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Sodium Tungstate Catalyzed Green and Rapid Synthesis of 2, 4, 5-Triarylimidazoles

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Abstract: One pot three component synthesis of 2, 4, 5-triaryl imidazoles was achieved by the condensation of aromatic aldehyde, benzil and ammonium acetate in ethanol catalyzed by sodium tungstate as a non-oxidative basic catalyst. The use of inexpensive catalyst, short reaction time and ethanol as the environmentally benign solvent makes the pesent protocl a valuable addition to the existing green protocols for the synthesis of triaryl imidazoles.
Keywords : Green, Sodium tungstate, 2, 4, 5-Triaryl imidazoles.

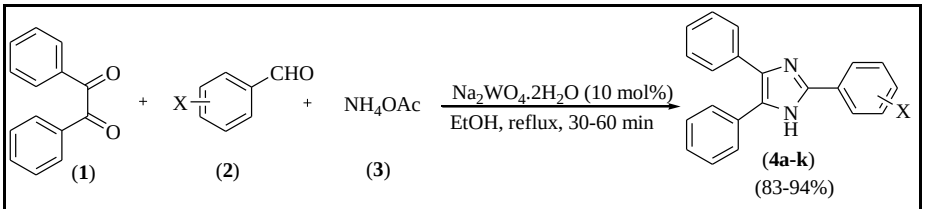
Introduction and Experimental

Sustainability is an important concept of green chemistry is which involves design and development of environmentally benign chemical processes[1]. Worldwide demand for green chemical processes and products needs the development of novel and cost-effective approaches in synthetic organic chemistry leading to environmental protection[2]. Rapid development of green chemistry is due to the recognition that environmentally benign processes are economical and long term viable.

Heterocyclic compounds comprise a major class of organic compounds. Imidazole; an electron rich five-membered aromatic heterocyclic compound is present in many therapeutically potent natural products and synthetic molecules of great biological significance. Imidazole ring possesses unique ability to bind with different enzymes and receptors in biological systems via weak interactions. The introduction of imidazole ring is an important strategy in drug discovery and organic synthesis thereby exhibiting numerous bioactivities including anticancer[3], anti-inflammatory[4], antitubercular[5], antioxidant[6], antibacterial[7] etc. It is a constituent of histidine amino acids, biotin and many alkaloids. Many drugs such as dacarbazine, ketoconazole, omeprazole etc contain imidazole ring skeleton in their structures. Thus imidazole is a medicinally privileged target in medicinal chemistry and drug discovery on account of several significant biological activities.

Literature is enriched with numerous reports for the synthesis of 2, 4, 5-triaryl imidazoles by one pot three component condensation of aldehyde, benzil and ammonium acetate using different catalysts such as various metal chlorides[8], NBS[9], tannic acid[10], Caro's acid/silica gel[11], $KMnO_4/CuSO_4$[12], SiO_2-$NaHSO_4$[13], $H_2SO_4 \cdot SiO_2$[14], morpholinium hydrogen sulphate[15], $NiCl_2 \cdot 6H_2O$[16], preyssler nanoparticles[17] etc. However many of the existing methodologies suffer from the adverse effects of toxic and hazardous waste, strong Lewis acids as catalysts, use of ionic liquids whose separation from the reaction mixture is a tedious task, prolong reaction time etc. Although literature is enriched with these methodologies; objective of the present study is to develop a simple, facile, cost effective and environmentally benign green approach with clean reaction profile for the synthesis of trisubstituted imidazoles.

Sodium tungstate ($Na_2WO_4.2H_2O$) is a simple, low cost and water soluble solid inorganic material which has emerged as an efficient catalyst for epoxidation of alkenes and oxidation of alcohols into the corresponding carbonyl compounds[18]. To the best of our knowledge and as per literature survey, only a few reports are available on the utility of sodium tungstate dehydrate as a catalyst[19]. As a part of our ongoing efforts in the development of new synthetic strategies for the synthesis of heterocyclic compounds[20]; in the present work we report sodium tungstate catalyzed green protocol for the synthesis of 2, 4, 5-triaryl substituted imidazoles via one pot three component condensation of aldehydes, benzil and ammonium acetate in ethanol under reflux within 30-60 min (**Scheme 1**).



Scheme 1: Sodium tungstate catalyzed rapid and green synthesis of 2,4,5-triaryl imidazoles

Chemicals were purchased from SD fine or Spectrochem chemical companies and were used without further purification. The progress of reaction was monitored using TLC plates silica gel precoated on aluminum using 30 % ethyl acetate: n-hexane as the mobile phase. Melting points of the products were recorded in capillaries open at one end and were uncorrected. The compounds were confirmed by comparison of their physical constants with literature values, ^{1}H NMR, IR and ESMS spectral data.

