

M. J. Joshi, P. B. Vekariya, B. L. Dodiya, R. M. Ghetiya, and H. S. Joshi*

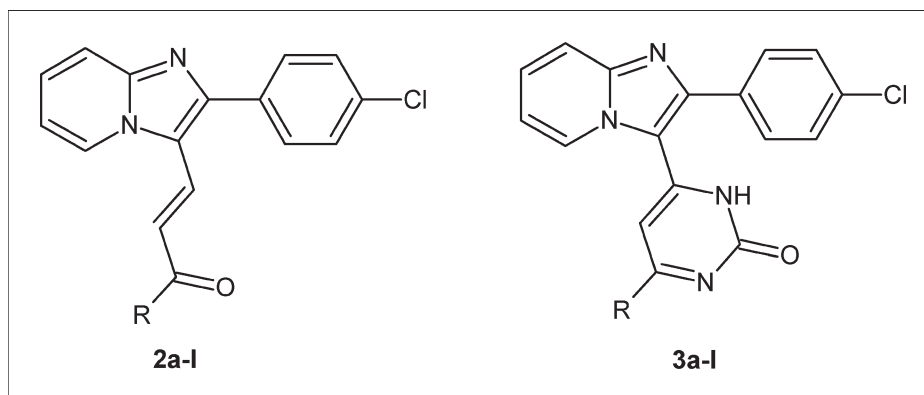
Chemical Research Laboratory, Department of Chemistry, Saurashtra University,
Rajkot-360005, India

*E-mail: drhsjoshi49@gmail.com

Received August 23, 2010

DOI 10.1002/jhet.787

Published online 15 October 2011 in Wiley Online Library (wileyonlinelibrary.com).



Heterosubstituted chalcones and oxypyrimidines were synthesized by the reaction of 2-(4-Chlorophenyl)imidazo[1,2-*a*]pyridine-3-carbaldehyde **1** and different aryl acetophenone in the presence of catalytic amount of 40% alkali to give (*2E*)-3-(2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-1-arylprop-2-en-1-ones **2a-I**. Compounds **2a-I** on reaction with urea in the presence of basic catalyst such as KOH to give 6-(2-(4-chlorophenyl)imidazo[1,2-*a*]pyridin-3-yl)-4-aryl pyrimidin-2(1*H*)-ones **3a-I**. Their IR, ¹H-NMR, MASS spectral data, and elemental analysis were in accord with assigned structure. All the newly synthesized compounds were screened for their antimicrobial activity.

J. Heterocyclic Chem., **49**, 130 (2012).

INTRODUCTION

Chalcones and oxypyrimidines are potential bioactive agents due to their wide spectrum of pharmacological activities such as anti-inflammatory [1], antimicrobial [2,3], calcium channel blockers [4], antihypertensive [5], analgesic [6], antitumor [7], antiviral [8], antibacterial [9], anti-HIV [10], anticancer [11], antimalarial [12], and antitubercular [13].

Our works are paying attention on introduction of chemical multiplicity in the molecular frame work, to synthesizing active molecules of widely different composition such as combination of two heterocyclic frame works to achieve good biological profile of the newly synthesized derivatives. So, we planned to synthesize some new chalcones and oxypyrimidines derivatives containing imidazo[1,2-*a*]pyridine moiety with hope that they may possess antimicrobial activities.

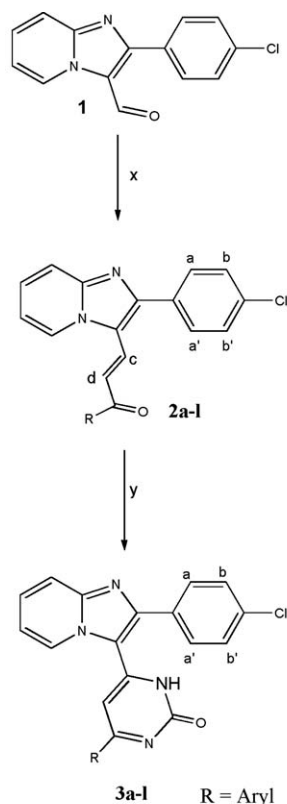
Imidazo[1,2-*a*]pyridine moieties represent important building blocks in both natural and synthetic bioactive compounds, which have been shown to possess diverse therapeutic activities [14,15]. The nature and the position of the substituent on the pyridinic moiety influence these activities [16].

