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Greener and Efficient Synthesis of Some Novel Substituted Azetidinones with 4-Amino Pyridine via γ-Ferrite as a Heterogenous Catalyst

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Abstract—*A new series of (3-chloro-2-oxo-4-substituted-Aryl-N-pyridine-4-yl-azetidinone) β –lactams (3a-3j) were synthesized via heterogenous catalysed reaction between 4 amino- pyridine and substituted aromatic benzaldehyde as a starting material by conventional in two steps. The structure of all the synthesized compounds were confirmed by chemical and spectral analysis such as IR,1H NMR,13C NMR and FAB-Mass.*

1. INTRODUCTION

Organic synthesis promoted by a solid heterogeneous catalyst have attracted wide spread interest and are advantageous because of operational simplicity, high selectivity, and clean separation of the product. Metal oxides has been recognized as a remarkably useful green heterogeneous catalyst to promote a wide range of organic reactions.[1] Herein we report a rapid and green approach to achieve highly substituted Azetidinones with pyridine in excellent yields in the presence of catalytic amount of γ-ferrite (Fe2O3) under controlled.

Pyridine derivatives of different heterocyclic nucleus have shown very important pharmacological properties like antifungal[2-4],antitubercular[5], antibacterial[6], antimicrobial[7], insecticidal[8] etc. Furthermore, different moieties of thiadiazole[9-10], thiazolidinone[11-12], and azetidinone[13-14] have also been reported to exhibit potent antifungal activities by several scientists. In the light of these observations, compounds of series.I were synthesized incorporating azetidinone moieties at 4-position of pyridine nucleus with a hope to develop better antifungal agents[15]. These compounds have been screened for their antifungal activity. 2-Azetidines have been extensively investigated by the organic chemists due to their close association with various types of biological activities[16]Azetidineones also have great importance because of the use of β-lactam derivatives as antibacterial agents.

2. MATERIALS AND METHODS

All Melting points were taken in open glass capillaries and are uncorrected. Progress of the reaction was monitored by TLC on pre-coated Silica gel-aluminium plates (Type 60 F254, Merck, Darmstadt, Germany) in MeOH:CHCl3 system (1:9). The spot was visualized by exposing exposure to UV-light (254 nm) or dry plate in iodine vapours. The IR spectra were recorder on shimadzu FT-IR 8300 (ν max in cm1) Spectrophotometer using (KBr disc) .[1]HNMR and [13]C-NMR spectra were measured on a JEOL DELTA-300 were spectrometer in DMSO-d6 at 300 MHz using TMS as an internal standard. Chemical shifts reported on δ scales. The FAB mass spectra were recorded on a JEOL SX-102 mass spectrometer. Elemental analyses were performed on a Carlo Erba-1108 analyser. The analytical data of all the compounds were highly satisfactory. For column chromatographic purification of the products, Merck silica Gel 60 (230-400 Mesh) was used. All chemicals were purchased from Sigma-Aldrich and the reagent grade chemicals were purchased from commercial sources and further purified before use.

2.1 General procedure for synthesis of Schiff bases compound (2a-2j)

4-Amino-pyridine (0.05 mol) was dissolved in 5 ml of ethanol in a 250 ml conical flask and was stirred at room temperature for 15 min to get a clear solution. To this solution, equimolar quantity (0.05 mol) of each substituted aryl aldehydes (in Ethanol) were added in presence of heterogenous catalyst γ-ferrite (Fe2O3) (in catalytic amount (0.01 mole%) and reaction mixture was refluxed with stirring up to 6–8 h at 70°C on magnetic stirrer. The reaction progress was monitored by TLC using mobile phase as chloroform: methanol (6:4).On completion of reaction, then allowed to cool. The product was purified over a column chromatography. The purified product was recrystallized from methanol at room temperature to give compound (2a-2j : Characterisation data of compounds (2a-2j) are presented below :

2.2 Synthesis of N-Benzylidenepyridin-4-amine2a

Yield:75.0%,m.p.91–93°C,Rf 0.75, IR (KBr,νcm-1) 1632 (C=N), 1615(C=N,pyridine), 1474(C=C,aromatic);1HNMR(DMSO d6)(δppm):8.2(s,1H,N=CH),8.7–7.8 (m,9H,aromatic); 13C-NMR:162.1(=CH),154.1 (pyridine), 135.2, 132.4, (benzene) .