General procedure for the sodium tungstate catalyzed synthesis of 2, 4, 5-triaryl substituted imidazoles:

A mixture of benzil (2 mmol), aldehyde (2 mmol), ammonium acetate (3 mmol) and sodium tungstate (10 mol %) in ethanol (2 mL) was refluxed at 80 ^{o}C for a specified time as mentioned in **Table 3**. Progress of the reaction was monitored by TLC (30% ethyl acetate: n-hexane). After completion of the reaction as indicated by TLC, the ethanol was evaporated and the reaction mass was poured onto ice cold water and filtered off the resulting solid which was further purified by recrystallization from ethanol.

The spectral data of representative compounds is mentioned below:

[2-(4'-Methoxyphenyl)-4, 5-diphenyl-1H-imidazole] (Table 1, Entry 2): Off white solid, M. P. 231-233 (^{o}C) ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm: 3.83 (3H, s, -OCH_3), 7.05 (d, 2H), 7.20-7.60 (m, 10 H), 8.05 (d, 2H), 12.5 (s, 1H, -NH). IR (KBr) cm^{-1} 3030, 2960, 1611, 1493, 1416, 1250, 1031, 697. ESMS: 327.29 (M+1).

[2-(4'-Thiomethoxy) phenyl-4, 5-diphenyl-1H-imidazole] (Table 1, Entry 3): Faint yellow solid, M. P. 240-242 (^{o}C) ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 2.45 (s, 3H, -SCH_3), 7.20-7.60 (m, 12H), 8.05 (d, 2H), 12.65 (1H, NH). IR (KBr) cm^{-1} 3028, 2834, 1603, 1485, 1380, 1024, 697. ESMS: 343.27 (M+1).

[2- (4'-Phenyl-phenyl)-4, 5-diphenyl-1H-imidazole] (Table 1, Entry 4): Cream yellow solid, M. P. 242-244 (^{o}C) ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.4 (d, 2H), 7.45 (m, 5H), 7.59 (m, 6H), 7.8 (dd, 4H), 8.2 (d, 2H), 13.0 (s, 1H, -NH) IR (KBr) cm^{-1} 3399, 3031, 1603, 1484, 1070 ESMS: 373 (M+1).

[2-(Benzo[d][1,3] dioxol-5-yl)-4, 5-diphenyl-1H-imidazole] (Table 1, Entry 5): White solid, M. P. 200-202(^{o}C) ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 6.10 (s, 2H), 7.05 (d, 2H), 7.20-7.70 (m, 12 H), 12.5 (s, 1H, -NH). IR (KBr) cm^{-1} 3057, 2882, 1604, 1482, 1236, 1070, 697. ESMS: 341.30 (M +1).

Result and Discussion

Initially a model condensation reaction was carried out on 4-hydroxy benzaldehyde, benzil and ammonium acetate using 10 mol% $Na_2WO_4.2H_2O$ in different solvents (**Table 1**).

Table 1: Optimization of reaction conditions for the synthesis of 2, 4, 5-triaryl substituted imidazoles

Entry	Conditions	Time	Yield (%)
1	THF	3 h	NR
2	MeOH	30 min	90
3	EtOH	45 min	92
4	IPA	60 min	81
5	EtOH: H_2O (1:1)	60 min	68
6	THF: H_2O (1:1)	60 min	NR
7	MeOH: H_2O (1:1)	60 min	70

Reactions were carried out with 4-hydroxybenzaldehyde (1 mmol), benzil (1 mmol) and ammonium acetate (1.5 mmol) under reflux using $Na_2WO_4.2H_2O$ (10 mol %) in respective solvent (1mL).

The model condensation reaction did not proceed in various solvents such as - THF or THF: H_2O. Also the reaction was found to be sluggish and not complete in aq. alcoholic media - EtOH:H_2O (1:1) or MeOH: H_2O (1:1) . The same reaction in isopropyl alcohol was not successful after 1 h. The reaction when carried out using $Na_2WO_4.2H_2O$ catalyst in merely methanol as the solvent requires 30 minutes and in ethanol it takes little more time (45 minutes) for completion under the same conditions. Since ethanol is comparatively more environmentally benign solvent rather than methanol; we chose ethanol as the reaction medium. Next we investigated the effect on catalyst concentration on the model reaction with 4-hydroxybenzaldehyde (**Table 2**).

