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Synthesis of Imidazo[1,2-*a*]pyridines: Triflic Anhydride-Mediated Annulation of 2*H*-Azirines with 2-Chloropyridines

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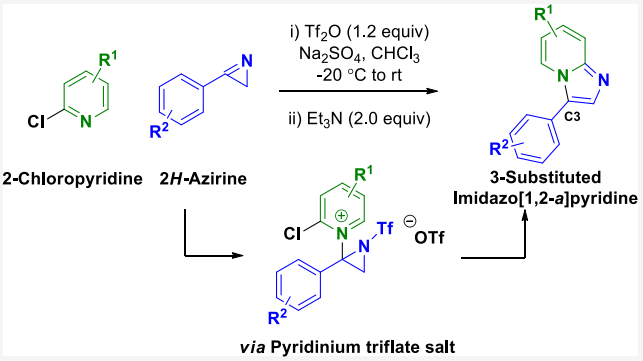
ABSTRACT: The discovery and optimization of a reaction between 2-chloropyridines and 2*H*-azirines producing imidazo[1,2-*a*]pyridines is described. The treatment of 2*H*-azirines with triflic anhydride (Tf_2O) forms an electrophilic 1-trifloyl-aziridin-2-yl triflate species which, when reacted *in situ* with 2-halopyridines, generates transient pyridinium salts. These salts were treated in the same pot with triethylamine (Et_3N), leading to the selective formation of C3-substituted imidazo[1,2-*a*]pyridines, an heterocyclic moiety commonly found in medicinal chemistry leads and drugs. Thorough optimization of the activation/cyclization resulted in yields ranging from 15 to 85% for a variety of substituted heterocycles.



INTRODUCTION

The synthesis and application of the imidazo[1,2-*a*]pyridine scaffold has seen considerable advancements in the last decade.[1] This bicyclic heterocycle is frequently encountered in many approved and commercialized drugs, clinical candidates, natural products, and functional materials.[2] For example, zolpidem (Ambien, **1**), miroprofen (**2**), soraprazan (remofuscin, **3**), and the more complex antibiotic rifaximin (xifaxan, **4**) all embed the imidazo[1,2-*a*]pyridine moiety (Figure 1). This bicycle showcases various positions that can be modified in order to modulate the physicochemical or pharmaceutical properties of a given target. Specifically, permutations of the C3-substituents of the imidazo[1,2-*a*]pyridine ring can have a profound effect on bioactivity.[3] New methods to affect such manipulations become important in the context of medicinal chemistry as the structure−activity relationship study around this heterocycle requires convergent synthetic methodologies for rapid and efficient modification of all positions.

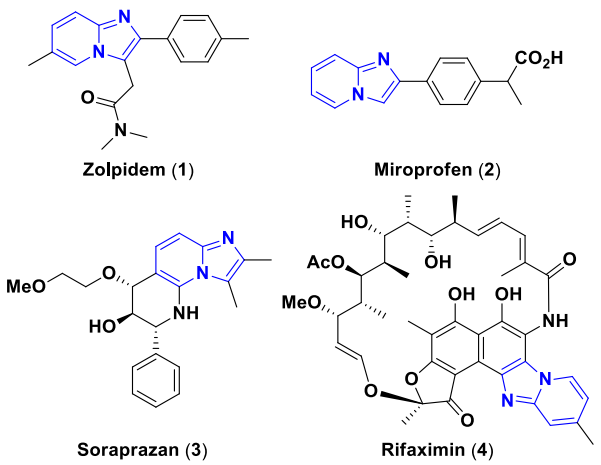


Figure 1. Examples of commercialized drugs containing the imidazo[1,2-*a*]pyridine moiety (highlighted in blue).

Correspondingly, many methodologies dedicated to diversifying the imidazo[1,2-*a*]pyridine scaffold were reported in recent years.[1,4] For instance, C−H functionalization reactions were specifically developed for the modulation of the C3-substituents of this heterocycle.[5] Strategies aimed at synthesizing the bicyclic core from simple fragments, and/or diversifying a pre-existing imidazo[1,2-*a*]pyridine ring, have also been recently disclosed.[1] However, there is still a need for convergent synthetic methods toward complex imidazo[1,2-*a*]pyridines from commercially available building blocks. In this context, we disclose herein the rapid assembly of these bicyclic heterocycles through the combination of 2*H*-azirines and 2-halopyridines in the presence of triflic anhydride (Tf_2O).

In 2017, the Maulide group reported conditions to synthesize tetrazolium triflate salts (**6**) from secondary amides (**5**) and alkyl azides (Scheme 1a).[6] It is well recognized that secondary amides can react in the presence of Tf_2O and a weak

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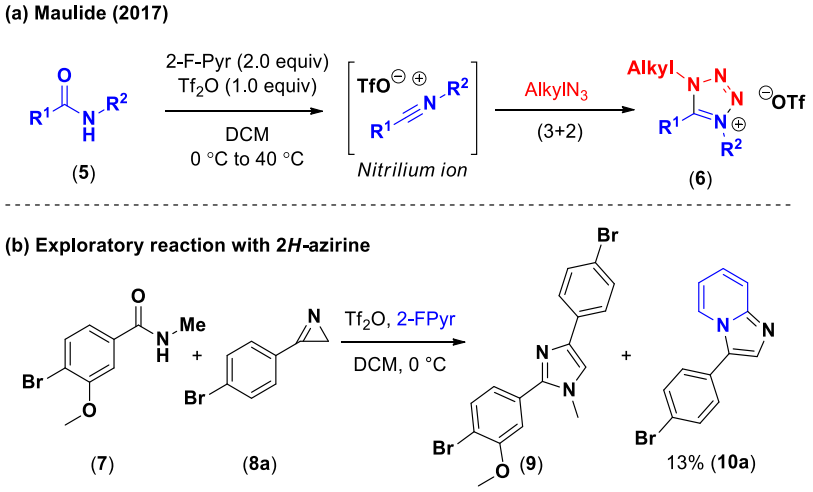
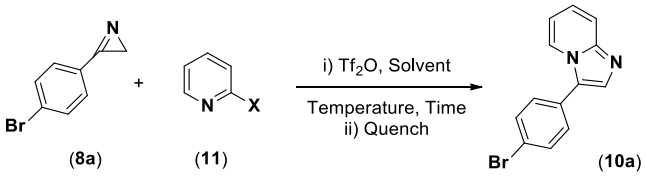
Scheme 1. Maulide's Conditions to Form Tetrazolium Salts 6 (a) and Extrapolation toward Imidazole 9 (b)