2.3 Synthesis of N-(4-Methoxybenzylidene) pyridin-4-amine : 2b

Yield: 72.8%, m.p.: 110–112°C, Rf 0.45, IR (KBr, ν cm-1):3031 (CH,CH3),1630 (C=N), 1615 (C=N,pyridine);1H-NMR (DMSO-d6)(δ ppm): 8.3 (s,1H,N=CH), 8.7–7.1 (m,8H, aromatic), 3.6 (s,3H,OCH3);13C-NMR: 163.2 (N=CH), 153.2, (pyridine),165.2, (benzene), 56.2 (OCH3).

2.4 Synthesis of N-(3,4-Dimethoxybenzylidene)pyridin-4-amine : 2c

Yield: 88.4%, m.p.: 125–127°C, Rf 0.58, IR (KBr, ν cm- 1): 1244 (Ar–OCH3),1630 (C=N), 1615 (C=N, pyridine), 1476(C=C, aromatic);1HNMR(DMSO-d6)(δ ppm): 8.3 (s,1H,N=CH), 8.7–7.1(m, 7H,aromatic),3.6 (s, 6H, OCH3);13C-NMR: 163.2 (=CH), 153.14.7 (benzene), 56.1 (OCH3).

2.5 Synthesis of N-(4 Bromobenzylidene)pyridin-4-amine: 2d

Yield: 78.2%, m.p.: 135–138°C, Rf 0.68, IR (KBr, ν cm- 1): 1630 (C=N), 1615 (C=N, pyridine), 1474(C=C, aromatic); 1H-NMR (DMSO-d6) (δ ppm): 8.3 (s,1H,N=CH), 8.4–7.1(m, 8H,aromatic),13C-NMR: 161.2 (=CH), 153.1 (pyridine),135.3(benzene)

2.6 Synthesis of N-(2 –Bromo -benzylidene) pyridin-4-amine : 2e

Yield:68.5%, m.p.: 131–134°C,Rf 0.63, IR (KBr, νcm-^{1}): 1630 (C=N), 1618 (C=N, pyridine), 1478(C=C,aromatic);1H-NMR(DMSO-d6)(δppm):8.3(s,1H,N=CH),8.4–7.3(m,8H,aromatic), 13C-NMR:160.1(=CH).153.1,148.2,114.2(pyridine), 135.3 (benzene)

2.7 Synthesis of N-(3 -Bromobenzylidene) pyridin-4-amine : 2f

Yield:62.5%, m.p.: 136–138°C, Rf 0.77, IR (KBr, ν cm- 1): 1618 (C=N, pyridine), 1474(C=C, aromatic);1H-NMR (DMSO-d6)(δ ppm): 8.3 (s,1H,N=CH), 8.4–7.4(m, 8H,aromatic),13C-NMR: 160.0 (=CH), 153.2,148.2,114.5 (pyridine),135.8, (benzene)

2.8 Synthesis of N-(3, 4,5,Trimethoxy-benzylidene) pyridin-4-amine : 2g

Yield:70%, m.p.: 142–145°C, Rf 0.74, IR (KBr,νcm-^{1}): 2865& 1170 (CH,OCH3), 1617(C=N,pyridine), 1472(C=C,aromatic);1H-NMR(DMSO-d6),(δppm):3.84(s,9H,OCH3), 8.3(s,1H,N=CH) 8.2–7.0 (m, 6H, aromatic), 13C-NMR:160.0(=CH),153.1 (pyridine),153.1 (benzene)

2.9 Synthesis of N-(3-methyl-benzylidene) pyridin-4-amine : 2h

Yield:64.5%, m.p.: 138–140°C, Rf 0.64, IR (KBr, ν cm-^{1}): 2927(CH3), 1618(C=N, Pyridine),1474(C=C Aromatic);1HNMR(DMSOd6)(δppm);2.51(s,3H,CH3)8.29(s, 1H,N=CH),8.47.2(m,8H,aromatic), 13CNMR:160.0(N=CH),153.1,141.3,114.0(5C,pyridine),138.4 (benzene)

2.10 Synthesis of N-(2-methoxy-benzylidene) pyridin-4-amine : 2i

Yield:79.5 %, m.p.: 178–180°C, Rf 0.74, IR (KBr, ν cm- 1): 2860, 1165 (OCH3) 1598(N=CH, azomet), 1618 (C=N, Pyridine),1478 (C=C Aromatic);1HNMR (DMSO-d6)(δppm);3.66(s,3H,OCH3),7.9(s,1H,N=CH),8.4-7.2(m,8H,aromatic,13CNMR:154.5(N=CH)

