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Rongalite as a Methylene Surrogate: Synthesis of Heterodiarylmethanes *via* C(sp^2)-H Functionalization

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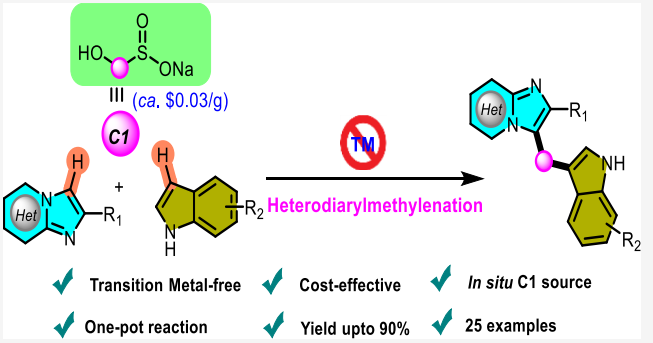
ABSTRACT: An efficient method for the synthesis of heterodiarylmethanes through the coupling of imidazo[1,2-*a*]pyridines and heteroarenes using indoles employing rongalite as a methylenating reagent has been developed. This regioselective C−H functionalization provides a wide range of heterodiarylmethanes of imidazo[1,2-*a*]pyridines and imidazo[2,1-*b*]thiazole. Here, rongalite plays a crucial role in generating a C1 unit in situ, which triggers the heterodiarylmethylation process. The use of inexpensive rongalite (ca. $0.03/1 g), mild reaction conditions, and gram-scale synthesis are some of the key features of this methodology.



INTRODUCTION

C1 homologation is a powerful tool for selectively introducing a methylene group (−CH_2) into parent compounds,[1] increasing their molecular diversity, and altering their organic framework to regulate physical and chemical properties such as lipophilicity and chemical reactivity.[2] Methylenation chemistry offers many advantages, including lengthening carbon chains, adding essential functionalities, and combining organic molecules to create valuable heterocyclic products.[3] In particular, the installation of methylene groups can dramatically improve the IC_{50} values of a specific drug.[4,5] Ideally, this process allows for the precise incorporation of the methylene unit between pre-existing molecular linkages, underscoring methylene's central role in advancing synthetic methodologies and expanding the diversity of chemical structures. A plethora of reagents were developed in this regard (e.g., diazomethane, ylides, carbenoid, etc.).[6,7] In recent years, the release of methylene under tunable reaction conditions has become an emerging area in organic synthesis. Researchers have explored the various sources of C1 synthon donors such as methanol, dimethyl sulfoxide (DMSO), *N*,*N*-dimethylformamide (DMF), *N*,*N*-dimethylacetamide (DMA), and tetramethyl urea in the presence of a suitable metal catalyst.[8] However, these methods require harsh reaction conditions, including the use of metals, toxic formalin, and long reaction time to provide C1 homologation.

Therefore, developing an alternate source of C1 homologation under transition-metal-free conditions has gained significant attention in synthetic organic chemistry. On the other hand, rongalite, an industrial product (ca. 0.03$/1g), is a potential source of both formaldehyde and sulfoxylate dianion and is widely used in organic synthesis.[9]

N-Heterocyclics are recognized for their high-end position as a valuable source of therapeutic agents in medicinal chemistry.[10] FDA databases reveal nearly 75% of small-molecule drugs contain a nitrogen heterocycle.[11] In particular, imidazo[1,2-*a*]pyridines are privileged scaffolds that are extensively utilized in the pharmaceutical industry due to their diverse biological properties.[12] Many pharmaceutical drugs on the market contain imidazopyridine derivatives as active ingredients such as zolpidem, necopidem, saripidem, and minodronic acid. Similarly, heterodiarylmethanes are also a privileged skeleton in several pharmaceutical drugs (Figure 1).

In addition, imidazo[1,2-*a*]pyridines are widely applied in material sciences because of their unique photophysical properties.[13] Imidazo[1,2-*a*]pyridine is a key structure that can be combined with other fragments to create complex molecules for potential use in drug discovery.[14] In recent years, there has been a great deal of interest in hybrid drugs, which aim to create potent new small molecules with combined biological effects. Indole is commonly known as the "Lord of the Rings" of heterocyclic compounds and is widely used in the synthesis of organic compounds due to its significant importance among heterocyclic structures.[15]

Imidazo[1,2-*a*]pyridines and indoles are commonly used in drug discovery programs and have been found in therapeutics for diseases like diabetes, cancers, and microbial infections.[16]

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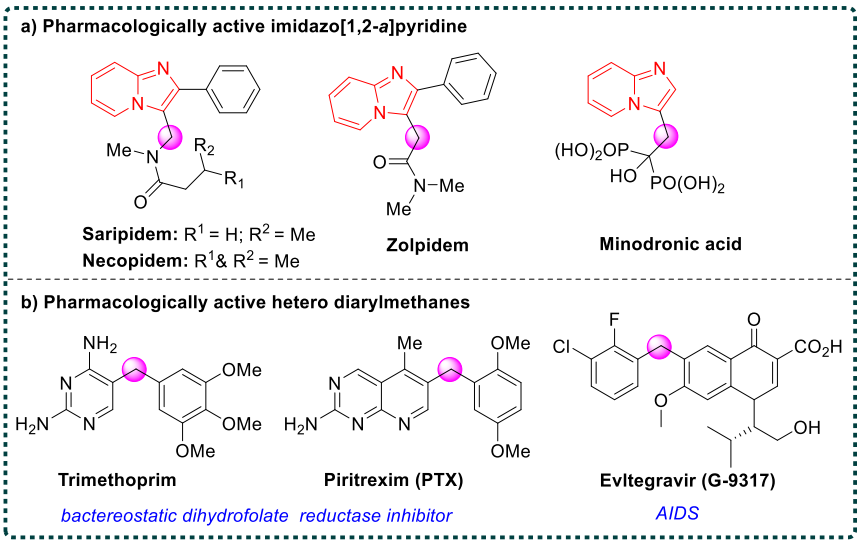
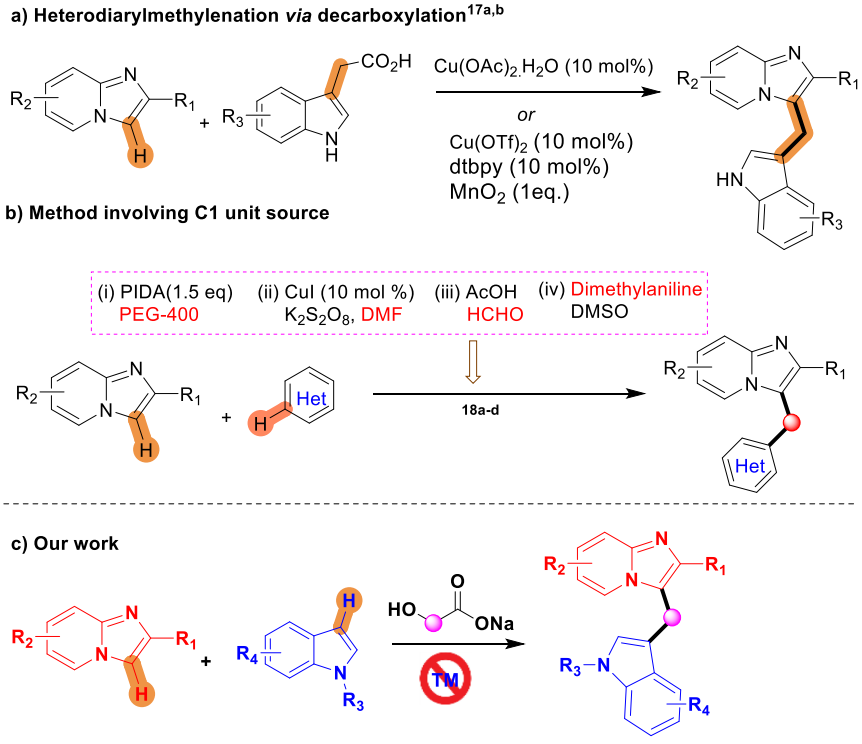


