Synthesis of Imidazo[1,2-*a*]pyridines and Imidazo[2,1-*b*]thiazoles Attached to a Cycloalkyl or Saturated Heterocycle Containing a Tertiary Hydroxy Substitution

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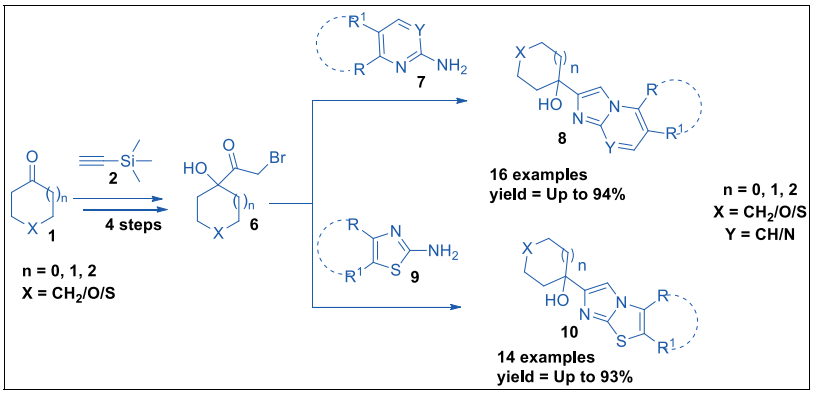


A new method has been developed for the synthesis of imidazo[1,2-*a*]pyridines, imidazo[2,1-*b*]thiazoles, and benzo[*d*]imidazo[2,1-*b*]thiazoles attached to a cycloalkyl or saturated heterocycle containing a tertiary hydroxy substitution. Readily available substituted 2-aminopyridines, 2-aminothiazoles, and 2-aminobenzothiazoles were treated with bromohydroxycycloalkyl ethanones to afford the desired products in good yields.

INTRODUCTION

Imidazoles attached to a cycloalkyl or saturated heterocyclic moiety, in which a hydroxyl group is positioned at the tertiary carbon, were found to be useful compounds in medicinal chemistry [1–3]. There are several reports that describe their uses as inhibitors of P-38 [1] and LXR kinase [2] and modulators of calcium channels [3] (Fig. 1A). Inclusion of a hydroxyl group, which is one of the methods to modulate physicochemical properties, is emphasized in these compounds. According to the empirical rules proposed by Lipinski and few others, physicochemical properties, such as cLogP and tPSA, play a key role in the observed oral bioavailability and permeability of a drug molecule [4a–4d]. Tuning these properties is considered as an important task in any drug discovery program. The hydroxy substituted compounds exhibit lower lipophilicity and higher polar surface area as compared with the corresponding des-hydroxy compounds. This substitution is also expected to impact the solubility and metabolic stability of the compounds. It has been shown that the hydroxyl substitution helps in improving the hERG and CYP liabilities in few cases [5–8].

As a part of our drug discovery program, we were interested in the synthesis of analogous imidazo[1,2-*a*]pyridines, imidazo[2,1-*b*]thiazoles, and benzo[*d*]imidazo[2,1-*b*]thiazoles attached to a cycloalkyl or saturated heterocycle containing a tertiary hydroxy substitution (Fig. 1B).

It was surprising to notice that there are no synthetic reports on imidazopyridines with a hydroxycycloalkyl substitution at the second position, while scouting through the literature. Few papers describe the synthesis of related hydroxyl substituted imidazo[1,2-*a*]pyridines, imidazo[2,1-*b*]thiazoles, and benzo[*d*]imidazo[2,1-*b*]thiazoles, but only dimethyl groups were explored as the alkyl groups in these reports (Fig. 2) [9–15].

In these related papers, the dimethyl group was introduced through the addition of methyl magnesium bromide to the ester group present on the imidazo[1,2-*a*]pyridines [11,12] or benzo[*d*]imidazo[2,1-*b*]thiazoles [13,14] (Fig. 3, Methods A and B). Our aim was to make the imidazo[1,2-*a*]pyridines, imidazo[2,1-*b*]thiazoles, and benzo[*d*]imidazo[2,1-*b*]thiazoles attached to cycloalkyl, tetrahydropyran, tetrahydrothiopyran, and piperidine moieties with a hydroxyl group present at the tertiary carbon (Fig. 1B). It would not be possible to incorporate the desired groups through the aforementioned methods. An alternative method could be possible if a Grignard reagent, prepared from the 2-bromoimidazo[1,2-*a*]

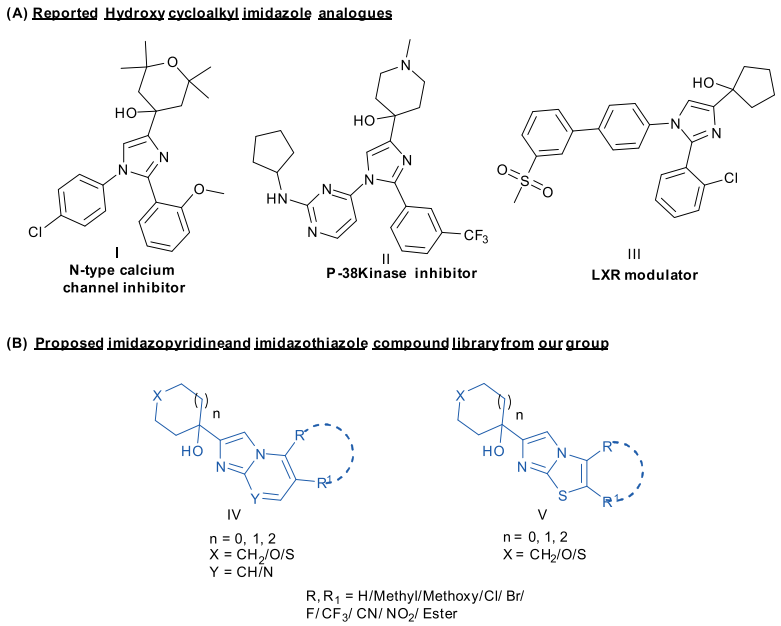


Figure 1. (A) Representative examples of imidazoles with *t*-hydroxy cycloalkyl substitution. (B) Proposed imidazo[1,2-*a*]pyridines and imidazo[2,1-*b*] thiazoles analogues from our group. [Color figure can be viewed at wileyonlinelibrary.com]

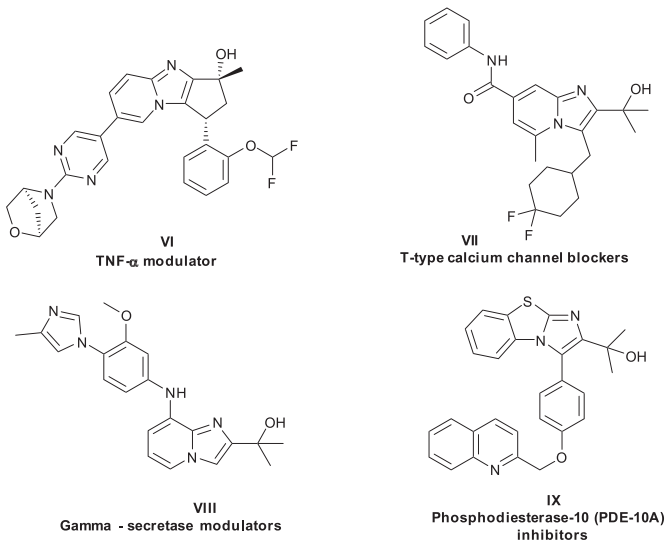


Figure 2. Representative examples of imidazo[1,2-*a*]pyridines and benzo[*d*]imidazo[2,1-*b*]thiazole with *t*-hydroxy substitution.