2.11 Synthesis of N-(4-Chloro-benzylidene) pyridin-4-amine : 2j

Yield:77.4 %, m.p.: 168–169°C, Rf 0.79, IR (KBr, ν cm-^{1}): IR: 747(C-Cl), 1560 (N=CH, azomet), 1618 (C=N, Pyridine),1478 (C=C Aromatic);1HNMR (DMSO-d6)(δppm)7.9(s,1H,N=CH),8.4-7.2 (m, 8H, aromatic), 13CNMR:159.5(N=CH),152.3, (5C,Pyridine)

2.12 General conventional method for synthesis of compound (3a-3j) :

A mixture of compound 2a-2j (0.01 mol) and Et3N (0.01 mol) in ethanol, ClCH2COCl(0.01 mol) was added drop wise. The well stirred (2 h) reaction mixture was refluxed on a steam bath for 5 h. The reaction mixture was cooled and excess of solvent was evaporated under reduced pressure. The solid obtained was purified by passing it through a chromatographic column packed with Silica gel using chloro-form/methanol (6:4 v/v) as eluant and recrystallised from ethanol to give compounds (3a-3j) :

2.13 Synthesis of N-(2-oxo-3-Chloro-4-phenyl-azetidine)pyridin-4-amine (3a) :

Yield:73.6 %, m.p.: 108–109°C, Rf 0.69, IR (KBr, ν cm-^{1}): IR: 3068(C–H), 1731 (C=O),1618 (C=N, Pyridine),1478 (C=C

Aromatic);1HNMR (DMSO-d6) (δppm): 8.51–7.26 (m,9H, Ar),5.02 (d, 1H,N–CH–Ar), 5.22 (d,1H,CH–Cl),13CNMR:162.22 (C=O), 62.6 (CH–Cl), 68.5 (N–CH–Ar). M/S, m /z: 258(M)$^+$, 260,259,261,2

2.14 Synthesis of N-[{4-(4-methoxyphenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3b) : Yield:63.7%, m.p.: 98–93°C, Rf 0.70, IR (KBr, ν cm^{-1}):IR: 3097 (C–H),1741 (C=O),1244 (Ar–OCH3).1617(C=N, Pyridine), 1478 (C=C Aromatic);1HNMR (DMSO-d6) (δppm): 8.56 –6.96 (m,8H,Ar),5.08 (d,1H,N–CH–Ar),5.42(d,1H,CH–Cl),3.73 (s, 3H, OCH3), 13C NMR: 162.22 (C=O), 62.2 (CH–Cl), 68.1 (N-CH –Ar). M/S, m /z: 288(M)$^+$, 290,289,291,290

2.16 Synthesis of N-[{4-(3,4-Dimethoxyphenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3c) :

Yield:63.7%, m.p.: 98–93°C, Rf 0.70, IR (KBr, ν cm^{-1}): IR: 3031 (CH,CH3),1728 (C=O),1241 (Ar–OCH3).1618 (C=N, Pyridine),1475 (C=C Aromatic);1HNMR (DMSO-d6) (δppm): 8.56 –6.76 (m,7H,Ar),5.08(d,1H,N–CH–Ar),5.44(d,1H,CH–Cl),3.83(s,6H,OCH3), 13CNMR:162.22 (C=O),155.2, 150.1,109.1(5C Of Pyridine),62.0 (CH–Cl),68.7(N-CH–Ar). M/S, m /z: 318(M)$^+$, 318,320,319,321, 320

2.17 Synthesis of N-[{4-(4-Bromophenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3d) :

Yield:63.4%, m.p.: 98–99°C, Rf 0.72, IR (KBr, ν cm^{-1}): IR: 3031 (CH,CH3),1728 (C=O), 642(Ar–Br).1618(C=N, Pyridine),1475 (C=C Aromatic);1HNMR (DMSO-d6) (δppm): 8.56 –7.96(m,8H,Ar),5.08(d,1H,N–CH–Ar),5.44(d,1H,CH–Cl),13CNMR:162.2(C=O),155.2,150, 109.1 (5C Of Pyridine),62.0 (CH–Cl), 68.3 (N-CH -Ar). M/S, m /z: 335(M)$^+$, 337,335,339,336,

