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UNWINDING ULTRASOUND ASSISTED CATALYST-FREE SYNTHESIS OF IMIDAZOPYRIDINE AND IMIDAZOTHIAZOLE MOIETIES: A NON-CONVENTIONAL SUSTAINABLE APPROACH

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ABSTRACT

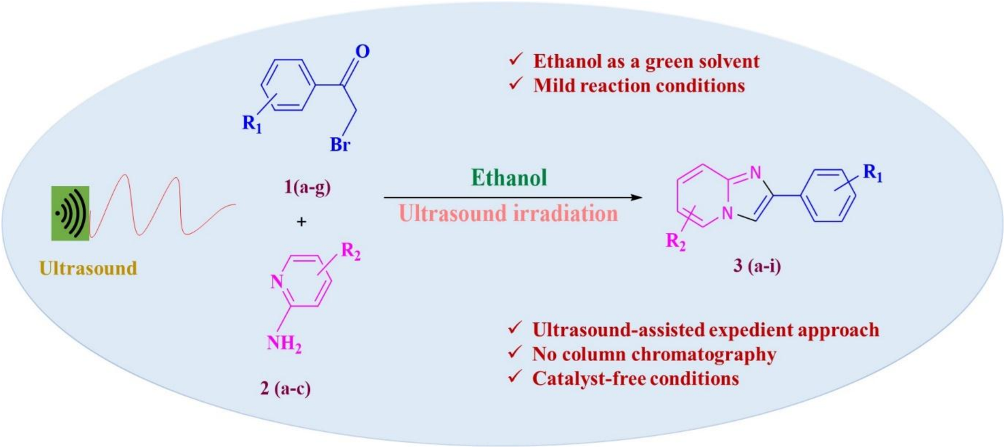
Momordica dioica Roxb., also known as spine gourd, is a nutritionally valuable dioecious plant with a wide range of pharmacological properties. It is rich in beta-carotene, proteins, calcium, phosphorus, and iron, making it a nutritious vegetable widely consumed in India. It exhibits antioxidant, hepatoprotective, anticancer, anti-ulcer, anti-inflammatory, antiallergic, nephroprotective, antimalarial, antidiabetic, and antibacterial activities due to its bioactive compounds. This underutilized plant holds promise for further research and development in natural medicine. There are lot many review articles already have been published in many different national and international journals. Although not much regarding its pharmacological activity in numerous disease has been discussed and explained smoothly. Therefore, a small attempt in this review article has been made to explain various pharmacological activity of Momordica dioica Roxb or spine gourd.

KEYWORDS: Momordica dioica Roxb., dioecious plant, Pharmacological actions.

ABSTRACT

An efficient, sustainable and environmentally benign approach has been established for the synthesis of imidazothiazoles and imidazopyridines using ethanol as a green solvent. The reaction was carried out at room temperature under ultrasonic irradiation and catalyst/metal-free conditions. The outstanding operational simplicity, practicality and versatility of this approach make it a promising alternative procedure to previously conventional reported methods. The present methodology provides excellent yields, easy isolation of products and no requirement of work-up or column chromatography purification. Thus, the reaction profile is clean, pollutant-free and economical with limited use of volatile solvents.

KEYWORDS: Ultrasonic irradiation, catalyst-free condition, metal-free condition, non-conventional method.



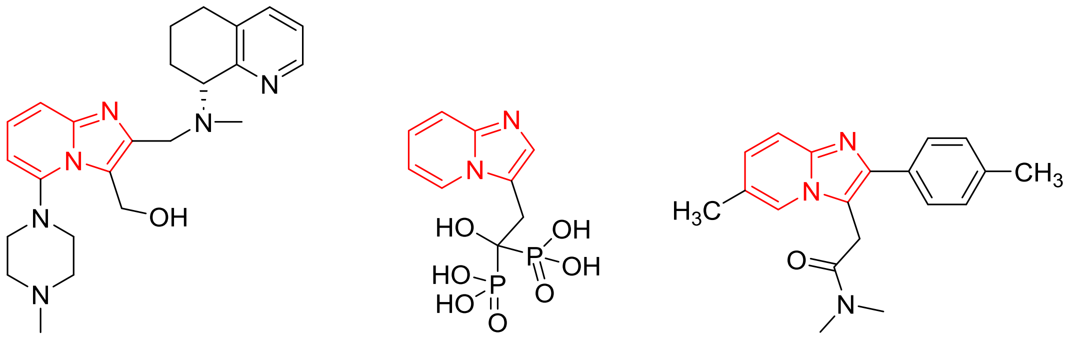
✓ Ethanol as a green solvent
✓ Mild reaction conditions

✓ Ultrasound-assisted expedient approach
✓ No column chromatography
✓ Catalyst-free conditions