Figure 1. Imidazo[1,2-*a*]pyridines and heterodiarylmethane containing pharmaceuticals.

Scheme 1. Strategies for the Formation of Diarylmethylenation. Adapted with Permission from ref 17b. Copyright 2021 Royal Society of Chemistry and ref 18a–bcd. Copyright 2016 and 2023 John Wiley and Sons



Therefore, it is desirable and significant to explore new methods for synthesizing imidazopyridine hybrids. Few reports are available for direct imidazopyridine hybrids, but the hybrids of indole-methylimidazopyridine have been less explored. The synthetic routes available for heterodiarylmethanes are (a) diarylmethylenation by decarboxylation[17] and (b) the use of a C-1 unit source.[18]

These methods require harsh reaction conditions such as the use of metals and toxic methylene sources. As a result, finding an alternative C1 unit source has become a key goal in diarylmethylenation strategies. Therefore, we aim to develop a novel method for the in situ generation of a C1 source to overcome the constraints associated with these methods. In this context, we are utilizing the rongalite, a commercially inexpensive reagent (ca. $0.03/g) as a C1 unit source under mild conditions for diarylmethylenation (Scheme 1c).

RESULTS AND DISCUSSION

To test the proposed hypothesis for the synthesis of the 3-((1*H*-indol-3-yl)methyl)-2-phenylimidazo[1,2-*a*]pyridine, we have initially set up a reaction with imidazo[1,2-*a*]pyridine **1a**, indole **2a**, and rongalite **3** in acetonitrile stirred at room temperature, but there is no change observed in the reaction progress (Table 1, entry 1).

However, starting material was consumed when the reaction mixture was heated in an oil bath to 80 °C and gave desired

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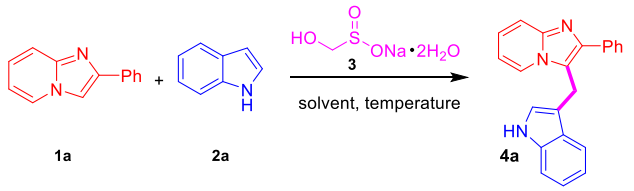
Table 1. Optimization of Reaction Condition[a]



entry	solvent	rongalite (equiv)	temp. (°C)	time (h)	yield (%)[b]
1	CH_3CN	1	rt	12	n.d[c]
2	CH_3CN	1	70	12	40
3	CH_2Cl_2	1	45	12	12
4	$CHCl_3$	1	65	12	10
5	DCE	1	70	12	10
6	toluene	1	80	10	45
7	THF	1	70	12	22
8	1,4-dioxane	1	70	12	20
9	MeOH	1	70	6	50
10	EtOH	1	70	6	55
11	DMF	1	70	5	68
12	DMF	1.5	70	5	75
13	DMF	2	80	5	90
14	DMF	2.5	80	5	90
15	DMSO	2	80	10	40
16	H_2O	2	80	24	n.d[c]

[a]All the reactions were conducted on a 1.0 mmol scale of **1a** (1.0 mmol), **2a** (1.0 mmol), and **3** (2.0 mmol) in solvent (2 mL), otherwise mentioned. [b]Isolated yields. [c]Not detected.

compounds **4a** in 40% yield (Table 1, entry 2). This promising result motivated us to further optimize and increase the product yield by modifying the reaction conditions. After initial screening, we switched to chlorinated solvents such as dichloromethane, chloroform, and dichloroethane but gave unsatisfactory yields (Table 1, entries 3−5). Further, we screened in toluene, THF, 1,4-dioxane, methanol, ethanol solvent (Table 1, entries 6−10), and DMF, which gave moderate yields. Surprisingly, DMF gave a 68% yield in 5 h (Table 1, entry 11). This led us to investigate the stoichiometry of rongalite and attempt the reaction with 1.5, 2.0, and 2.5 equiv, with 2.0 equiv of rongalite yielding a 90% product yield (1, entries 12−14). Unfortunately, DMSO and H_2O solvents are inefficient for this methodology to yield the desired product (Table 1, entries 15−16).

After testing various solvents, we determined that DMF is the most effective reaction medium for producing the compound with a high yield. The established conditions for synthesizing diarylmethane are as follows: imidazo[1,2-*a*]-pyridine **1a** (1.0 mmol), indole **2a** (1.0 mmol), and rongalite **3** (2.0 mmol) in 2 mL of DMF solvent at 80 °C in an oil bath for 5 h.

After optimizing the reaction conditions for the metal-free protocol of heterodiarylmethanes between imidazo[1,2-*a*]-pyridines, indoles, and rongalite in DMF, we concentrated on the scope of the substitutions on both the imidazo[1,2-*a*]pyridines and indoles; the results are shown in Scheme 2. Fortunately, the substitution such as methyl, −F, −Br, −Ph, methoxy, and −Cl on both the imidazo-[1,2-*a*]pyridine and indoles is well tolerated, given the corresponding 3-((1*H*-indol-3-yl)methyl)-2-phenylimidazo[1,2-*a*]pyridine derivative in good to excellent yields (Scheme 2a, **4a−4p**), and also *N*-methyl, *N*-butyl, *N*-allyl indoles reacted with imidazo-[1,2-*a*]pyridine and gave good yields (Scheme 2a, **4q−4s**). Further, the above methodology was extended for the synthesis of other heteroarene, i.e., imidazo[2,1-*b*]thiazole and benzo[*d*]imidazo-[2,1-*b*]-thiazole. Notably, these substrates also showed similar reactivity patterns of imidazo[1, 2-*a*]pyridines and furnished the titled compounds in excellent yield (Scheme 2b, **6a−6f**).

Finally, we have tested our method in gram scale for industrial applications with 5 g scale and obtained target compounds **4a** in 90% yield (Scheme 3).

