International Journal of Engineering and Technical Research (IJETR)
ISSN: 2321-0869, Volume-2, Issue-3, March 2014

Novel, rapid and efficient one-pot synthesis of substituted Imidazoles

Hossein Dianat, Alireza Nazif, Saeid Salimi

***Abstract*— Novel, efficient and fast method for the synthesis of 8-aryl-7*H*-acenaphtho[1,2-*d*]imidazole derivatives, catalyzed by Iron(III) *p*-toluenesulfonate under ultrasonic irradiation at room temperature was reported. A series of imidazoles was synthesized in excellent yields from aromatic aldehydes, acenaphthylene-1,2-dione and ammonium acetate**

***Index Terms*— One-pot, 8-aryl-7 H-acenaphtho [1,2-*d*] imidazole, Iron(III) *p*-toluenesulfonate.**

I. INTRODUCTION

The incorporation of five-membered azole ring fragments into organic materials have continued to arouse considerable attention in various areas of molecular sciences such as organic lighting, organic field effect transistor, fluorescence sensing and emission switching/signaling research fields [1-3].

A literature survey reveals that aryl imidazoles have been found to possess a wide spectrum of biological activity such as antibacterial [1], antirheumatoid arthritis [2], antitubercular [3], antiviral [4], anti-inflammatory [5] and anticancer activities [6-9]. Specifically, it has been revealed from the literature that imidazoles fused with indole nucleus possess various biological activities [10-14] including anticancer activity especially against breast cancer.

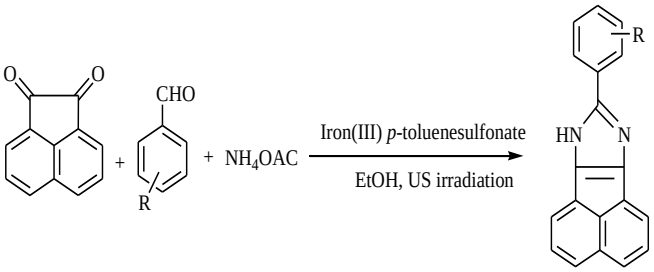
Since, we have made an attempt to synthesize and screen aryl imidazoles which are biological interest [15], in the present study, one-pot three component reactions of acenaphthylene-1,2-dione, various aromatic aldehydes and ammonium acetate in the presence of catalytic amount of Iron(III) *p*-toluenesulfonate under ultrasonic irradiation have been carried out and the corresponding 8-aryl-7H-acenaphtho[1,2-*d*]imidazoles were obtained in excellent yields and short reactiom times (Scheme 1). To the best of our knowledge, the one-pot synthesis of 8-aryl-7H-acenaphtho[1,2-*d*]imidazole and its derivatives employing efficient, inexpensive, heterogeneous and stable Iron(III) *p*-toluenesulfonate catalyst has not been reported up to now. This study provides rapid, mild and efficient method for synthesis imidazole derivatives in a one-pot three component condensation.

Manuscript received March 20, 2014.

Hossein Dianat, Department of Chemistry, Sarvestan Branch, Islamic Azad University, Iran.

Alireza Nazif, Department of Chemistry, Sarvestan Branch, Islamic Azad University, Iran

Saeid Salimi, Department of Chemistry, Sarvestan Branch, Islamic Azad University, Iran



Scheme 1. Synthetic route to synthesis of imidazole derivatives

II. EXPERIMENTAL

General procedure for preparation of 8-aryl-7H-acenaphtho[1,2-d]imidazole derivatives:
A mixture of aromatic aldehyde (1 mmol), acenaphthylene-1,2-dione (1 mmol), ammonium acetate (3.5 mmol) and Iron(III) *p*-toluenesulfonate (5 mol%) in ethanol (10 mL) was stirred at room temperature under ultrasonic irradiation using ultrasonic cleaner with a frequency of 40 KHz and a nominal power 100 W for the appropriate time (Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, as indicated by TLC, the catalyst was filtered off, washed several times with methanol and dried in oven at 70 ^{o}C to reuse in further reactions. The solvent was evaporated under reduce pressure to obtained crude product which was purified by short column chromatography on silica gel (300-400 mesh) using ethyl acetate/petroleum ether mixture (1:9, v/v) as eluent. The spectra data of the selected compounds are as follows:

8-phenyl-7H-acenaphtho[1,2-d]imidazole **(1):** ^{1}H NMR (100 MHz, DMSO-d6): δ 7.1-7.35 (m, 3H), 7.45 (d, 2H, J = 7.2 Hz), 7.55-7.80 (m, 4H), 7.95 (d, 2H, J = 5.2 Hz), 11.55 (s, NH). ^{13}C NMR (75 MHz, DMSO-d6): 123.5, 125.4, 127.2, 127.9, 128.1, 128.3, 129.1, 129.6, 129.8, 132.4, 134.7, 150.5. Found for $C_{19}H_{12}N_2$: C, 84.92; H, 4.47; N, 10.39; Calcd.: C, 85.05; H, 4.51; N, 10.44. EIMS m/z: 268 (M+).