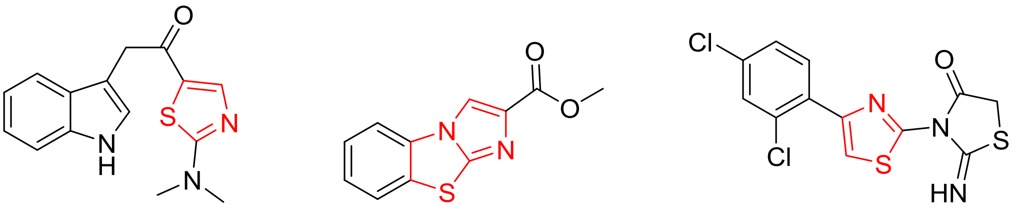
INTRODUCTION

Heterocyclic compounds widely exist in various natural products, biological compounds, drugs, and functional materials.[1] Many synthetic targets that are biologically active, such as natural compounds and medicines, contain nitrogen-containing heterocycles.[2-4] Therefore, synthetic chemists have been paying close attention to the synthesis and functionalization of nitrogen-containing heterocycles.[5] Imidazopyridine and imidazolthiazoles are such biologically significant heterocycles Imidazopyridine derivatives have a wide range of biological activities, which makes them very appealing heteroaromatic units.[6] Specifically, imidazo[1,2-a]pyridine has been identified as a major core in numerous medicines, including minodronic acid, olprinone, zolimidine, and alpidem.[7] Medicinal and biological properties of imidazopyridine, such as their anticancer[8], antimicrobial[9-11], anti-inflammatory[12], antibacterial, anxiolytic, ulcer-healing, antiviral, antiprotozoal, antiherpes, and antiapoptotic properties, GABA receptor ligand[13] and calcium channel antagonist[14] are well-known. It has recently been discovered that a derivative of imidazo[1,2-a]pyrimidine exhibits remarkable in vivo tumor growth suppression in prostate cancer that is resistant to castration (CRPC).[15] Specifically, 3-substituted imidazo[1,2-a]pyridines are recognized as preferred scaffolds. As an illustration, the C3- alkylated imidazo[1,2-a]pyridines are frequently included in commercially accessible medications, including the hypnotics Zolpidem and the anti-HIV GSK812397 (Fig.1).[16] Similarly, Thiazoles are mostly connected with medicinal chemistry and have been used significantly in the development of drugs to treat bacterial infections, hypertension, allergies[17], inflammation[18], and HIV infections[19], hypnotics[20], schizophrenia[21] pain management[22], novel bacterial DNA gyrase B[23], fibrinogen receptor antagonists with antithrombotic properties[24] and so on. Its biological abilities are outstanding exhibiting properties including anticancer[25], antifungal[26], antibacterial[27], anti-inflammatory[28], antitubercular[29], anticonvulsant[30], diuretic[31], neuroprotective and antioxidant activity.[32]

In the pursuit of exploring the sustainable alternatives to conventional procedures ultrasonic-irradiation techniques brought to be the best method relative to waste reduction and energy conservation.[33-37] Under ultrasonic irradiation, organic transformations can be achieved in the paucity of catalyst.[38] Ultrasonic vibrations create an array of small cavitation bubbles within the solution. These small bubbles generate micro-jets that can produce a fine emulsion between the starting precursors, as they rapidly ascend and explode abruptly.[39] Further, the reaction solution and local temperature increase due to the powerful collapse of these small bubbles.[40] This provides sufficient energy to surpass the energy barrier.[41] To expand the application of ultrasound in the synthesis of heterocyclic compounds, herein, we report a synthesis of imidazopyridines and imidazothiazole motifs under ultrasound irradiation.



Anti-HIV agent **Minodronic acid** **Zolpidem**



Anticancer agent **Nonsedative anxiolytic** **Antifungal agent**

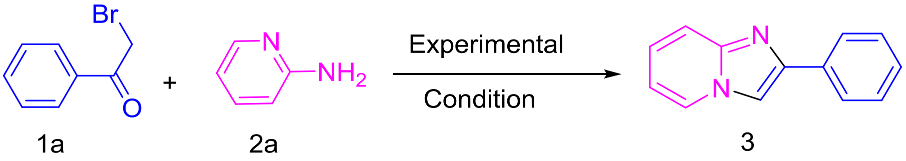
Figure 1: Some medicinally important derivatives imidazopyridine and imidazothiazole.

RESULTS AND DISCUSSION

In the beginning of our quest for an efficient and environmentally friendly approach for producing 2-arylimidazo fused heterocycles, we chose a model reaction to prepare 2-phenyl-imidazo[1,2-*a*] pyridine using phenacyl bromide (**1a**, 1mmol) and 2-aminopyridine (**2a**, 1 mmol) as substrates under ultrasound irradiation. We investigated the effect of various green solvents in this study, in addition to the reaction time, as described in Table 1. Our investigation started with the reaction of 2-aminopyridine 1a (0.5 mmol) and 2-bromoacetophenone 2a (0.5 mmol) under neat condition at room temperature (RT). After sonication for 120 min, desired product(3a) was obtained in 68% isolated yield (Table 1, Entry 1). After obtaining this result, we focused on screening various environmentally friendly solvents, including water, ethanol, glycerol, glycerol: water (3:1), PEG-400, ethyl lactate and under various rection condition (entries 2-8). The best result (Table 1, Entry 3) was observed in ethanol under ultrasound irradiation at ambient conditions to furnish the desired product, 2-phenyl-imidazo[1,2-*a*] pyridine in a 96% yield just in 30min, proving that the efficient energy-transfer by the ultrasonic irradiation can promote a fast reaction. The isolated compound was characterized by its elemental and spectral (^{1}H-NMR, IR and ^{13}C-NMR) studies. The overall results are documented in Table 1.

