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Synthesis and antifungal activity 2, 6-bis (subtituted phenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl)-4-(subtituted phenyl) pyridine derivatives

S. N. Mokale*, Grover D. G, Maheshwari T. Shete

Dr. Rafiq Zakaria Campus, Y. B. Chavan College of Pharmacy, Aurangabad(M. S.), India

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ABSTRACT

*Novel series of 2, 6-bis (subtituted phenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl)-4-(subtituted phenyl) pyridine antifungal agents having 1, 4- dihydropyridine ring and imidazole pharmacophore (**4a-4p**) were prepared successively by condensation of 1-(4-chlorophenyl)-2-(1H-imidazol-1-yl) ethanone with aromatic aldehyde and ammonium acetate. The chemical structures of the compound were confirmed by ^{1}H NMR, IR and mass spectral data. The compounds were screened for antifungal activity against pathogenic fungal strains.*

Keywords: Antifungal, 1, 4- dihydropyridine, antifungal agent.

INTRODUCTION

1, 4-Dihydropyridyl compounds are important class of pyridine derivatives which posses a wide spectrum of biological activities [1]. 1, 4-Dihydropyridines (1, 4-DHP) belong to a class of nitrogen-containing heterocyclic having a six member ring. Much attention has been devoted to exploring their pharmacological activities [2]. Nowadays, dihydropyridine derivatives are widely used in the therapy of many diseases depending on the kind and place of substitution on the dihydropyridine rings. The fungal infection is become a serious medical problem because of the difficulty of its control in immunocompromised individuals and because of the emergence of multidrug resistant fungi, although a variety of antifungal drugs have been developed [3]. Until the 1970s, fungal infections had generally been considered curable and thus the demand for new antifungal drugs had been very low [4].

From the literature survey it is observed that no efforts have been made for developments of a molecular scaffold containing these two important cores i.e. 1, 4- dihydropyridine ring and imidazole group. In view of this we have attempted the synthesis novel of series of 2, 6-bis (subtituted phenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl)-4-(subtituted phenyl) pyridine derivatives (**Figure-1**).

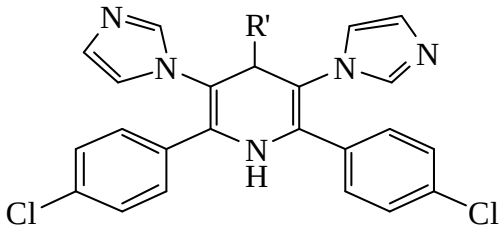


Figure-1

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and are reported as not corrected. FT-IR spectra (KBr) were run on a Jasco FT-IR 4000 spectrometer. NMR spectra were recorded on a Bruker avance II 400 spectrometer with 500.13 MHz in $CDCl_3$ or DMSO solvents using TMS as an internal standard. Mass spectra were obtained on a Shimadzu GCMS-QP 1000 EX instrument at 70 eV.

Synthesis of 2-bromo-1- (4-chlorophenyl) ethanone (2)

Place a solution of 0.25 M of P-Chloroacetophenone in 100 ml of glacial acetic acid in a 500 ml flask. Add bromine (0.25 M, 12.5 ml) slowly (30 min) from a dropping funnel ***(CAUTION)*** [7]. Shake the mixture vigorously during the addition and keep the temperature below 20^0C. p-bromophenacyl bromide commences to separate as needles after about half of the bromine has been introduced. When the addition s complete, cool the mixture in ice-water, filter the crude product at pump and wash it with 50% alcohol until colourless (about 100 ml required). Recrystallized from rectified (or industrial) spirit (400 ml). The yield of pure p-bromophenacyl bromide (Colourless needles, m.p 109^0C) is 50g (72%).

Synthesis of 1-(4-chlorophenyl)-2-(1H-imidazol-1-yl) ethanone (3)

1H-Imidazole (0.72 g, 10.59 mmol) was added to a solution of bromoderivative (1.00 g, 3.52 mmol) in chloroform ($CHCl_3$) (25 ml) and the mixture was stirred at room temperature for 2 h[7]. The mixture was evaporated to dryness and recrystallized using methanol. (yield 75%).