pyridine, is added to a cyclo alkanone (Fig. 3, Method D) [15]. This would yield the required products, but the reported synthesis of the Grignard precursors 2-bromoimidazo[1,2-*a*]pyridine and 6-bromoimidazo[2,1-*b*] thiazole is difficult and also low yielding (Fig. 3, Method D) [16]. It is also important to note that there are no reports on the preparation of Grignard reagents from these bromo analogues. In another method, reaction of 2-aminopyridines with (*Z*)-5-(bromomethylene)-4,4-dimethyl-1,3-dioxolan-2-on afforded the cyclized product (Fig. 3, Method C) [17]. We assumed that the cyclization of 2-aminopyridines and 2-aminothiazoles with a bromohydroxycycloalkyl ethanone could be a much facile route to synthesize the desired compound in a divergent fashion (Fig. 4, Method E). Lack of synthetic reports for the desired compounds and the special status of imidazopyridines [18,19], imidazothiazoles [20], and benzoimidazothiazoles [21] as privileged scaffolds in medicinal chemistry encouraged us to attempt this reaction. Herein, we present the results on the synthesis

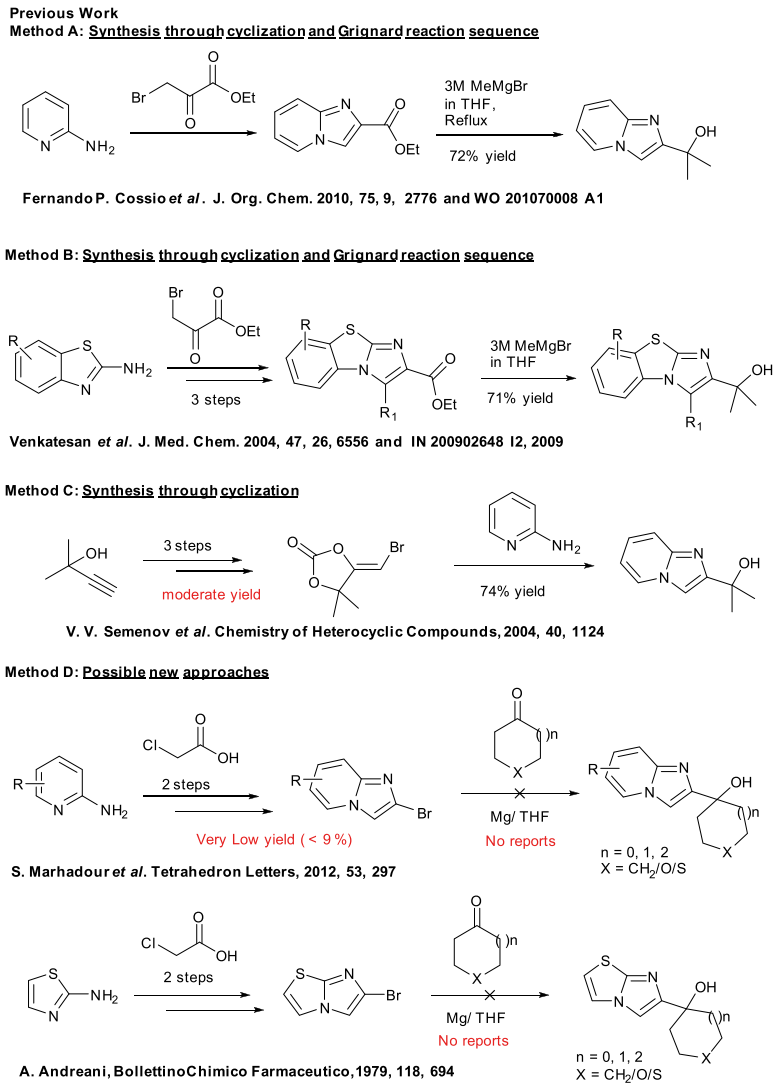


Figure 3. Known synthesis of imidazo[1,2-*a*]pyridines and imidazo[2,1-*b*]thiazoles with *t*-hydroxy cycloalkyl substitution. [Color figure can be viewed at wileyonlinelibrary.com]

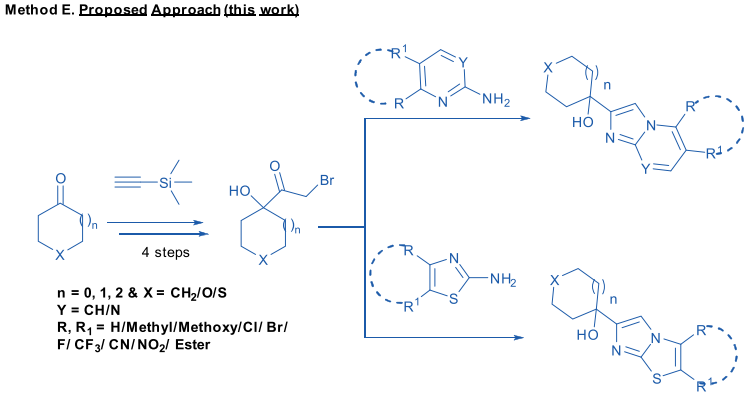


Figure 4. Proposed approach to synthesis of imidazo[1,2-*a*]pyridines and imidazo[2,1-*b*]thiazoles with *t*-hydroxy cycloalkyl substitution. [Color figure can be viewed at wileyonlinelibrary.com]

of these privileged scaffolds attached to a cycloalkyl or saturated heterocyclic groups, with a hydroxyl group placed at the tertiary carbon.

RESULTS AND DISCUSSION

Our first step was to synthesize some known *t*-hydroxy substituted acylbromides [22] and few more unknown analogues. After careful optimization, various hydroxy substituted acylbromide precursors **6a–6e** were prepared from **5a–5e** (Scheme 1). Cyclization of 2-bromo-1-(1-hydroxycyclohexyl)ethan-1-one **6a** with 2-aminopyridine **7a** was investigated as a test case under different experimental conditions to obtain imidazopyridine **8a**. The attempted reaction conditions are depicted in Table 1 (Entries 1–12). The reaction did not work in the absence of a base (Entries 1 and 2, Table 1). Poor yield was observed when the reaction was performed at ambient temperature (Entry 3, Table 1). The reaction was attempted with various bases in different solvents at heating conditions (Entries 4–12, Table 1). The best conversion for the cyclization was obtained with $NaHCO_3$ as the base in 1,4-dioxane solvent at 110°C (Entry 6, Table 1).

The substrate scope was further expanded to various 2-aminopyridines, and the results are summarized in Scheme 2. The product yields were not affected by the

Scheme 1. Synthesis of various *t*-hydroxy cycloalkyl and saturated heterocyclic acylbromides. Reaction conditions: (a) Trimethylsilyl acetylene **2** (1.2 mmol), n-BuLi (1.3 M in n-hexane) (1.2 mmol), THF, −78 °C to RT, 2 h, yield 82–95%; (b) K_2CO_3 (2.5 mmol), methanol, RT, 12 h, yield 91–99%; (c) HgO (catalytic), conc. H_2SO_4 (catalytic), acetone, 60°C, 3 h, yield 65–74%; and (d) compounds **5a–5e** (1.0 mmol), Br_2 (1.0 mmol), methanol, 0 °C to RT, 6 h. [a]Isolated yield in step d. [b]Isolated as 90% pure material.