8-(4-nitrophenyl)-7H-acenaphtho[1,2-d]imidazole **(2):** ^{1}H NMR (100 MHz, DMSO-d6): δ 7.35-7.60 (m, 4H), 7.75 (d, 2H, J = 5.5 Hz), 7.95 (d, 2H, J = 8.2 Hz), 8.15 (d, 2H), 11.75 (s, 1H, N–H). Found for $C_{19}H_{11}N_3O_2$: C, 72.75; H, 3.51; N, 13.38; Calcd.: C, 72.84; H, 3.54; N, 13.41. EIMS m/z: 313 (M+).

8-(4-methoxyphenyl)-7H-acenaphtho[1,2-d]imidazole **(3)**: ^{1}H NMR (100 MHz, DMSO-d6): δ 3.75 (s, 3H), 6.85 (d, 2H, J = 7.8 Hz), 7.25 (d, 2H, J = 7.5 Hz), 7.5-7.8 (m, 4H), 8.05 (d, 2H, J = 7.5 Hz), 12.10 (s, NH). ^{13}C NMR (75 MHz, DMSO-d6): 57.6, 112.7, 119.4, 125.3, 126.5, 126.8, 127.3, 127.9, 129.0, 131.6, 133.5, 145.8, 157.9. Found for

$C_{20}H_{14}N_2O$: C, 80.41; H, 4.67; N, 9.33; Calcd.: C, 80.52; H, 4.73; N, 9.39. EIMS m/z: 298 (M+).

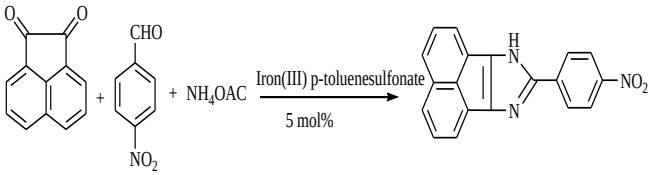
8-p-tolyl-7H-acenaphtho[1,2-d]imidazole **(5)**: ^{1}H NMR (100 MHz, DMSO-d6): δ 2.30 (s, 3H), 7.22 (d, 2H, J = 8.2 Hz), 7.40 (d, 2H, J = 8.5 Hz), 7.55-7.85 (m, 4H), 7.95 (d, 2H, J = 9.2 Hz), 11.85 (s, NH). Found for $C_{20}H_{14}N_2$: C, 84.93; H, 5.05; N, 9.87; Calcd.: C, 85.08; H, 5.00; N, 9.92. EIMS m/z: 282 (M+).

8-(naphthalen-1-yl)-7H-acenaphtho[1,2-d]imidazole **(8):** ^{1}H NMR (100 MHz, DMSO-d6): 7.25-7.40 (m, 4H), 7.50–7.65 (m, 5H), 7,85(dd, 2H, J_1 = 4.5 Hz, J_2 = 5 Hz), 8.07 (d, 2H, J = 7.6 Hz), 11.45 (s, NH). Found for: $C_{23}H_{14}N_2$:C, 86.58; H, 4.39; N, 8.72; Calcd.: C, 86.77; H, 4.43; N, 8.80. EIMS m/z: 318 (M+).

8-(4-(7H-acenaphtho[1,2-d]imidazol-8-yl)phenyl)-7H-acenaphtho[1,2-d]imidazole **(11):** ^{1}H NMR (100 MHz, DMSO-d6): 7.45 (s, 4H), 7.55-7.65 (m, 4H), 7.65-7.85 (m, 4H), 7.95 (d, 4H, J = 9.4 Hz), 11.45 (s, 2H, NH). ^{13}C NMR (75 MHz, DMSO-d6): 122.5, 126.4, 127.2, 127.8, 128.3, 129.6, 129.9, 131.2, 135,7, 150.5. Found for: $C_{32}H_{18}N_4$: C, 83.77; H, 3.91; N, 12.15; Calcd.: C, 83.82; H, 3.96; N, 12.22. EIMS m/z: 458 (M+).

