IJMPR 2023, 7(6), 75-79

International Journal of Modern Pharmaceutical Research

www.ijmpronline.com

ISSN: 2319-5878
IJMPR
Research Article

SJIF Impact Factor: 5.273

AN EFFICIENT BIO ACTIVE SYNTHESIS OF 1-BENZYL-2-(4-CHLOROPHENYL)-4, 5-DIPHENYL-1H-IMIDAZOLE ANALOGOUS

T. L. K. Swaroopa, B. Rambabum B. Priyanka and Dr. N. KrishnaRao*

PRISM PG & DG College, (Affiliated to Andhra university), Visakhapatnam, India.

Received on: 08/04/2023

Revised on: 28/04/2023

Accepted on: 18/05/2023

***Corresponding Author**

Dr. N. KrishnaRao

PRISM PG & DG College, (Affiliated to Andhra university), Visakhapatnam, India.

ABSTRACT

A reliable an efficient synthetic method has been developed for five series of 1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (5).These moieties can be synthesized by the 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (3) with substituted (bromomethyl)benzene (4) in the presence of strong base such as triethyl amine and methylene dichloride at reflux. The compound (3) can be prepared from benzil, ammonium acetate, and aromatic aldehyde by using KIO_4 a nontoxic and inexpensive catalyst. The Structural features of the titled compounds have been evaluated from their analytical data, IR, Mass, 1H NMR. The antibacterial activity of all synthesized compound has been performed by using filter paper disc method against gram positive and gram negative bacteria.

KEYWORDS: 2-(4-chlorophenyl) -4,5-diphenyl- 1H-imidazole,substituted (bromomethyl) benzene, Benzil, chloro benzaldehyde, papain catalyst**,** Antimicrobial activity.

INTRODUCTION

Multi substituted imidazole and derivatives are an important class of compounds in the field of organic synthesis and medicinal chemistry. They exhibit a broad range of biological properties such as, inhibitors of p38 MAP Kinase,[1] B-Raf kinase,[2] anti-HIV.[3] anticonvulsant.[3] HIV-1 protease,[4] calcium antagonist and inhibitors of thromboxane A2 synthesase,[5] therapeutic agent,[6] antihistaminic,[7] tranquilizer,[8] antimuscarinic,[9] antiarthritic,[10] cardiotonic,[11] HMG CoA reductase(HMGR),[12] and antitumor agents.[13] In recent years substituted imidazoles are substantially used as Ionic liquids,[14] Literature survey reveals that several methods have been developed for the synthesis of 2,4,5-triaryl-1H-imidazoles by three component cyclocondensation of 1,2-diketone, -hydroxy ketone with aldehydes and ammonium acetate, which comprises the use of ionic liquids,[15] silica sulphuric acid,[16] refluxing in acetic acid [17a-b], alum.[18a] sulphanilic acid,[18b] $NiCl2.6H_2O$,[19] H_3PO_4,[20] CAN,[21] grinding with I2,[22] from N-acylated -amino in presence of triphenyl phosphine followed by coupling with Pd catalyst.[23] Recently, Konwar, et al. reported the synthesis of imidazole using $InCl_3.H_2O$.[24] In present work based on the multistep an efficient bio active synthesis of 1-benzyl-2-(4-chlorophenyl)-4, 5-diphenyl-1H-imidazole analogous by conventional method.

MATERIALS AND METHODS

Experimental

All chemicals, reagents and solvents were procured from Merck Chemical Company and all the raw materials were used without further purification. The melting points of the newly synthesized derivatives were limited by the Gallenkamp melting point apparatus. Nuclear magnetic resonance spectra were recorded newly synthesized derivatives by the Bruker -400 AVANCE spectrometer (1HNMR400MHz and 13C NMR 100MHz) using Tetramethylsilane (TMS) as an internal standard. The mass spectra were measured on a Liquid Chromatography Mass Spectrometry (LCMS) Agilent mass spectrometer.Themicroanalyses of the new derivatives for C, H and N were performed on a Perkin-Elmer elemental analyzer. The bacterial cultures were purchased from Microbial type Culture Collection, Institute of Microbial Technology, and Chandigarh, India. Dimethyl sulphoxide (DMSO) and Streptomycin and Fluconazole were used as negative and positive controls, respectively. The experiments were carried out in triplicates.