To gain mechanistic insight into one-pot heterodiarylmethylation, we conducted control experiments (Scheme 4). First, we carried out control experiments on 2-phenylimidazo-[1,2-*a*]pyridine **1a** (1.0 mmol) and indole **2a** (1.0 mmol) in 2 mL of DMF at 80 °C without rongalite **3** (Scheme 4a). However, this failed to produce target compound **4a**. This result indicates that C1 is sourced from rongalite. Next, we repeated the same reaction in the presence of rongalite **3** (2.0 mmol) and recorded the HRMS data of the samples at different intervals. These samples showed the formation of (2-phenylimidazo[1,2-*a*]pyridin-3-yl)methanol **7** (Scheme 4b). The adduct of (1*H*-indol-3-yl)methanol **9** was not detected in HRMS, indicating that rongalite primarily reacts with phenylimidazo[1,2-*a*]pyridine **1a**. Finally, the heterodiarylmethylation reaction was conducted in the presence of a radical quencher, TEMPO (3.0 mmol), in 2 mL of DMF at 80 °C. No progress in the reaction was observed to provide **4a** (Scheme 4c). However, the formation of a TEMPO adduct with imidazo-[1,2-*a*]pyridine **8** was observed when the HRMS of the sample was recorded (Scheme 4c).

The plausible reaction mechanism pathway is proposed for the heterodiarylmethanes via metal-free coupling between imidazo[1,2-*a*]pyridines or imidazo[2,1-*b*]thiazole and indoles, based on control experiments and literature reports (Scheme 5).[17−20]

In the first step, rongalite dissociates and generates formaldehyde in situ under thermal conditions.[19] Next, the formaldehyde may further react with electronically rich heterocyclic imidazo[1,2-*a*]pyridines or imidazo[2,1-*b*]-thiazole. The C-3 position of imidazo[1,2-*a*]pyridine forms an intermediate **I** upon reaction with formaldehyde, which then rearomatizes to form compound (2-phenylimidazo[1,2-*a*]pyridin-3-yl)methanol **7** (detected by HRMS). Upon dehydration of intermediate **7**, Michael acceptor 3-methyl-ene-2-phenyl-3*H*-imidazo[1,2-*a*]pyridin-4-ium **III** is formed. Subsequently, indole π electrons attack intermediate **III** via Michael addition to form intermediate **IV**, which then undergoes aromatization to produce the desired product **4a** (Scheme 5).

CONCLUSIONS

In this study, rongalite, a cost-effective reagent, was utilized as a powerful in situ methylenating agent for the synthesis of heterodiarylmethanes under metal-free conditions. This strategy demonstrates a wide functional group tolerance and offers the corresponding 3-((1*H*-indol-3-yl)methyl)-2-phenylimidazo[1,2-*a*]pyridines and 5-((1*H*-indol-3-yl)-methyl)-6-phenylimidazo[2,1-*b*]thiazoles in good to excellent yields under mild conditions. We anticipate that this approach will be a convenient, economical, and practical tool to synthesize structurally diversified heterodiarylmethanes. Additionally, this protocol has been tested for large-scale industrial applications.

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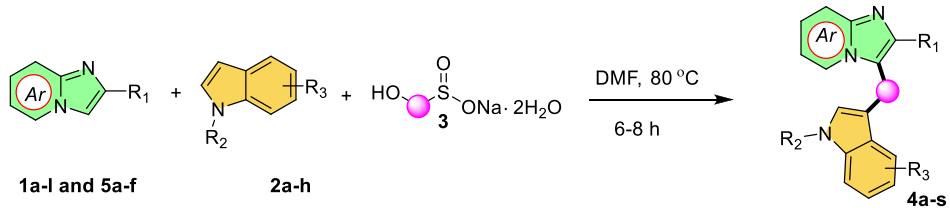
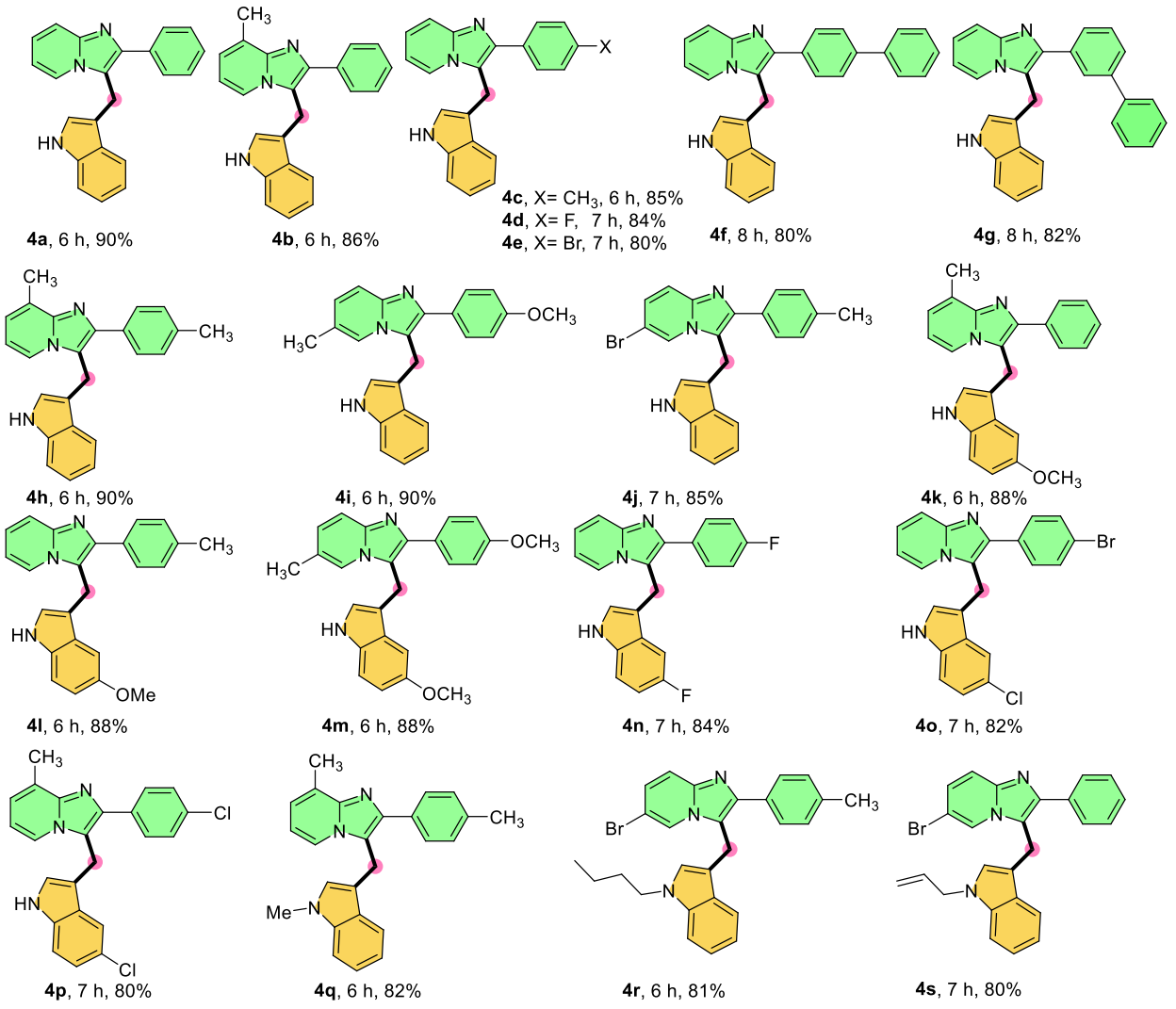
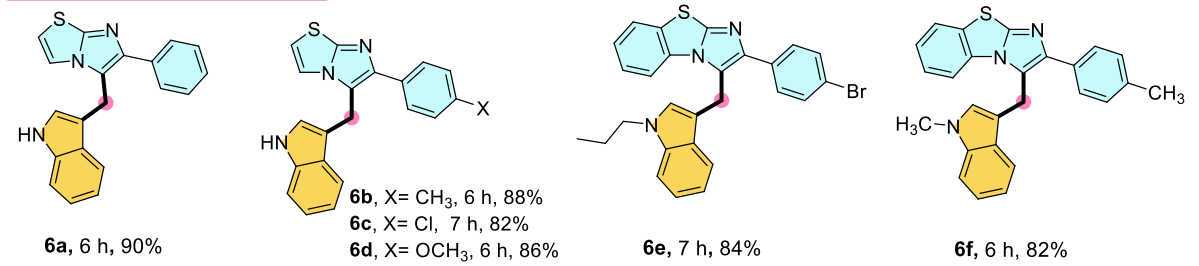
Scheme 2. Substrate Scope of 3-((1*H*-Indol-3-yl)methyl)-2-phenylimidazo[1,2-*a*]pyridine[a]