In order to further improve the yield and decrease the reaction time, we tried to increase the reaction temperature under ultrasound irradiation. The effect, however, was not remarkable (Table 1). Consequently, it was indicated that there was no remarkable temperature effect on this reaction.

Table 1: Optimization of Reaction Conditions for the Synthesis of 2-phenyl imidazo [1,2-*a*] pyridines under ultrasound irradiation.

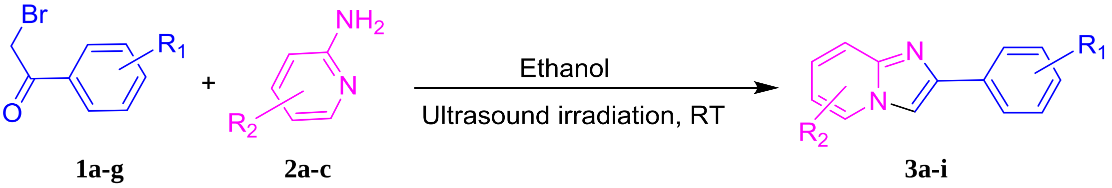


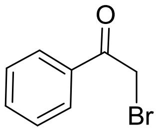
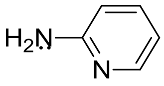
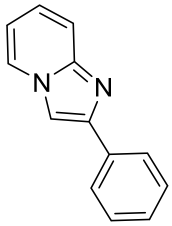
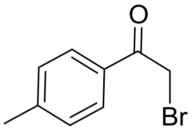
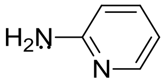
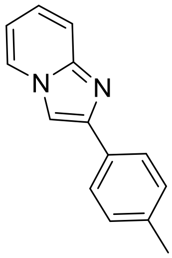
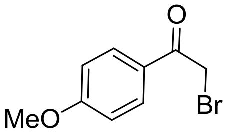
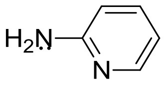
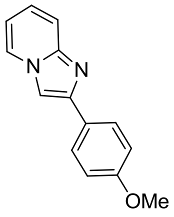
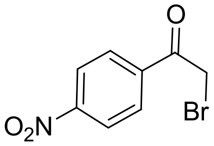
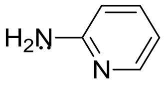
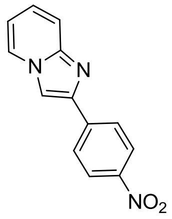
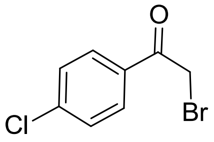
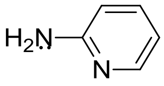
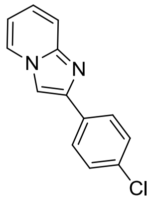
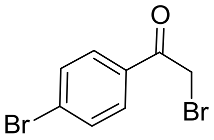
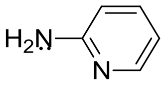
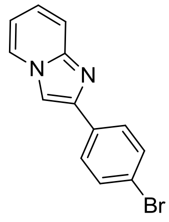
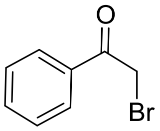
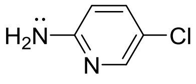
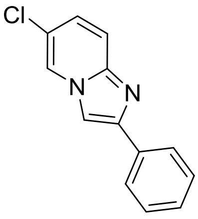
Entry	Solvent	Method	Temp	Time (min.)	Yield(%)^{a,b}
1.	Neat	Ultrasound	RT	120	68
			50	110	69
			70	100	71
2.	Water	Ultrasound	RT	300	40
			50	270	42
			70	240	45
3.	**Ethanol**	**Ultrasound**	**RT**	**30**	**96**
			50	25	96
			70	20	97
4.	Glycerol	Ultrasound	RT	40	90
5.	Glycerol: Water (4:1)	Ultrasound	50	45	93
6.	PEG-400	Ultrasound	50	60	89
7.	Ethyl lactate	Ultrasound	RT	60	91
8.	Ethanol	Stirring	RT	780	37
			80	420	45