Preparation of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole:

Take dry and clean four necks RBF. The charge the ethanol into RBF at room temperature which is also fitted on the magnetic stirrer possesses hot plate. The charge a mixture of substituted aromatic aldehydes (1.2 mmol), benzil, and ammonium acetate (1.1mmol) into RBF at mixture carried out 70^0C. The catalyst KIO_4 added into the reaction .Before start the reaction, papain added into the reaction mixture and reaction continued in 3hrs at same temperature and monitored by TLC (ethyl acetate and n-hexane). After the completion of the reaction, crude poured in cold water and add 10 mL of 5% saturated solution of sodium bi carbonate added into

the solution and charge with ethyl acetate. The organic layer separated and washed with solution of Brain. Finally separated the organic layer and distilled off under vacuums. The desired product separated by column chromatography and also recrystallized with ethanol 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole.

Characterization 2-(4-chlorophenyl)-4, 5-diphenyl-1H-imidazole

Orange brown solid; Yield-90%; m.p- 218^{0}C; Rf-0.45 (n-hexane: EtOAc – 6:4); ^{1}HNMR(400Mz,$CDCl_3$) ppm:12.847(s,1H,NH-imidazole),7.924-7.742(m,4H,Ar-H),7.484-7.284(m,5H,Ar-H) ; 13CNMR (100MHz,$CDCl_3$) ppm: 179.62, 136.26, 132.43, 130.86, 129.46,129.09, 128.89,128.56,128.22,127.85,127.44; LCMS (m/z): 332.41(M+2). Molecular formulae: $C_{21}H15N_2Cl$; Elemental Analysis: Calculated C-76.25, H-4.57, N-8.47; Obtained: C-76.18, H-4.56, N - 8.53.

General procedure of 1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

Take dry and clean four necks RBF. The charge the methylene dichloride into RBF at room temperature which is also fitted on the magnetic stirrer possesses hot plate. The charge a mixture of substituted (bromomethyl) benzene and 2-(4-chlorophenyl)-4, 5-diphenyl-1H-imidazole (1mmol) into RBF at mixture carried out 40^{0}C. Before start the reaction, the strong base such as and triethyl amine added into the reaction mixture and reaction continued in 5hrs at same temperature and monitored by TLC (ethyl acetate and n-hexane). After the completion of the reaction, crude poured in cold water and add 10 mL of 10% HCl added into the solution and charge with ethyl acetate. The organic layer separated and washed with solution of Brain. Finally separated the organic layer and distilled off. The desired product separated by column chromatography and also recrystallized with ethanol 1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole.

Characterization 1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole

1.1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (5a)

Brownsolid,yields-79%;m.p-255-257^{0}C.1HNMR(400Mz,$CDCl_3$)ppm:8.082-7.894(m,4H, Ar-H),7.472-7.294(m,8H,Ar-H),7.046-6.874(m,2H,Ar-H),5.123(s,2H,-CH_2-);^{13}CNMR (100MHz, $CDCl_3$)ppm: 150.29, 132.45, 131.66, 129.43, 129.04, 128.75, 128.48, 128.22, 128.02, 127.95, 127.49, 126.67, 125.33, 46.65. LCMS (m/z): 422.22(M+2). Molecular formulae: $C_{28}H_{21}N_2Cl$. Elemental Analysis: Calculated C-79.89,H-5.03,N-6.66. Obtained: C-79.81, H-5.02, N-6.72.