RESULTS AND DISCUSSION

The synthesis of chalcones **2a-I** and oxypyrimidines **3a-I** were performed from the following steps shown in reaction (Scheme 1). The required compound **1** [17] has been prepared by the literature methods. The compounds **2a-I** were synthesized by reacting compound **1** with different aryl ketones in the presence of catalytic amount of 40% alkali in ethanol. Compounds **2a-I** on reaction with urea in the presence of basic catalyst such as KOH give compounds **3a-I**. The purity of all the newly synthesized compounds was checked on TLC. The structures of the synthesized compounds were assigned on the basis of spectral data such as IR, ¹H-NMR, MASS spectral analysis, and elemental analysis. All the newly synthesized compounds were in full agreement with the proposed structures.

Antimicrobial activity. The antimicrobial activity was assayed by using the cup-plate agar diffusion method [18] by measuring the zone of inhibition in mm. Newly synthesized compounds were screened *in vitro* for their antimicrobial activity against varieties of bacterial strains such *Bacillus megaterium* ATCC 14518, *Staphylococcus aureus* ATCC 25923, *Escherichia coli*

Scheme 1. Synthesis of chalcones and oxypyrimidines.



Reagents and conditions: (x) 40 % KOH, ethanol, RT.
(y) Alcoholic KOH, urea, ethanol, reflux

ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, and fungi *Aspergillus niger* ATCC 9029 at 40 $\mu\text{g}/\text{mL}$ concentration. Standard drugs such as Amoxicillin, Benzyl penicillin, Ciprofloxacin, Erythromycin, and Griseofulvin were used for the comparison purpose. The results are given in Table 1.

From the result of antimicrobial data, compounds **2g**, **2h**, **2i**, **2j**, **3g**, **3h**, **3i**, and **3j** were active and compounds **2a**, **2d**, **2k**, **3a**, **3e**, **3f**, and **3l** were moderately active against *B. megaterium*. Same as compounds **2i**, **2j**, **3g**, **3i**, and **3k** were active, whereas compounds **2g**, **2k**, **2i**, **3a**, **3c**, **3h**, and **3l** were moderately active against *S. aureus*. Further compounds **2g**, **2i**, **2l**, **3e**, **3h**, **3i**, **3j**, and **3k** were active and compounds **2b**, **2c**, **2k**, **3b**, **3d**, **3g**, and **3l** show moderate activity against *E. coli*. In case of *P. aeruginosa* compounds **2i**, **3d**, **3i**, and **3j** were active and compounds **2e**, **2j**, **2h**, **3f**, **3h**, and **3k** were moderately active. Against *A. niger* compounds **2h**, **2i**, **2j**, **3e**, **3i**, and **3j** were active, whereas compounds **2g**, **2f**, **2k**, **3a**, **3d**, **3h**, and **3k** were moderately active. Remaining compounds did not show any promising activity against tested bacteria and fungi.

The structure–activity relationship studies revealed that compounds **2i** and **3i** containing SO_2CH_3 group

present in 4-position in both cases, that is, chalcone and oxypyrimidines, show potent activities against all bacteria. Also compound **3j** containing **F** group at the 3-position exhibited very good antimicrobial activities against *B. megaterium*, *S. aureus*, *E. coli*, and *P. aeruginosa* and antifungal activity against *A. niger*.

EXPERIMENTAL

Melting points were determined on electrothermal apparatus using open capillaries and are uncorrected. Thin layer chromatography was accomplished on 0.2-mm precoated plates of silica gel G60 F254 (Merck, St. Louis, MO). Visualization was made with UV light (254 and 365 nm) or with an iodine vapor. IR spectra were recorded on a FTIR-8400 spectrophotometer (Shimadzu, Kyoto, Japan), using DRS prob. $^1\text{H-NMR}$ spectra were recorded on a Bruker AVANCE II (400 MHz) spectrometer (Bruker, Rheinstetten, Germany), in CDCl_3 . Chemical shifts are expressed in δ ppm downfield from TMS as an internal standard. Mass spectra were determined using direct inlet probe on a GCMS-QP 2010 mass spectrometer (Shimadzu, Kyoto, Japan). Elemental analysis was performed on a Carlo-Erba EA 1108 elemental analyzer (Waltham, MA). Solvents were evaporated with a Laborota 4000 efficient rotary evaporator (Heidolph, Germany). All reagents were purchased from Fluka (New Delhi, India), Sigma Aldrich (New Delhi, India), Merck (St. Louis, MO), and Rankem (New Delhi, India) and used without further purification.

Procedure for synthesis of 2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-carbaldehyde (1). To the solution of 2-(4-chlorophenyl)imidazo[1,2-a]pyridine (2.28 g, 0.01 mol) in DMF (25 mL) phosphorus oxychloride (3.06 g, 0.02 mol) was added at room temperature under stirring. The mixture was heated to 80°C for 5.0 h. The resulting solution was evaporated to dryness *in vacuo*, and the residue was treated with cold water, filtered, and crystallized from methanol to give pure product. Yield 64%, mp 196°C .