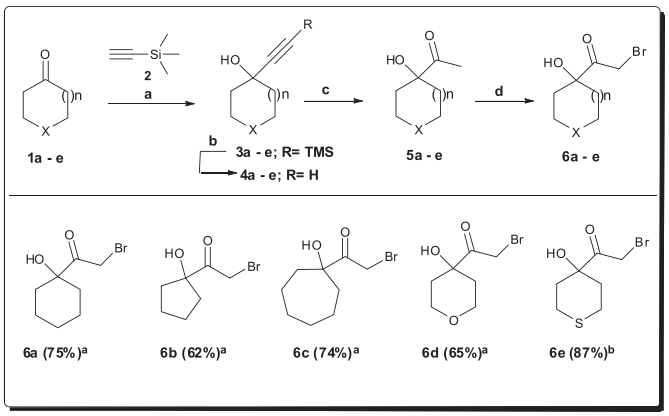
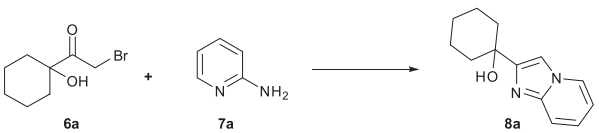


Table 1

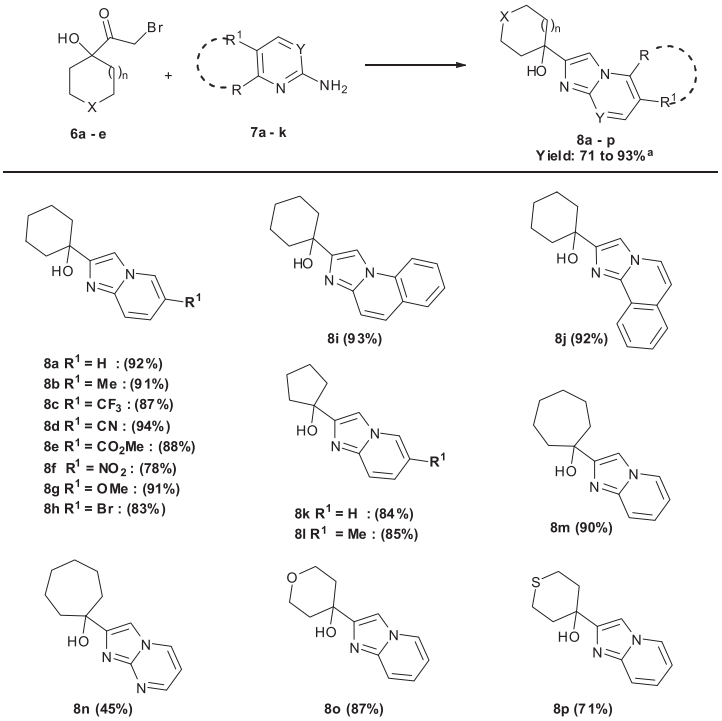
Optimization of the reaction conditions of 1-(imidazo[1,2-*a*]pyridin-2-yl)cyclohexan-1-ol (**8a**).



Entry	Conditions	**8a** (yield %)[a]
1	Ethanol, 90 °C, 12 h	0
2	1,4-Dioxane, 110 °C, 12 h	0
3	K_2CO_3, 1,4-dioxane, RT, 12 h	10
4	K_2CO_3, 1,4-dioxane, 110 °C, 12 h	54
5	$KHCO_3$, 1,4-dioxane, 110 °C, 12 h	75
6	$NaHCO_3$, 1,4-dioxane, 110 °C, 12 h	92
7	Na_2CO_3, 1,4-dioxane, 110 °C, 12 h	60
8	Cs_2CO_3, 1,4-dioxane, 110 °C, 12 h	65
9	$NaHCO_3$, ethanol, 80 °C, 12 h	71
10	$NaHCO_3$, acetonitrile, 90 °C, 12 h	68
11	$NaHCO_3$, ethyl acetate, 80 °C, 12 h	62
12	$NaHCO_3$, DMF, 80 °C, 12 h	57

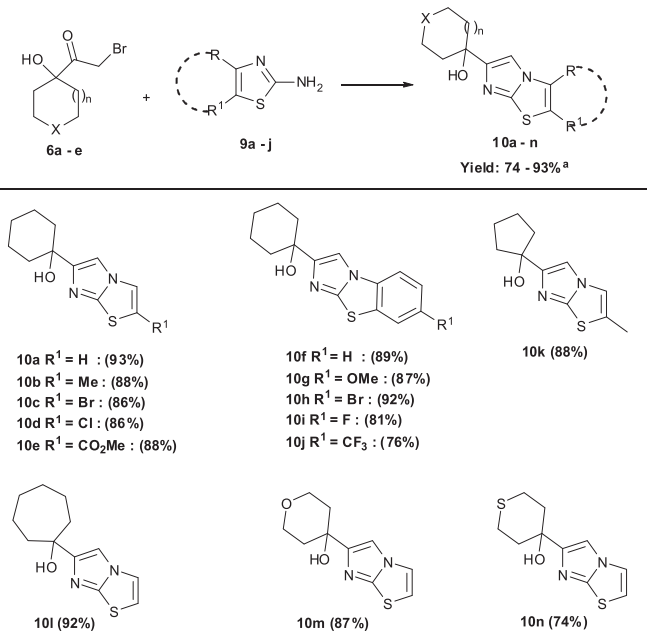
[a]Isolated yield.

Scheme 2. Synthesis of **8a–8p**. Reaction conditions: **7a–7k** (1.0 mmol), *t*-hydroxy acyl bromides **6a–6e** (1.5 mmol), $NaHCO_3$ (2.5 mmol), 1,4-dioxane, 110 °C, 12 h. [a]Isolated yield.



electronic nature of substituents on the aminopyridines as exemplified by the products obtained (compounds **8a–8h)**. 2-Bromo-1-(1-hydroxycyclopentyl)ethan-1-one **6b** and 2-bromo-1-(1-hydroxy-cycloheptyl)ethan-1-one **6c** were also found to be good and afforded compounds **8k**, **8l**, and **8m**, respectively. Similar results were obtained while treating 2-bromo-1-(4-hydroxytetrahydro-2*H*-pyran-4-yl)ethan-1-one **6d** and 2-bromo-1-(4-hydroxytetrahydro-2*H*-thiopyran-4-yl)ethan-1-one **6e** with 2-aminopyridine **7a**. The corresponding cyclized products

Scheme 3. Synthesis of **10a–10n**. Reaction conditions: **9a–9j** (1.0 mmol), *t*-hydroxy acyl bromides **6a–6e** (1.5 mmol), $NaHCO_3$ (2.5 mmol), 1,4-dioxane, 110 °C, 12 h. [a]Isolated yield.



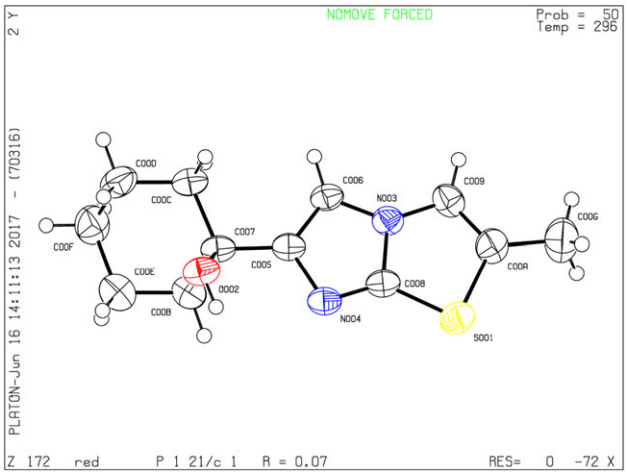


Figure 5. X-ray crystal structure of **10b** (CCDC1559566). [Color figure can be viewed at wileyonlinelibrary.com]

8o and **8p** were obtained in good yields. 2-Aminoquinoline **7i** and 1-aminoisoquinoline **7j** were also found to be good substrates under these reaction conditions and resulted in compounds **8i** and **8j**. 2-Aminopyrimidine **7k** afforded the cyclized product **8n** in moderate yield. It is also note worthy to mention that many of these products offer further scope for modification due to the presence of bromo (compound **8h**), nitro (compound **8f**), cyano (compound **8d**), methoxy (compound **8g**), and carboxyl groups (compound **8e**). Reactions such as reduction, amidation, demethylation followed by etherification, Suzuki coupling, and Buchwald coupling are few of the possible modifications that could be attempted on these reactive functional groups.