a) with imidazo[1,2-*a*]pyridine



b) with imidazo[2,1-*b*]thiazol



[a]All the reactions were conducted on a 1 mmol scale of **1a−l** (1 mmol), **2a−h** (1 mmol), and **3** (2 mmol) in DMF solvent (2 mL). [b]Isolated yields.

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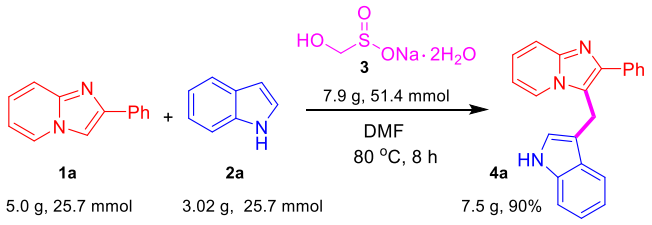
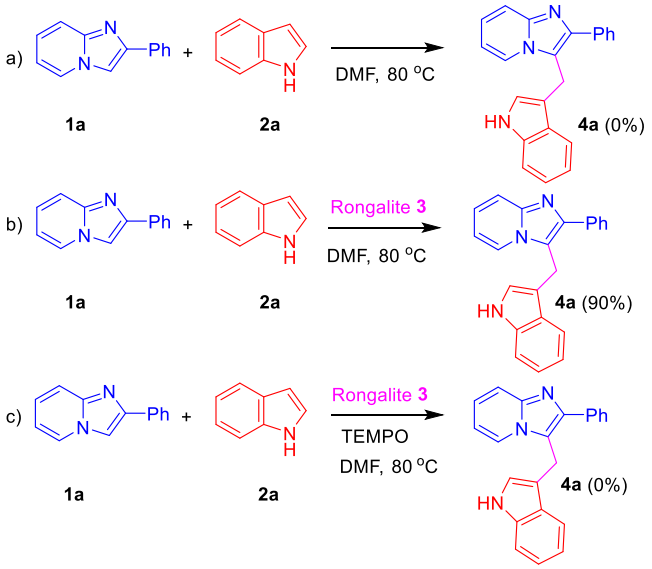
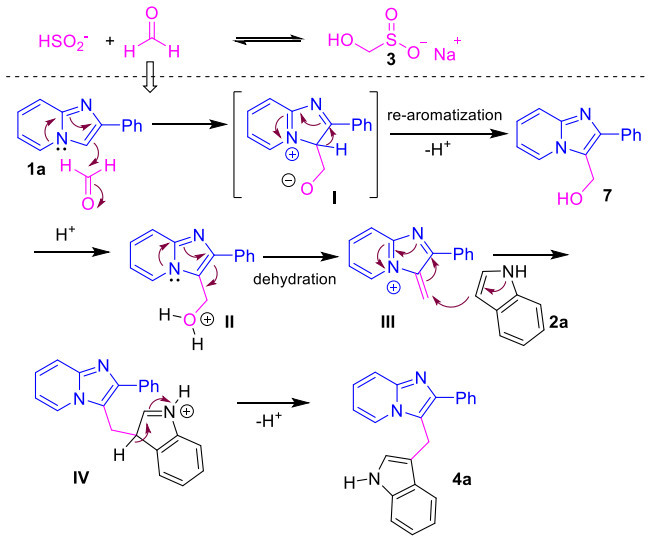
Scheme 3. Gram-Scale Synthesis of Compound 4a



Scheme 4. Control Experiments



Scheme 5. Plausible Mechanism



EXPERIMENTAL SECTION

General Information. All chemicals and solvents were purchased from Alfa Aesar, Spectrochem, SRL, and Finar and used as received. Imidazo-[1,2-*a*]pyridine **1a**−**l** and imidazo[2,1-*b*]thiazoles **5a**−**f** were prepared from literature reports,[1,2] and rongalite **3** was purchased from Sisco Research Laboratories Pvt. Ltd. The conformation of the reactions was monitored using analytical thin layer chromatography (TLC) Merck silica gel G/GF $_{254}$ plates, and UV-Cabinet was used for visualization of compound spots on TLC plate. Purification of compounds using column chromatography was performed with the Rankem silica gel (60−120 mesh). Spectral analysis for Fourier transform infrared was recorded using a PerkinElmer IR spectrometer. Finding the melting points of solid compounds was determined by open capillaries using the Stuart SMP30 melting point apparatus and is uncorrected. NMR (^{1}H, ^{13}C, and ^{19}F) spectra of all the synthesized compounds were recorded on a Bruker AVANCE HD (400 MHz/100 MHz) spectrometer using $CDCl_3$ and DMSO-d_6 as solvents and TMS as an internal standard. The data of the compounds was recorded as chemical shifts (δ ppm) (multiplicity, coupling constant (Hz), and integration). Abbreviations for the multiplicity are as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and dd = doublet of doublet. The mass spectrum analysis was recorded in a Bruker-micro-TOF MS analyzer.

General Procedure for the Synthesis of 2-Arylimidazo[1,2-*a*]pyridines. To an oven-dried 50 mL round-bottom flask were added 2-bromo-1-arylethanone (2.51 mmol) and pyridin-2-amine (2.51 mmol) in 10 mL of ethanol, and then $NaHCO_3$ (3.76 mmol) was added.[21] The resulting mixture was refluxed in an oil bath for 3 h; after completion of the reaction, the solvent was evaporated under a vacuum, EtOAc (3 × 10 mL) was added and washed with excess water. The organic layers were dried on Na_2SO_4 and evaporated to give 2-arylimidazo[1,2-*a*]pyridines, which were used directly in the next step without further purification.