General procedure for the preparation of final derivatives (4a-4p)

The Hantzsch synthesis was carried out by taking 0.0039 M of substituted aldehyde, 0.0078 M of 1-(4-chlorophenyl)-2-(1H-imidazol-1-yl)ethanone and 0.0039 M of ammonium acetate in a 25 ml round bottomed flask containing 10 ml of ethanol to which calculated amount of potassium carbonate was added [8]. Each mixture was stirred at room temperature for the required time. Progress of the reaction was monitored by thin layer chromatography (TLC). Subsequently, the reaction mixture was filtered for removal of catalyst, was poured into ice-cold water (to remove ammonium acetate), and then washed using ethyl acetate. The organic layer was in turn soaked with sodium sulfate (to remove traces of water) and concentrated. The crude products was purified by recrystallisation from ethanol: water (95:5) and isolated products were characterized by NMR and mass spectroscopy.

4-(2, 6-bis (4-chlorophenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl) pyridin-4-yl) phenol (4a)

Compound 3 was obtained as white solid (57.03%); m.p.: $180\text{-}182^0$C; IR (KBr) ν [cm^{-1}]: 3410, 3389, 1683, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300MHz) δ [ppm]: 4.79 (s) 1H, DHP, 5.0-6.3 (s) 1H, phenol, 7.14-7.32 (d) 6H, Imidazole, 7.40-7.46 (d) 7H, benzene, 8.14 (s) 2H, Imidazole;

R_F=0.42 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =526.4 $M^{(+)}$. Anal. Calcd. for $C_{29}H_{21}Cl_2N_5O$: C, 66.17; H, 4.02; N, 13.30. Found: C, 66.87; H, 4.22; N, 13.74.

4-(2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridin-4-yl)-N,N-dimethylbenzenamine (4b)

Compound 4 was obtained as white solid (53%); m.p.: 185-187^{0}C; IR (KBr) v [cm^{-1}]: 3389, 1683, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.79 (s) 1H, DHP, 2.85-3.0 (s) 6H, N,N-dimethyl, 7.14-7.32 (d) 6H, Imidazole, 7.40-7.46 (d) 7H, benzene, 8.14 (s) 2H, Imidazole; R_F=0.5 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =553.4 $M^{(+)}$. Anal. Calcd. for $C_{31}H_{26}Cl_2N_6$: C, 65.04; H, 4.58; N, 14.68. Found: C, 65.47; H, 4.32; N, 14.84.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(3,4,5-trimethoxy phenyl)pyridine (4c)

Compound 5 was obtained as white solid (60%); m.p.: 125-127^{0}C; IR (KBr) v [cm^{-1}]: 3446, 3143, 1683, 1489, 1285, 1229, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.79 (s) 1H, DHP, 3.73-3.83 (s) 9H, ether, 7.14-7.32 (d) 6H, Imidazole, 7.40-7.46 (d) 7H, benzene, 8.14 (s) 2H, Imidazole; R_F=0.76 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =600.4 $M^{(+)}$. Anal. Calcd. for $C_{32}H_{27}Cl_2N_5O_3$: C, 64; H, 4.53; N, 11.66. Found: C, 64.37; H, 4.72; N, 11.84.