Encouraged by the positive results obtained for the synthesis of imidazo[1,2-*a*]pyridines, we extended the reaction scope to various substituted 2-aminothiazoles (compounds **10a–10e** and **10k–10n**, Scheme 3) and 2-aminobenzothiazoles (compounds **10f–10j**, Scheme 3). Both these chemo types emulated the reactivity and tolerability of 2-aminopyridines, and yields of the products obtained were comparable. The structure of compound **10b** is assigned through X-ray crystallography (Fig. 5).

CONCLUSIONS

In conclusion, we have synthesized imidazo[1,2-*a*] pyridines, imidazo[2,1-*b*]thiazoles, and benzo[*d*] imidazo[2,1-*b*]thiazoles attached to cycloalkyl or saturated heterocyclic moieties with a hydroxyl group placed at the tertiary carbon. The earlier methods reported for related compounds were not suitable to prepare the desired compounds. This work is complimentary to the earlier reports and filled some of the gaps observed in them. Cyclization of 2-aminopyridines and 2-aminothiazoles with bromohydroxycycloalkyl or saturated heterocyclic ethanones was found to be a much facile route to synthesize the desired compounds in a divergent fashion.

EXPERIMENTAL

All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware. Dried THF and 1,4-dioxane were purchased from Leonid Chemicals Pvt Ltd, India. Chromatographic separations were carried out by flash chromatography systems using Hi-Purit Flash Column Silica (NP) columns. Analytical thin-layer chromatography was performed on EM Reagent 0.25-nm silica gel 60-F254 aluminum sheets.

^{1}H NMR was recorded on a Varian (400 MHz) spectrometer and is reported in ppm (δ) from tetramethylsilane (δ 0.0 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet), coupling constants (Hz), and integration. ^{13}C NMR was recorded on a Varian (100 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million from tetramethylsilane with solvent resonance as the internal standard ($CDCl_3$: δ 77.0 and DMSO: 40.0 ppm). High-resolution mass spectra were obtained on WATERS Q-TOF Premier-HAB213 spectrometer in ESI mode. Melting points were recorded using Buchi melting point apparatus, and temperatures were collected.

Procedure for the synthesis of compounds 3a–3e. ***1-((Trimethylsilyl)ethynyl)cyclohexanol (3a)***. A stirred solution of ethynyltrimethylsilane (**2**) (8.70 mL, 0.061 mol) in dry THF (50 mL) was added n-BuLi (1.3 M in hexane) (47 mL, 0.061 mol) at −78 °C, and the reaction mixture was stirred for 45 min at the same temperature followed by addition of cyclohexanone (**1a**) (5.0 g, 0.050 mol) in dry THF (50 mL) at −78 °C. The resulting mixture was stirred for 1 h at −78 °C and warmed to room temperature slowly continued for 30 min. The reaction mixture was quenched with saturated NH_4Cl aqueous solution (100 mL) at 0 °C. The organic layer was separated, the aqueous layer was extracted with ethyl acetate (2 × 100 mL). The combined extracts were washed with water (2 × 100 mL) and brine solution (50 mL) and dried over anhydrous Na_2SO_4,; solvent was filtered and evaporated under reduced pressure to obtain the crude product. The crude was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (0.5% to 8%) as an eluting solvent to afford the desired product. (9.5 g, 95% yield) as white solid. ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.24 (s, 1H), 1.68 (t, J = 7.0 Hz, 2H), 1.60–1.52 (m, 2H), 1.43–1.41 (m, 4H), 1.39–1.21 (m,

2H), 0.11 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.43, 86.54, 67.25, 39.99, 25.33, 23.14, 0.51; ESI-MS $[M + H]^+$ *m/z* 196.19.

Compounds **3b–3e** were prepared according to the procedure followed for **3a**.

1-((Trimethylsilyl)ethynyl)cyclopentanol (3b). Viscous liquid (10 g, 93% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.12 (s, 1H), 1.80–1.71 (m, 4H), 1.68–1.54 (m, 4H), 0.10 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 112.60, 84.95, 73.07, 42.40, 23.48, 0.46; ESI-MS $[M + H]^+$ *m/z* 182.85.

1-((Trimethylsilyl)ethynyl)cycloheptanol (3c). Viscous liquid (9.5 g, 92% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.12 (s, 1H), 1.83–1.78 (m, 2H), 1.65 (t, *J* = 11.8 Hz, 2H), 1.55–1.37 (m, 8H), 0.11 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 113.35, 85.72, 70.41, 43.01, 27.87, 22.27, 0.46; ESI-MS $[M + H]^+$ *m/z* 211.1.

4-((Trimethylsilyl)ethynyl)tetrahydro-2H-pyran-4-ol (3d). White solid (8.1 g, 82% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.91–3.87 (m, 2H), 3.66–3.60 (m, 2H), 2.06 (s, 1H), 1.92–1.81 (m, 2H), 1.81–1.74 (m, 2H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 108.00, 89.55, 66.01, 64.87, 39.91, 0.12; ESI-MS $[M + H]^+$ *m/z* 199.2.

4-((Trimethylsilyl)ethynyl)tetrahydro-2H-thiopyran-4-ol (3e). White solid (8.5 g, 92% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.54 (s, 1H), 2.62 (t, *J* = 4.4 Hz, 4H), 1.97–1.94 (m, 2H), 1.71–1.65 (m, 2H), 0.13 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 110.71, 88.54, 66.39, 40.73, 25.47, 0.44; ESI-MS $[M + H]^+$ *m/z* 215.1.

Procedure for the synthesis of compounds 4a–4e. ***1-Ethynylcyclohexanol (4a).*** A stirred solution of 1-((trimethylsilyl)ethynyl)cyclohexanol (**3a**) (5.0 g, 0.025 mol) in methanol (75 mL) was added K_2CO_3 (8.79 g, 0.063 mol) at room temperature, and the reaction mixture was stirred for 12 h at room temperature. Methanol was evaporated under reduced pressure; crude residue was diluted with water (100 mL) and extracted with ethyl acetate (2 × 100 mL). The combined extracts were washed with water (50 mL) and brine solution (50 mL) and dried over anhydrous Na_2SO_4, solvent was filtered and evaporated under reduced pressure to obtain crude product. The crude product was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (1% to 10%) as an eluting solvent to afford the desired product. Viscous liquid (3.0 g, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 1H), 1.96 (s, 1H), 1.93–1.86 (m, 2H), 1.72–1.68 (m, 2H), 1.61–1.56 (m, 4H), 1.54–1.51 (m, 1H), 1.29–1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 87.75, 72.03, 68.49, 25.06, 23.08; ESI-MS $[M + H]^+$ *m/z* 124.18.

Compounds **4b–4e** were prepared according to the procedure followed for **4a**.

1-Ethynylcyclopentanol (4b). Viscous liquid (3.0 g, 99% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.13 (s, 1H), 3.19 (s, 1H), 1.80–1.55 (m, 8H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 89.74, 72.70, 72.58, 42.25, 23.37; ESI-MS $[M + H]^+$ *m/z* 111.2.

1-Ethynylcycloheptanol (4c). Viscous liquid (3.0 g, 92% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.12 (s, 1H), 3.17 (s, 1H), 1.85–1.79 (m, 2H), 1.67 (t, *J* = 11.4 Hz, 2H), 1.50–1.37 (m, 8H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 90.67, 72.82, 69.97, 43.04, 28.11, 22.05; ESI-MS $[M + H]^+$ *m/z* 139.2.

4-Ethynyltetrahydro-2H-pyran-4-ol (4d). Viscous liquid (3.0 g, 94% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.93–3.88 (m, 2H), 3.69–3.63 (m, 2H), 2.55 (s, 1H), 2.19 (s, 1H), 1.96–1.96 (m, 2H), 1.84–1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 86.45, 72.91, 65.36, 64.59, 39.70; ESI-MS $[M + H]^+$ *m/z* 127.2.

4-Ethynyltetrahydro-2H-thiopyran-4-ol (4e). White solid (3.0 g, 91% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86–2.79 (m, 2H), 2.74–2.69 (m, 2H), 2.56 (s, 1H), 2.22–2.16 (m, 2H), 2.04 (s, 1H), 1.96–1.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 86.17, 73.78, 67.45, 40.42, 25.74; ESI-MS $[M + H]^+$ *m/z* 143.1.