General procedure for synthesis of (2E)-3-[2-(4-chlorophenyl)imidazo[1,2-a]pyridin-3-yl]-1-arylprop-2-en-1-one (2a-l). The mixture of 2-(4-chlorophenyl)imidazo[1,2-a]pyridine-3-carbaldehyde (2.56 g, 0.01 mol) and aryl acetophenone (0.01 mol) in ethanol (25 mL) was stirred at room temperature for 24 h in the presence of catalytical amount of 40% KOH. The resulting solution was poured on to crushed ice, and thus the solid separated was filtered and crystallized from ethanol to give analytically pure product (**2a-l**).

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-phenyl-prop-2-en-1-one (2a). Yield 62%; m.p. $156\text{--}158^\circ\text{C}$; IR (KBr): 3015, 1655, 1591, 1509, 1170, 785 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz CDCl_3): δ , 7.33 (d, 2H, Ar-Ha,a'), 7.42 (d, 2H, Ar-Hb,b'), 7.51 (d, 1H, —CHc), 7.63 (m, 4H, imidazo[1,2-a]pyridine-H), 7.71 (d, 1H, —CHd), 7.81 (m, 5H, Ar-H); MS: m/z : 359 $[\text{M}^+]$; Anal. Calcd. for $\text{C}_{22}\text{H}_{15}\text{ClN}_2\text{O}$: C, 73.64; H, 4.21; N, 7.81% Found: C, 73.62; H, 4.17; N, 7.83%.

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-(4-methylphenyl)prop-2-en-1-one (2b). Yield 58%; m.p. $146\text{--}148^\circ\text{C}$; IR (KBr): 3021, 1645, 1583, 1480, 1153, 788 cm^{-1} ; $^1\text{H-NMR}$ (400 MHz CDCl_3): δ 2.70 (s, 3H, —CH₃), 7.08 (d, 2H, Ar-Ha,a'), 7.28 (d, 2H, Ar-Hb,b'), 7.33 (d, 1H, —CHc), 7.51 (m, 4H, imidazo[1,2-a]pyridine-H), 7.62 (d, 1H, —CHd),

Table 1
Antimicrobial screening results of compounds **2a–l** and **3a–l**.

Compound	R	Zones of inhibition in mm				
		Antibacterial activity				Antifungal activity
		<i>B. megaterium</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>A. niger</i>
2a	C ₆ H ₅ [−]	16	10	11	10	11
2b	4-CH ₃ -C ₆ H ₄ [−]	10	11	16	13	13
2c	2-CH ₃ -C ₆ H ₄ [−]	10	13	14	10	12
2d	2,4-(CH ₃) ₂ -C ₆ H ₃ [−]	14	12	11	11	11
2e	4-OCH ₃ -C ₆ H ₄ [−]	13	10	13	14	12
2f	2,4-(Cl) ₂ -C ₆ H ₃ [−]	12	10	12	13	15
2g	4-Cl-C ₆ H ₄ [−]	20	17	20	12	16
2h	3-Cl-C ₆ H ₄ [−]	21	13	12	14	20
2i	4-SO ₂ CH ₃ -C ₆ H ₄ [−]	20	18	18	18	21
2j	3-F-C ₆ H ₄ [−]	18	19	12	16	19
2k	3-NO ₂ -C ₆ H ₄ [−]	14	14	16	15	13
2l	4-NO ₂ -C ₆ H ₄ [−]	12	17	19	10	11
3a	C ₆ H ₅ [−]	16	16	10	10	17
3b	4-CH ₃ -C ₆ H ₄ [−]	13	12	17	13	11
3c	2-CH ₃ -C ₆ H ₄ [−]	12	14	10	12	12
3d	2,4-(CH ₃) ₂ -C ₆ H ₃ [−]	12	11	16	19	14
3e	4-OCH ₃ -C ₆ H ₄ [−]	17	11	20	11	18
3f	2,4-(Cl) ₂ -C ₆ H ₃ [−]	15	10	11	15	11
3g	4-Cl-C ₆ H ₄ [−]	18	20	16	13	12
3h	3-Cl-C ₆ H ₄ [−]	22	15	18	15	15
3i	4-SO ₂ CH ₃ -C ₆ H ₄ [−]	22	19	18	21	20
3j	3-F-C ₆ H ₄ [−]	19	17	19	20	21
3k	3-NO ₂ -C ₆ H ₄ [−]	13	21	20	17	17
3l	4-NO ₂ -C ₆ H ₄ [−]	17	15	17	13	13
Amoxicillin	–	25	25	20	22	00
Benzyl penicillin	–	18	19	21	21	00
Ciprofloxacin	–	20	15	22	16	00
Erythromycin	–	22	21	19	23	00
Greseofulvin	–	00	00	00	00	26