4-(2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridin-4-yl)-2-methoxyphenol (4d)

Compound 6 was obtained as white solid (55.86%); m.p.: 175-179^{0}C; IR (KBr) v [cm^{-1}]: 3450, 3446, 3143, 1683, 1489, 1285, 1229, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.79 (s) 1H, DHP, 3.73-3.83 (s) 3H, ether, 5.0-5.5 (s) 1H, phenol, 7.14-7.32 (d) 6H, Imidazole, 7.40-7.46 (d) 7H, benzene, 8.14 (s) 2H, Imidazole; R_F=0.64 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =556.4 $M^{(+)}$. Anal. Calcd. for $C_{30}H_{23}Cl_2N_5O_2$: C, 64.75; H, 4.17; N, 12.59. Found: C, 64.47; H, 4.32; N, 12.44.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(3-nitrophenyl)pyridine (4e)

Compound 7 was obtained as white solid (50.86%); m.p.: 195-198^{0}C; IR (KBr) v [cm^{-1}]: 3396, 3079, 1671, 1519, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.79 (s) 1H, DHP, 7.99-8.0 (s) 2H, nitro, 7.14-7.32 (d) 6H, Imidazole, 7.40-7.46 (d) 7H, benzene; R_F=0.41 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =555.4 $M^{(+)}$. Anal. Calcd. for $C_{29}H_{20}Cl_2N_6O_2$: C, 62.71; H, 3.63; N, 15.13. Found: C, 62.47; H, 3.52; N, 15.23.

5-(2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridin-4-yl)-2-methylphenol (4f)

Compound 8 was obtained as white solid (63%); m.p.: 170-173^{0}C; IR (KBr) v [cm^{-1}]: 3450, 3396, 3079, 1671, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 5.0 (s) 1H, phenol, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.41-6.77 (d) 3H, benzene; R_F=0.36 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =526.4 $M^{(+)}$. Anal. Calcd. for $C_{29}H_{21}Cl_2N_5O$: C, 66.17; H, 4.02; N, 13.30. Found: C, 66.37; H, 4.22; N, 13.54.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-phenylpyridine (4g)

Compound 9 was obtained as white solid (60%); m.p.: 182-184^{0}C; IR (KBr) v [cm^{-1}]: 3389, 3091, 1680, 1489, 1274, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 7.06-7.14 (d) 5H, benzene; R_F=0.36 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =510.4 $M^{(+)}$. Anal. Calcd. for $C_{29}H_{21}Cl_2N_5$: C, 68.24; H, 4.15; N, 13.72. Found: C, 68.45; H, 4.32; N, 13.84.

4-(2-chlorophenyl)-2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridine (4h)

Compound 10 was obtained as white solid (65%); m.p.: 118-120^{0}C; IR (KBr) v [cm^{-1}]: 3389, 3091, 1683, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 7.00-7.15 (d) 4H, benzene; R_F=0.48 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =544.8 $M^{(+)}$. Anal. Calcd. for $C_{29}H_{20}Cl_3N_5$: C, 63.93; H, 3.70; N, 12.85. Found: C, 63.57; H, 3.62; N, 12.64.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-p-tolylpyridine (4i)

Compound 11 was obtained as white solid (55%); m.p.: 173-175^{0}C; IR (KBr) v [cm^{-1}]: 3371, 3091, 1680, 1489, 1274, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.94 (d) 4H, benzene, 2.35 (s) 3H, methyl; R_F=0.6 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =524.4 $M^{(+)}$. Anal. Calcd. for $C_{30}H_{23}Cl_2N_5$: C, 68.71; H, 4.42; N, 13.35. Found: C, 68.45; H, 4.32; N, 13.64.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(thiophen-2-yl)pyridine (4j)

Compound 12 was obtained as white solid (50%); m.p.: 153-155^{0}C; IR (KBr) v [cm^{-1}]: 3389, 3091, 1683, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.60 (d) 3H, thiophene; R_F=0.85 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =516.4 $M^{(+)}$. Anal. Calcd. for $C_{27}H_{19}Cl_2N_5S$: C, 62.79; H, 3.71; N, 13.56. Found: C, 62.47; H, 3.52; N, 13.43.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(4-nitrophenyl) pyridine (4k)

Compound 13 was obtained as white solid (60%); m.p.: 160-162^{0}C; IR (KBr) v [cm^{-1}]: 3396, 3079, 1671, 1519, 1488, 1328, 1091; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.60 (d) 3H, thiophene; R_F=0.85 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =555.4 $M^{(+)}$.Anal. Calcd. for $C_{29}H_{20}Cl_2N_6O_2$: C, 62.71; H, 3.63; N, 15.13. Found: C, 62.87; H, 3.42; N, 15.33.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(2,5-dimethoxy phenyl) pyridine (4l)