2.18 Synthesis of N-[{4-(2-Bromophenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3e) :

Yield:75.6%, m.p.: 97–99°C, Rf 0.76, IR (KBr, ν cm^{-1}):IR: 3091 (C–H,CH3),1735(C= O),644 (Ar–Br),1617 (C=N, Pyridine),1475 (C=C Aromatic);1HNMR (DMSO-d6) (δppm):8.56 –7.16(m,8H,Ar),5.08(d,1H,N–CH–Ar),5.44(d,1H,CH–Cl),13CNMR:162.22(C=O),155.3, 150.2,109.1(5C Of Pyridine),61.8(CH–Cl),64.7(N-CH–Ar). M/S, m /z: 318(M)$^+$, 318,320,319,321

2.19 Synthesis of N-[{4-(3-Bromophenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3f) :

Yield:75.6%, m.p.: 93–95°C, Rf 0.72, IR (KBr, ν cm^{-1}): 3094 (C–H,CH3),1745(C= O),636(Ar–Br),1615 (C=N, Pyridine),1478 (C=C Aromatic);1HNMR (DMSO-d6) (δppm):8.56 –7.26(m,8H,Ar),5.08(d,1H,N–CH–Ar),5.41(d,1H,CH–Cl), 13CNMR:162.21(C=O), 63.8(CH–Cl),69.7(N-CH–Ar). M/S, m /z: 335(M)$^+$

2.20 Synthesis ofN-[{4-((3,4,5-Trimethoxyphenyl)3-Chloro-2-oxo-azetidine)pyridin-4-amine (3g) :

Yield:73.7%, m.p.: 97–99°C, Rf 0.73, IR (KBr, ν cm^{-1}): IR: 3073 (CH,CH3),1747 (C=O),1248 (Ar–OCH3) 1620 (C=N, Pyridine),1479 (C=C Aromatic); 1HNMR (DMSO-d6) (δppm): 8.56 –6.66 (m,6H,Ar), 5.03(d,1H,N–CH–Ar),5.44(d,1H,CH–Cl),3.89 (s,9H, OCH3), 13C NMR: 162.2 (C=O), 62.0 (CH–Cl), 69.7 (N-CH –Ar).

2.21 Synthesis of N-[{4-((3 –methyl-phenyl)3-Chloro-2-oxo-azetidine)pyridin-4-amine (3h):

Yield:61.2%, m.p.: 145–148°C, Rf 0.69, IR (KBr, ν cm-^{1}): IR: 1547(N -CH),1612(C=N, Pyridine),1469(C=C Aromatic); 1HNMR (DMSO-d6) (δppm);2.31(s,3H,CH3), 8.59,7.02(m,8H,aromatic),

5.06(d,1H,N–CH–Ar),5.44(d,1H,CHCl),13CNMR:162.2(C=O), 158.1,150.7,109.1(5C Of Pyridine),62.0 (CH–Cl), 68.7 (N-CH –Ar). M/S, m /z: 272(M)$^+$,

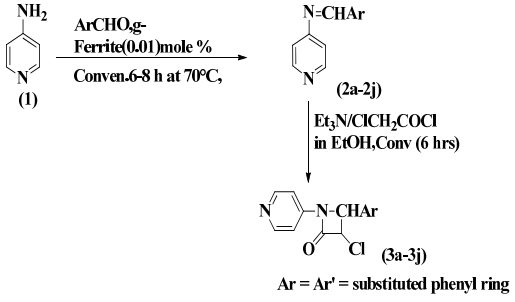
2.22 Synthesis of N-[{4-((2 –methoxyphenyl)3-Chloro-2-oxo-azetidine)pyridin-4-amine (3i):

Yield:64.8%, m.p.: 108–110°C, Rf 0.71, IR (KBr, ν cm^{-1}): 3097 (C–H),1738 (C=O),1249(Ar–OCH3).1614 (C=N, Pyridine),1472(C=CAromatic);1HNMR (DMSO-d6)(δppm): 8.56 –6.92 (m,8H,Ar),5.08 (d,1H,N–CH–Ar),5.46(d,1H,CH–Cl),3.83 (s, 3H, OCH3), 13C NMR: 162.12 (C=O),155,162.8 (CH–Cl), 62.1 (N-CH–Ar).125.4,154.8