General Procedure for the Synthesis of 6-Phenylimidazo-[2,1-*b*]thiazoles. In an oven-dried 50 mL round-bottom flask, phenacyl bromide (1.0 mmol), 2-aminothiazole (1.0 mmol), and $NaHCO_3$ (1.5 mmol) were dissolved in 5 mL of ethanol and stirred at 80 °C in an oil bath for 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with water and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine solution, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The product was purified by column chromatography on silica gel with EtOAc/petroleum ether (10/90) as the eluent.

General Procedure for the Preparation of Substituted 3-((1*H*-Indol-3-yl)methyl)-2-phenylimidazo[1,2-*a*]pyridine (4a−4s). To a clean and dry round-bottom flask equipped with a magnetic bead were added imidazo-[1, 2-*a*] pyridine **1a** (1.0 mmol), indole **2a** (1.0 mmol), and rongalite **3** (2 mmol) in 2 mL of DMF solvent. The reaction mixture was allowed to stir in an oil bath at 80 °C for 6−8 h for completion. After completion of the reaction (monitored by TLC), the reaction mixture was poured into an ice-cold water and extracted with ethyl acetate (3 × 10 mL), dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture was separated by using column chromatography with silica gel (100−200 mesh) by eluting with ethyl acetate/hexanes as a mobile phase.

General Procedure for the Preparation of Substituted 5-((1*H*-Indol-3-yl)methyl)-6-phenylimidazo[2,1-*b*]thiazole and 3-((1*H*-Indol-3-yl)methyl)-2-phenylbenzo[*d*]imidazo[2,1-*b*]-thiazole (6a−6f). To a clean and dry round-bottom flask equipped with magnetic beads were added indole **2a** (1.0 mmol), 6-phenylimidazo[2,1-*b*]thiazole or 2-phenylbenzo[*d*]imidazo[2,1-*b*]-thiazole **5a** (1.0 mmol), and rongalite **3** (2.0 mmol) in DMF solvent (2 mL). The reaction mixture was allowed to stir in an oil bath at 80 °C for 6−8 h for completion. After conforming the reaction (monitored by TLC), the reaction mixture was poured into ice cold water, extracted with ethyl acetate (3 × 10 mL), dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude mixture was separated by using column chromatography with silica gel (100−200 mesh) by eluting with ethyl acetate/hexanes as a mobile phase.

3-((1*H*-Indol-3-yl)methyl)-2-phenyl*H*-imidazo[1,2-*a*]-pyridine (4a). The product was purified by column chromatog-

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raphy[17,18] (EtOAc/hexanes = 15:85) (292 mg, 90%), brown solid, mp 160−162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 7.73 (d, J = 7.0 Hz, 2H), 7.67 (d, J = 7.1 Hz, 1H), 7.56 (t, J = 8.8 Hz, 2H), 7.30−7.28 (m, 1H), 7.26 (d, J = 3.8 Hz, 1H), 7.23−7.19 (m, 1H), 7.18−7.12 (m, 2H), 7.10−7.02 (m, 2H), 6.55 (t, J = 6.8 Hz, 1H), 6.45 (s, 1H), 4.43 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.8, 143.2, 136.8, 134.5, 128.7, 128.2, 127.7, 127.0, 124.2, 123.9, 122.4, 122.2, 119.6, 118.6, 118.4, 117.3, 112.0, 111.5, 110.9, 20.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{18}N_3$, 324.1495; found, 324.1496.

3-((1*H*-Indol-3-yl)methyl)-8-methyl-2-phenyl*H*-imidazo[1,2-*a*]pyridine (4b). The product was purified by column chromatography[17,18] (EtOAc/hexanes = 20:80) (289 mg, 86%), brown solid, mp 142−144 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.74 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.9 Hz, 2H), 7.29 (t, J = 7.1 Hz, 3H), 7.21 (t, J = 7.3 Hz, 1H), 7.16 (d, J = 5.0 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.88 (d, J = 6.8 Hz, 1H), 6.50 (t, J = 6.8 Hz, 1H), 6.47 (s, 1H), 4.41 (s, 2H), 2.62 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.1, 142.5, 136.7, 134.5, 128.6, 128.4, 127.6, 127.2, 127.0, 123.2, 122.4, 122.1, 121.7, 119.6, 118.7, 118.6, 112.2, 111.4, 111.2, 20.8, 17.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{23}H_{20}N_3$, 338.1652; found, 338.1647.

3-((1*H*-Indol-3-yl)methyl)-2-*p*-tolyl*H*-imidazo[1,2-*a*]pyridine (4c). The product was purified by column chromatography[17] (EtOAc/hexanes = 20:80) (287 mg, 85%), brown solid, mp 106−108 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.69 (d, J = 6.5 Hz, 1H), 7.63 (t, J = 7.3 Hz, 3H), 7.56 (d, J = 7.4 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 7.09 (dd, J = 18.3, 7.6 Hz, 4H), 6.59 (t, J = 6.4 Hz, 1H), 6.51 (s, 1H), 4.44 (s, 2H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.5, 142.8, 137.6, 136.8, 131.2, 129.4, 128.1, 126.9, 124.4, 123.8, 122.5, 122.1, 119.7, 118.6, 118.0, 117.1, 112.2, 111.5, 111.0, 21.3, 20.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{23}H_{20}N_3$, 338.1652; found, 338.1654.

3-((1*H*-Indol-3-yl)methyl)-2-(4-fluorophenyl)*H*-imidazo[1,2-*a*]pyridine (4d). The product was purified by column chromatography[17] (EtOAc/hexanes = 15:85) (286 mg, 84%), white solid, mp 178−180 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.75−7.70 (m, 3H), 7.64 (d, J = 9.0 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 8.1 Hz, 1H), 7.18 (d, J = 4.8 Hz, 1H), 7.15−7.08 (m, 2H), 7.01 (t, J = 8.6 Hz, 2H), 6.64 (t, J = 6.7 Hz, 1H), 6.54 (s, 1H), 4.44 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.9 (d, $^1J_{C-F}$ = 250 Hz), 144.3, 141.5, 136.8, 129.9 (d, $^3J_{C-F}$ = 8 Hz), 126.8, 124.9, 123.9, 122.6, 122.0, 119.8, 118.5, 118.2, 117.0, 115.8 (d, $^2J_{C-F}$ = 20 Hz), 112.6, 111.5, 110.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −114.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{17}FN_3$, 342.1401; found, 342.1401.

3-((1*H*-Indol-3-yl)methyl)-2-(4-bromophenyl)*H*-imidazo[1,2-*a*]pyridine (4e). The product was purified by column chromatography (EtOAc/hexanes = 15:85) (322 mg, 80%), brown solid, mp 193−195 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 2H), 7.70 (d, J = 6.9 Hz, 1H), 7.61 (d, J = 8.4 Hz, 2H), 7.58−7.53 (m, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.1 Hz, 1H), 7.20−7.15 (m, 2H), 7.10 (t, J = 8.9 Hz, 2H), 6.61 (t, J = 6.6 Hz, 1H), 6.49 (s, 1H), 4.42 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.6, 141.6, 136.8, 133.1, 131.9, 129.7, 126.8, 124.8, 123.8, 122.7, 122.0, 121.9, 119.8, 118.5, 117.2, 112.5, 111.5, 110.7, 20.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{17}BrN_3$, 402.0600; found, 402.0609 (Br peak 404.0592).