7.75 (m, 4H, Ar-H); MS: *m/z*: 373[M⁺]; Anal. Calcd. for C₂₃H₁₇ClN₂O: C, 74.09; H, 4.60; N, 7.51% Found: C, 74.05; H, 4.56; N, 7.48%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(2-methylphenyl)prop-2-en-1-one (**2c**). Yield 65%; m.p. 187–189°C; IR (KBr): 3010, 1659, 1595, 1474, 1090, 781 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 2.93 (s, 3H, −CH₃), 7.17 (d, 2H, Ar-Ha,a'), 7.24 (d, 2H, Ar-Hb,b'), 7.41 (d, 1H, −CHc), 7.59 (m, 4H, imidazo[1,2-*a*]pyridine-H), 7.73 (d, 1H, −CHd), 7.87 (m, 4H, Ar-H); MS: *m/z*: 386[M⁺]; Anal. Calcd. for C₂₃H₁₇ClN₂O: C, 74.09; H, 4.60; N, 7.51% Found: C, 74.08; H, 4.56; N, 7.48%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(2,4-dimethylphenyl)prop-2-en-1-one (**2d**). Yield 62%; m.p. 152–154°C; IR (KBr): 3023, 1649, 1605, 1487, 1124, 798 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 3.04 (s, 6H, −CH₃), 6.79 (d, 2H, Ar-Ha,a'), 7.23 (d, 2H, Ar-Hb,b'), 7.48 (d, 1H, −CHc), 7.73 (m, 4H, imidazo[1,2-*a*]pyridine-H), 7.82 (d, 1H, −CHd), 7.93 (m, 3H, Ar-H); MS: *m/z*: 387[M⁺]; Anal. Calcd. for C₂₄H₁₉ClN₂O: C, 74.51; H, 4.95; N, 7.24% Found: C, 74.47; H, 4.92; N, 7.23%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(4-methoxyphenyl)prop-2-en-1-one (**2e**). Yield 67%; m.p. 214–216°C; IR (KBr): 3016, 1645, 1593, 1503, 1221, 1107, 781 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 3.84 (s, 3H,

−OCH₃), 6.62 (d, 2H, Ar-Ha,a'), 6.75 (d, 2H, Ar-Hb,b'), 6.90 (d, 1H, −CHc), 7.22 (m, 4H, imidazo[1,2-*a*]pyridine-H), 7.56 (d, 1H, −CHd), 7.71 (m, 4H, Ar-H); MS: *m/z*: 389[M⁺]; Anal. Calcd. for C₂₃H₁₇ClN₂O₂: C, 71.04; H, 4.41; N, 7.20% Found: C, 71.03; H, 4.38; N, 7.17%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(2,4-dichlorophenyl)prop-2-en-1-one (**2f**). Yield 58%; m.p. 198–200°C; IR (KBr): 3019, 1658, 1591, 1481, 1083, 785 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 6.62 (d, 2H, Ar-Ha,a'), 6.72 (d, 2H, Ar-Hb,b'), 6.92 (d, 1H, −CHc), 7.21 (m, 4H, imidazo[1,2-*a*]pyridine-H), 7.55 (d, 1H, −CHd), 7.73 (m, 3H, Ar-H); MS: *m/z*: 428[M⁺]; Anal. Calcd. for C₂₂H₁₃Cl₃N₂O: C, 61.78; H, 3.06; N, 6.55% Found: C, 61.75; H, 3.05; N, 6.49%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(4-chlorophenyl)prop-2-en-1-one (**2g**). Yield 55%; m.p. 180–182°C; IR (KBr): 3027, 1663, 1580, 1460, 1097, 773 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 6.69 (d, 2H, Ar-Ha,a'), 6.78 (d, 2H, Ar-Hb,b'), 6.94 (d, 1H, −CHc), 7.27 (m, 4H, imidazo[1,2-*a*]pyridine-H), 7.58 (d, 1H, −CHd), 7.78 (m, 4H, Ar-H); MS: *m/z*: 393[M⁺]; Anal. Calcd. for C₂₂H₁₄Cl₂N₂O: C, 67.19; H, 3.59; N, 7.12% Found: C, 67.16; H, 3.58; N, 7.15%.