Procedure for the synthesis of compounds 5a–5e. ***1-(1-Hydroxycyclohexyl)ethanone (5a).*** A stirred solution of 1-ethynylcyclohexanol (**4a**) (3.0 g, 0.025 mol) in acetone/water (60 mL/6 mL, 10:1) was added catalytic amount of conc. H_2SO_4 (0.05 mL) and HgO (0.313 g, 0.0014 mol) at RT, and the mixture was stirred for 3 h at 60 °C. Solvent was evaporated under reduced pressure; crude residue was diluted with DCM (100 mL) and filtered on celite bed washed with DCM (2 × 50 mL). The filtrate was washed with 10% sodium bicarbonate solution (50 mL), water (50 mL), and brine solution (50 mL) and dried over Na_2SO_4, solvent was filtered and evaporated under reduced pressure to obtain crude product. The crude product was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (1% to 10%) as an eluting solvent to afford the desired product. Viscous liquid (2.3 g, 68% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.01 (s, 1H), 2.11 (s, 3H), 1.59–1.39 (m, 9H), 1.29–1.21 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 214.46, 73.31, 33.31, 25.50, 24.81, 21.26; ESI-MS $[M + H]^+$ *m/z* 143.2.

Compounds **5b–5e** were prepared according to the procedure followed for **5a**.

1-(1-Hydroxycyclopentyl)ethanone (5b). Viscous liquid (2.3 g, 66% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.13 (s, 1H), 2.16 (s, 3H), 1.82–1.79 (m, 2H), 1.71–1.68 (m, 2H), 1.55–1.52 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 213.54, 86.99, 38.19, 25.85, 24.74; ESI-MS $[M + H]^+$ *m/z* 129.2.

1-(1-Hydroxycycloheptyl)ethanone (5c). Viscous liquid (2.5 g, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.62 (s, 1H), 2.23 (s, 3H), 1.84–1.78 (m, 4H), 1.70–1.68 (m, 2H), 1.63–1.57 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

212.53, 80.75, 37.67, 29.06, 23.55, 23.12; ESI-MS $[M + H]^+$ *m/z* 157.2.

1-(4-Hydroxytetrahydro-2H-pyran-4-yl)ethanone (5d). Viscous liquid (2.2 g, 65% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.38 (s, 1H), 3.62–3.56 (m, 4H), 2.14 (s, 3H), 1.75–1.68 (m, 2H), 1.37 (d, *J* = 13.6 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 213.05, 74.76, 62.88, 33.51, 24.60; ESI-MS $[M + H]^+$ *m/z* 145.2.

1-(4-Hydroxytetrahydro-2H-thiopyran-4-yl)ethanone (5e). Viscous liquid (2.4 g, 71% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.72 (s, 1H), 3.18–3.11 (m, 2H), 2.44 (d, *J* = 14.0 Hz, 2H), 2.26 (s, 3H), 2.12–2.03 (m, 2H), 1.71 (d, *J* = 13.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.73, 76.30, 34.41, 25.50, 23.18; ESI-MS $[M + H]^+$ *m/z* 161.1.

Procedure for the synthesis of compounds 6a–6e. ***2-Bromo-1-(1-hydroxycyclohexyl)ethanone (6a).*** A stirred solution of 1-(1-hydroxycyclohexyl)ethanone (**5a**) (2.3 g, 0.016 mol) in methanol (50 mL) was added bromine solution (0.831 mL, 0.016 mol) at 0 °C over a period of 15 min, slowly warmed to room temperature, and continued for 6 h at RT. The reaction mixture was diluted with DCM (150 mL) washed with 10% aq. sodium bicarbonate solution (100 mL), water (50 mL), and brine solution (50 mL) and dried over Na_2SO_4, solvent was filtered and evaporated under reduced pressure to obtain crude product. The crude was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (1% to 10%) as an eluting solvent to afford the desired product. Viscous liquid (2.68 g, 75% yield); ^{1}H NMR (400 MHz, DMSO-d_6): δ 5.32 (s, 1H), 4.65 (s, 2H), 1.60–1.50 (m, 7H), 1.44–1.42 (m, 2H), 1.21–1.15 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 207.19, 77.96, 36.12, 33.78, 25.29, 21.04; ESI-MS $[M + H]^+$ *m/z* 221.09.

Compounds **6b–6e** were prepared according to the procedure followed for **6a**.

2-Bromo-1-(1-hydroxycyclopentyl)ethanone (6b). Viscous liquid (1.0 g, 62% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.21 (s, 2H), 2.78 (s, 1H), 2.10–2.04 (m, 2H), 1.94–1.88 (m, 2H), 1.85–1.77 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.90, 87.47, 40.03, 30.54, 24.95; ESI-MS $[M + H]^+$ *m/z* 207.12.

2-Bromo-1-(1-hydroxycycloheptyl)ethanone (6c). Viscous liquid (1.1 g, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.25 (s, 2H), 2.65 (s, 1H), 1.98–1.92 (m, 2H), 1.75–1.58 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.16, 81.90, 38.44, 31.09, 29.13, 22.49; ESI-MS $[M + H]^+$ *m/z* 235.12.

2-Bromo-1-(4-hydroxytetrahydro-2H-pyran-4-yl)ethanone (6d). Viscous liquid (1.0 g, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.23 (s, 2H), 3.87–3.70 (m, 4H), 2.99 (bs, 1H), 2.17–2.09 (m, 2H), 1.57–1.49 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.46, 76.06, 62.90, 34.52, 29.80; ESI-MS $[M + H]^+$ *m/z* 223.0.

2-Bromo-1-(4-hydroxytetrahydro-2H-thiopyran-4-yl) ethanone (6e). Off white solid (1.3 g, 87% yield, 90% purity); ^{1}H NMR (400 MHz, DMSO-d_6): δ 4.67 (s, 2H), 4.42 (s, 1H), 2.89–2.82 (m, 2H), 2.39–2.33 (m, 2H), 1.85–1.74 (m, 4H); ESI-MS $[M + H]^+$ *m/z* 239.29.

Procedure for the synthesis of compounds 8a–8p. ***1-(Imidazo[1,2-a]pyridin-2-yl)cyclohexanol (8a).*** A mixture of 2-bromo-1-(1-hydroxycyclohexyl)ethanone (**6a**) (1.5 mmol, 1.5 equiv.) and substituted 2-aminopyridine (**7a**) (1 mmol, 1 equiv.) was taken in 1,4-dioxane (10 mL) in a sealed tube; $NaHCO_3$ (2.5 mmol, 2.5 equiv.) was added at room temperature and stirred at 110 °C for 12 h. After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with ethyl acetate (100 mL) washed with water (30 mL). The organic phase was dried over anhydrous Na_2SO_4;solvent was filtered and evaporated under reduced pressure to obtain crude product. It was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (10% to 70%) as an eluting solvent to afford the desired product as off white solid (105 mg, 92% yield); m.p.: 190.3–191.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.45 (d, *J* = 6.8 Hz, 1H), 7.72 (s, 1H), 7.44 (d, *J* = 9.6 Hz, 1H), 7.13 (t, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 6.6 Hz, 1H), 4.64 (s, 1H), 1.93–1.87 (m, 2H), 1.66–1.54 (m, 5H), 1.26–1.23 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.95, 144.13, 127.15, 124.25, 116.86, 111.89, 108.67, 70.05, 38.12, 25.84, 22.13; HRMS (ESI) *m/z* calcd for $C_{13}H_{16}N_2O$ $[M + Na]^+$, 239.1160; found 239.1160.

Compounds **8b–8p** were prepared according to the procedure followed for **8a**.