3-((1*H*-Indol-3-yl)methyl)-2-([1,1′-biphenyl]-4-yl)imidazo-[1,2-*a*]pyridine (4f). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (318 mg, 80%), brown solid, mp 101−102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 7.90 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 6.8 Hz, 1H), 7.66 (t, J = 7.3 Hz, 2H), 7.60 (t, J = 8.5 Hz, 4H), 7.44−7.36 (m, 3H), 7.32 (t, J = 7.3 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 7.20−7.11 (m, 2H), 6.64 (t, J = 6.7 Hz, 2H), 6.59 (s, 1H), 4.56 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 144.4, 141.9, 140.5, 140.1, 137.0, 133.4, 128.9, 128.6, 127.4, 127.2, 126.9, 124.6, 124.1, 122.5, 121.9, 119.1, 118.9, 118.3, 116.9, 112.3, 111.8, 109.7, 20.8 HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{28}H_{22}N_3$, 400.1808; found, 400.1792.

3-((1*H*-Indol-3-yl)methyl)-2-([1,1′-biphenyl]-3-yl)imidazo-[1,2-*a*]pyridine (4g). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (328 mg, 82%), brown solid, mp 105−107 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.89 (s, 1H), 8.26 (d, J = 6.8 Hz, 1H), 8.07 (s, 1H), 7.86 (d, J = 9.3 Hz, 1H), 7.69−7.63 (m, 2H), 7.59−7.52 (m, 3H), 7.43−7.30 (m, 5H), 7.29−7.23 (m, 1H), 7.10 (t, J = 7.0 Hz, 1H), 7.03−6.84 (m, 3H), 4.65 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6): δ 144.3, 141.8, 140.9, 140.4, 137.1, 135.9, 129.8, 129.4, 128.0, 127.2., 127.1, 126.5, 126.1, 125.0, 124.7, 123.2, 121.8, 119.8, 119.0, 118.8, 117.3, 112.5, 112.1, 110.3, 20.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{28}H_{22}N_3$, 400.1808; found, 400.1828.

3-((1*H*-Indol-3-yl)methyl)-8-methyl-2-*p*-tolyl*H*-imidazo[1,2-*a*]pyridine (4h). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (316 mg, 90%), brown solid, mp 195−197 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (s, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.58 (dd, J = 12.1, 7.4 Hz, 2H), 7.32 (d, J = 8.1 Hz, 1H), 7.19 (s, 1H), 7.13 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 7.2 Hz, 1H), 6.91 (d, J = 6.8 Hz, 1H), 6.54 (t, J = 6.8 Hz, 2H), 4.43 (s, 2H), 2.64 (s, 3H), 2.28 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.7, 142.1, 137.6, 136.7, 129.4, 128.3, 127.0, 123.6, 122.4, 122.1, 121.7, 119.6, 118.6, 118.4, 112.3, 111.4, 111.2, 21.3, 20.7, 17.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{24}H_{22}N_3$, 352.1808; found, 352.1815.

3-((1*H*-Indol-3-yl)methyl)-2-(4-methoxyphenyl)-6-methylimidazo[1,2-*a*]pyridine (4i). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (331 mg, 90%), white solid, mp 121−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 7.73 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 9.0 Hz, 1H), 7.58 (s, 1H), 7.42 (d, J = 8.1 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.19 (t, J = 7.4 Hz, 1H), 7.04 (d, J = 9.2 Hz, 1H), 6.91 (d, J = 8.5 Hz, 2H), 6.61 (s, 1H), 4.48 (s, 2H), 3.80 (s, 3H), 2.21 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.4, 143.2, 141.8, 136.9, 129.4, 128.0, 126.9, 126.2, 122.5, 122.3, 122.1, 121.3, 119.7, 118.6, 117.3, 116.1, 114.2, 111.5, 111.1, 55.3, 20.7, 18.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{24}H_{22}N_3O$, 368.1757; found, 368.1764.

3-((1*H*-Indol-3-yl)methyl)-6-bromo-2-*p*-tolyl*H*-imidazo[1,2-*a*]pyridine (4j). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (375 mg, 85%), brown solid, mp 151−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.91 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 7.8 Hz, 1H), 7.53 (d, J = 9.5 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.16 (t, J = 7.7 Hz, 5H), 6.57 (s, 1H), 4.48 (s, 2H), 2.34 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 143.8, 143.0, 138.0, 136.9, 130.8, 129.5, 128.0, 127.6, 126.8, 123.7, 122.6, 122.0, 199.7, 118.6, 118.5, 117.7, 111.6, 110.4, 106.9, 21.3, 20.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{23}H_{19}BrN_3$, 416.0757; found, 416.0740. (Br peak 418.0722).

3-((5-Methoxy-1*H*-indol-3-yl)methyl)-2-*p*-tolyl*H*-imidazo-[1,2-*a*]pyridine (4k). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (323 mg, 88%), brown solid, mp 98−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.76 (d, J = 6.9 Hz, 1H), 7.68 (t, J = 7.4 Hz, 3H), 7.21 (d, J = 8.8 Hz, 1H), 7.17−7.11 (m, 3H), 6.91 (d, J = 2.3 Hz, 1H), 6.83 (dd, J = 8.8, 2.4 Hz, 1H), 6.66 (td, J = 6.8, 0.8 Hz, 1H), 6.60−6.57 (m, 1H), 4.43 (s, 2H), 3.74 (s, 3H), 2.30 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.2, 144.1, 137.9, 131.8, 129.5, 128.2, 127.2, 124.8, 123.8, 122.7, 118.1, 116.9, 112.8, 112.5, 112.1, 110.5, 100.2, 55.9, 21.3, 20.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{24}H_{22}N_3O$, 368.1757; found, 368.1758.

3-((5-Methoxy-1*H*-indol-3-yl)methyl)-2-*p*-tolyl*H*-imidazo-[1,2-*a*]pyridine (4l). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (325 mg, 88%), brown solid, mp 191−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (s, 1H), 7.70−7.67 (m, 2H), 7.57 (t, J = 7.9 Hz, 2H), 7.32 (d, J = 8.1 Hz, 1H), 7.20−7.15 (m, 2H), 7.12−7.07 (m, 1H), 6.90 (d, J = 6.8 Hz, 1H), 6.86−6.84 (m, 2H), 6.53 (t, J = 6.8 Hz, 2H), 4.41 (s, 2H), 3.73 (s, 3H), 2.63 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.3, 144.8, 142.1, 136.7, 129.6, 127.0, 123.3, 122.5, 122.0, 121.6, 119.7, 118.6, 118.0, 114.1, 112.2, 111.4, 55.3, 20.8, 17.3 HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{24}H_{22}N_3O$, 368.1757; found, 368.1745.