(2*E*)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-*a*]pyridin-3-yl)-1-(3-chlorophenyl)prop-2-en-1-one (**2h**). Yield 65%; m.p. 149–151°C; IR (KBr): 3012, 1652, 1601, 1478, 1118, 797 cm^{−1}; ¹H-NMR (400 MHz CDCl₃): δ 6.59 (d, 2H, Ar-Ha,a'), 6.82 (d,

2H, Ar-Hb,b'), 6.99 (d, 1H, —CHc), 7.34 (m, 4H, imidazo[1,2-a]pyridine-H), 7.61 (d, 1H, —CHd), 7.71 (m, 4H, Ar-H); MS: m/z : 393[M⁺]; Anal. Calcd. for C₂₂H₁₄Cl₂N₂O: C, 67.19; H, 3.59; N, 7.12% Found: C, 67.18; H, 3.62; N, 7.10%.

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-(4-methylsulfonylphenyl)prop-2-en-1-one (2i). Yield 62%; m.p. 177–179°C; IR (KBr): 3056, 1645, 1588, 1491, 1084, 773 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 2.97 (s, 3H, —SO₂CH₃), 6.61 (d, 2H, Ar-Ha,a'), 6.76 (d, 2H, Ar-Hb,b'), 7.03 (d, 1H, —CHc), 7.24 (m, 4H, imidazo[1,2-a]pyridine-H), 7.51 (d, 1H, —CHd), 7.88 (m, 4H, Ar-H); MS: m/z : 437[M⁺]; Anal. Calcd. for C₂₃H₁₇ClN₂O₃S: C, 68.22; H, 4.23; N, 6.92% Found: C, 68.21; H, 4.22; N, 6.91%.

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-(3-fluorophenyl)prop-2-en-1-one (2j). Yield 64%, m.p. 211–213°C; IR (KBr): 3010, 1643, 1610, 1510, 1163, 790 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 6.64 (d, 2H, Ar-Ha,a'), 6.76 (d, 2H, Ar-Hb,b'), 6.97 (d, 1H, —CHc), 7.31 (m, 4H, imidazo[1,2-a]pyridine-H), 7.59 (d, 1H, —CHd), 7.78 (m, 4H, Ar-H); MS: m/z : 377[M⁺]; Anal. Calcd. for C₂₂H₁₄ClFNO: C, 70.12; H, 3.74; N, 7.43% Found: C, 70.09; H, 3.73; N, 7.40%.

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-(3-nitrophenyl)prop-2-en-1-one (2k). Yield 57%; m.p. 172–174°C; IR (KBr): 3005, 1649, 1581, 1497, 1149, 795 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 7.03 (d, Ar-Ha,a'), 7.19 (d, 2H, Ar-Hb,b'), 7.41 (d, 1H, —CHc), 7.58 (m, 4H, imidazo[1,2-a]pyridine-H), 7.71 (d, 1H, —CHd), 7.93 (m, 4H, Ar-H); MS: m/z : 404[M⁺]; Anal. Calcd. for C₂₂H₁₄ClN₃O₃: C, 65.43; H, 3.49; N, 10.41% Found: C, 65.45; H, 3.47; N, 10.39%.

(2E)-3-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-1-(4-nitrophenyl)prop-2-en-1-one (2l). Yield 59%; m.p. 167–169°C; IR (KBr): 3005, 1649, 1581, 795 cm⁻¹. ¹H-NMR (400 MHz CDCl₃) δ 7.07 (d, 2H, Ar-Ha,a'), 7.23 (d, 2H, Ar-Hb,b'), 7.49 (d, 1H, —CHc), 7.64 (m, 4H, imidazo[1,2-a]pyridine-H), 7.69 (d, 1H, —CHd), 8.03 (m, 4H, Ar-H); MS: m/z : 404[M⁺]; Anal. Calcd. for C₂₂H₁₄ClN₃O₃: C, 65.43; H, 3.49; N, 10.48% Found: C, 65.41; H, 3.46; N, 10.47%.

General procedure for synthesis of 6-[2-(4-Chlorophenyl)imidazo[1,2-a]pyridin-3-yl]-4-aryl pyrimidin-2(1H)-one (3a–l). The mixture of (2E)-3-(2-(2,4-dichlorophenyl)imidazo[1,2-a]pyridin-3-yl)-1-4-aryl-prop-2-en-1-one (0.01 mol) and urea (0.77 g, 0.01 mol) in ethanol (20 mL) was refluxed in the presence of alcoholic KOH for 8 h. The excess solvent was distilled off under reduced pressure *in vacuo*, and the residue was neutralized with dilute HCl, and thus, the separated solid was filtered out and crystallized from ethanol to give pure product (3a–l).