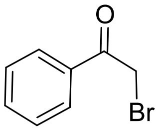
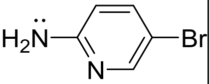
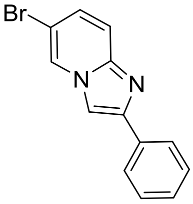
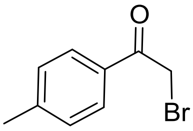
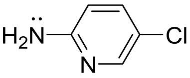
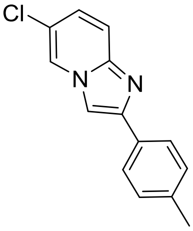
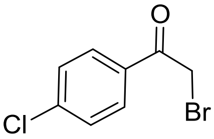
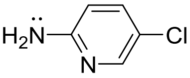
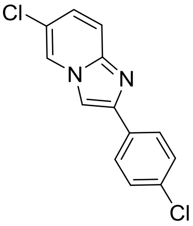
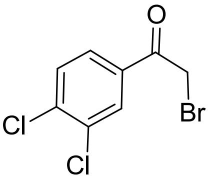
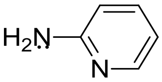
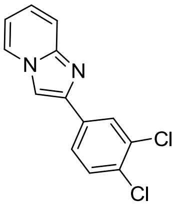
[a] All reactions were carried out with phenacyl bromide (**1a**) (1 mmol) and 2-amino pyridine (**2a)** (1mmol) using 5ml ethanol under ultrasound irradiation. [b] Isolated yields.

After finding the optimal conditions for performing this reaction, we employed the devised methodology to produce a variety of substituted imidazopyridines [Table 2]. All of the compounds were adequately synthesized in short reaction times and with good to excellent yields. Whenever, using phenacyl bromides with an electron withdrawing group on the phenyl ring, higher yields and faster reactions were generally seen, whereas when an electron donating group was present on the phenyl ring, the reaction slowed down and the product yield was decreased.

Table 2: Substrate scope[a]

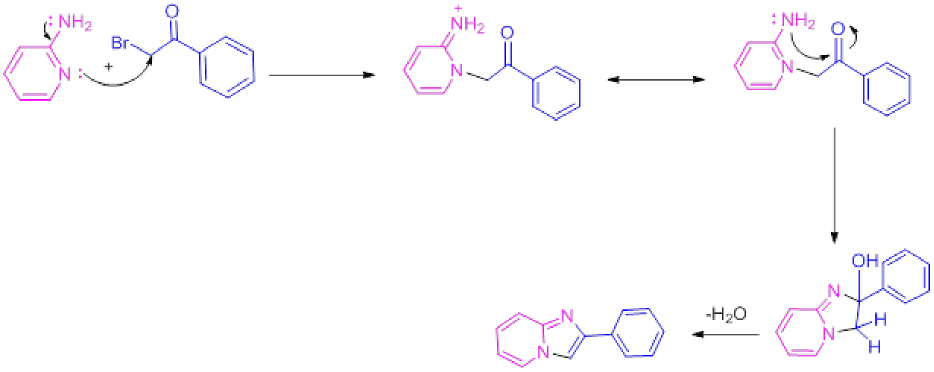


Entry	1	2	Product	Time (min)	Yield[b] (%)	M. P. (°C)
1.	 **1a**	 **2a**	 **3a**	**30**	**96**	**136-138**
2.	 **1b**	 **2a**	 **3b**	**30**	**90**	**136-138**
3.	 **1c**	 **2a**	 **3c**	**55**	**89**	**132-134**
4.	 **1d**	 **2a**	 **3d**	**20**	**96**	**264-266**
5.	 **1e**	 **2a**	 **3e**	**35**	**92**	**212-214**
6	 **1f**	 **2a**	 **3f**	**30**	**93**	**217-219**
7.	 **1a**	 **2b**	 **3g**	**35**	**89**	**212-214**

8.	 **1a**	 **2c**	 **3h**	**30**	**90**	**197-199**
9.	 **1b**	 **2b**	 **3i**	**40**	**89**	**227-229**
10.	 **1e**	 **2b**	 **3j**	**80**	**86**	**213-215**
11	 **1g**	 **2a**	 **3k**	**25**	**94**	**166-168**

[a] All reactions were carried out with the respective o-phenacyl bromides **1a-g** (1 mmol), and respective 2-aminopyridines **2a-c** (1mmol), in 5 mL of ethanol solvent system at room temperature under ultrasound irradiation; [b] Yields reported are isolated yields.

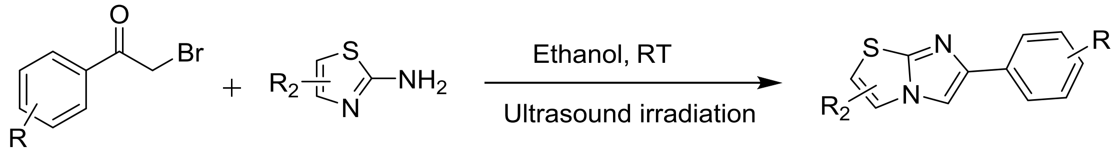
A possible mechanism pathway for the synthesis of imidazo[1,2-a] pyridine is shown in (Scheme 1). The nucleophilic attack of 2-aminopyridine's ring nitrogen[42,43] on phenacyl bromide is speculated to be the initial stage for the condensation of 2-aminopyridine and phenacyl bromide. This is followed by intramolecular cyclization and simultaneous dehydration, which yields the required imidazo[1,2-a] pyridine.