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3-((5-Methoxy-1*H*-indol-3-yl)methyl)-2-(4-methoxyphenyl)-6-methyl*H*-imidazo[1,2-*a*]pyridine (4m). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (351 mg, 88%), brown solid, mp 163−164 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.68−7.64 (m, 2H), 7.61 (dd, J = 7.8, 1.1 Hz, 1H), 7.51−7.48 (m, 2H), 7.33 (dt, J = 8.1, 1.0 Hz, 1H), 7.22−7.19 (m, 1H), 7.12 (ddd, J = 8.0, 7.0, 1.1 Hz, 1H), 6.93 (dd, J = 9.3, 1.6 Hz, 1H), 6.86−6.82 (m, 2H), 6.53 (dd, J = 2.5, 1.3 Hz, 1H), 4.41 (s, 2H), 3.73 (s, 3H), 2.14 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.2, 154.0, 143.7, 142.7, 132.0, 129.3, 127.3, 127.1, 122.9, 121.5, 121.3, 117.3, 116.3, 114.1, 112.5, 112.2, 110.7, 100.3, 55.9, 55.2, 20.8, 18.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{25}H_{24}N_3O_2$, 398.1863; found, 398.1855.

3-((5-Fluoro-1*H*-indol-3-yl)methyl)-2-(4-fluorophenyl)*H*-imidazo[1,2-*a*]pyridine (4n). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (302 mg, 84%), white solid, mp 180−182 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.99 (s, 1H), 8.19 (d, J = 6.9 Hz, 1H), 7.87 (dd, J = 8.5, 5.5 Hz, 2H), 7.62 (d, J = 9.0 Hz, 1H), 7.36−7.22 (m, 5H), 7.01 (td, J = 5.1, 2.4 Hz, 2H), 6.95−6.83 (m, 3H), 4.56 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6): δ 163.3 (d, $^1J_{C-F}$ = 240 Hz), 158.2 (d, $^1J_{C-F}$ = 230 Hz), 144.2, 141.1, 133.7, 131.8, 131.7, 130.2 (d, $^3J_{C-F}$ = 10 Hz), 127.2 (d, $^3J_{C-F}$ = 10 Hz), 125.3, 124.9, 124.7, 119.0, 117.2, 116.1 (d, $^2J_{C-F}$ = 20 Hz), 113.0 (d, $^3J_{C-F}$ = 10 Hz), 112.4, 110.3 (d, $^4J_{C-F}$ = 10 Hz), 110.0, 109.7, 103.5 (d, $^2J_{C-F}$ = 30 Hz), 20.2. ^{19}F NMR (376 MHz, DMSO-d_6): δ −114.7, −125.05. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{16}F_2N_3$, 360.1307; found, 360.1301.

2-(4-Bromophenyl)-3-((5-chloro-1*H*-indol-3-yl)methyl)*H*-imidazo[1,2-*a*]pyridine (4o). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (362 mg, 82%), brown solid, mp 196−198 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.71 (d, J = 6.8 Hz, 1H), 7.60 (t, J = 9.3 Hz, 3H), 7.43 (t, J = 9.5 Hz, 3H), 7.30 (s, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.06 (dd, J = 8.5, 1.6 Hz, 1H), 6.66 (t, J = 6.7 Hz, 1H), 6.54 (s, 1H), 4.40 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.6, 141.6, 137.1, 132.9, 131.9, 129.7, 128.6, 125.4, 124.9, 123.7, 122.6, 122.1, 120.6, 119.4, 118.2, 117.3, 112.6, 111.5, 111.0, 20.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{16}BrClN_3$, 436.0211; found, 436.0227 (Br peak 438.0207).

3-((5-Chloro-1*H*-indol-3-yl)methyl)-2-(4-chlorophenyl)-8-methyl*H*-imidazo[1,2-*a*]pyridine (4p). The product was purified by column chromatography (EtOAc/hexanes = 20:80) (325 mg, 80%), red solid, mp 191−193 °C. ^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$): δ 10.74 (s, 1H), 7.85−7.74 (m, 3H), 7.46−7.34 (m, 4H), 7.02 (d, J = 6.4 Hz, 1H), 6.96 (dd, J = 8.5, 1.5 Hz, 1H), 6.78−6.68 (m, 2H), 4.50 (s, 2H), 2.63 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, DMSO-d_6 + $CDCl_3$): δ 144.6, 137.4, 133.2, 129.7, 128.8, 127.2, 126.7, 125.5, 123.5, 122.1, 119.5, 119.3, 112.7, 111.6, 110.0, 20.6, 17.0. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{23}H_{18}Cl_2N_3$, 406.0872; found, 406.0886.

8-Methyl-3-((1-methyl-1*H*-indol-3-yl)methyl)-2-*p*-tolyl*H*-imidazo[1,2-*a*]pyridine (4q). The product was purified by column chromatography (EtOAc/hexanes = 15:85) (300 mg, 82%), brown solid, mp 111−113 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.0 Hz, 2H), 7.57 (t, J = 8.9 Hz, 2H), 7.25 (d, J = 8.0 Hz, 1H), 7.21(t, J = 7.5 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.09 (t, J = 7.3 Hz, 1H), 6.89 (d, J = 6.8 Hz, 1H), 6.52 (t, J = 6.8 Hz, 1H), 6.42 (s, 1H), 4.42 (s, 2H), 3.57 (s, 3H), 2.64 (s, 3H), 2.29 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 145.0, 142.6, 137.5, 137.3, 131.8, 129.3, 128.2, 127.4, 127.2, 126.7, 122.9, 122.0, 121.6, 119.1, 118.8, 118.4, 112.0, 109.9, 32.7, 21.3, 20.7, 17.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{25}H_{24}N_3$, 366.1965; found, 366.1976.

6-Bromo-3-((1-butyl-1*H*-indol-3-yl)methyl)-2-*p*-tolyl*H*-imidazo[1,2-*a*]pyridine (4r). The product was purified by column chromatography (EtOAc/hexanes = 15:85) (380 mg, 81%), brown solid, mp 105−107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.71 (d, J = 8.0 Hz, 2H), 7.58 (dd, J = 8.6, 4.8 Hz, 2H), 7.36 (d, J = 8.3 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 7.21 (dd, J = 6.9, 4.4 Hz, 3H), 7.14 (t, J = 7.4 Hz, 1H), 6.54 (s, 1H), 4.50 (s, 2H), 4.00 (t, J = 7.0 Hz, 2H), 2.37 (s, 3H), 1.71 (dt, J = 14.6, 7.1 Hz, 2H), 1.26−1.20 (m, 2H), 0.86 (t, J = 7.3 Hz, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.0, 143.1, 137.8, 136.9, 131.1, 129.5, 128.1, 127.4, 125.7, 123.8, 122.0, 119.2, 118.9, 118.6, 118.0, 109.8, 108.7, 106.7, 46.1, 32.2, 21.3, 20.9, 20.1, 13.7. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{27}H_{27}BrN_3$, 472.1383; found, 472.1380 (Br peak 474.1363).