base to form highly electrophilic iminium triflates or nitrilium ions.[7] Following such activation, alkyl azides can therefore add to these electrophiles *via* formal (3 + 2) cycloadditions to form a range of substituted tetrazolium triflate salts (**6**). We were initially inspired by Maulide's conditions as we hypothesized that alkyl azides could be replaced by 1-vinyl azides (or 2*H*-azirines) toward the synthesis of 1,2,4-trisubstituted imidazoles (Scheme 1b). To test this hypothesis, we first treated amide **7** in the presence of 2*H*-azirine **8a** under the reported optimized conditions [Tf_2O, 2-fluoropyridine (2-FPyr), DCM, 0 °C], expecting to form imidazole **9**. Following LCMS monitoring of the reaction, we observed some residual starting materials (**8a** and **7**) along with trace amounts of a product with a mass consistent with **9**. Among the products formed, we unexpectedly identified the imidazo[1,2-*a*]pyridine **10a** (13% yield).[8] This product stems from the reaction between an equivalent of **8a** and an equivalent of the base used in the reaction (2-FPyr). Intrigued by this result, we further investigated the possibility to obtain selectively the imidazo-[1,2-*a*]pyridine by omitting the addition of the secondary amide **7** in the activation step while varying the nature of the base. Interestingly, when 2*H*-azirine **8a** was treated in the presence of 2-chloropyridine (2-ClPyr) with Tf_2O, the C3-substituted imidazo[1,2-*a*]pyridine **10a** was isolated in 38% yield (Table 1). This regioselectivity preference for C3 is complementary to a closely related transformation reported in 2014 by the Adimurthy group, where C2-substituted imidazo-[1,2-*a*]pyridines were formed selectively when pyridines reacted with 1-vinyl azides in the presence of CuI.[9] Encouraged by these results, we decided to delve further into optimizing these conditions toward **10a**.

Table 1. Optimization of Reaction Conditions[a]



entry	solvent (M)	temp. (°C)	quench	yield **10a** (%)[b]
1	DCM	−78 to rt	$NaHCO_3$	35 (38)[c]
2[d]	DCM	−78 to rt	$NaHCO_3$	29
3[e]	DCM	−78 to rt	$NaHCO_3$	40
4	DCM	−20 to rt	$NaHCO_3$	20
5	DME	−20 to rt	$NaHCO_3$	0
6	Tol.	−20 to rt	$NaHCO_3$	20
7	$CHCl_3$	−20 to rt	$NaHCO_3$	34
8[f]	$CHCl_3$	−20 to rt	$NaHCO_3$	42
9[f]	$CHCl_3$	−20 to rt	NaOH 1 M	41
10[f]	$CHCl_3$	−20 to rt	citric acid 10%	7
11[f]	$CHCl_3$	−20 to rt	sat. NaCl	0
12[f]	$CHCl_3$	−20 to rt	Et_3N (2.0 equiv)	93 (80)[c]
13[f]	$CHCl_3$	−20 to rt	Bu_4NOH (2.0 equiv)	22
14[f,g]	$CHCl_3$	−20 to rt	Et_3N (2.0 equiv)	82
15[f,h]	$CHCl_3$	−20 to rt	Et_3N (2.0 equiv)	74

[a]Reaction conditions: **8a** (1.0 equiv), Tf_2O (1.2 equiv), 2-chloropyridine **11a** (2.0 equiv), −78 °C to rt, 16 h, then $NaHCO_3$ sat. aq. [b]Refers to ^1H NMR yield using 1,3,5-trimethoxybenzene as the internal standard. [c]Isolated yield in parentheses. [d]Tf_2O (1.5 equiv). [e]2-ClPyr (5.0 equiv). [f]Anhydrous Na_2SO_4 was added. [g]2-FPyr (2.0 equiv) used instead of 2-ClPyr. [h]2-BrPyr (2.0 equiv) used instead of 2-ClPyr.

RESULTS AND DISCUSSION

To capitalize on the initial findings, we set out to identify parameters that could improve the efficiency of the reaction (Table 1). First, we varied the amount of Tf_2O and base while fixing 2*H*-azirine **8a** and 2-chloropyridine **11a** as the reactants (entries 1−3). These modifications did not improve the reaction profile as we only observed slightly better yields of **10a** if a large excess of 2-ClPyr is employed (entry 3). Modulating the solvent showed that the reaction is best performed in chlorinated solvents, in this case with $CHCl_3$, similar to what is known in Tf_2O-mediated amide activations (entries 4−7).[7] The temperature was also adjusted at −20 °C to avoid solidification of $CHCl_3$ (and some other solvents screened).[10] During optimization, we observed that the reactions were sensitive to the presence of residual water. This led us to the use of strictly anhydrous solvents and desiccants (see Scheme 3 for more details). Consequently, addition of an external desiccant such as 3 Å MS or anhydrous Na_2SO_4 to $CHCl_3$ gave a cleaner reaction profile (42% *vs* 34%, entries 8 *vs* 7). Furthermore, we saw a sharp difference in yield for **10a** when the reaction is quenched with a basic solution *versus* an acidic aqueous medium (entries 8−11). While