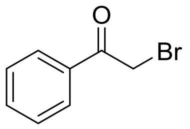
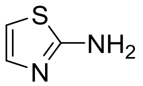
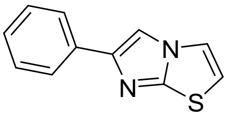
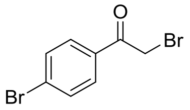
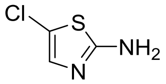
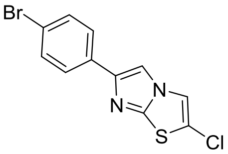
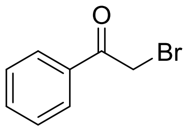
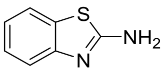
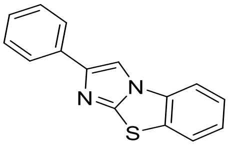
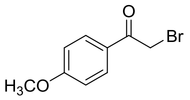
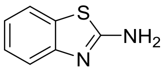
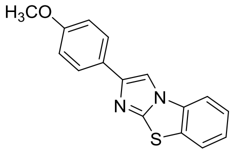
Scheme1. Plausible mechanism for synthesis of imidazopyridine.

We substituted 2-aminopyridine with additional compounds, 2-amino thiazole derivatives, as synthons to demonstrate the adaptability of the disclosed approach. The reaction proceeded as expected with both of these starting materials; however, the yields for the 2-aminopyridine were comparatively higher than those for the 2-amino thiazole.

Table 3: Substrate scope[a]



1(a-c) **4(a-c)** **5(a-d)**

Entry	1	2	Product	Time (min)	Yield (%)	M. P. (℃)
1.	 1a	 4a	 5a	60	91	138-141
2.	 1b	 4b	 5b	90	85	232-234
3.	 1a	 4c	 5c	120	84	108-110
4.	 1c	 4c	 5d	140	80	178-180

[a]All reactions were carried out with the respective o-phenacyl bromides **1a-c**(1 mmol), and 2-aminothiazo **4a-c**(1mmol) in 5 mL ethanol system at room temperature under ultrasound irradiation; [b]Yields reported are isolated yields.

CONCLUSION

Finally, we have developed a catalyst free, simple, quick, and highly efficient green synthetic approach with ultrasound support for a new broad spectrum of interesting functionalized 2-phenyl imidazo [1,2-*a*] pyridine and imidazo[2,1-a] thiazole in ethanol at ambient condition. This protocol's significant advantages include the use of readily available, affordable starting materials that are commercially available; energy efficiency; short reaction times; operational simplicity and clean reaction profiles; reusability of reaction media; ease of product isolation and purification without the need of column chromatography; large-scale synthetic applicability; excellent yields; and high atom economy, all of which satisfy various aspects of green and sustainable chemistry. Use of ultrasound, eco-efficiency, greener reagents, use of green solvents, absence of bases and catalyst requirements, ease of workup, quick reaction times, and the strategy is appealing as well as successful than the other methods proposed due to its high product yield and short reaction time.

ACKNOWLEDGEMENTS

We sincerely thank SAIF, Punjab University, Chandigarh, for providing micro-analyses and spectra. The author Surya Pratap Verma is thankful to CSIR, New Delhi, for the award of Senior Research Fellowship (SRF), authors S. K. Tiwari and Vikas Yadav are thankful to CSIR and UGC, New Delhi respectively, for the award of Senior Research Fellowship (SRF). Kartikey Yadav is also thankful to UGC, New Delhi for Resarch fellowship.

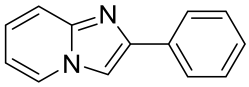
EXPERIMENTAL SECTION

General information: Sonication was carried out utilizing an ultrasound probe- sonicator (Model: VCX 130) manufactured by Sonics with a 20 kHz frequency and 130 W of energy. NMR spectra were recorded on a Bruker Avance-II 400FT spectrometer at 400 MHz (^{1}H) and 100 MHz (^{13}C) in DMSO or $CDCl_3$ using TMS as an internal reference. Infrared spectra were recorded using a Shimadzu (FT-IR 8400S) FT-IR spectrophotometer using KBr disc. All chemicals were reagent grade and purchased from Aldrich, Merck, and Qualigens and were used without further purification. The reactions were monitored using pre-coated Aluminium TLC plates of silica gel G/UV-254 of 0.25 mm thickness (Merck 60 F-254). Melting points were determined by open glass capillary method and were uncorrected.

General procedure for the synthesis of 2-aryl [1, 2-*a*] imidazoheterocycles

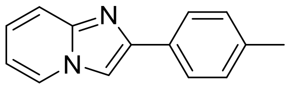
An equimolar mixture of phenacyl bromide (1; 1 mmol) and 2-Amino pyridine/2-Amino thiazole (2; 1 mmol) was added to 5 ml of ethanol in an oven dried round bottom flask under ultrasonic irradiation. Then the reaction progress was monitored by TLC. On completion of the reaction, about 10 ml of the distilled water was added to quench the reaction. A solid mass precipitated out, which was then filtered off. The crude product was then purified by washing it several times with distilled water. The yield of the obtained product was 80-96%. Then the product was confirmed by IR, ^{1}H and ^{13}C spectra. All the synthesized compounds are known and were characterized by comparison of their spectral data as reported in the previous literatures.