1-(6-Methylimidazo[1,2-a]pyridin-2-yl)cyclohexanol (8b). Off white solid (96 mg, 91% yield); m.p.: 201–202.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.25 (s, 1H), 7.62 (s, 1H), 7.35 (d, *J* = 8.8 Hz, 1H), 6.99 (d, *J* = 9.2 Hz, 1H), 4.60 (s, 1H), 2.22 (s, 3H), 1.91–1.85 (m, 2H), 1.68–1.53 (m, 5H), 1.45–1.42 (m, 2H), 1.28–1.22 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.53, 143.07, 127.36, 124.61, 121.07, 116.21, 108.38, 70.00, 38.15, 25.84, 22.13, 17.95; HRMS (ESI) *m/z* calcd for $C_{14}H_{18}N_2O$ $[M + Na]^+$, 253.1317; found 253.1317.

1-(6-(Trifluoromethyl)imidazo[1,2-a]pyridin-2-yl) cyclohexanol (8c). Off white solid (76 mg, 87% yield); m. p.: 204.2–205.7 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.17 (s, 1H), 7.89 (s, 1H), 7.65 (d, *J* = 10.0 Hz, 1H), 7.36 (d, *J* = 9.2 Hz, 1H), 4.83 (s, 1H), 1.93–1.87 (m, 2H), 1.72–1.56 (m, 5H), 1.47–1.44 (m, 2H), 1.29–1.21 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.18, 143.96, 127.02 (q, $J_{C–F}$ = 5.8 Hz), 124.53 (q, $J_{C–F}$ = 268.8 Hz), 119.70 (q, $J_{C–F}$ = 4.0 Hz), 117.77, 114.47 (q, $J_{C–F}$ = 33.3 Hz), 110.55, 70.14, 37.92, 25.75, 21.96; HRMS (ESI) *m/z* calcd for $C_{14}H_{15}F_3N_2O$ $[M + Na]^+$, 307.1034; found 307.1037.

2-(1-Hydroxycyclohexyl)imidazo[1,2-a]pyridine-6-carbonitrile (8d). Off white solid (95 mg, 94% yield); m.p.: 200.2–201.4 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.27 (s, 1H), 7.83 (s, 1H), 7.62 (d, *J* = 9.6 Hz, 1H), 7.40 (d, *J* = 9.2 Hz, 1H), 4.86 (s, 1H), 1.93–1.86 (m, 2H), 1.72–1.56 (m, 5H), 1.47–1.44 (m, 2H), 1.29–1.21 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.50, 143.60, 134.50, 124.24, 117.77, 117.72, 110.24, 96.72, 70.12, 37.82, 25.72, 21.92; HRMS (ESI) *m/z* calcd for $C_{14}H_{15}N_3O$ [M + Na]$^+$, 264.1113; found 264.1114.

Methyl 2-(1-hydroxycyclohexyl)imidazo[1,2-a]pyridine-6-carboxylate (8e). Pale yellow solid (79 mg, 88% yield); m.p.: 203.5–203.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (s, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.57–7.51 (m, 2H), 3.94 (s, 3H), 2.49 (s, 1H), 2.00–1.96 (m, 2H), 1.92–1.88 (m, 2H), 1.64–1.59 (m, 2H), 1.42–1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.33, 156.56, 145.32, 129.99, 124.06, 116.62, 116.29, 108.43, 70.68, 52.37, 37.92, 25.46, 21.99; HRMS (ESI) *m/z* calcd for $C_{15}H_{18}N_2O_3$ [M + Na]$^+$, 297.1215; found 297.1207.

1-(6-Nitroimidazo[1,2-a]pyridin-2-yl)cyclohexanol (8f). Pale yellow solid (73 mg, 78% yield); m.p.: 238.2–239.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.84 (s, 1H), 8.01 (s, 1H), 7.86 (d, *J* = 9.6 Hz, 1H), 7.61 (d, *J* = 9.6 Hz, 1H), 4.96 (s, 1H), 1.98–1.86 (m, 2H), 1.69–1.57 (m, 5H), 1.48–1.45 (m, 2H), 1.26–1.21 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.80, 144.43, 136.53, 128.48, 118.46, 116.26, 111.75, 70.21, 37.74, 25.70, 21.87; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}N_3O_3$ [M + Na]$^+$, 284.1011; found 284.1012.

1-(6-Methoxyimidazo[1,2-a]pyridin-2-yl)cyclohexanol (8g). Pale brown solid (90 mg, 91% yield); m.p.: 150.3–151.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.44 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 9.6 Hz, 1H), 3.81 (s, 3H), 2.57 (bs, 1H), 1.97–1.92 (m, 4H), 1.87–1.78 (m, 3H), 1.38–1.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.20, 149.18, 141.71, 119.70, 117.41, 108.45, 107.66, 70.53, 56.19, 38.12, 25.56, 22.15; HRMS (ESI) *m/z* calcd for $C_{14}H_{18}N_2O_2$ [M + Na]$^+$, 269.1266; found 269.1263.

1-(6-Bromoimidazo[1,2-a]pyridin-2-yl)cyclohexanol (8h). Pale brown solid (75 mg, 83% yield); m.p.: 195.7–196.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.47 (s, 1H), 7.45 (d, *J* = 10.4 Hz, 1H), 7.21 (dd, *J* = 1.6 Hz, *J* = 1.6 Hz, 1H), 2.51 (s, 1H), 2.01–1.73 (m, 7H), 1.70–1.58 (m, 2H), 1.41–1.28 (m, 1H); ^{13}C NMR (100 MHz, CDCl3): δ 155.41, 143.17, 127.93, 125.75, 117.97, 107.71, 106.76, 70.61, 38.03, 25.47, 22.02; HRMS (ESI) *m/z* calcd for $C_{13}H_{15}BrN_2O$ [M + Na]$^+$, 317.0265, 319.0245; found 317.0264, 318.9096.

1-(Imidazo[1,2-a]quinolin-2-yl)cyclohexanol (8i). Pale brown solid (85 mg, 93% yield); m.p.: 182.1–183.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.47 (s, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.54–7.48 (m, 2H), 7.46–7.43 (m, 1H), 2.57 (bs, 1H), 2.10–2.04 (m, 2H), 1.98–1.94 (m, 2H), 1.87–1.78 (m, 2H), 1.67–1.57 (m, 3H), 1.46–1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.40, 143.27, 132.70, 129.11, 128.74, 126.06, 124.54, 123.27, 116.94, 115.04, 105.98, 70.69, 38.12, 25.58, 22.18; HRMS (ESI) *m/z* calcd for $C_{17}H_{18}N_2O$ [M + Na]$^+$, 289.1317; found 289.1315.

1-(Imidazo[2,1-a]isoquinolin-2-yl)cyclohexanol (8j). Off white solid (84 mg, 92% yield); m.p.: 149.5–150.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.42 (s, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 2.96 (bs, 1H), 2.04–1.97 (m, 5H), 1.88–1.79 (m, 2H), 1.65–1.60 (m, 2H), 1.43–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.34, 142.22, 129.38, 127.98, 126.81, 123.78, 123.42, 123.05, 112.85, 108.76, 70.33, 38.36, 25.65, 22.25; HRMS (ESI) *m/z* calcd for $C_{17}H_{18}N_2O$ [M + H]$^+$, 267.1497; found 267.1495.

1-(Imidazo[1,2-a]pyridin-2-yl)cyclopentanol (8k). Pale yellow solid (90 mg, 84% yield); m.p.: 150.1–151.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 6.8 Hz, 1H), 7.55 (d, *J* = 8.8 Hz, 1H), 7.51 (s, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 7.0 Hz, 1H), 2.60 (bs, 1H), 2.20–2.15 (m, 2H), 2.04–1.97 (m, 4H), 1.89–1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.99, 144.96, 125.65, 124.53, 117.25, 112.20, 107.41, 80.39, 41.31, 23.93; LCMS (ESI) *m/z* calcd for $C_{12}H_{14}N_2O$ [M + Na]$^+$, 225.1004; found 225.1008.