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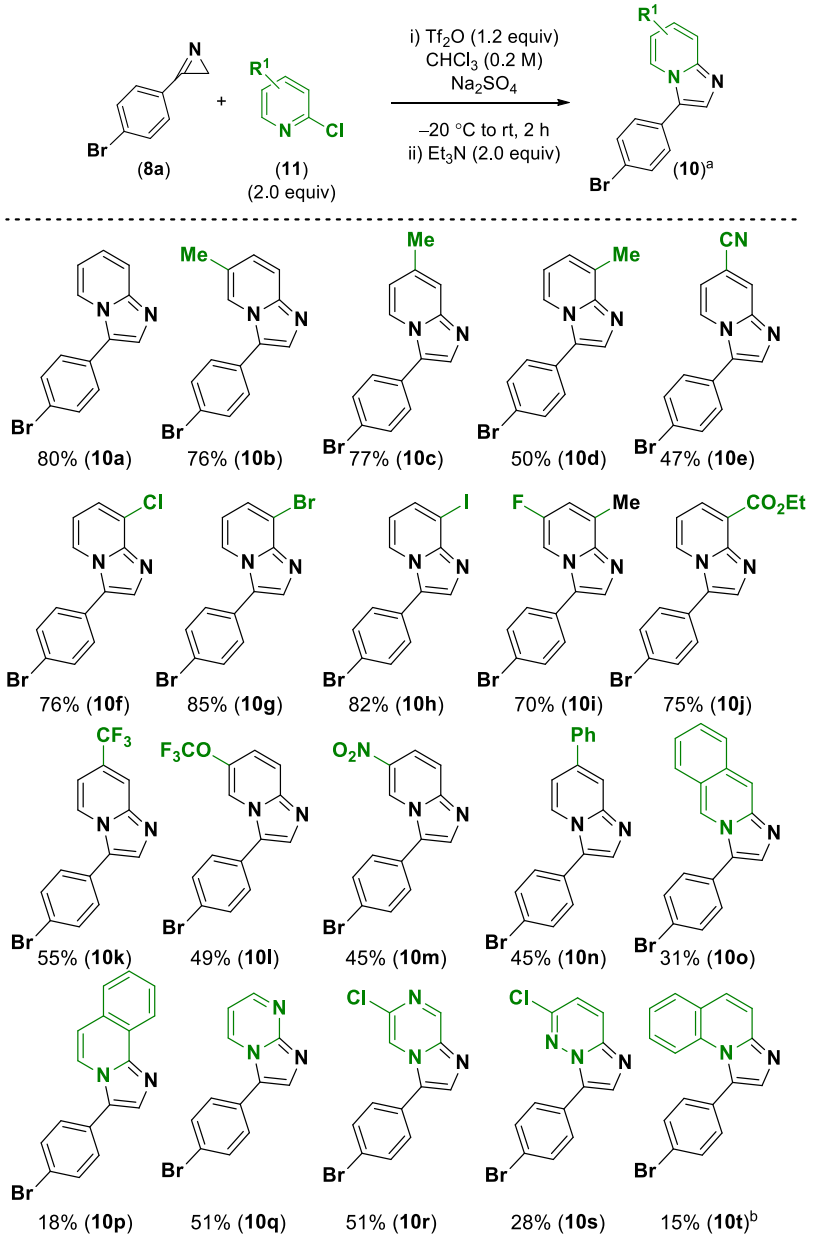
Table 2. Substrate Scope of Imidazo[1,2-*a*]pyridines: Variation of the 2-Chloropyridine



[a]Isolated yields. [b]The reaction was treated with Et_3N (2.0 equiv) for 16 h at 80 °C.

moderate yields were obtained when the reactions are quenched with either aqueous saturated $NaHCO_3$ or 1 M NaOH (42 and 41%, respectively, entries 8–9), the desired product was barely observed in the crude ^1H NMR of similar reactions quenched with citric acid (10% wt) or saturated aqueous NaCl solutions. These results prompted us to instead quench the reaction with anhydrous organic bases (entries 12–13). Notably, in the presence of 2.0 equiv of anhydrous Et_3N, we saw complete and clean conversion to **10a** (93% yield by ^1H NMR) and obtained 80% yield of the desired compound after purification. Substitution of 2-ClPyr by either 2-FPyr (82%, entry 14) or 2-BrPyr (74%, entry 15) was still productive toward **10a**, but to a lesser extent than with 2-ClPyr.

With a set of reaction conditions identified which provided high yields for the formation of **10a**, we set out to demonstrate the scope of this activation-cyclization sequence with respect to the 2-chloropyridine component (**11a–11t**, see the Reagents section in the Supporting Information) (Table 2). Methyl substitution at position 5 (76%, **10b**), position 4 (77%, **10c**), and position 3 (50%, **10d**) of the 2-chloropyridine were well tolerated. 2-Chloropyridines substituted with halogens (Cl, Br, I, and F) gave clean conversions of **8a** and among the best performing reactions (70 to 85% yields, entries **10f–i**). Imidazo[1,2-*a*]pyridines substituted with a nitrile (**10e**, 47%), an ester (75%, **10j**), trifluoromethyl (55%, **10k**), trifluoromethoxy (49%, **10l**), and nitro (45%, **10m**) were also formed in satisfactory yields after treatment with Et_3N. The reactions giving 4-phenyl-imidazo[1,2-*a*]pyridine (**10n**), imidazo[1,2-*b*]isoquinoline (**10o**), and imidazo[2,1-*a*]-isoquinoline (**10p**) were found to be sluggish and lower yields for the heterocycles were obtained (45, 31 and 18%). This methodology can also be performed with 2-chloropyrimidine,

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2,5-dichloropyrazine, and 3-chloropyridazine providing a quick access to other poly-nitrogen-containing bicyclic heterocycles (**10q**−**s**, 28−51%). When the reaction was first performed with 2-chloroquinoline, no conversion to the desired heterocycle **10t** was observed. However, after a quick reoptimization of the reaction conditions for this substrate,[10] an encouraging 15% yield was obtained for **10t** when the reaction is heated at 80 °C for 16 h after the addition of Et_3N.

During the study of this reaction, we found that certain 2-halopyridines were not productive and gave no conversion toward the desired imidazo[1,2-*a*]pyridines (Figure 2). For

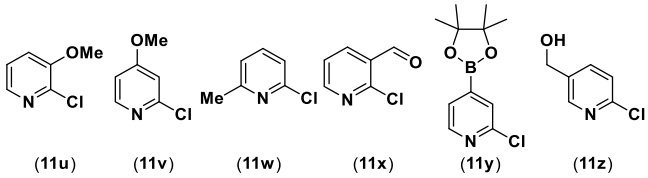
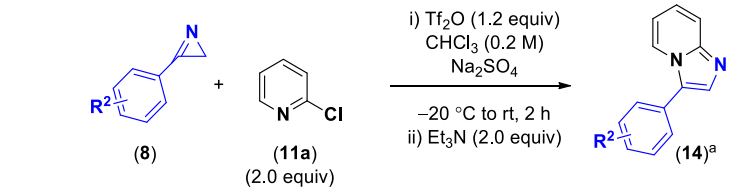