2.2-(4-chlorophenyl)-1-(4-methoxybenzyl)-4,5-diphenyl-1H-imidazole(5b)

Brown red solid, yields-89%; m.p-253-255 0C. ^{1}HNMR(400Mz,$CDCl_3$)ppm:8.092-7.621 (m,4H,Ar-H),7.475-7.285(m,5H,Ar-H),7.102-6.956(m,4H,Ar-H),5.026 (s,2H,-CH_2-), 3.725 (s,3H,-OCH3);^{13}CNMR(100MHz,$CDCl_3$)ppm: 154.65, 150.07, 136.33, 131.67, 130.25, 129.66, 129.15, 128.74, 128.56, 128.15, 128.07, 127.85, 127.53, 117.64, 56.86, 47.31. LCMS (m/z): 452.27(M+2). Molecular formulae: $C_{29}H_{23}N_2O_4$ Elemental Analysis: Calculated C-77.54.,H-5.14,N-6.2. Obtained: C-77.46, H-5.12, N-6.23.

3.2-(4-chlorophenyl)-1-(4-methylbenzyl)-4,5-diphenyl-1H-imidazole(5c):

PaleBrownsolid,yields-88%m.p-267-269^{0}C.1HNMR (400Mz,$CDCl_3$)ppm:8.125-7.625(m, 4H,Ar-H),7.492-7.326 (m,5H,Ar-H), 7.126-7.062(m,4H,Ar-H),5.125 (s,2H,-CH_2-), 1.672 (s,3H, ,-CH3),^{13}CNMR (100MHz,$CDCl_3$)ppm: 154.76, 140.35, 137.62, 134.61, 132.09, 131.50, 129.61, 129.17, 128.87, 128.53, 128.32, 128.09, 127.62, 127.34, 126.56, 46.56, 20.37 LCMS (m/z): 436.36(M+2); Molecularformulae: $C_{29}H_{23}N_2Cl$; Elemental Analysis: Calculated C-80.08.,H-5.33,N-6.44. Obtained: C-80.00, H-5.32, N-6.50.

4.1-(4-chlorobenzyl)-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (5d)

Redsolid,yields-90%m.p-271-273^{0}C.1HNMR (400Mz,$CDCl_3$) ppm:8.135-7.676(m,4H,Ar-H), 7.494-7.326 (m,6H,Ar-H),7.442(d,J=7.6Hz,2H,Ar-H),5.256 (s,2H,-CH_2-).13CNMR (100MHz, $CDCl_3$)ppm: 155.62, 140.65, 137.33, 134.65, 130.39, 129.96, 129.42, 128.87, 128.62, 128.45, 128.25, 127.77, 126.65, 46.28 LCMS(m/z): 456.22(M+2). Molecular formulae: $C_{28}H_2ON_2$ .Elemental Analysis: Calculated C-73.85.,H-4.43,N-6.15. Obtained: C-73.78, H-4.42, N-6.22.

5.2-(4-chlorophenyl)-1-(4-nitrobenzyl)-4,5-diphenyl-1H-imidazole (5e)

Redsolid,yields-84%;m.p-256-258^{0}C.1HNMR (400Mz, CDCl3)ppm:8.046-7.825 (m,5H,Ar-H), 7.492-7.294 (m,8H,Ar-H),5.245(s,2H,-CH_2-).^{13}CNMR (100MHz, $CDCl_3$) ppm: 154.76, 143.66, 140.65, 139.09, 135.35, 134.74, 130.66, 129.72, 129.34, 128.94, 128.55, 128.31, 128.19,127.65,123.35, 45.62.LCMS (m/z): 467.28 (M+2). Molecularformule: $C_{28}H_{20}N_3O_2Cl$. .Elemental Analysis: Calculated C-72.18.,H-4.33,N-9.02. Obtained: C-72.10, H-4.31, N-9.12.

3. Biological Evaluation

3.2.1. Antibacterial assay

50 mL sterile conical flask of nutrient broth was inoculated with the test organisms and incubated at 36^{0}C overnight. By using a sterile pipette, 0.5 mL of the broth culture of each test organism was added to 60 mL of molten agar, mixed well and maintained at 45^{0}C. Sterile agar test plates of each test organism were prepared by pouring inoculated medium with uniform thickness. The agar was allowed to set and harden and wells of 4 mm diameter were cut at equidistant using a sterilecork borer. Agar plugs were removed. 100 lg/mL of test solutions (5a–e) were prepared in DMSO and were introduced into the wells using micropipette. The agar plates were kept at room temperature for 1.5hrs for better diffusion of solution into the medium. The plates were incubated for