Compound 14 was obtained as white solid (58.6%); m.p.: 178-181^{0}C; IR (KBr) v [cm^{-1}]: 3446, 3143, 1683, 1489, 1285, 1229, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.46-6.54 (d) 3H, benzene (O-C), 3.73 (s) 6H, ether; R_F=0.45 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =570.4 $M^{(+)}$. Anal. Calcd. for $C_{31}H_{25}Cl_2N_5O_2$: C, 65.27; H, 4.42; N, 12.28. Found: C, 65.17; H, 4.62; N, 12.34.

2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)-4-(4-methoxyphenyl) pyridine (4m)

Compound 15 was obtained as white solid (65.74%); m.p.: 120-122^{0}C; IR (KBr) v [cm^{-1}]: 3446, 3143, 1683, 1489, 1285, 1229, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 6.65-6.95 (d) 4H, benzene (O-C), 3.73 (s) 3H, ether; R_F=0.65 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =540.4 $M^{(+)}$.Anal. Calcd. for $C_{30}H_{23}Cl_2N_5O$: C, 66.67; H, 4.29; N, 12.96. Found: C, 66.57; H, 4.42; N, 12.84.

2, 4, 6-tris(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridine (4n)

Compound 16 was obtained as white solid (55.74%); m.p.: 112-114^{0}C; IR (KBr) v [cm^{-1}]: 3389, 3091, 1683, 1488, 1328, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 7.00-7.15 (d) 4H, benzene; R_F=0.54 (ethyl acetate/

n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =544.8 $M^{(+)}$.Anal. Calcd. for $C_{29}H_{20}Cl_3N_5$: C, 63.93; H, 3.70; N, 12.85. Found: C, 63.77; H, 3.82; N, 12.74.

2,6-bis(4-chlorophenyl)-4-(furan-2-yl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridine (4o)
Compound 17 was obtained as white solid (61.74%); m.p.: 173-175^{0}C; IR (KBr) v [cm^{-1}]: 3446, 3143, 1683, 1489, 1285, 1229, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.7 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 5.88-7.21 (d) 3H, furan; R_F=0.58 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =500.3 $M^{(+)}$. Anal. Calcd. for $C_{27}H_{19}Cl_2N_5O$: C, 64.81; H, 3.83; N, 14.00. Found: C, 64.67; H, 3.62; N, 14.24.

2-(2,6-bis(4-chlorophenyl)-1,4-dihydro-3,5-di(1H-imidazol-1-yl)pyridin-4-yl)pyridine (4p)
Compound 18 was obtained as white solid (65.74%); m.p.: 135-137^{0}C; IR (KBr) v [cm^{-1}]: 3371, 3091, 1680, 1489, 1274, 1092; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ [ppm]: 4.4 (s) 1H, DHP, 7.1-7.7 (d) 6H, Imidazole, 7.22-7.24 (d) 8H, benzene, 7.22-8.67 (d) 4H, benzene; R_F=0.36 (ethyl acetate/ n-butanol(4:1)). MS (TOF, 1.99 e4): *m/z* =511.4 $M^{(+)}$. Anal. Calcd. for $C_{28}H_{20}Cl_2N_6$: C, 65.76; H, 3.94; N, 16.43. Found: C, 65.57; H, 3.72; N, 16.54.

RESULTS AND DISCUSSION

Chemistry

The final 2, 6-bis (subtituted phenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl)-4-(subtituted phenyl) pyridine derivatives (**4a-4p**) were prepared by the reactions of 1-(4-chlorophenyl)-2-(1H-imidazol-1-yl) ethanone with commercially available aromatic aldehydes and ammonium acetate in the presence of catalytic amounts of potassium carbonate in EtOH under reflux condition (**Scheme 1**). The physicochemical properties of final compounds were summarized in **Table1**.