1-(6-Methylimidazo[1,2-a]pyridin-2-yl)cyclopentanol (8l). Pale yellow solid (85 mg, 85% yield); m.p.: 147.8–148.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.44 (d, *J* = 9.2 Hz, 1H), 7.41 (s, 1H), 6.99 (d, *J* = 9.2 Hz, 1H), 2.29 (s, 1H), 2.19–2.09 (m, 2H), 2.05–1.99 (m, 4H), 1.84–1.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.71, 144.00, 127.62, 123.73, 121.71, 116.50, 107.11, 80.34, 41.23, 23.91, 18.00; HRMS (ESI) *m/z* calcd for $C_{13}H_{16}N_2O$ [M + Na]$^+$, 239.1160; found 239.1162.

1-(Imidazo[1,2-a]pyridin-2-yl)cycloheptanol (8m). Pale yellow solid (110 mg, 90% yield); m.p.: 141.3–142.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, *J* = 6.8 Hz, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.47 (s, 1H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 6.4 Hz, 1H), 2.82 (bs, 1H), 2.19–2.13 (m, 2H), 2.10–2.04 (m, 2H), 1.85–1.77 (m, 2H), 1.73–1.68 (m, 2H), 1.67–1.58 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.50, 144.73, 125.68, 124.37, 117.38, 112.11, 106.99, 74.23, 41.94, 29.48, 22.26; HRMS (ESI) *m/z* calcd for $C_{14}H_{18}N_2O$ [M + Na]$^+$, 253.1317; found 253.1317.

1-(Imidazo[1,2-a]pyrimidin-2-yl)cycloheptanol (8n). Pale yellow solid (54 mg, 45% yield); m.p.: 151.5–152.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 1.6 Hz, 1H), 8.38 (d, *J* = 6.0 Hz, 1H), 7.44 (s, 1H), 6.86–6.83 (m, 1H), 3.64 (bs, 1H), 2.20–2.14 (m, 2H), 2.09–2.04 (m, 2H), 1.79–1.61 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ

157.37, 149.62, 147.80, 133.17, 108.62, 105.09, 74.37, 41.80, 29.52, 22.24; HRMS (ESI) *m/z* calcd for $C_{13}H_{17}N_3O$ [M + Na]$^+$, 254.1269; found 254.1273.

4-(Imidazo[1,2-a]pyridin-2-yl)tetrahydro-2H-pyran-4-ol (8o). Off white solid (100 mg, 87% yield); m.p.: 158.2–159.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.48 (d, *J* = 6.4 Hz, 1H), 7.78 (s, 1H), 7.47 (d, *J* = 9.2 Hz, 1H), 7.16 (t, *J* = 8.0 Hz, 1H), 6.82 (t, *J* = 6.6 Hz, 1H), 5.02 (s, 1H), 3.77–3.72 (m, 2H), 3.65–3.62 (m, 2H), 2.16–2.07 (m, 2H), 1.62 (d, *J* = 12.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.67, 144.26, 127.27, 124.58, 116.95, 112.11, 108.93, 67.66, 63.59, 38.27; HRMS (ESI) *m/z* calcd for $C_{12}H_{14}N_2O_2$ [M + Na]$^+$, 241.0953; found 241.0950.

4-(Imidazo[1,2-a]pyridin-2-yl)tetrahydro-2H-thiopyran-4-ol (8p). Pale brown solid (85 mg, 71% yield); m.p.: 171.9–172.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 7.2 Hz, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.44 (s, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.78 (t, *J* = 6.8 Hz, 1H), 3.25–3.18 (m, 2H), 3.06 (bs, 1H), 2.52 (d, *J* = 13.6 Hz, 2H), 2.27–2.15 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.76, 144.64, 125.83, 124.76, 117.42, 112.44, 106.91, 68.62, 39.07, 24.22; HRMS (ESI) *m/z* calcd for $C_{12}H_{14}N_2OS$ [M + Na]$^+$, 257.0725; found 257.0725.

Procedure for the synthesis of compounds 10a–10n. ***1-(Imidazo[2,1-b]thiazol-6-yl)cyclohexanol (10a).*** A mixture of 2-bromo-1-(1-hydroxycyclohexyl)ethanone (**6a**) (1.5 mmol, 1.5 equiv.) and substituted 2-aminothiazole (**9a**) (1 mmol, 1 equiv.) was taken in 1,4-dioxane (10 mL) in a sealed tube; $NaHCO_3$ (2.5 mmol, 2.5 equiv.) was added at room temperature and stirred at 110 °C for 12 h. After completion of the reaction (thin-layer chromatography), the reaction was cooled to room temperature and diluted with ethyl acetate (100 mL) washed with water (30 mL). The organic phase was dried over anhydrous Na_2SO_4, solvent was filtered and evaporated under reduced pressure to obtain crude product. It was purified by flash column chromatography on silica gel using a mixture of ethyl acetate and n-hexane (10% to 70%) as an eluting solvent to afford the desired product as off white solid (106 mg, 93% yield); m.p.: 171.0–172.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.80 (d, *J* = 4.0 Hz, 1H), 7.50 (s, 1H), 7.12 (d, *J* = 4.4 Hz, 1H), 4.51 (s, 1H), 1.86–1.79 (m, 2H), 1.68–1.50 (m, 5H), 1.43–1.40 (m, 2H), 1.26–1.23 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 157.26, 147.73, 120.37, 112.27, 108.84, 69.95, 38.01, 25.84, 22.19; HRMS (ESI) *m/z* calcd for $C_{11}H_{14}N_2OS$ [M + H]$^+$, 223.0905; found 223.0898.

Compounds **10b–10n** were prepared according to the procedure followed for **10a**.

1-(2-Methylimidazo[2,1-b]thiazol-6-yl)cyclohexanol (10b). Off white solid (94 mg, 88% yield); m.p.: 159.1–160.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (s, 1H), 7.06 (s, 1H), 2.39 (s, 3H), 1.96–1.84 (m, 4H), 1.80–1.71 (m, 2H), 1.68–1.59 (m, 3H), 1.38–1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.66, 148.50, 126.04, 115.07, 107.07, 70.60, 37.88, 25.61, 22.26, 13.99; HRMS (ESI) *m/z* calcd for $C_{12}H_{16}N_2OS$ [M + H]$^+$, 237.1062; found 237.1061.

1-(2-Bromoimidazo[2,1-b]thiazol-6-yl)cyclohexanol (10c). Pale yellow solid (50 mg, 86% yield); m.p.: 140.5–141.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 1H), 7.31 (s, 1H), 2.26 (s, 1H), 1.94–1.83 (m, 5H), 1.79–1.77 (m, 3H), 1.68–1.54 (m, 1H), 1.38–1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.98, 148.17, 119.60, 107.86, 101.17, 70.68, 37.79, 25.53, 22.14; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}BrN_2OS$ [M + H]$^+$, 301.0010 and 302.9990; found 301.0012 and 303.0000.

1-(2-Chloroimidazo[2,1-b]thiazol-6-yl)cyclohexanol (10d). Pale yellow solid (64 mg, 86% yield); m.p.: 154.7–155.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H), 7.29 (s, 1H), 2.26 (bs, 1H), 1.95–1.83 (m, 5H), 1.79–1.70 (m, 3H), 1.69–1.55 (m, 1H), 1.38–1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.94, 146.22, 119.04, 117.10, 107.96, 70.68, 37.82, 25.53, 22.15; HRMS (ESI) *m/z* calcd for $C_{11}H_{13}ClN_2OS$ [M + Na]$^+$, 279.0335; found 279.0335.

Methyl 6-(1-hydroxycyclohexyl)imidazo[2,1-b]thiazole-2-carboxylate (10e). Off white solid (78 mg, 88% yield); m.p.: 218.3–219.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.39 (s, 1H), 3.92 (s, 3H), 2.27 (s, 1H), 1.97–1.84 (m, 4H), 1.80–1.70 (m, 2H), 1.67–1.58 (m, 2H), 1.39–1.28 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.67, 157.81, 149.99, 124.65, 120.90, 108.80, 70.76, 52.75, 37.67, 25.49, 22.06; HRMS (ESI) *m/z* calcd for $C_{13}H_{16}N_2O_3S$ [M + Na]$^+$, 303.0779; found 303.0782.