3-((1-Allyl-1*H*-indol-3-yl)methyl)-6-bromo-2-phenyl*H*-imidazo[1,2-*a*]pyridine (4s). The product was purified by column chromatography (EtOAc/hexanes = 15:85) (355 mg, 80%), red solid, mp 104−106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.82 (d, J = 7.2 Hz, 2H), 7.59 (dd, J = 8.7, 4.3 Hz, 2H), 7.41 (t, J = 7.4 Hz, 2H), 7.35 (d, J = 8.8 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 7.22 (dd, J = 9.6, 1.5 Hz, 1H), 7.16 (t, J = 7.4 Hz, 1H), 6.57 (s, 1H), 5.90 (ddd, J = 22.2, 10.4, 5.3 Hz, 1H), 5.14 (d, J = 10.2 Hz, 1H), 4.99 (d, J = 17.9 Hz, 1H), 4.62 (d, J = 5.2 Hz, 2H), 4.53 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 144.0, 143.2, 137.1, 134.0, 133.3, 128.8, 128.2, 128.0, 127.5, 127.4, 125.7, 123.8, 123.3, 119.5, 118.9, 118.8, 118.1, 117.3, 110.0, 109.4, 106.8, 48.8, 20.8. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{25}H_{21}BrN_3$, 442.0913; found, 442.0911 (Br peak 444.0893).

3-((6-Phenylimidazo[2,1-*b*]thiazol-5-yl)methyl)-1*H*-indole (6a). The product was purified by column chromatography (EtOAc/hexanes = 25:75) (298 mg, 90%), red solid, mp 62−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 1H), 7.66 (d, J = 7.2 Hz, 2H), 7.46 (d, J = 7.9 Hz, 1H), 7.33−7.26 (m, 3H), 7.20 (t, J = 7.4 Hz, 1H), 7.17−7.12 (m, 1H), 7.08−7.03 (m, 1H), 6.94 (d, J = 4.5 Hz, 1H), 6.65 (s, 1H), 6.55 (d, J = 4.5 Hz, 1H), 4.36 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.3, 143.7, 136.7, 134.6, 128.7, 127.5, 127.2, 126.9, 122.5, 122.3, 120.4, 119.7, 118.6, 117.6, 112.1, 111.9, 111.5, 21.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{16}N_3S$, 330.1059; found, 330.1059.

3-((6-*p*-Tolylimidazo[2,1-*b*]thiazol-5-yl)methyl)-1*H*-indole (6b). The product was purified by column chromatography (EtOAc/hexanes = 30:70) (305 mg, 88%), brown solid, mp 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (s, 1H), 7.62 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 7.9 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.0 Hz, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.09 (t, J = 7.4 Hz, 1H), 6.92 (d, J = 4.5 Hz, 1H), 6.63 (s, 1H), 6.51 (d, J = 4.5 Hz, 1H), 4.38 (s, 2H), 2.32 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.2, 143.8, 137.0, 136.7, 131.8, 129.4, 127.4, 126.9, 122.4, 122.3, 120.2, 119.6, 118.6, 117.6, 111.9, 111.8, 111.5, 21.5, 21.3. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{21}H_{18}N_3S$, 344.1216; found, 344.1213.

3-((6-(4-Chlorophenyl)imidazo[2,1-*b*]thiazol-5-yl)methyl)-1*H*-indole (6c). The product was purified by column chromatography[18] (EtOAc/hexanes = 30:70) (300 mg, 82%), orange solid, mp 130−131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.57 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 7.8 Hz, 1H), 7.28 (d, J = 8.2 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.13 (d, J = 7.6 Hz, 1H), 7.05 (t, J = 7.4 Hz, 1H), 6.94 (d, J = 4.5 Hz, 1H), 6.62 (s, 1H), 6.55 (d, J = 4.5 Hz, 1H), 4.32 (s, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.5, 142.5, 136.7, 133.1, 128.8, 128.7, 126.8, 122.6, 122.2, 120.7, 119.8, 118.5, 117.5, 112.5, 111.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3S$, 364.0670; found, 364.0671.

5-((1*H*-Indol-3-yl)methyl)-6-(4-methoxyphenyl)imidazo[2,1-*b*]thiazole (6d). The product was purified by column chromatography (EtOAc/hexanes = 30:70) (312 mg, 86%), brown solid, mp 120−125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (s, 1H), 7.59−7.56 (m, 2H), 7.45 (d, J = 7.9 Hz, 1H), 7.26 (d, J = 8.2 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H), 7.06−7.01 (m, 1H), 6.90 (d, J = 4.5 Hz, 1H), 6.83−6.80 (m, 2H), 6.62−6.60 (m, 1H), 6.49 (d, J = 4.5 Hz, 1H), 4.31 (s, 2H), 3.70 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.9, 148.1, 143.7, 136.7, 128.7, 127.5, 126.9, 122.4, 122.3, 119.7, 119.6, 118.6, 117.6, 114.1, 112.1, 111.7, 111.5, 55.3, 21.5.

2-(4-Bromophenyl)-3-((1-propyl-1*H*-indol-3-yl)methyl)-benzo[*d*]imidazo[2,1-*b*]thiazole (6e). The product was purified by column chromatography (EtOAc/hexanes = 30:70) (380 mg, 84%), orange solid, mp 139−140 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dt, J = 13.6, 6.7 Hz, 3H), 7.52 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 7.33 (t, J = 6.8 Hz, 2H), 7.25 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 7.1 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 6.61 (s, 1H), 4.55 (s, 14H), 3.88 (t, J = 7.0 Hz, 2H), 1.64 (dd, J = 14.4, 7.2 Hz, 2H), 0.67 (t, J = 7.4 Hz, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 147.1, 137.0,

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132.7, 132.5, 131.9, 130.3, 128.9, 127.0, 126.4, 126.2, 124.8, 124.2, 122.7, 122.2, 121.7, 119.3, 118.7, 113.9, 110.0, 109.9, 48.0, 23.4, 22.2, 11.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{27}H_{23}BrN_3S$, 500.0791; found, 500.0786 (Br peak 502.0786).

3-((1-Methyl-1*H*-indol-3-yl)methyl)-2-(*p*-tolyl)benzo[*d*]-imidazo[2,1-*b*]thiazole (6f). The product was purified by column chromatography (EtOAc/hexanes = 30:70) (294 mg, 82%), brown solid, mp 191−193 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.9 Hz, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.33 (t, J = 8.4 Hz, 1H), 7.26 (t, J = 7.9 Hz, 2H), 7.15 (dd, J = 10.4, 4.6 Hz, 2H), 7.12−7.05 (m, 3H), 6.58 (s, 1H), 4.56 (s, 2H), 3.58 (s, 3H), 2.27 (s, 3H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 146.7, 144.2, 137.1, 133.0, 131.2, 130.4, 129.4, 127.3, 126.2, 124.3, 124.1, 122.1, 122.0, 119.2, 118.7, 113.7, 110.9, 109.6, 32.8, 22.1, 21.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{22}N_3S$, 408.1529; found, 408.1528.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.4c02143.

Experimental details, procedures, and spectral data for all new compounds (PDF)

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The manuscript was written through the contributions of all authors.

Notes

The authors declare no competing financial interest.

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