2-Phenylimidazo[1,2-a] pyridine (3a)



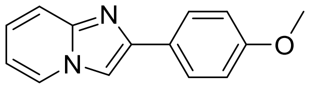
Yellow powder, Yield: 96%; M.P.:136-138˚C; IR (KBr, cm^{-1}): 3124, 1646, 1484, 1365, 750, 712; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.16 (dd, *J* 1.04, 1.03, 1H), 8.06(d, 2H), 7.72 (s, 1H), 7.60 (d, *J* 9.14, 1H), 7.45 (dd, 2H), 7.42 (t, *J* 7.22, 2H), 7.35 (d, 1H), 7.32 (d, *J* 7.33, 1H), 7.18-7.15 (m, 1H), 6.68 (d, *J* 6.78, 1H); ^{13}C NMR ($CDCl_3$) (δ, ppm): 144.9, 144.6, 134.6, 129.5, 127.53, 126.86, 126.5, 123.4, 116.3, 113.3, 109.6; MS (ESI): m/z 194; found 195 $(M+H)^+$; Anal calcd for $C_{13}H_{10}N_2$: 195.0923 Found: 195.09.

2-p-Tolylimidazo[1,2-a] pyridine (3b)



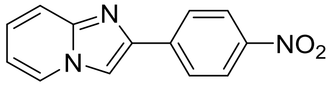
Yellow powder; Yield: 90%; M.P.:142-144˚C, IR (KBr, cm^{-1}): 3026, 1642, 1476, 1374, 826, 744 ; ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 8.18 (d, 1H, J= 6.8 Hz), 7.94 (d, 2H, J= 8.0 Hz), 7.86 (s, 1H), 7.64-7.51 (m, 1H), 7.28 (d, 2H, J 7.9 Hz), 7.22-7.17 (m, 1H), 6.62-6.56 (m, 1H), 2.52(s, 3H); ^{13}C NMR ($CDCl_3$) (δ, ppm): 145.96, 135.09, 133.02, 132.16, 128.43, 125.46, 124.54, 122.42, 113.38, 111.03, 24.23; ES-MS (m/z): 209 $([M+H]^+$, 100).

2-(4-Methoxyphenyl)-imidazo[1,2-a] pyridine (3c)



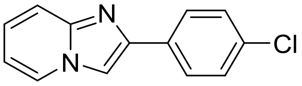
Light yellow powder; Yield: 89%; M.P.:132-134˚C, IR (KBr, cm^{-1}): 2956, 2834, 1618, 932, 746, 632, 538, 452; ^{1}H (400 MHz, $CDCl_3$) (δ, ppm): 8.14 (d, *J* = 6.77, 1H), 7.92 (dd, *J*= 1.95, 1.94, 2H), 7.72(s, 1H), 7.58 (d, *J* 9.08, 1H), 7.22-7.20(m, 1H), 6.93 (dd, *J* =1.97-1.94, 2H), 6.72 (dd, *J*= 0.82-0.81, 1H), 3.78 (s, 3H, OCH_3); ^{13}CNMR($CDCl_3$)(δ, ppm): 158.92, 144.85, 128.38, 126.48, 125.96, 124.62, 117.18, 114.34, 112.44, 107.76, 55.42; ES-MS (m/z): 225 $([M+H]^+$,100).

2-(4-nitrophenyl)imidazo[1,2-*a*] pyridine (3d)



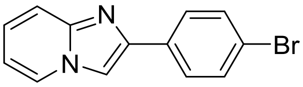
Reddish powder; Yield: 94%; M.P.: 264-266°C; IR (KBr, cm^{-1}): 3107, 1636, 1508, 1335, 854, 718; ^{1}HNMR(400 MHz, $CDCl_3$)(δ, ppm): 8.36-8.30 (2H, m), 8.19 (1H, dt, *J*= 6.82,1.03 Hz), 8.14-8.12 (2H, m), 8.06 (1H, s), 7.54 (1H, dd, *J*= 9.07, 0.74 Hz), 7.32 (1H, m), 6.78 (1H, td, *J*= 6.74, 1.02 Hz); ^{13}C NMR (DMSO-d6)(δ, ppm): 148.05, 146.13, 143.09, 141.05, 128.32, 125.63, 125.08, 124.82, 117.08, 112.39, 111.04.