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-phenylpyrimidin-2(1H)-one (3a). Yield 63%; m.p. 168–170°C; IR (KBr): 3351, 3015, 1658, 1591, 1433, 1107, 785 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.31 (s, 1H, —Hh), 7.04 (q, 2H, Ar-Ha,a') 7.26 (d, 2H, Ar-Hb,b'), 7.41 (m, 4H, imidazo[1,2-a]pyridine-H), 7.57 (m, 5H Ar-H), 7.81 (s, 1H —NH); MS: m/z : 399[M⁺]; Anal. Calcd. for C₂₃H₁₅ClN₄O: C, 69.26; H, 3.79; N, 14.05% Found: C, 69.21; H, 3.83; N, 14.04%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(4-methylphenyl)pyrimidin-2(1H)-one (3b). Yield 54%; m.p. 192–194°C; IR (KBr): 3293, 3019, 1650, 1587, 1463, 1129, 780 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 3.23 (s, 3H, —CH₃), 5.42 (s, 1H, —Hh), 7.13 (q, 2H, Ar-Ha,a') 7.34 (d, 2H, Ar-Hb,b'), 7.46 (m, 4H, imidazo[1,2-a]pyridine-H), 7.63 (m, 4H,

Ar-H), 7.93 (s, 1H —NH); MS: m/z : 413[M⁺]; Anal. Calcd. for C₂₄H₁₇ClN₄O: C, 69.82; H, 4.15; N, 13.57 % Found: C, 69.76; H, 4.19; N, 13.48%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(2-methylphenyl)pyrimidin-2(1H)-one (3c). Yield 61%; m.p. 175–177°C; IR (KBr): 3317, 3024, 1652, 1589, 1451, 1136, 779 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 3.27 (s, 3H, —CH₃), 5.37 (s, 1H, —Hh), 7.16 (q, 2H, Ar-Ha,a') 7.31 (d, 2H, Ar-Hb,b'), 7.51 (m, 4H, imidazo[1,2-a]pyridine-H), 7.67 (m, 4H, Ar-H), 7.90 (s, 1H —NH); MS: m/z : 413[M⁺]; Anal. Calcd. for C₂₄H₁₇ClN₄O: C, 69.82; H, 4.15; N, 13.57 % Found: C, 69.81; H, 4.12; N, 13.55%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(2,4-dimethylphenyl)pyrimidin-2(1H)-one (3d). Yield 58%; m.p. 152–154°C; IR (KBr): 3329, 3024, 2990, 1658, 1581, 1375, 1130, 784 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 3.37 (s, 6H, —CH₃), 5.49 (s, 1H, —Hh), 7.21 (q, 2H, Ar-Ha,a') 7.38 (d, 2H, Ar-Hb,b'), 7.61 (m, 4H, imidazo[1,2-a]pyridine-H), 7.74 (m, 3H, Ar-H), 8.01 (s, 1H —NH); MS: m/z : 427[M⁺]; Anal. Calcd. for C₂₅H₁₉ClN₄O: C, 70.34; H, 4.49; N, 13.12% Found: C, 70.38; H, 4.37; N, 13.09%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(4-methoxyphenyl)pyrimidin-2(1H)-one (3e). Yield 72%; m.p. 183–185°C; IR (KBr): 3227, 3029, 2954, 1649, 1570, 1367, 1104, 786 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 3.73 (s, 3H, —OCH₃), 5.47 (s, 1H, —Hh), 7.09 (q, 2H, Ar-Ha,a') 7.21 (d, 2H, Ar-Hb,b'), 7.57 (m, 4H, imidazo[1,2-a]pyridine-H), 7.65 (m, 4H, Ar-H), 7.80 (s, 1H —NH); MS: m/z : 429[M⁺]; Anal. Calcd. for C₂₄H₁₇ClN₄O₂: C, 67.21; H, 4.00; N, 13.06 % Found: C, 67.17; H, 4.07; N, 13.11%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(2,4-dichlorophenyl)pyrimidin-2(1H)-one (3f). Yield 67%; m.p. 212–215°C; IR (KBr): 3262, 3018, 1659, 1590, 1453, 1133, 791 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 6.22 (s, 1H, —Hh), 7.12 (q, 2H, Ar-Ha,a') 7.38 (d, 2H, Ar-Hb,b'), 7.46 (m, 4H, imidazo[1,2-a]pyridine-H), 7.61 (m, 3H, Ar-H), 7.87 (s, 1H, —NH); MS: m/z : 468[M⁺]; Anal. Calcd. for C₂₃H₁₃Cl₃N₄O: C, 59.06; H, 2.80; N, 11.98% Found: C, 59.13; H, 2.76; N, 11.93 %.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(4-chlorophenyl)pyrimidin-2(1H)-one (3g). Yield 34%; m.p. 195–197°C; IR (KBr): 3319, 3029, 1665, 1587, 1093, 796 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.53 (s, 1H, —Hh), 7.11 (q, 2H, Ar-Ha,a') 7.25 (d, 2H, Ar-Hb,b'), 7.49 (m, 4H, imidazo[1,2-a]pyridine-H), 7.67 (m, 4H, Ar-H), 7.92 (s, 1H —NH); MS: m/z : 433[M⁺]; Anal. Calcd. for C₂₃H₁₄Cl₂N₄O: C, 63.76; H, 3.26; N, 12.93% Found: C, 63.71; H, 3.30; N, 12.88%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(3-chlorophenyl)pyrimidin-2(1H)-one (3h). Yield 46%; m.p. 221–222°C; IR (KBr): 3312, 3019, 1672, 1588, 1128, 781 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.45 (s, 1H, —Hh), 7.19 (q, 2H, Ar-Ha,a'), 7.30 (d, 2H, Ar-Hb,b'), 7.54 (m, 4H, imidazo[1,2-a]pyridine-H), 7.70 (m, 4H, Ar-H), 7.95 (s, 1H —NH); MS: m/z : 433[M⁺]; Anal. Calcd. for C₂₃H₁₄Cl₂N₄O: C, 63.76; H, 3.26; N, 12.93% Found: C, 63.73; H, 3.21; N, 12.90%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-[4(methylsulfonyl)phenyl]pyrimidin-2(1H)-one (3i). Yield 43%; m.p. 186–188°C; IR (KBr): 3315, 3034, 1666, 1589, 1139, 785 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.35 (s, 1H, —Hh), 7.06