24h at35^{0}C. The zone inhibitory diameter tested derivatives formed after incubation around each well was measured in millimeter (mm) using antibiotic zone scale. The assay was carried out in triplicates. The drug controlled solvent was used as DMSO and also the antibacterial activity of the test compounds was compared with standard references is **"Ciprafloxin".**

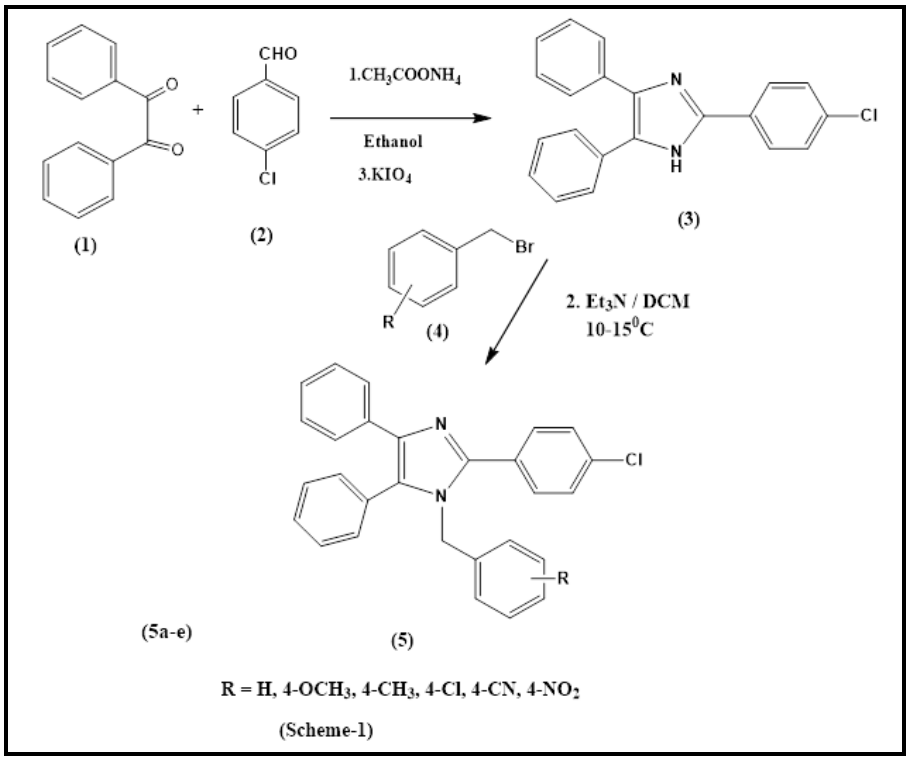
3.2.2. Antifungal assay

Sterile molten potato dextrose agar (PDA) medium was inoculated with 50 mL of fungal spore suspension aseptically and maintained at 45^{0}Ctemperature. The inoculated medium was mixed well and poured immediately in sterilized petriplates. Then five wells of 6 mm diameter were punched using sterile borer and filled with 100 lg/mL of test compounds (4a-4o) as well as sterile DMSO 100% as negative control. Plates were incubated for 24 h at 35^{0}C. Antifungal activity was determined by measuring the zone of inhibition. The zones produced by the test compounds were compared with the "**ketoconazole.**

RESULTS AND DISCUSSION

3.1. Chemistry

The starting material A reliable an efficient synthetic method has been developed for five series of 1-benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (5).These moieties can be synthesized by the 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (3) with substituted (bromomethyl)benzene (4) in the presence of strong base such as triethyl amine and methylene dichloride at reflux. The compound (3) can be prepared from benzil, ammonium acetate, and aromatic aldehyde by using KIO_4 a nontoxic and inexpensive catalyst (Scheme 1).