Antifungal Screening

The final derivatives (**4a-4p)** were evaluated for their antifungal activity against (**Table 2**) representative strains of yeasts: *Candida albicans* ATCC 100231 (*C. albicans*),: *Aspergillus flavus* NCL 535/NRRL 2211 (*A. flavus*) and *Aspergillus fumigatus* 867/06 (*A. fumigatus*) according to an agar disc diffusion method by using Micropipettes.

The zone of inhibition of the compounds varied from 2 mm to 32 mm, compounds **4i** and **4m** having the biggest zone of inhibition (**Table 2**). This value is smaller than values obtained for commercially available drugs with imidazole / or chloro phenyl moieties (e.g. clotrimazole revealed growth inhibition zone ranging 36 mm in the concentration 100 µg/mL). In this regard **4i** and **4m** showed significant antifungal activity and results were comparable to that of reference standard Clotrimazole. Growth of *C. albicans* was inhibited by compounds **4e, 4h, 4i, 4m** and the biggest zone of inhibition sized 32 mm. On the other hand **4f, 4k** and **4l** have shown moderate antifungal activity. *A. flavus* species was sensitive to **4e**, **4l, 4m** and the most effective was **4l** (size of growth inhibition zone ranged 14 mm). Derivatives **4a-4p** was found to posses less antifungal activity against *A. fumigates*

The result suggested that all the compounds posses good antifungal activity with percent inhibition ranging from 27.77 % to 88.88 %. As mentioned in the literature [5, 6], we also noticed that diazole rings, such as imidazole inhibit growth of fungus.