(q, 2H, Ar-Ha,a'), 7.37 (d, 2H, Ar-Hb,b'), 7.47 (m, 4H, imidazo[1,2-a]pyridine-H), 7.53 (m, 4H, Ar-H), 7.87 (s, 1H —NH); MS: *m/z*: 476[M⁺]; Anal. Calcd. for C₂₄H₁₇ClN₄O₃S: C, 65.65; H, 3.75; N, 13.03% Found: C, 65.64; H, 3.73; N, 13.02%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(3-fluorophenyl)pyrimidin-2(1H)-one (3j). Yield 68%; m.p. 216–218°C; IR (KBr): 3296, 3025, 1658, 1566, 1146, 781 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.40 (s, 1H, —Hh), 7.15 (q, 2H, Ar-Ha,a'), 7.33 (d, 2H, Ar-Hb,b'), 7.53 (m, 4H, imidazo[1,2-a]pyridine-H), 7.69 (m, 4H, Ar-H), 7.91 (s, 1H —NH); MS: *m/z*: 417[M⁺]; Anal. Calcd. for C₂₃H₁₄ClFN₄O: C, 66.27; H, 3.39; N, 13.44% Found: C, 66.24; H, 3.36; N, 13.44%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(3-nitrophenyl)pyrimidin-2(1H)-one (3k). Yield 55%; m.p. 169–171°C; IR (KBr): 3252, 3015, 1648, 1561, 1124, 786 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.61 (s, 1H, —Hh), 7.17 (q, 2H, Ar-Ha,a'), 7.21 (d, 2H, Ar-Hb,b'), 7.46 (m, 4H, imidazo[1,2-a]pyridine-H), 7.62 (m, 4H, Ar-H), 7.97 (s, 1H —NH); MS: *m/z*: 444[M⁺]; Anal. Calcd. for C₂₃H₁₄ClFN₅O₃: C, 62.24; H, 3.18; N, 15.78% Found: C, 62.25; H, 3.14; N, 15.78%.

6-(2-(4-Chlorophenyl)H-imidazo[1,2-a]pyridin-3-yl)-4-(4-nitrophenyl)pyrimidin-2(1H)-one (3l). Yield 40%; m.p. 185–187°C; IR (KBr): 3335, 3062, 1663, 1556, 1453, 1124, 789 cm⁻¹; ¹H-NMR (400 MHz CDCl₃): δ 5.65 (s, 1H, —Hh), 7.20 (q, 2H, Ar-Ha,a'), 7.39 (d, 2H, Ar-Hb,b'), 7.51 (m, 4H, imidazo[1,2-a]pyridine-H), 7.67 (m, 4H, Ar-H), 8.05 (s, 1H —NH); MS: *m/z*: 444[M⁺]; Anal. Calcd. for C₂₃H₁₄ClFN₅O₃: C, 62.24; H, 3.18; N, 15.78% Found: C, 62.21; H, 3.14; N, 15.76%.