III. RESULTS AND DISCUSSION

In our initial search for appropriate reaction conditions, three component reaction of acenaphthylene-1,2-dione, ammonium acetate and benzaldehyde to synthesize the 8-(4-nitrophenyl)-7*H*-acenaphtho[1,2-*d*]imidazole as a model reaction was chosen to find the optimum solvent (Table 1).



Solvent	Ethanol	Dichloromethane	Acetonitril	Toluene	Chloform	THF
Yield[a,b]	90	71	82	60	73	40
Reusability[c]	90[d]	88[e]	87[f]	85[g]	~ 80[h]	-

a) All the reactions were carried out under ultrasonication for 60 min at r.t.

b) Isolated yields. c) Reusability of the recovered catalyst was investigated in ethanol as the optimum solvent. d-h) Reusability of the recovered catalyst in new runs (from run 2 [d] to run 6 [h]).

Table 1. Influence of solvent on Iron (III) *p*-toluenesulfonate / US-catalyzed reaction acenaphthylene-1,2-dione and ammonium acetate and benzaldehyde and reusability study.

As shown in the Table 1, the best yield was obtained when ethanol was used as a solvent in the presence of 5 mol% catalyst under ultrasonication. As it can be seen in Table 1, the catalyst could be reused without significant loss of its catalytic activity until at least 4 times. It is noteworthy that when the model reaction was performed in the absence of ultrasonic irradiation, the moderate chemical yield of 76% was obtained in 30 min at room temperature. Therefore, in order to describe a time saving and efficient methodology for synthesis of imidazole derivatives, further studies were performed in the presence of ultrasonication.

Using the reaction conditions established as above, various 8-aryl-7H-acenaphtho[1,2-d]imidazole were synthesized in excellent yields by the reaction of different aromatic aldehydes, acenaphthylene-1,2-dione and ammonium acetate and the results are summarized in Table 2. In all cases, aromatic aldehydes bearing either electron-donating or electron-withdrawing groups reacted successfully and the corresponding products were isolated in excellent yields. It is worthy to note that the condensation of 2-chlorobenzaldehyde and 2-flurobenzaldehyde also afforded the desired 8-(2-fluorophenyl)-7H-acenaphtho[1,2-d]imidazole and 8-(2-chlorophenyl)-7H-acenaphtho[1,2-d]imidazole respectively (entries 9, 10) in good yields indicating that the present method doesn't suffer from steric hindrance. The reaction of 1-naphtaldehyde also gave the corresponding

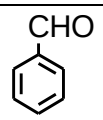
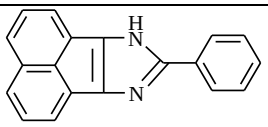
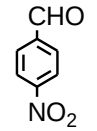
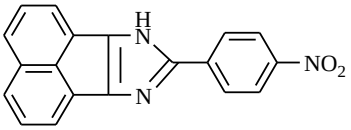
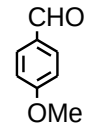
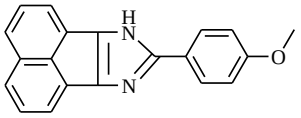
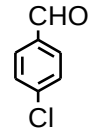
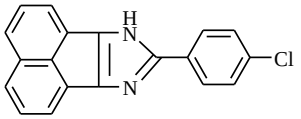
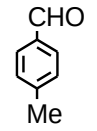
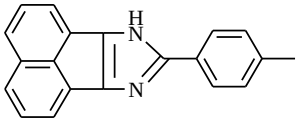
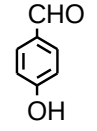
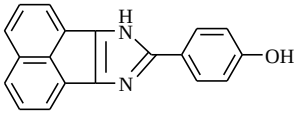
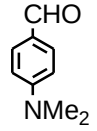
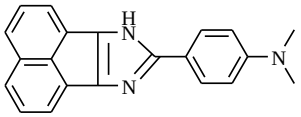
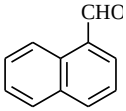
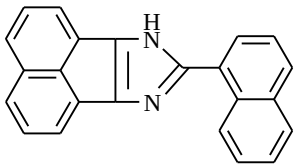
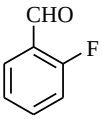
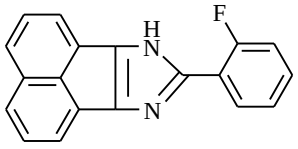
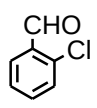
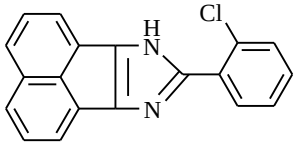
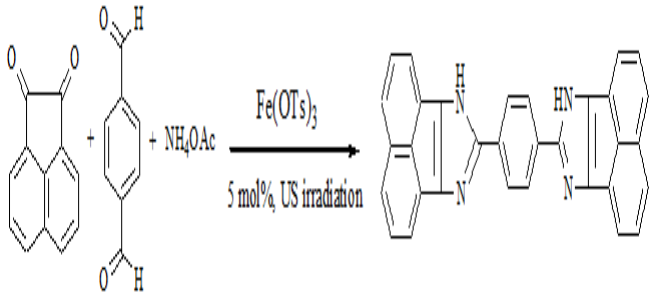
Entry	Aldehyde	Product	Time (min)	Yield (%)[a]
1			45	88
2			40	90
3			50	84
4			53	85
5			60	85
6			62	82
7			70	84
8			54	87
9			48	88
10			52	86