1-(Benzo[d]imidazo[2,1-b]thiazol-2-yl)cyclohexanol (10f). Off white solid (81 mg, 89% yield); m.p.: 178–179 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.0 Hz, 1H), 7.60 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 2.35 (s, 1H), 2.04–1.96 (m, 2H), 1.93–1.89 (m, 2H), 1.83–1.73 (m, 2H), 1.66–1.55 (m, 3H), 1.43–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.90, 147.06, 132.30, 130.22, 126.10, 124.68, 124.35, 112.51, 106.41, 70.79, 37.82, 25.58, 22.26; HRMS (ESI) *m/z* calcd for $C_{15}H_{16}N_2OS$ [M + H]$^+$, 273.1062; found 273.1064.

1-(7-Methoxybenzo[d]imidazo[2,1-b]thiazol-2-yl) cyclohexanol (10g). Off white solid (73 mg, 87% yield); m. p.: 140.2–142.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54 (s, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 2.4 Hz, 1H), 6.98 (dd, *J* = 2.4 Hz, *J* = 2.4 Hz, 1H), 3.86 (s, 1H), 2.34 (s, 1H), 2.04–1.99 (m, 2H), 1.96–1.88 (m, 2H), 1.82–1.74 (m, 2H), 1.62–1.56 (m, 3H), 1.42–1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.05, 155.43, 146.38, 131.39, 126.55, 113.30, 112.97, 108.73, 106.40, 70.72, 55.90, 37.84, 25.60, 22.25; HRMS (ESI) *m/z* calcd for $C_{16}H_{18}N_2O_2S$ [M + Na]$^+$, 325.0987; found 325.0988.

1-(7-Bromobenzo[d]imidazo[2,1-b]thiazol-2-yl)cyclohexanol (10h). Pale yellow solid (70 mg, 92% yield); m.p.: 140.9–141.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (s,

1H), 7.58 (s, 1H), 7.55 (d, J = 8.4 Hz, 1H), 7.42 (d, J = 8.8 Hz, 1H), 2.31 (s, 1H), 2.04–1.96 (m, 2H), 1.91–1.88 (m, 2H), 1.82–1.73 (m, 2H), 1.70–1.60 (m, 3H), 1.42–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.35, 146.76, 131.98, 131.27, 129.27, 126.89, 117.25, 113.55, 106.63, 70.81, 37.76, 25.53, 22.15; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}BrN_2OS$ $[M + Na]^+$, 372.9986 and 374.9966; found 372.9990 and 374.9971.

1-(7-Fluorobenzo[d]imidazo[2,1-b]thiazol-2-yl)cyclohexanol (10i). Pale brown solid (70 mg, 81% yield); m.p.: 130–131.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (s, 1H), 7.50 (dd, J = 4.4 Hz, J = 4.4 Hz, 1H), 7.41 (dd, J = 2.0 Hz, J = 2.4 Hz, 1H), 7.18–7.14 (m, 1H), 2.17–1.99 (m, 2H), 1.96–1.88 (m, 2H), 1.82–1.60 (m, 5H), 1.41–1.33 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.58 (d, $J_{C–F}$ = 244 Hz), 156.07, 146.68, 131.47 (d, $J_{C–F}$ = 10.1 Hz), 128.85, 113.76 (d, $J_{C–F}$ = 24.8 Hz), 113.12 (d, $J_{C–F}$ = 9.3 Hz), 111.41 (d, $J_{C–F}$ = 27.1 Hz), 106.63, 70.77, 37.79, 25.56, 22.18; HRMS (ESI) *m/z* calcd for $C_{15}H_{15}FN_2OS$ $[M + Na]^+$, 313.0787; found 313.0784.

1-(7-(Trifluoromethyl)benzo[d]imidazo[2,1-b]thiazol-2-yl) cyclohexanol (10j). Pale yellow solid (59 mg, 76% yield); m.p.: 167.1–167.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.51 (s, 1H), 8.20 (d, J = 8.4 Hz, 1H), 8.17 (s, 1H), 7.87 (d, J = 8.8 Hz, 1H), 4.76 (s, 1H), 1.88 (t, J = 11.2 Hz, 2H), 1.68–1.60 (m, 4H), 1.52–1.46 (m, 3H), 1.26–1.21 (m, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.00, 146.51, 135.08, 130.56, 125.38 (q, $J_{C–F}$ = 32.5 Hz), 124.55 (q, $J_{C–F}$ = 271.1 Hz), 124.11 (q, $J_{C–F}$ = 3.8 Hz), 123.03 (q, $J_{C–F}$ = 3.8 Hz), 114.13, 109.28, 70.00, 37.78, 25.81, 22.14; HRMS (ESI) *m/z* calcd for $C_{16}H_{15}F_3N_2OS$ $[M + H]^+$, 341.0935; found 341.0925.

1-(2-Methylimidazo[2,1-b]thiazol-6-yl)cyclopentanol (10k). Pale yellow solid (86 mg, 88% yield); m.p.: 163.1–164.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (s, 1H), 7.06 (s, 1H), 2.39 (s, 3H), 2.36 (s, 1H), 2.07–2.00 (m, 2H), 1.98–1.95 (m, 4H), 1.81–1.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 153.37, 148.82, 125.89, 115.02, 106.95, 80.44, 40.84, 23.80, 13.95; HRMS (ESI) *m/z* calcd for $C_{11}H_{14}N_2OS$ $[M + Na]^+$, 245.0725; found 245.0719.

1-(Imidazo[2,1-b]thiazol-6-yl)cycloheptanol (10l). Pale brown solid (108 mg, 92% yield); m.p.: 122.4–124.1°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.34 (m, 2H), 6.77 (d, J = 4.4 Hz, 1H), 2.54 (bs, 1H), 2.15–2.09 (m, 2H), 2.05–1.99 (m, 2H), 1.81–1.65 (m, 7H), 1.57–1.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.12, 149.13, 118.44, 111.99, 107.04, 74.43, 41.61, 29.55, 22.24; HRMS (ESI) *m/z* calcd for $C_{12}H_{16}N_2OS$ $[M + Na]^+$, 259.0881; found 259.0885.

4-(Imidazo[2,1-b]thiazol-6-yl)tetrahydro-2H-pyran-4-ol (10m). Off white solid (96 mg, 87% yield); m.p.: 142.0–143.2°C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.84 (d, J = 4.4 Hz, 1H), 7.59 (s, 1H), 7.18 (d, J = 4.4 Hz, 1H), 4.95 (bs, 1H), 3.74–3.69 (m, 2H), 3.62–3.59 (m, 2H), 2.07–1.97 (m, 2H), 1.60 (d, J = 12.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.63, 148.00, 120.49, 112.88, 109.21, 67.49, 63.60, 38.14; HRMS (ESI) *m/z* calcd for $C_{10}H_{12}N_2O_2S$ $[M + Na]^+$, 247.0517; found 247.0528.

4-(Imidazo[2,1-b]thiazol-6-yl)tetrahydro-2H-thiopyran-4-ol (10n). Pale brown solid (88 mg, 74% yield); m.p.: 174.0–175.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 4.4 Hz, 1H), 7.32 (s, 1H), 6.81 (d, J = 4.8 Hz, 1H), 3.20–3.13 (m, 2H), 2.72 (s, 1H), 2.53–2.48 (m, 2H), 2.25–2.18 (m, 2H), 2.17–2.00 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.52, 149.17, 118.50, 112.49, 107.02, 68.81, 38.84, 24.29; HRMS (ESI) *m/z* calcd for $C_{10}H_{12}N_2OS_2$ $[M + H]^+$, 241.0469; found 241.0456.

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