(Scheme-1)

The structures of the desired compounds were characterized by ^{1}HNMR, ^{13}C NMR, mass spectral and elemental analyses. 1H NMR spectrum showed two singlets at δ 12.847 which were due to presence of imidazole N-H respectively. Further, the imidazole N-H and aromatic proton on imidazole ring resonated at δ 8.135 and 6.623 which confirm the structure. The mass spectrum of 5e exhibited molecular ion peak at m/z = 467.28(M+2), which is in agreement with the molecular formula $C_{28}H_{20}N_3O_2Cl$,

4.2. Bio evaluation

4.2.1. Antimicrobial activity

The evaluation of newly obtained derivatives and also well characterized compounds (5a-e) were screened for in vitro antibacterial potent activity against Gram (+Ve) bacteria, Gram (-Ve) bacteria and antifungal potent activity against AspergillusNiger, Candida albicans and Aspergillus favus using agar well diffusion assay and the test compounds were expressed in mm by zones of inhibition as shown in Table-I and Table-II..

4.2.2. Antibacterial activity

The evaluation of in vitro antibacterial activity of the titled derivatives (4a-4o) were compared with standard references as a" Ciprafloxin'' as collected in (Table-I). As indicated in Table-I, most of the synthesized derivatives generally exhibited potent activity against all the tested bacterial strains. Compound "5d" exhibited excellent antibacterial activity against gram-positive bacterial strains viz; E.coli, P.aeruginose and gram negative bacterial strains viz; B.subtilis and

Staphylococcus aureus respectively due to such compounds possess halogen atoms. The derivatives, "5b and 5c" and 4m showed moderate to good active potential against bacterial strains. The compounds"5a and 5e" exhibited low activity against bacterial strains due to compounds having highly electron withdrawing groups These results evidenced that the compounds having electron releasing groups showed moderate to good activity than the compounds having electron withdrawing groups. The compounds containing halogen atoms exhibited excellent active potential.

Table-I: In vitro antibacterial activity of the newly synthesized compounds (5a-e): Zones of inhibition (mm) of compounds 5a–5e against tested bacterial strains.

Entry	Anti-Bacterial Activity			
	Gram(+ve) bacteria		Gram(-ve) bacteria	
	E. coli	P. aureoginosa	B. subtilis	S. aureus
5a	07	09	06	08
5b	13	15	18	16
5c	16	17	15	17
5d	21	22	23	24
5e	04	06	08	06
Ciprafloxin	27	27	30	30
DMSO				

Ciprafloxin was used as standard. a 100 lg/mL of compound in each well.
Values are average of three readings.

Antifungal activity

The comparison of the evaluation in vitro antifungal activity of the titled compounds (5a-e) were compared with standard drug" Ketonozole.'' as collected in (Table-II). The in vitro antifungal potent activity of the titled compounds (5a-e) was investigated against AspergillusNiger, Candida albicans and Aspergillus favus using agar well diffusion assay and zones of inhibition of the test compounds were expressed in mm as shown in Table-II. Compounds "5d "expected significant potent activity against the fungal strain. The compounds containing "5b and 5c "were observed to be good active potential against tested fungal strain. Compounds "5a, 5b, 5c, 5e" have demonstrated significant antifungal activity comparable to reference drug. From the results it is reveals that most of the titled derivatives showed significant potent activity whereas few of derivatives showed moderate potent activities against Aspergillusfavus as shown in Table-II. The results of the desired tested compounds evidenced that the having electron donating groups of compounds exhibited excellent potent activity while the compounds having electron attracting groups exhibited moderate to good against the fungal stains.

Table-II: Antifungal activity of the synthesized compounds (5a-e); Zones of inhibition (mm)a of compounds (5a–5e) against tested fungal strains.

Entry	Anti-Fungal Activity		
	Aspergillus Niger	Candida albicans	Aspergillusfavus
5a	08	05	07
5b	10	09	07
5c	12	11	12
5d	19	21	20
5e	21	20	21
Ketonozole	25	25	25
DMSO			

4. CONCLUSIONS

In conclusion, we have perceived that papain can catalyze efficiently the one-pot synthesis of a large number of tri- substituted imidazoles at moderate temperature under conventional method conditions. Present multi step synthesis offers very attractive features such as reduced reaction times, higher yields, and economic viability of the catalyst, when compared with MW method as well as sonic methods as well as with other catalysts, which will have wide scope in organic synthesis. We expect this method will find extensive applications in the field of combinatorial chemistry, diversity-oriented synthesis, heterogeneous catalytic systems, and drug discovery.