2-(4-Chlorophenyl)-imidazo[1,2-a] pyridine (3e)



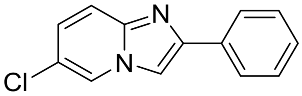
Yellowish powder; Yield: 92%; M.P.: 212- 213°C, IR (KBr, cm^{-1}): 2924, 1636, 942, 836, 754; ^{1}HNMR(400 MHz, $CDCl_3$)(δ, ppm): 8.14 (d, *J*= 6.78, 1H), 7.84 (d, *J*= 8.52, 2H), 7.80 (s, 1H), 7.65 (d, *J* = 9.15, 1H), 7.35 (d, *J* =8.52, 2H), 7.22 (t, *J* 7.17, 1H), 6.84 (t, *J* =6.60, 1H); ^{13}CNMR($CDCl_3$)(δ, ppm): 147.04, 145.16, 134.28, 132.63, 129.82, 127.32, 125.76, 124.19, 117.63, 113.7, 109.53; MS (ESI): *m/z* (%) 229 $([M+H]^+$, 100).

2-(4-Bromophenyl)-imidazo[1,2-a]pyridine (3f)



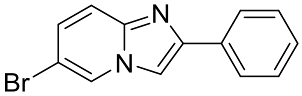
Yellow powder; Yield: 93%; M.P.: 217-219°C; IR (KBr, cm^{-1}): 3086, 1642, 1468, 1372, 828, 738; ^{1}H NMR (400 MHz, $CDCl_3$)(δ, ppm): 8.16 (d, 1H, J= 6.3 Hz), 7.72 (s, 1H), 7.68 (d, 2H, J=7.5 Hz), 7.56 (d, 2H, J= 8.3 Hz), 7.42 (d, 1H, J 9.0 Hz), 6.69-6.62 (m, 1H), 6.46-6.36 (m, 2H), ^{13}CNMR($CDCl_3$)(δ, ppm): 148.06, 144.28, 136.06, 135.32, 133.41, 130.32, 127.73, 125.68, 117.02, 113.06, 109.43; ES-MS (m/z): 272 $([M+H]^+$, 100).

6-bromo-2-phenylimidazo[1,2-a]pyridine (3g)



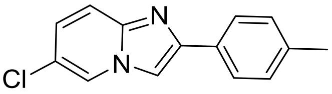
White solid; Yield: 89%; M.P.: 212-214^{o}C; IR (KBr, cm^{-1}): 1636, 768; ^{1}H NMR (CDCl3, 400 MHz) (δ, ppm): 8.86-8.84 (dd, 1H), 8.39 (s, 1H), 8.16(d, 2H), 7.52 (dd, 2H), 7.41(d, 1H), 7.39-7.31 (m, 2H); ^{13}C NMR (CDCl3)(δ,ppm):147.02, 134.13, 132.02, 130.09, 129.62, 129.06, 128.83, 127.58, 127.45, 124.06, 123.40, 117.16, 114.03; ES-MS (m/z): 229 $([M+H]^+$, 100).

6-bromo-2-phenylimidazo[1,2-a]pyridine (3h)



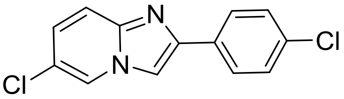
Pale Yellow solid; Yield: 90%; M.P.: 197-199°C; IR (KBr, cm^{-1}): 1638, 778; ^{1}H NMR (400 MHz ,CDCl3) (δ, ppm): 8.24-8.25 (m, 1H), 7.92-7.95 (m, 2H), 7.80 (s, 1H), 7.54(d, *J*=8 Hz, 1H), 7.42-7.47(m, 2H), 7.34-7.38(m, 1H), 7.24-7.25(m, 1H); ^{13}C NMR (CDCl3) (δ, ppm): 146.6, 144.1, 133.2, 128.9, 128.5, 128.3, 126.2, 125.7, 118.2, 108.4, 107.2; ES-MS (m/z): 272 ([M+H]$^+$, 100).

6-chloro-2-(p-toly)imidazo[1,2-*a*]pyridine (3i)



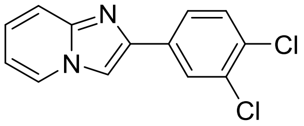
Pale yellow solid; Yield:89%; M.P.:227-229°C; IR (KBr, cm^{-1}): 1628, 1628, 1533, 1565; ^{1}H NMR (400MHz, CDCl3) (δ, ppm): 8.24 (d, 1H), 7.85(s, 1H), 7.68(d, 1H), 7.49-7.44(m, 2H), 7.37 (t, 1H), 7.22-7.17 (m, 2H), 2.39(s, 3H); ^{13}C NMR (CDCl3) (δ, ppm): 148.7, 137.2, 134.01, 133.09, 129.18, 128.65, 127.96, 123.52, 122.05, 120.18, 120.12, 16.02; ES-MS (m/z): 243 ([M+H]$^+$, 100).