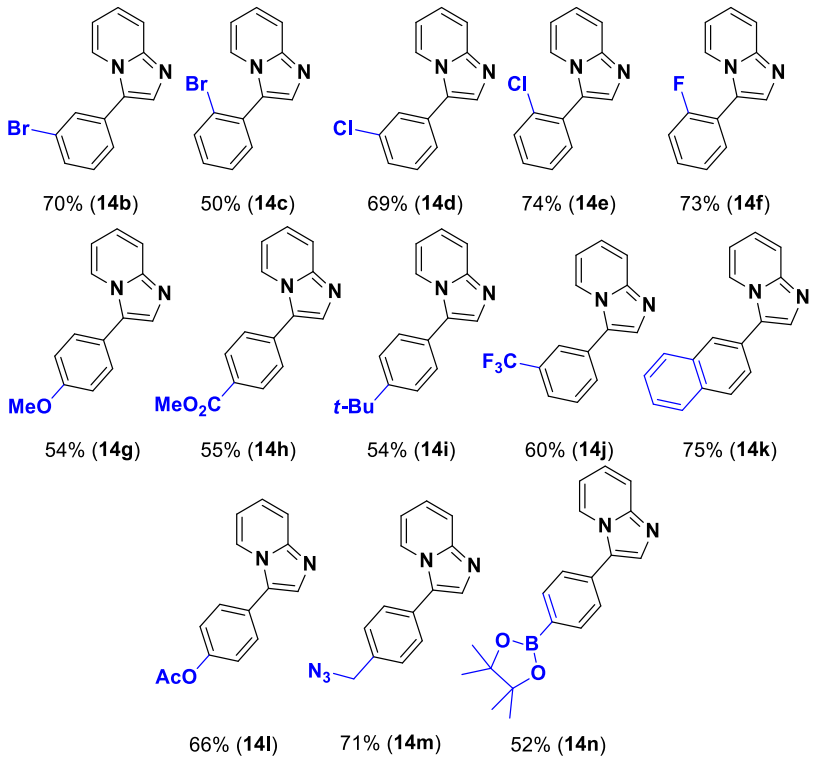
Figure 2. 2-Chloropyridines which were unproductive under the optimized reaction conditions.

example, electron-rich pyridines such as **11u** and **11v**, as well as 2-chloropyridines possessing substitution at the 6-position such as 2-chloro-6-methylpyridine (**11w**), failed to give desired products. In these cases, we observed possible formation of pyridinium intermediates by LCMS analysis of the crude mixtures (analogous to **19g**, *vide infra*). Potentially, these pyridinium species might be too stable to undergo base-mediated cyclization toward the desired compounds. In addition, it was found that 2-chloropyridines containing an aldehyde (**11x**), a boronic ester (**11y**), or a primary alcohol (**11z**) also failed to generate desired imidazo-pyridine products, which could be due to either the instability of the obtained products or to competition with 2*H*-azirines for Tf_2O activation.

A variety of 2*H*-azirines (**8**) were then investigated toward the formation of imidazo[1,2-*a*]pyridines (**14**) using our optimized conditions with 2-chloropyridine **11a** (Table 3). These 2*H*-azirines were synthesized from their corresponding styrenes **12** (and 1-vinyl azides **13**) following literature protocols (see Experimental Section).[11,12] Generally, we found that most of the 2*H*-azirines (**8**) tested under the optimized conditions gave moderate yields of the corresponding imidazo[1,2-*a*]pyridines (**14**). Aryl-substituted 2*H*-azirines containing a halogen at position 2, 3, or 4 of the phenyl ring were all tolerated (**14b**−**14e**) as well as electron-rich and electron-poor aryl functionalities (**14f**−**14k**). Notably, imidazo[1,2-*a*]pyridines substituted with an alkyl azide or pinacol boronic ester were effectively obtained, which could

Table 3. Substrate Scope of Imidazo[1,2-*a*]pyridines: Variation of the 2*H*-Azirine





[a]Isolated yields.

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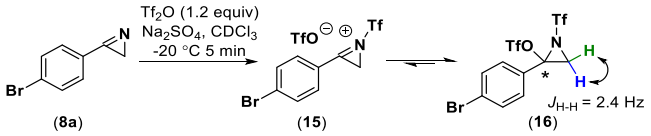
provide synthetic handles for further functionalization through click chemistry or transition-metal-catalyzed cross-couplings (**14m**, **14n**). In the counterpart, a few 2*H*-azirines substituted on the methylene moiety were tested under the optimized conditions, but they did not provide substantial amount of their corresponding imidazo[1,2-*a*]pyridines.

To gain more insight into the reaction, we selected a few control experiments. An initial reaction between the 2*H*-azirine **8a** and a slight excess of Tf_2O in anhydrous $CDCl_3$ was initiated without the inclusion of any 2-halopyridine derivative (Scheme 2). A rapid and complete reaction was observed to

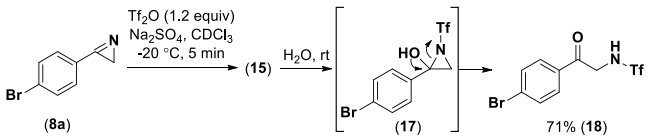
Scheme 2. Formation of a Transient 1-Triflyl-aziridin-2-yl *N*-Triflate 16



take place to form a transient and reactive intermediate in solution. Attempts to isolate this intermediate were unsuccessful as it rapidly hydrolyzed under air and moisture. However, this intermediate was sufficiently stable in solution to be characterized *in situ*. We hypothesized that the 2*H*-azirine **8a** is initially activated through nucleophilic attack of the nitrogen lone pair onto the highly electrophilic Tf_2O giving rise to an *N*-triflyl azirinium triflate salt (**15**). This iminium ion would then equilibrate to the more stable and neutral 1-triflyl-aziridin-2-yl *N*-triflate (**16**); its structure is supported by ^{1}H NMR (Supporting Information, pages **S8**−**S10**).[10] The methylene singlet at 1.83 ppm in $CDCl_3$ of the starting material **8a** is now observed as a pair of doublets at 3.67 and 3.57 ppm, respectively, after activation. Both protons are now diastereotopic because of the formation of a chiral center α- to the aryl ring and *N*-Tf moiety. Moreover, both doublets have a small *J* coupling constants of 2.4 Hz, suggesting that the strained aziridine 3-membered ring is conserved.[13]