6. AKOWNLDEMENT

We would like to acknowledge PRISM PG &DG College, Visakhapatnam for providing us laboratory facility to carry out project work.

REFERENCES

1. Lee, J.C.; Laydon, J.T.; McDonnell, P.C.; Gallagher, T.F.; Kumar, S.; Green, D.; cNulty, .; Blumenthal, M.J.; Keys, J.R.; Vatter, S.W.L.; Strickler, J.E.; McLaughlin, M.M.; iemens, I.R.; Fisher, S.M.; Livi, G.P.; White, J.R.; Adams, J.L.; Young, P.R. A protein kinase involved in the regulation of inflammatory cytokine biosynthesis. Nature, 1994; 372-739.
2. Takle, A.K.; Brown, M.J.B.; Davies, S.; Dean, D.K.; Francis, G.; Gaiba, A.; Hird, A.W.; King, F.D.; Lovell, P.J.; Naylor, A.; Reith, A.D.; Steadman, J. G.; Wilson, D.M. The identification of potent, selective and CNS penetrant furan-based inhibitors of B-Raf kinase. Bioorg. Med. Chem. Lett., 2006; 16: 378-81.
3. Renukadevi, P.; Biradar, J.S.; Hiremath, S.P.; Manjunath, S.Y.ynthesis and antimicrobiasl activity of 1,2-Disubstituted-4-[5'-Substituted-2'-phenyl indole-3'-yl) methylene] imidazolin-5(4H)-ones. Indian J. Heterocycl. Chem., 1997; 6: 277-280.
4. Paul, W.B. Heterocyclic HIV-1 protease inhibitors. Org. Lett., 1999; 1(2): 249-252.
5. Cozzi, P.; Carganico, G.; Fusar, D.; Grossoni, M.; Menichincheri, M.; Pinciroli, V.; onani, R.; Vaghi, F.; Salvati, P. Dihydropyridines Imidazoles Thromboxane-A ynthase/antagonists & inhibitors. J. Med. Chem, 1993; 36: 2964-2972.
6. Chengzhi, Z.; Sepehr, S.; Edmund, J. M.; Sonja, K.; Jennifer, C. R.; Khalid, D. B.; Ross, D.; Adnan, M. M. 2,4,5-Trisubstituted imidazoles: novel nontoxic modulators of P-glycoprotein mediated, multidrug resistance, Bioorg Med Chem Lett., 2000; 10(23): 2603-2605.
7. Robert, A. T.; Charles, F. H.; Caesar, R. S. Studies on imidazole I. 4-methyl imidazole and related compounds. J. Am. Chem. Soc., 1949; 71(8): 2801-2803.
8. Shealy, Y.E.; Montogomery, J.A.; Loster, W.R. Antitumor activity of triazenoimidazoles. J. Biochem. Pharmacol., 1962; 11: 674.
9. Miyachi, H.; Kiyota, H.; Segawa, M. Novel imidazole derivatives with subtype-selective antimuscarinic activity. Bioorg Med. Chem. Lett., 1998; 18: 2163-2168.
10. Sharpe, T.R.; Cherkovsky, S.C.; Hewes, W.E.; Smith, D.H.; Gregory, W.A.; Haber, S.B.; Leadbetter, M.R.; Whitney, J.G. Preparation, antiarthritic and analgesic activity of 4,5-diaryl-2-(substituted thio)-1H-imidazoles and their sulfoxides and sulfones. J. Med. Chem., 1985; 28: 1188-1194.
11. Ila Sircar, Bradley L. Duell, James A. Bristol, Ronald E. Weishaar, Dale B. Evans Cardiotonic agents. 5. 1,2-Dihydro-5-[4-(1Himidazol-1-yl)phenyl]-6-methyl-2- oxo-3-pyridinecarbonitriles and related compounds. Synthesis and inotropic activity. J. Med. Chem., 1987; 30: 1023-1029.