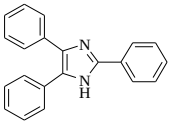
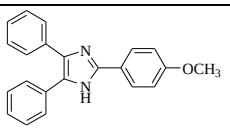
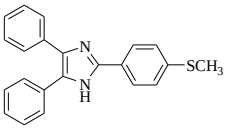
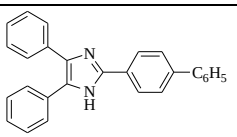
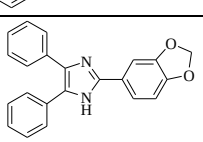
Table 2: Effect of catalyst concentration on the synthesis of 2, 4, 5-triaryl substituted imidazoles

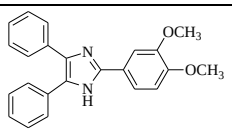
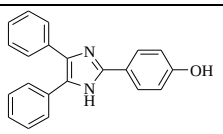
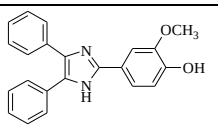
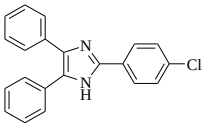
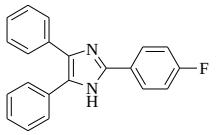
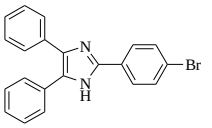
Entry	Catalyst (mol%)	Yield (%)[@]
1	5	80
2	10	92
3	15	94
4	20	94

[@]Yields of reactions isolated after 45 min in EtOH (1mL) under reflux.

Under these optimized reaction conditions several aldehydes were screened for the reaction with benzil and ammonium acetate (**Table 3**).

Table 3: Yields of sodium tungstate catalyzed green synthesis of 2, 4, 5-triaryl substituted imidazoles

Entry	Aldehyde (X)	Product	Time (min)	Yield (%)[#]	M. P. (^oC) [Ref]
1	H		30	83	268-270 [17]
2	4-OCH_3		30	88	231-233 [12]
3	4-SMe		30	86	240-242 [17]
4	4-C_6H_5		60	94	242-244 [Present work]
5	3,4-Methylene dioxy		60	89	200-202

6	3,4-$(OCH_3)_2$		30	90	217-218 [17]
7	4-OH		45	92	268-270 [10]
8	3-OCH_3, 4-OH		45	87	218-220 [10]
9	4-Cl		30	90	259-261 [10]
10	4-F		30	86	188-190 [17]
11	4-Br		45	84	261-263 [17]

[#]Isolated yields on the reaction of aldehyde (2 mmol), benzil (2 mmol) and ammonium acetate (3 mmol) using $Na_2WO_4.2H_2O$ (10 mol %) in EtOH under reflux.

Conclusion

The present protocol reports utility of sodium tungstate dihydrate as a simple, inexpensive commercially available basic catalyst in short reaction time making it a green approach for the synthesis of 2, 4, 5-triaryl substituted imidazoles. The use of ethanol as the comparatively environmentally friendly solvent, clean reaction profile, short reaction time and higher yields of the corresponding products makes the present protocol a valuable addition to the existing methods for the synthesis of these heterocyclic compounds.

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References

1. Dastan, A., Kulkarni, A. and Torok, B. Environmentally benign synthesis of heterocyclic compounds by combined microwave-assisted heterogeneous catalytic approaches. Green Chemistry 2012, 14, 17-37.
2. Varma, R. S. Solvent-free organic syntheses using supported reagents and microwave irradiation. Green Chemistry 1999, 1, 43-55.
3. Elahian, F., Akbari, M., Ghasemi, M., Behtooee, N., Taheri, M. and Amini, M. Synthesis and anticancer activity of 2, 4, 5-triaryl imidazole derivatives. Letters in Drug Design & Discovery 2014, 11, 840-843.
4. Gallagher, T.F., Fier-Thompson, S.M., Garigipati, R.S., Sorenson, M.E., Smietana, J.M., Lee, D., Bender, P.E., Lee, J.C., Laydon, J.T., Griswold, D.E. Chabot-Fletcher, M.C., Breton, J.J. and Adams, J.L. 2, 4, 5- triarylimidazole inhibitors of IL-1 biosynthesis. Bioorganic and Medicinal Chemistry Letters 1995, 5, 1171-1176.
5. Gupta, P., Hameed, S. and Jain, R. Ring-substituted imidazoles as a new class of anti-tuberculosis agents. European Journal of Medicinal Chemistry 2004, 39, 805-814.