Compound **18** was also observed by LCMS and ^{1}H NMR when the reaction solvent was not anhydrous or when some water was added after the activation step of the reaction (Scheme 3). We suspect that the formation of this ketone

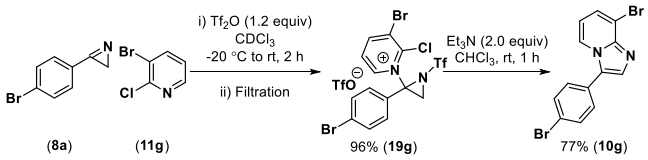
Scheme 3. Formation of *N*-Triflyl Acetophenone Derivative 18



arose from hydrolysis of the activated intermediate **15** observed previously (see Scheme 2). In the presence of water, the iminium ion could be substituted by water forming an unstable hemiaminal intermediate **17** which could ring-open to the observed *N*-triflyl α-amino acetophenone **18**.[14] Moreover, ^{1}H NMR signals from this ketone (minor contaminant) can be seen in the ^{1}H NMR of **16** alluded to previously. The formation of **18** also supports the activation of **8a** with Tf_2O *via* the nitrogen lone pair.

Following these results, we investigated whether formation of stable pyridinium salts was occurring in this reaction. To do this, we revisited the reaction between 2*H*-azirine **8a** and 3-bromo-2-chloropyridine **11g** as we previously observed that a precipitate was gradually formed with this pyridine prior to Et_3N addition (Scheme 4). Performing this reaction in $CDCl_3$

Scheme 4. Interception of a Pyridinium Salt 19g and Subsequent Formation of 10g



without inclusion of Na_2SO_4 or triethylamine led to the formation of a white suspension, which could be isolated by filtration. Characterization of this reaction intermediate by LCMS and NMR in THF-d_8 led to its assignment as bench stable pyridinium-aziridine salt **19g** (96% yield). The structure of this compound was supported by ^{1}H NMR wherein the aziridine methylene signal is again observed as a pair of doublets with small *J* coupling constants of 1.5 Hz observed at 4.71 and 4.51 ppm, respectively. Importantly, independent treatment of this isolated pyridinium salt in $CHCl_3$ with 2.0 equiv of Et_3N procured **10g** in 77% yield. This result supports the hypothesis that pyridinium salts such as **19g** could be productive intermediates in the reaction mechanism toward the formation of imidazo[1,2-*a*]pyridines.

With the information above, our proposed mechanism for the formation of imidazo[1,2-*a*]pyridines **10** and **14** is shown in Scheme 5. First, 2*H*-azirines **8** are chemoselectively activated by Tf_2O in the presence of 2-chloropyridines[15] to provide electrophilic 1-triflyl-aziridin-2-yl *N*-triflates **16** (in equilibrium with **15**). The selective activation of azirines over 2-chloropyridines is supported by previous observations from the Movassaghi group that 2-chloropyridine and Tf_2O does not provide a stable and viable *N*-triflyl pyridinium salt in chlorinated solvents, even at −78 °C.[16] Intermediate **15** then reacts with a 2-chloropyridine derivatives to provide stable pyridinium salts such as **19**. From this intermediate, two pathways are possible: pathway A (in blue) involves a [1,3]-sigmatropic rearrangement of **19**, which leads to a bicyclic salt such as **20a**. Neutralization/tautomerization of **20a** is possible *via* addition of a base such as Et_3N to provide **21**. The second pathway (B, in red) involves a base-mediated ring-opening of **19** to form a zwitterionic intermediate **20b**, which is followed by intramolecular S_NAr to form **21**. Elimination of the *N*-triflate group with concomitant rearomatization procures the observed heterocycles **10** and **14**. We were unable to isolate intermediates such as **20a,b**−**22**; however, an analogous reaction was already reported by the Yoo group,[17] wherein similar *N*-quinolinium zwitterion dipoles could cyclize to form the corresponding imidazo[1,2-*a*]quinolines.

To support the applicability of the developed method, we targeted the synthesis of a highly potent Mnk_1/Mnk_2 inhibitor **25** disclosed in 2018 by the Nacro group (Scheme 6).[18] Compound **25** is originally prepared *via* commercially available 6-bromoimidazo[1,2-*a*]pyrazine in five steps. We thought that such a compound could also be easily accessed using our reported conditions starting from 2*H*-azirine **8l**, synthesized in three steps from 4-acetoxystyrene, and 2,5-dichloropyrazine (**11r**). Applying our optimized conditions on a 2.95 mmol scale of **8l**, we were delighted to isolate the corresponding

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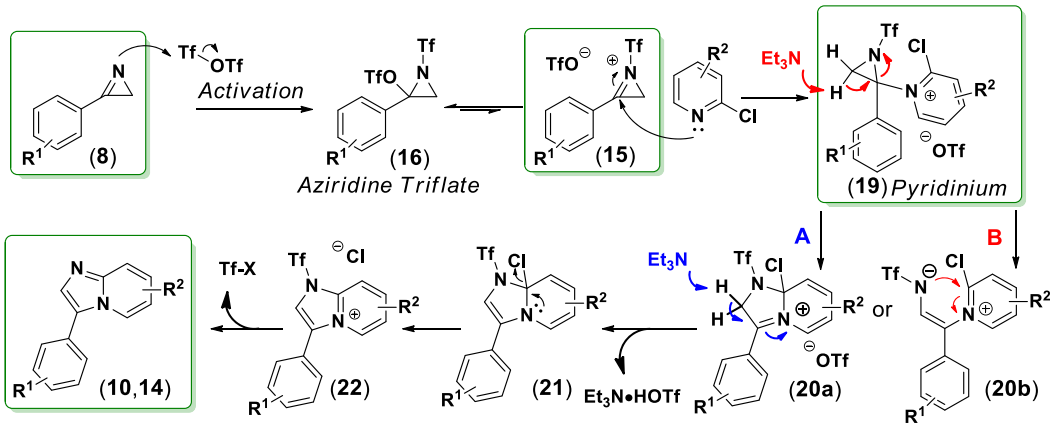
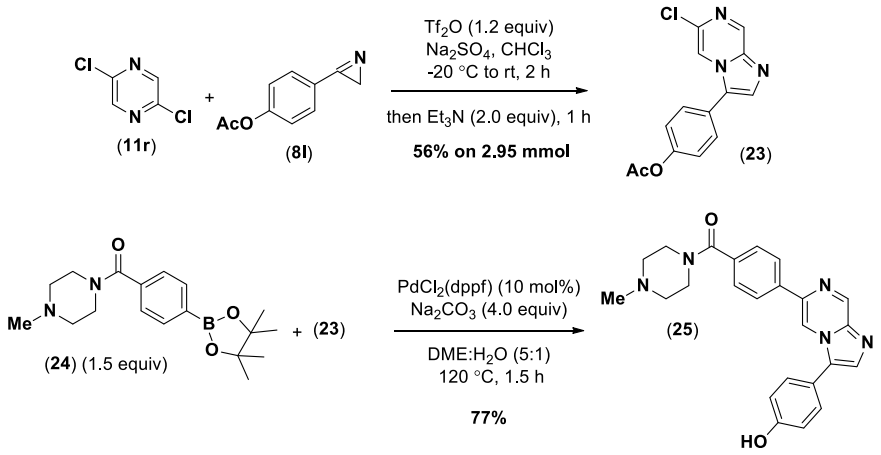
Scheme 5. Proposed Mechanism for the Formation of Imidazo[1,2-*a*]pyridines 10 and 14