12. Chuen, C.; Bailey, E. J.; David, H.; David, F. H.; Julie, L. H.; Graham, G. A. I.; Paul, S. J.; Suzanne, E. K.; Barrie, E. K. Inhibitors of cholesterol biosynthesis. 1. 3,5-Dihydroxy-7-(Nimidazolyl)-6-heptenoates and -heptanoates, a novel series of 3-hydroxy-3-methylglutarate-CoA reductase inhibitors. J. Med. Chem., 1996; 36: 3646-3657.
13. Wang, L.; Woods, K.W.; Li, Q.; Barr, K.J.; McCroskey, R.W.; Hannick, S. M.; Gherke, L.; Credo, R.B.; Hui, Y.H.; Marsh, K.; Warner, R.; Lee, J.Y.; Zielinsky-Mozng, N.; Frost, D.; Rosenberg, S.H.; Sham, H.L. Potent, Orally active heterocycle-based combretastatin A-4 analogues: synthesis, structure-activity relationship, pharmacokinetics, and in vivo antitumor activity evaluation J. Med. Chem., 2002; 45: 1697-1711.
14. (a) Dupont, J.; de Souza, R.F.; Suarez, P.A.Z. Ionic liquid (molten salt) phase organometallic catalysis. Chem. Rev., 2002; 102: 3667.
15. Siddiqui, S.A.; Narkhede, U.C.; Palimkar, S.S.; Daniel, T.; Lahoti, R.J.; Srinivasan, K.V. Room temperature ionic liquid promoted improved and rapid synthesis of 2,4,5-triaryl imidazoles from aryl aldehydes and 1,2-diketones or -hydroxyketone. Tetrahedron, 2005; 61: 3539-3546.
16. Shaabani, A.; Rahmati, A. Silica sulfuric acid as an efficient and recoverable catalyst for the synthesis of trisubstituted imidazoles. J. Mol. Catal. A Chem., 2006; 249: 246-248.
17. (a) Sarshar, S.; Siev, D.; Mjalli, M.M. Imidazole libraries on solid support. Tetrahedron Lett, 1996; 37: 835-838;
18. (a) Mohammadi, A. A.; Mivechi, M.; Kefayati, H. ChemInform abstract: potassium aluminum sulfate (Alum): an efficient catalyst for the one-pot synthesis of trisubstituted imidazoles. Monatsh Chem., 2008; 139: 935-937.
19. Heravi, M.M.; Bakhtiari, K.; Oskooie, H.A.; Taheri, S. Synthesis of 2,4,5-triaryl-imidazoles catalyzed by NiCl2·6H2O under heterogeneous system. J. Mol.Catal. A Chem., 2007; 263, 279.
20. Liu, J.; Chem, J.; Zhao, J.; Zhao, Y.; Li, L.; Zhang, H. A modified procedure for the synthesis of 1-arylimidazoles. Synthesis, 2003; 17: 2661-2266.
21. Sangshetti, J.N.; Kokare, N.D.; Kotharkara, S.A.; Shinde, D.B. A new series of 4-substituted 3H-1,2,3,5-oxathiadiazole 2-oxides bearing 1,2. J. Chem. Sci., 2008; 120(5): 463-467.
22. Parveen, A.; Ahmed, M.D.; Rafi, S.K.; Shaikh, K.A.; Deshmukh, S.P.; Pawar, R.P. Efficient synthesis of 2,4,5-triaryl substituted imidazoles under solvent free conditions at room temperature. Arkivoc, 2007; 12-18.
23. Zhong, Y.L.; Lee, J.; Reamer, R. A.; Askin, D. Divergent and Regioselective synthesis of 1,2,4- and 1,2,5-trisubstituted imidazoles. J. Org. Chem., 2008; 73(17): 6816- 6823.
24. Sharma, S.D.; Hazarika, P.; Konwar, D. An efficient and one-pot synthesis of 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted imidazoles catalyzed by InCl3·3H2O. Tetrahedron Lett., 2008; 49: 2216-2220.