestingly, the electronic properties of the substituents have virtually no effect on yields. More specifically, the reaction of a benzaldehyde with an electron-donating or an electron-withdrawing group furnishes product **4** in high yield.

In a similar way, phenanthraquinone **5** was allowed to react with five substituted benzaldehydes. As shown in Table 3, these reactions produce the desired 2-arylphenanthrimidazoles **6** in excellent yields, and the substituent on the aldehyde,

Table 1 Optimizing the reaction conditions[a].



1 2 3 4a

Entry	Catalyst	Catalyst (mmol%)	NH_4OAc (mmol)	Time (h)	Yield (%)[b]
1	F_3CCOOH	10	6	5	65
2	H_3BO_3	10	6	5	69
3	CH_3SO_3H	10	6	5	73
4	p-$CH_3C_6H_5SO_3H$	10	6	5	77
5	p-$NH_2C_6H_5SO_3H$	10	6	5	80
6	NH_2SO_3H	10	6	5	85
7	NH_2SO_3H	2.5	6	5	75
8	NH_2SO_3H	5	6	5	80
9	NH_2SO_3H	15	6	5	85
10	NH_2SO_3H	10	8	5	89
11	NH_2SO_3H	10	10	4	93

[a]The amount of benzaldehyde was 2 mmol and benzil was 2 mmol; [b]isolated yields.

whether electron-donating or -withdrawing, has no effect on the yield.

Conclusions

We have developed a simple and efficient three-component condensation reaction for the synthesis of 2,4,5-triarylimidazoles and 2-arylphenanthrimidazoles using sulfamic acid as an efficient, cost-effective and eco-friendly catalyst.

Experimental section

General

Melting points were determined on X4 melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded using KBr discs on a Nicolet 6700 fourier transform infrared (FT-IR) spectrophotometer. ^{1}H-NMR spectra were recorded on the Varian Inova-300 MHz spectrometer using tetramethylsilane (TMS) as internal standard and DMSO-d_6 as a solvent. Mass spectra (EI, 70 eV) were obtained on a Shimadzu SIL-10A Auto Injector liquid chromatography-mass spectrometry (LC-MS). Thin layer chromatography (TLC) was carried out on GF254 silica gel plates.

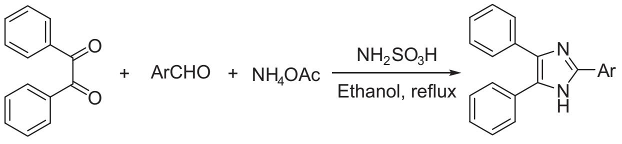
General procedure for the preparation of 2,4,5-triarylimidazoles 4 and 2-arylphenanthrimidazoles 6

A mixture of benzil or phenanthraquinone (2 mmol), a benzaldehyde (2 mmol), ammonium acetate (10 mmol) and sulfamic acid (10 mmol%) in ethanol (10 ml) was stirred and heated under reflux until the reaction was completed as monitored by TLC. Then, the mixture was poured onto crushed ice and the resulting solid was filtered and crystallized from ethanol. Known compounds **4a–k** (Table 2), **6a** and **6g** (Table 3) showed ^{1}H nuclear magnetic resonance (NMR) spectra that were virtually identical with those reported.

2-(4-Trifluoromethylphenyl)-4,5-diphenyl-1*H*-imidazole (4l) White crystals; ^{1}H NMR: δ 8.27 (d, *J*=8 Hz, 2H), 7.83 (d, *J*= 8 Hz, 2H), 7.59–7.18 (m, 10H); IR: 3402, 3057, 1602, 1588, 1496, 1441 cm^{-1}; MS: m/z 365 ([M+1]$^+$, 100).

2-(2,4-Dichlorophenyl)-1*H*-phenanthro[9,10-*d*]imidazole (6b) White crystals; ^{1}H NMR: δ 8.84 (d, J=8 Hz, 2H), 8.59 (d, J= 8 Hz, 2H), 7.94 (d, J=8 Hz, 1H), 7.87 (s, 1H), 7.73–7.60 (m, 5H); IR: 3440, 3083, 1614, 1588, 1515 cm^{-1}; MS: m/z 363 (M$^+$, 100).

Table 2 Sulfamic acid catalyzed synthesis of 2,4,5-triarylimidazoles **4a–l**.