2.23 Synthesis of N-[{4-((4–Chlorophenyl) 3-Chloro-2-oxo-azetidine)pyridin-4-amine (3j):

Yield:67.4%,m.p.:155159°C,Rf 0.81,IR (KBr,νcm^{1}): 745(CCl),1618(C=N,Pyridine), 1478 (C=CAromatic); 1HNMR(DMSO-d6) (δppm):8.56–7.43(m,8H,Ar),5.08 (d,1H,N–CH–Ar),5.48(d,1H,CH–Cl), 13C NMR: 162.12 (C=O),155.2,150.4,109.0 (5C Of Pyridine),62.2 (CH–Cl),69.1(N-CH-Ar). M/S, m /z: 288(M)$^+$

SCHEME-1



3. RESULTS AND DISCUSSION

The Schiff bases from 4-Amino-Pyridine with various substituted aromatic aldehydes were synthesized according to reaction scheme and characterized by FTIR, 1H-NMR,13C-NMR and Mass, and elemental analysis in order to verify their purity. All the spectral characterization data were found to support the Schiff base of amino pyridine. FTIR data proved the formation of Schiff's bases as the N=C peak appeared in the region of 1615–1638 $cm^{-1}$and diminished of the peaks for –NH2 and –C=O groups.In case of 1HNMR and 13C-NMR, the δ values 8.3 and 163–175 for N=C group confirmed the formation of 4-amino pyridine Schiff-base and its Azitidinone derivatives. Azitidinone derivatives (3a-3j)were prepared from 4 amino pyridine by the Schiff base cyclization in presence of tri-ethylamine and chloroacetylchloride. we tried the reaction with series of Lewis acids such as ZnCl2,AlCl 3,FeCl3 SiO2/Fe2O3, and with γ-ferrite also. The range of yield observed were 50–55,45–47, 45–48, 40–42 and 60–85% respectively. Thus, γ-ferrite (Fe2O3) was found to be highly efficient catalyst for the synthesis of imines and imine derived Azitidinone derivatives also. The formation of (2a-j) was supported by the appearance of signals at d 8.62-7.93 ppm due to -N=CH in the1H NMR spectra and IR spectra, the bands at 1598-1647 cm^{-1} (N=CH- , acyclic),Azetidinone derivatives (3a-3j) exhibited CHCl proton of β -lactam ring as doublet at δ 3.77–4.62 ppm. And N-CH proton as multiplet at δ 4.85–5.64 ppm. The structures were further confirmed by the mass spectra which exhibited the molecular ion peaks at their respective molecular weights.

4. CONCLUSION

We have synthesized some 4 amino pyridine Schiff base and its Azetidinone derivatives by green conventional method. With the help of heterogenous catalyst, the yield of product was increased from 60% upto 85% as compared to without green conventional method. By using heterogenous catalyst the reactions which reduced the time and formation of By-product.

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REFERENCES

[1] Ya ma waki, J.; Ando, T. Chem. Le tt. 1979, 755.
[2] Clark, J. H. Chem. Rev. 1980, 80, 429.
[3] Patrick G L and Kinsmar O S, Eur. J. Med. Chem. 31, 1996, 615-624.
[4] Hishmat O H, Abdel Galil F M and Farrag D S, Pharmazie, 45, 1990, 793-795.
[5] Buschmann E, Sauter M, Ammermann E, and Pommer, E H, Chem. Abst. 105, 1986, -772.
[6] Doshi R, Kagthara P, and Parekh H, Indian J. Chem. 38, 1999, 348-352.
[7] Hoehn H and Fr. Wemande, Chem. Abstr. 93, 1980, 980.
[8] Bhatt A H, Parekh M H, Parikh K A and Parikh A R, J. Indian Chem. Soc. 40, 2001, 57-21.
[9] Molla B S, Pharanna C S , Poojary B, Raw K S , Shridhar K, and Bhatt U G. Indian J. Chem. 43, 2004 864-868.
[10] Padhy A K, Nag V L, and Panda C S, Indian J. Chem. 38, 1999, 998-1001.
[11] Rani R R, Bhalerao U T, and Rahman M F, Indian J. Chem. 29, 1990, 995-998.
[12] Datta N J, Khunt R C, and Parikh A R, Indian J. Chem. 41, 2002, 2133-435.
[13] Abdel Rahman R M, EL Gendy Z, and Fawzy M M, J. Indian Chem. Soc. 68, 1991, 628-630.
[14] Anna A, Silivo G, Giuseppe M, and Lucio M, Eur. J. Med. Chem. 23, 1988, 149-154.
[15] Fernardes Y J, and Parekh H, J. Inst. Chem. 63, 1991, 119-120.
[16] Gehlot, D., and Vohra, A. Advances in plant sci., 1998, 1, 109-111.