Scheme 6. Synthesis of the Highly Potent Mnk_1/Mnk_2 Inhibitor



imidazo[1,2-*a*]pyrazine **23** in 56% yield. This reaction sets the stage for a Suzuki cross-coupling between commercially available boronic ester **24** and **23** to procure inhibitor **25** in 77%. Considering that aqueous basic conditions are employed in the Suzuki coupling, we were pleased to observe complete hydrolysis of the aryl acetate in this coupling to directly provide the desired target compound.

CONCLUSIONS

General conditions to synthesize C3-substituted imidazo[1,2-*a*]pyridines were found. The reaction was optimized to give up to 93% NMR yield, and 85% isolated yield for the desired bicyclic heterocycles. The scope of the reaction with respect to 2-chloropyridine and 2*H*-azirines was investigated, giving over 30 examples of imidazo[1,2-*a*]pyridines with various substitution patterns. We were able to identify and characterize key intermediates of the reaction. These studies support the implication of transient pyridinium salts in the mechanism of the reaction as they were shown to proceed toward the formation of the desired heterocycles under basic conditions. Extension of the concepts presented in this study to the synthesis of other heterocycles is currently under investigation.

EXPERIMENTAL SECTION

General Information. Routine ^{1}H NMR spectra were recorded on 400, or 500 MHz spectrometers (Oxford or Bruker) at ambient temperature. NMR solvents, *d*-chloroform ($CDCl_3$), d_6-dimethylsulfoxide (DMSO-d_6), and d_8-tetrahydrofuran (THF-d_8), were purchased from commercial suppliers and used without further purification. Spectra were processed using the automatic phasing and polynomial baseline correction features of the software. Spectral data are reported as follows: chemical shift {multiplicity [singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), sextuplet (sex), multiplet (m), apparent (app), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplets (dt)], coupling constant, integration}. Chemical shifts are reported in parts per million (δ), and coupling constants are reported in hertz. ^{1}H resonances are referenced to solvent residual peaks for $CDCl_3$ (7.26 ppm), DMSO-d_6 (2.50 ppm), or THF-d_8 (3.58 ppm or 1.73 ppm).[19] Routine $^{13}C\{^1H\}$-NMR spectra were recorded on Brucker or Oxford 400 or 500 MHz spectrometer with protons fully decoupled. $^{13}C\{^1H\}$ Resonances are reported in parts per million relative to solvent residual peaks for $CDCl_3$ (77.2 ppm), DMSO-d_6 (39.52 ppm), or THF-d_8 (67.57 or 25.37 ppm).[19] Structural assignments were made with additional information from gCOSY, gHSQC, and HMBC 2D NMR experiments (for **10a**, see the Supporting Information). Routine ^{19}F-NMR spectra were recorded on Oxford or Brucker 400 or 500 MHz spectrometer. ^{19}F Resonances are reported in ppm relative to 0.1% 1,1,1-trifluorotoluene added as the internal standard, with literature resonance peak at −63.72 ppm.

High-resolution liquid chromatography−mass spectrometry (MS) was performed by the DMPK group at Paraza Pharma Inc on a Q Exactive Plus Hybrid Quadrupole-Orbitrap Mass Spectrometer using a XBridge BEH C18 2.1 × 30 mm, 2.5 μm column set at 50 °C. An ESI ionization source was used with the following parameters: resolution of 140,000, AGC target of 3.00×10^6, maximum IT 25 ms, scan range of 100−700 m/z, and positive/negative polarity. Direct injection high-resolution MS (HRMS) analysis was performed by Centre Régional de Spectrométrie de Masse de l'Université de

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Montréal on a Agilent TOF 6224 with an ESI ionization source using positive polarity and a scan range of 100−3200 m/z. The HPLC-UV/MS instrumentation for crude analysis consisted of a Waters Alliance 2695 with a column heater coupled with a ZQ 4000 mass spectrometer. The MS was equipped with an electrospray ionization (ESI) source and used in scan mode (100−1200 amu, source temperature: 150 °C) for both positive and negative ionization. The HPLC was equipped with a Waters photodiode array detector (PDA) 2998 (range used: 195−320 nm). The analytical method was developed on a XBridge C18 column (3.5 μm particle size, 4.6 × 30 mm) with a 10 mM buffer (ammonium formate pH 3.8 or ammonium bicarbonate pH 10)—A % and acetonitrile—B % as the mobile phase. A flow rate of 3 mL/min at 25 °C was set and the following gradient was used: 5% B isocratic for 0.2 min, 5%−100% B in 1.8 min, 100% B for 1 min. Fourier-transform infrared spectroscopy (FTIR) spectral acquisition was performed at Neomed Institute on a Nicolet 6700 FTIR from Thermo Scientific equipped with ATR module, model Smart iTR. Scan range: 4000−450 cm^{-1}.