6. Satyanarayana, V.S.V. and Sivakumar, A. An efficient and novel one-pot synthesis of 2, 4, 5-triaryl-1H-imidazoles catalyzed by $UO_2(NO_3)_2 \cdot 6H_2O$ under heterogeneous conditions. Chemical Papers 2011, 5, 65 19-526.
7. Khan, M.S., Siddiqui, S.A., Siddiqui, M.S.R.A., Goswami, U., Srinivasan, K.V. and Khan, M.I. Antibacterial activity of synthesized 2, 4, 5-trisubstituted imidazole derivatives. Chemical Biology & Drug Design 2008, 72, 197-204.
8. Marques, M.V., Ruthner, M.M., Fontoura, L.A.M. and Russowsky D. Metal chloride hydrates as Lewis acid catalysts in multicomponent synthesis of 2,4,5-triarylimidazoles or 2,4,5-triaryloxazoles. Journal of the Brazilian Chemical Society, 2012, 23, 171-179.
9. Maleki, B. and Ashrafi, S.S. N-Bromosuccinimide catalyzed three component one-pot efficient synthesis of 2, 4, 5-triaryl-1H-imidazoles from aldehyde, ammonium acetate, and 1, 2-diketone or α-hydroxyketone. Journal of the Mexican Chemical Society 2014, 58, 76-81.
10. Shitole, N.V., Shitole, B.V., Kakde, G.K. and Shingare, M.S. Tannic acid catalyzed an efficient synthesis of 2, 4, 5-Triaryl-1H-imidazole. Orbital Electronic Journal of Chemistry 2013, 5, 35-39.
11. Pourshamsian, K., Montazeri, N. and Asadyan, S. Caro's acid-silica gel: An efficient and reusable catalyst for the synthesis of 2, 4, 5- trisubstituted imidazoles under solvent-free conditions. Journal of Applied Chemical Research 2014, 8, 53-59.
12. Khorramabadi-zad, A., Azadmanesh, M. and Mohammadi, S. One-pot, simple and efficient synthesis of triaryl-1h-imidazoles by $KMnO_4/CuSO_4$. South African Journal of Chemistry 2013, 66, 244-247.
13. Hatamjafari, F. and Khoastehkouhi, H. A New method for synthesis of 2,4,5-triaryl-1H-imidazole derivatives using SiO_2-$NaHSO_4$ under solvent-free conditions. Oriental Journal of Chemistry 2014, 30, 329-331.
14. Maleki, B. , Shirvan, H. K., Taimazi, F. and Akbarzadeh, E. Sulfuric acid immobilized on silica gel as highly efficient and heterogeneous catalyst for the one-pot synthesis of 2, 4, 5-triaryl-1H-imidazoles. International Journal of Organic Chemistry 2012, 2, 93- 99.
15. Marzouk, A.A., Abbasov, V.M. and Talybov, A.H. Short time one-spot synthesis of 2, 4, 5-trisubstituted imidazoles using morpholinium hydrogen sulphate as green and reusable catalysts. Chemistry Journal 2012, 2, 179-184.
16. Heravi, M. M., Bakhtiari, K., Oskooie, H. A., Taheri, S. Synthesis of 2, 4, 5-triaryl-imidazoles catalyzed by $NiCl_2 \cdot 6H_2O$ under heterogeneous system. Journal of Molecular Catalysis: A 2007, 263, 279-281.
17. Gharib, A., Khorasani, B.R.H., Jahangir, M. and Roshani, M. Synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted-1H-imidazole derivatives and or 2,4,5-triaryloxazoles using of silica-supported preyssler nanoparticles. Bulgerian Chemical Communications 2014, 46, 165-174.
18. Bakhtiari, L., Mohadeszadeh, S., Noyori, R., Aokib, M. and Satoc, K. Green oxidation with aqueous hydrogen peroxide. Chemical Communications 2003, 1977-1986.
19. Khodabakhshi, S. and Baghernejad, M. Sodium tungstate: The first application as non-oxidative catalyst in organic synthesis. Journal of the Chinese Chemical Society 2014, 61, 521-524.
20. Tekale, S.U., Pagore, V.P., Kauthale, S.S. and Pawar, R.P. La_2O_3/TFE: An efficient system for room temperature synthesis of Hantzsch polyhydroquinolines. Chinese Chemical Letters 2014, 25, 1149-1152.

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