Table 2. Results of imidazole derivatives synthesis

Furthermore,4-(7H-acenaphtho [1,2-d]imidazol-8-yl)phenyl) -7H-acenaphtho [1,2-d]imidazole was synthesized successfully with the one-pot reaction of acenaphthylene-1,2-dione, benzene 1,4-di-carbaldehyde and ammonium acetate in EtOH. The structure of the corresponding product has been shown in Scheme 2. The product was obtained after 55 min in 90% yield (Scheme 2, compound 11).



Scheme 2. Synthesis of 8-(4- (7H-acenaphtho [1,2-d]imidazol-8-yl) phenyl)-7H- acenaphtho [1,2-d] imidazole (**11**).

CONCLUSION

In conclusion, a fast and efficient synthesis of novel acenaphtho[1,2-*d*]imidazole derivatives is described, in the presence of Iron(III) *p*-toluenesulfonate. The methodology is compatible with a series of functional groups attached to the aromatic aldehydes.

REFERENCES

[1] I. Devi, P. J. Bhuyan, *Tetrahedron Lett*., **2004**, 45, 8625.
[2] S. H., Mashraqui, M. B. Patil, H. D. Mistry, S. Ghadigaonkar, A. Meetsma, *Chem. Lett*. **2004**, 33, 1058.
[3] A. Chetia, , C, J. Saikia, K. C. Lekhok, R. C. Boruah, *Tetrahedron Lett*., **2004**, 45, 2649.
[4] Gunay N. S., Capan G., Ulusoy N., Ergenc N., Otuk G., Kaya D., *IL Farmaco*, **54**, 826-831 (1999).
[5] Sisko J., Mellinger M., *Pure Appl. Chem.*, **74**, 1349-1357 (2002).
[6] Gupta P., Hameed S., Jain R., *Eur. J. Med. Chem.*, **39**, 805-814 (2004).
[7] Kocabalkanli A., Schinazi R. F., *IL Farmaco*, **57**, 993-997 (2002).
[8] Puratchikodi A., Nallu M., Gopalakrishnan S., *Ind. J. Hetrocycl. Chem.*, **14**, 149-150 (2004).
[9] Reddy Sastry C. V., Srinivasa Rao K., Rastogi K., Jain M. L., *Ind. J.Chem.*, **30**, 480-483 (1991).
[10] Kumar R., Lown J. W., *Eur. J. Med. Chem.*, **40**, 641-654 (2005).
[11] Foroumadi A., Mirzaei M., Shafiee A., *IL Farmaco*, **56**, 621-623 (2001).
[12] Frantz D. E., Morency L., Soheili A., Murry J. A., Grabowski E. J. J., Tillyer R. D., *Org. Lett.*, **6**, 843-846 (2004).
[13] James D. A., Koya K., Li H., Chen S., Xia Z., Ying W., Wu Y., Sun L., *Bioorg. Med. Chem. Lett.*, **16**, 5164-5168 (2006).
[14] Dolensky B., Nam G., Deng W., Narayanan J., Fan J., Kirk K. L., *J. Fluorine Chem.*, **125**, 501-508 (2004).
[15] Gyanendra Kumar Sharma, Devender Pathak. *Chem. Pharm. Bull*. **58**(3) 375—380 (2010).