2-(2,4-Dichlorophenyl)-6-methylimidazo[1,2-a]pyridine (3j)



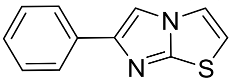
Yellowish white solid; Yield: 86%; M.P.:213-215°C; IR (KBr, cm^{-1}): 2986, 1656, 1155, 1086, 566; ^{1}H NMR (400MHz, CDCl3) (δ, ppm):) 8.45(d, *J* =8.55,1H), 8.24 (s, 1H), 7.86 (s, 1H), 7.56(d, *J* =9.33,1H), 7.42 (d, *J* =2.13, 1H), 7.38 (dd, *J* =2.16, 2.07, 1H), 7.12(dd, *J* =1.47,1.50, 1H); ^{13}C NMR (CDCl3) (δ, ppm): 146.36, 142.25, 134.13, 133.35, 131.44, 131.02, 130.53, 128.73, 126.62, 124.12, 123.15, 117.80, 113.5, 18.03; MS (ESI): *m/z* (%), 263 ([M+H]$^+$, 100).

2-(3,4-dichlorophenyl)imidazo[1,2-*a*]pyridine (3k)



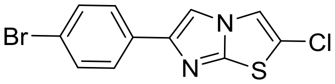
Yellowish powder; Yield: 94%; M.P.: 166-168°C; IR(KBr, cm^{-1}): 3072, 1638, 1456, 1128, 832, 748; ^{1}H (500 MHz, $CDCl_3$)(δ, ppm): 7.94 (1H, d, *J* = 6.7 Hz), 7.98 (1H, d, *J* = 1.71 Hz), 7.72 (1H, s), 7.60 (1H, dd, *J* = 8.24, 1.76 Hz), 7.52 (1H, d, *J* = 9.04 Hz), 7.38 (1H, d, *J* = 8.55 Hz), 7.12(1H, t, *J*= 7.89 Hz), 6.79 (1H, t, *J* = 6.48 Hz); ^{13}C (125 MHz, $CDCl_3$) (δ, ppm): 146.07, 142.35, 134.74, 133.62, 132.68, 131.54, 128.64, 126.77, 125.76, 125.01, 117.86, 112.07, 108.12.

6-phenylimidazo [2, 1-b]thiazole (5a)



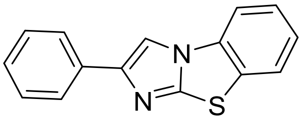
Yield: 91%; M.P.: 138-141°C; IR(KBr, cm^{-1}): 3038, 2822, 1612, 1566, 1528, 1475, 1414; ^{1}H NMR (400 MHz, DMSO*d*6): (δ, ppm): 8.18 (1H, s), 7.90-7.89 (1H,d, J=4.48), 7.85-7.82 (2H, d), 7.40-7.38 (2H, t), 7.26 (1H, t), 7.22-7.20 (1H, d, J=4.44); MS (ESI) *m/z*: 201[M+H]; Anal. Calcd.for C11H8N2S: C, 65.67; H, 4.13; N, 13.64; Found: C, 65.55; H,3.72; N, 13.16.

6-(4-bromophenyl)-2-chloroimidazo[2, 1-b]thiazole (5b)



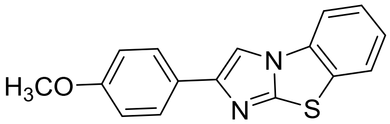
Yield: 85%; M.P.: 232-234°C; IR(KBr, cm^{-1}): 1546, 1183, 985, 742; ^{1}H NMR (400 MHz, DMSO*d*6) (δ, ppm): 8.36 (1H, s), 8.26 (1H, s), 7.84 (2H, d, *J*=8.4), 7.65 (2H, d, *J*=8.4); MS (ESI) *m/z*: 312 [M+H]; Anal. Calcd. for $C_{11}H_6BrClN_2S$: C,42.23; H, 1.95; N, 8.96; Found: C, 39.55; H, 1.70; N, 8.07.

2-Phenyl-benzo[d]imidazo[2,1-*b*]thiazole (5c)



Yield: 84%; M.P.: 108-110°C; IR(KBr, cm^{-1}): 3426, 2336, 1578; 1H NMR (400 MHz, CDCl3) (δ, ppm): 7.92 (s, 1H); 7.92-7.89 (m, 1H), 7.70-7.68 (m, 1H), 7.61-7.59 (m, 1H), 7.02-6.50 (m, 6H); MS (ESI) *m/z*: 251 [M+H]; Anal. Calcd. for $C_{15}H_{10}N_2S$: C,71.92; H, 4.09; N, 11.22; Found: C, 71.68; H, 3.81; N, 10.69.

2-(4-Methoxyphenyl)-benzo[*d*]imidazo[2,1-*b*]thiazole (5d)



Yield: 80%; M.P.: 178-180°C; IR(KBr, cm^{-1}): 3418, 2942,1612, 1465; ^{1}H NMR (400 MHz, CDCl3) (δ, ppm): 7.92(s, 1H), 7.76- 7.70 (m, 2H), 7.57-7.54 (m, 1H), 7.50-7.49 (m, 1H), 7.36-7.30 (m, 2H), 6.96-6.94 (m, 2H), 3.88 (s, 3H); MS (ESI) *m/z* : 281 [M+H]; Anal. Calcd. for $C_{16}H_{12}N_2OS$: C, 68.45; H, 4.36; N, 9.96; Found: C, 68.28; H, 4.26; N, 9.62.

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