Analytical thin-layer chromatography (TLC) was performed using 60 Å Silica Gel F254 precoated plates (0.25 mm thickness). TLC plates were visualized by irradiation with a UV lamp and, if necessary, revealed using chemical stains cerium ammonium molybdenate (CAM), potassium permanganate ($KMnO_4$), or iodine on silica gel. Normal-phase manual column chromatography was performed using 60 Å silica gel (32−62 μm) with an appropriate mobile phase composition and gradient. Normal-phase automated column chromatography was performed using a Biotage Isolera, Yamazen, or Isco Rf flash purification systems equipped with a 10, 25, 50, 100, or 340 g SNAP Ultra or Isco Gold columns.

Synthesis of 1-Vinylazide from Treatment of the Corresponding Styrenes with ICl/*t*-BuOK (Procedure A, Adapted from the Literature).[11] CAUTION: Iodine azide (IN_3) is generated *in situ* in this reaction and should always be kept in solution. IN_3 is a known toxic and explosive compound. Manipulation of IN_3 should be performed under a well ventilated area with appropriate personal protective equipment.Organic azides are potentially explosive substances that can decompose with the slight input of energy from external sources, always work behind a blast shield. To a stirred solution of ICl (1.50 equiv) in anhydrous MeCN (2.6 M) at −20 °C (*i*PrOH/H_2O, 1:1 with dry ice bath) was added solid sodium azide (2.5 equiv) portionwise at −20 °C while keeping the internal temperature of the reaction below −10 °C. The reaction was stirred for 1 h at −20 °C and then the reaction mixture was warmed to 0 °C (ice/water bath). A solution of styrene **12** (1.0 equiv) in anhydrous MeCN (2.6 M) was then added dropwise. The reaction was stirred for 1 h at 0 °C before being quenched by dropwise addition of 10% wt aqueous solution of $Na_2S_2O_3$ under stirring until color changed to a yellow or translucent solution. The mixture was partitioned between diethyl ether and water (1:1) while being transferred to an extraction funnel. The organic layer was separated and washed with a 10% wt aqueous solution of $Na_2S_2O_3$ (1×) and then brine (2×). The organic solution was then dried over anhydrous Na_2SO_4 and filtered over a sintered funnel, and the filtrate was evaporated to dryness (rotary evaporator bath temperature ≤25 °C). ^1H NMR of the crude showed complete conversion of the styrene to the saturated addition product. The crude residue was dissolved in diethyl ether (0.3 M), and solution was cooled to 0 °C. KO*t*Bu (1.5 equiv) was added in one portion. The reaction became black, and a solid precipitated out of the mixture. The suspension was stirred for 1 h while warming to 0 °C to rt. The crude was filtered over a silica gel pad with a layer of Celite on top. The pad was rinsed using diethyl ether, and the filtrate was concentrated *in vacuo*. The residual vinyl azide (**13**) was generally clean enough by ^1H NMR to continue to the next step without purification.

Synthesis of 1-Vinyl Azides from Dibromination of the Corresponding Styrenes (Procedure B, Adapted from the Literature).[12] *Bromination of Alkenes and Styrenes.* Bromine (1.0 equiv) in CCl_4 (0.7 M) was added to a stirred and cooled (water bath, 15−20 °C) solution of the corresponding styrene (1.0 equiv) in CCl_4 (0.7 M) in a round-bottom flask. After the addition was completed, the mixture was stirred for 2 h and the solvent was removed with a stream of air. The crude dibromide was then directly used in the next step without purification.

Substitution and Elimination. The dibrominated product (1.0 equiv) was dissolved in DMSO (0.67 M). Solid sodium azide (1.5 equiv) was added portionwise into the solution (over 45 min) at rt. Over the course of the reaction, we usually noted that the mixture became a thick suspension/gel. The reaction was stirred overnight at rt. The elimination step was then triggered by addition of a solution of NaOH (1.0 equiv) in deionized water (0.5 M). Stirring was continued at room temperature, and the reaction was monitored by ^1H NMR. Upon completion, the mixture was poured into an aqueous solution of 2% wt of sodium bicarbonate, and the reaction was diluted with DCM until two layers were obtained. The aqueous solution was extracted with DCM (2×), and the organic layers were combined. The extracts were washed with water (4×), and the solvent was removed in vacuo to give the crude product. Purification was done by flash column chromatography (heptanes/EtOAc) to yield the corresponding 1-vinyl azides **13**.

Thermolysis of Vinyl Azides toward 2*H*-Azirines (Procedure C, Adapted from the Literature).[12] CAUTION: Heating of organic azides may cause explosion, always work behind a blast shield in a well ventilated area and with appropriate personal protective equipment. To a round-bottom flask equipped with a reflux condenser was added 1-vinyl azide **13** (1.0 equiv) along with toluene (0.2 M). The solution was heated at 115−120 °C (at reflux) in an oil bath for 2 h (or until the thermolysis was complete as observed by ^1H NMR analysis of an aliquot of the reaction in $CDCl_3$). The reaction was then cooled to rt, and the solvent was evaporated *in vacuo*. The crude product was used as is or purified by flash column chromatography (heptanes/EtOAc) to yield the corresponding 2*H*-azirines (**8**). Note: Because the 2*H*-azirines were found to decompose if stored at room temperature, it is appropriate to store them in a freezer at −20 °C over long periods of time (>24 h). We observed minimal decomposition of 2*H*-azirines at −20 °C if stored neat over multiple months.

3-(4-Bromophenyl)-2H-azirine ***8a***.[20] Synthesized according to procedures A and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 5.7 g (43.7 mmol scale), 67% over three steps. Obtained as an orange solid. The product corresponds to literature characterization. ^1H NMR (400 MHz, $CDCl_3$): δ 7.79−7.76 (m, 2H), 7.73−7.70 (m, 2H), 1.81 (s, 2H).

3-(3-Bromophenyl)-2H-azirine ***8b***. Synthesized according to procedures A and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 1.9 g (15.6 mmol scale), 63% over three steps. Obtained as a yellow oil. ^1H NMR (500 MHz, $CDCl_3$): δ 8.08−7.98 (m, 1H), 7.89−7.81 (m, 1H), 7.71 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.49−7.38 (m, 1H), 1.81 (s, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 165.4, 135.9, 132.5, 130.8, 128.1, 127.6, 123.2, 20.3. IR ν: 3049, 2978, 2894, 1742, 1591, 1565, 1473, 1418, 1310, 1291 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for C_8H_7BrN, 195.9757; found, 195.9756.