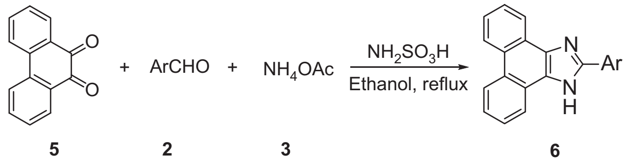


1 2 3 4a-l

Entry	2	Aryl	Time (h)	Product	Yield (%)[a]	Mp (°C)[b] (found)	Mp (°C) (reported)$^{\text{Literature}}$
1	**2a**	C_6H_5	4	**4a**	93	277–279	274–276[c]
2	**2b**	2,4-$Cl_2C_6H_3$	5	**4b**	94	177–179	175–178[d]
3	**2c**	4-MeC_6H_4	4	**4c**	95	235–238	233–235[d]
4	**2d**	4-BrC_6H_4	4	**4d**	91	267–268	265[e]
5	**2e**	2-ClC_6H_4	3	**4e**	92	199–201	195–196[c]
6	**2f**	3-$NO_2C_6H_4$	3	**4f**	95	>300	>300[d]
7	**2g**	4-$OMeC_6H_4$	4	**4g**	93	231–232	227–228[c]
8	**2h**	4-ClC_6H_4	3	**4h**	95	263–265	262–264[d]
9	**2i**	4-$N(Me)_2C_6H_4$	4	**4i**	92	256–257	256–259[d]
10	**2j**	2-Furyl	4	**4j**	89	241–243	242[e]
11	**2k**	4-OHC_6H_4	4	**4k**	90	265–267	268–269[c]
12	**2l**	4-$F_3CC_6H_4$	5	**4l**	90	273–275	

[a]Isolated yields; [b]after crystallization; [c](Gadekara et al., 2009); [d](Samai et al., 2009); [e](Chary et al., 2008).

Table 3 Sulfamic acid catalyzed synthesis of 2-arylphenanthrimidazoles **6**.



Entry	2	Aryl	Time	Product	Yield (%)[a]	Mp (°C)[b] (found)	Mp (°C) (reported)Literature
1	**2a**	C_6H_5	5	**6a**	93	>300	314–315[c]
2	**2b**	2,4-$Cl_2C_6H_3$	4	**6b**	90	245–246	
3	**2d**	4-BrC_6H_4	4	**6d**	91	264–267	
4	**2g**	4-$OMeC_6H_4$	4	**6g**	92	250–253	254–255[c]
5	**2l**	4-$F_3CC_6H_4$	5	**6l**	93	241–243	

[a]Isolated yields; [b]after recrystallization; [c](Behmadi et al., 2009).

2-(4-Bromophenyl)-1*H*-phenanthro[9,10-*d*]imidazole (6d) White crystals; ^1H NMR: δ 8.83 (d, *J*=8 Hz, 2H), 8.53 (d, *J*= 8 Hz, 2H), 8.24 (d, *J*=8 Hz, 2H), 7.79 (d, *J*=8 Hz, 2H, Ar–H), 7.72 (t, *J*=8 Hz, 2H), 7.62 (t, *J*=8 Hz, 2H); IR: 3425, 3069, 1653, 1616, 1539, 1475, 1457 cm^{-1}; MS: m/z 373 (M^+, 90), 375 ($[M+2]^+$, 100).

2-(4-Trifluoromethylphenyl)-1*H*-phenanthro[9,10-*d*]imidazole (6l) White crystals, ^1H NMR: δ 8.93 (t, *J*=8 Hz, 2H), 8.65 (t, *J*= 8 Hz, 2H), 8.59 (d, *J*=8 Hz, 2H), 8.04 (d, *J*=8 Hz, 2H), 7.88–7.68 (m, 4H); IR: 3458, 3077, 1619, 1588, 1529, 1454 cm^{-1}. MS: m/z 363 ($[M+1]^+$, 100).

Acknowledgments

We acknowledge financial support from the Research Program of Science and Technology from the Bureau of Education of Jiangxi Province, China (No.: GJJ10736) and the Youth Science Foundation of Jiangxi Educational Committee, China (No.: GJJ11232).

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Received August 30, 2011; accepted October 19, 2011