CONCLUSIONS

In conclusion, we have described efficient synthesis of imidazo[1,2-a]pyridine systems containing chalcones and oxopyrimidines. Imidazo[1,2-a]pyridine is the key intermediate in the formation of these heterocyclic compounds. Although there are not many imidazo[1,2-a]pyridine fused to chalcones or oxopyrimidines, a number of them are incorporated into a wide variety of therapeutically important compounds possessing a broad spectrum of biological activities. In this connection, we have synthesized chalcones and oxopyrimidines.

Biological activity data indicate imidazo[1,2-a]pyridine systems containing oxopyrimidines ring show potent activity, Finally, we concluded that oxopyrimidine ring

increases biological activity with imidazo[1,2-a]pyridine nucleus while chalcone is moderate active.

Acknowledgments. Authors are thankful to Department of Chemistry for providing laboratory facilities. The authors are also thankful for facilities and grants given under UGC-SAP for Department Research Support (DRS) and Department of Science & Technology (DST), New Delhi for Fund for Improvement of Science & Technology (FIST). Authors are also thankful to RSIC Chandigarh for providing ¹H-NMR spectral analysis of the compounds.

REFERENCES AND NOTES

- [1] Bahekar, S. S.; Shinde, D. B. *Acta Pharm* 2003, 53, 223.
- [2] Ladani, M. J.; Tala, S. D.; Akbari, J. D.; Dhaduk, M. F.; Joshi, H. S. *J Indian Chem Soc* 2009, 86, 104.
- [3] Rival, Y.; Grassy, G.; Michel, G. *Chem Pharma Bull* 1992, 40, 1170.
- [4] Sanfilippo, P. J.; Urbanski, M.; Press, J. B.; Dubinsky, B.; Moore, J. B., Jr. *J Med Chem* 1988, 31, 2221.
- [5] Pathak, P.; Kaur, R.; Kaur, B. *ARKIVOC* 2006, xvi, 160.
- [6] Veerachamy, A.; Durairaj, S.; Viswas, R. S. *ARKIVOC* 2006, xvi, 149.
- [7] Huang, Y. L.; Lin, C. F.; Lee, Y. J.; Li, W. W.; Chao, T. C. *Bio Org Med Chem* 2003, 11, 145.
- [8] Shigeta, S.; Mori, S.; Watanabe, F.; Saneyoshi, M. *Antivir Chem Chemother* 2002, 13, 67.
- [9] Somnath, N.; Richa, P.; Manish, K.; Shukla, P. K.; Sanjay, B. *Bio Org Med Chem* 2006, 16, 3824.
- [10] Cheenpracha, S.; Karalai, C.; Ponglimanont, C.; Subhadhirasakul, S.; Supinya, T. *Bioorg Med Chem* 2006, 14, 1710.
- [11] Nimavat, K. S.; Popat, K. H.; Vasoya, S. L.; Joshi, H. S. *Indian J Heterocycl Chem* 2003, 12, 217.
- [12] Whittingham, J. L.; Leal, I.; Nguyen, C.; Kasinathan, G.; Bell, E. *Structure (Camb.)* 2005, 13, 329.
- [13] Popat, K. H.; Purohit, D. H.; Chovatia, P. T.; Joshi, H. S. *J Indian Chem Soc* 2005, 82, 940.
- [14] Silvestre, J.; Leeson, P. A.; Castaner, J. *Drugs Future* 1998, 23, 598.
- [15] Hamdouchi, C.; Blas, J.; Prado, M.; Gruber, J.; Heinz, B. A.; Vance, L. *J Med Chem* 1999, 42, 50.
- [16] Lhassani, M.; Chavignon, O.; Chezal, J. M.; Teulade, J. C.; Chapat, J. P.; Snoeck, R.; Andrei, G.; Balzarini, J.; De Clercq, E.; Gueiffier, A. *Eur J Med Chem* 1999, 34, 271.
- [17] Burkholder, C.; Dolbier, W. R.; Medebielle, M.; Ait-Mohand, S. *Tetrahedron Lett* 2001, 42, 3077.
- [18] (a) Barry, A. L. In *The Antimicrobial Susceptibility Test: Principle and Practices*; Lea, I.; Febiger, Eds.; CBS Publishers and Distributors, Philadelphia, PA, USA, 1976; p 180; (b) Barry, A. L. *Biol Abstr* 1976, 64, 25183.