Table 1: Physico-chemical properties of compounds 4a-4p

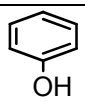
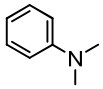
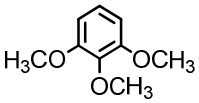
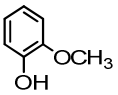
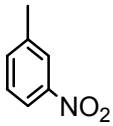
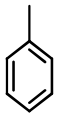
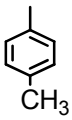
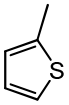
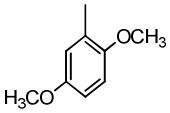
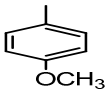
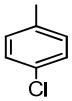
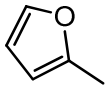
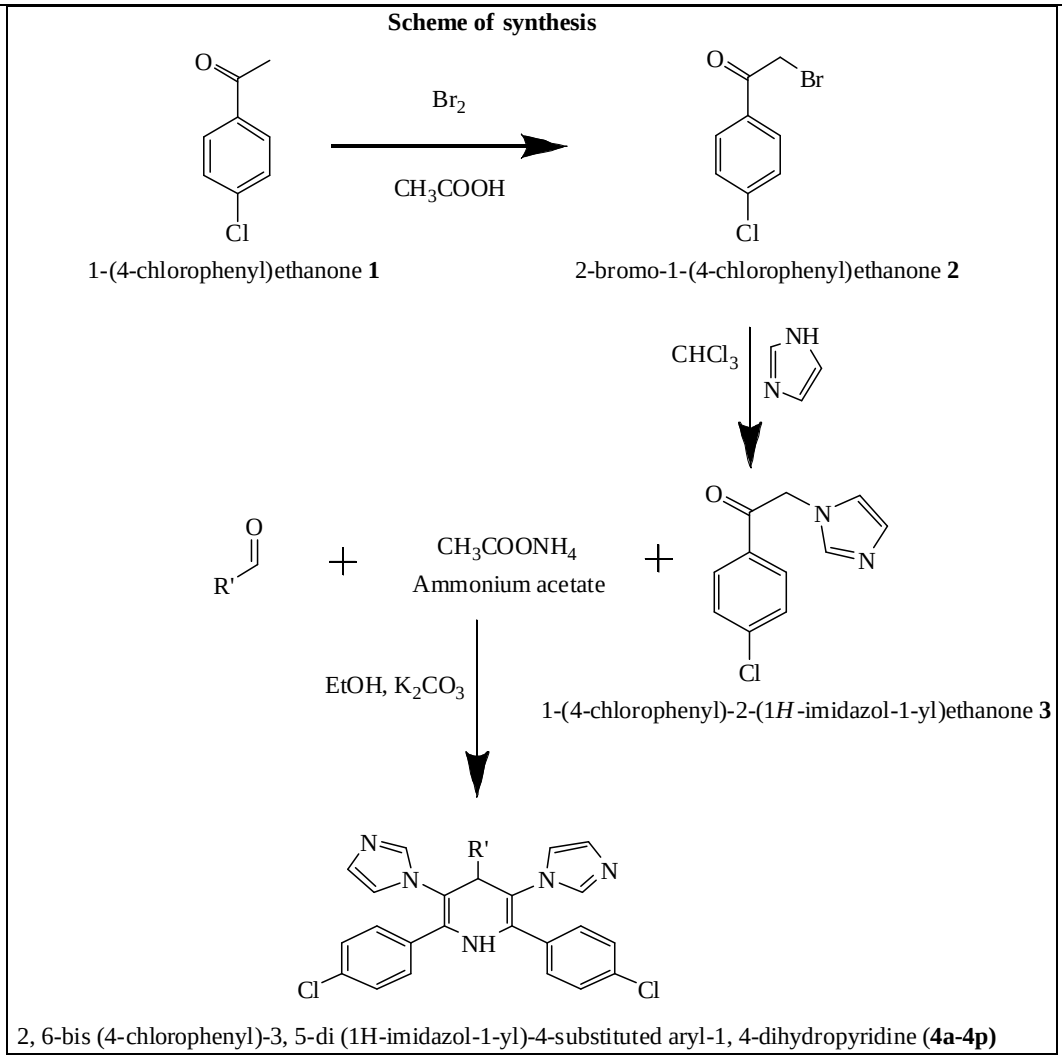
Compound	R'	m.p.(°C)	Yield (%)	Rf Value
4a		180-182	57	0.42
4b		188-190	53	0.5
4c		128-130	77	0.76
4d		175-177	55	0.64
4e		190-192	41	0.41
4f		173-175	48	0.36
4g		185-187	70	0.36
4h		121-123	68	0.48
4i		170-172	74	0.6
4j		153-155	82	0.85
4k		163-165	87	0.78
4l		181-183	88	0.45
4m		123-125	70	0.65
4n		115-117	80	0.54
4o		173-175	84	0.58
4p		138-140	74	0.36

Table 2. Antifungal activities of derivatives 4a-4p

Compound	*C. albicans*	*A.flavus*	*A.fumigatus*
4a	20	-	-
4b	16	2	4
4c	22	-	-
4d	26	-	2
4e	30	12	-
4f	24	4	6
4g	22	6	2
4h	30	12	4
4i	32	2	6
4j	21	4	2
4k	26	8	-
4l	26	14	8
4m	32	10	4
4n	22	2	6
4o	12	4	2
4p	10	6	10
Clotrimazole	36	40	32

Scheme of synthesis



2, 6-bis (4-chlorophenyl)-3, 5-di (1H-imidazol-1-yl)-4-substituted aryl-1, 4-dihydropyridine (**4a-4p)**

CONCLUSION

In summary, this paper describes the synthesis and spectral characterization 2, 6-bis (subtituted phenyl)-1, 4-dihydro-3, 5-di (1H-imidazol-1-yl)-4-(subtituted phenyl) pyridine derivatives. The structures of new derivatives were characterized by ^{1}H-NMR, IR and MS. The synthesized compounds were evaluated for their antifungal activity against representative strains of yeasts. The notable antifungal effect of certain compounds confirms that these are a good basis for the production of a number of new, possibly physiologically 1, 4- dihydropyridine derivatives.

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