3-(2-Bromophenyl)-2H-azirine ***8c***.[21] Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 2.74 g (16.4 mmol scale), 86% over three steps. Obtained as a yellow solid. The product corresponds to literature characterization. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86−7.83 (m, 1H), 7.75−7.72 (m, 1H), 7.53−7.41 (m, 2H), 1.89 (s, 2H).

3-(3-Chlorophenyl)-2H-azirine ***8d***. Synthesized according to procedures A and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 2.2 g (21.6 mmol scale), 63% over three steps. Obtained as an orange oil. ^1H NMR (500 MHz, DMSO-d_6): δ 7.96 (ddd, J = 2.0, 1.5, 0.4 Hz, 1H), 7.90−7.88 (m, 1H), 7.77 (ddd, J = 8.1, 2.2, 1.1 Hz, 1H), 7.70−7.67 (m, 1H), 1.77 (s, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6): δ 165.2, 134.2, 133.2, 131.6, 128.9, 127.9, 127.1, 19.7. IR ν: 3051, 2980, 1743, 1569, 1475, 1456, 1475, 1456, 1424, 1412, 1312, 1292 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for C_8H_7ClN, 152.0262; found, 152.0261.

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3-(2-Chlorophenyl)-2H-azirine ***8e***.[22] Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 2.87 g (21.6 mmol scale), 87% over three steps. Obtained as an orange oil. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (dd, J = 7.2 Hz, 1.6 Hz, 1H), 7.55 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.52 (dt, J = 7.2 Hz, 1.6 Hz, 1H), 7.46 (dt, J = 7.2 Hz, 1.6 Hz, 1H), 1.85 (s, 2H).

3-(2-Fluorophenyl)-2H-azirine ***8f***. Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 2.85 g (24.6 mmol scale), 85% over three steps. Obtained as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.84 (m, 1H), 7.62−7.59 (m, 1H), 7.38−7.35 (m, 1H), 7.29−7.27 (m, 1H), 1.80 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 162.3, 161.8 (d, ^1J = 260.8 Hz, J_{C-F}), 134.9 (d, ^3J = 8.8 Hz, J_{C-F}), 131.4 (d, ^4J = 1.3 Hz, J_{C-F}), 124.8 (d, ^3J = 3.8 Hz, J_{C-F}), 116.6 (d, ^2J = 20.2 Hz, J_{C-F}), 114.4 (d, ^2J = 11.3 Hz, J_{C-F}), 18.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.0 (s). IR ν: 3303, 3065, 2103, 1612, 1579, 1485, 1451, 1212 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for C_8H_7FN, 136.0557; found, 136.0556.

3-(4-Methoxyphenyl)-2H-azirine ***8g***.[22] Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 2.85 g (22.4 mmol scale), 86% over three steps. Obtained as an orange solid. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H), 1.74 (s, 2H).

Methyl 4-(2H-Azirin-3-yl)benzoate ***8h***.[23] Synthesized according to procedures B and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 56 mg (4.62 mmol scale), 22% over four steps. Obtained as an orange solid. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.8 Hz, 2H), 8.01 (d, J = 8.8 Hz, 2H), 4.00 (s, 3H), 1.88 (s, 2H).

3-(4-(tert-Butyl)phenyl)-2H-azirine ***8i***.[23] Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 2.75 g (17.4 mmol scale), 91% over three steps. Obtained as an orange oil. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.5 Hz, 2H), 1.78 (s, 2H), 1.39 (s, 9H).

3-(3-(Trifluoromethyl)phenyl)-2H-azirine ***8j***. Synthesized according to procedures A and C. The product was found to be pure enough to use without flash chromatography, 4.55 g (24.6 mmol scale), 88% over three steps. Obtained as an orange oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (s, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.87 (d, J = 7.5 Hz, 1H), 7.72 (dd, J = 8.0, 7.5 Hz, 1H), 1.88 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6): δ 165.2, 132.8, 130.7, 130.2 (q, ^2J = 32.8 Hz, J_{C-F}), 129.6 (q, ^3J = 4.0 Hz, J_{C-F}), 126.1, 125.7 (q, ^3J = 3.5 Hz, J_{C-F}), 123.6 (q, ^1J = 273.4 Hz, J_{C-F}), 19.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −64.1 (s). IR ν: 3076, 2877, 1653, 1611, 1489, 1447, 1419, 1325 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_9H_7F_3N$, 186.0525; found, 186.0525.

3-(Naphthalen-2-yl)-2H-azirine ***8k***.[22] Synthesized according to procedures B and C. Purified using a gradient of 100% heptanes to 50% EtOAc in 50% heptanes, 876 mg (12.0 mmol scale), 60% over 4 steps. Obtained as an orange solid. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H), 8.03−7.98 (m, 3H), 7.92 (d, J = 8.0 Hz, 1H), 7.61−7.50 (m, 2H), 1.89 (s, 2H).

3-(4-Acetoxyphenyl)-2H-azirine ***8l***. Synthesized according to procedures B and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 1.87 g (30.8 mmol scale), 35% over four steps. Obtained as an orange solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.05−7.89 (m, 2H), 7.50−7.37 (m, 2H), 2.32 (s, 3H), 1.73 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, DMSO-d_6): δ 169.1, 164.6, 154.2, 130.9, 123.3, 122.6, 21.0, 19.2. IR ν: 3495, 3047, 2975, 2887, 1751, 1599, 1502, 1415, 1368, 1191 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{10}H_{10}NO_2$, 176.0706; found, 176.0706.

3-(4-(Azidomethyl)phenyl)-2H-azirine ***8m***.[23] Synthesized according to procedures B and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 121 mg (12 mmol scale), 9% over four steps. Obtained as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 8.1 Hz, 2H), 4.47 (s, 2H), 1.81 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 165.5, 140.5, 130.0, 128.6, 125.4, 54.5, 19.8. IR ν: 3047, 2978, 2888, 2208, 1735, 1605, 1417, 1279, 1264, 1208 cm^{-1}. HRMS (ESI/Q-TOF) m/z: [M + H]$^+$ calcd for $C_9H_9N_4$, 173.0822; found, 173.0818.

3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2H-azirine ***8n***.[24] Synthesized according to procedures B and C. Purified using a gradient of 100% heptanes to 40% EtOAc in 60% heptanes, 410 mg (4.35 mmol scale), 44% over four steps. Obtained as an orange solid. The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.0 Hz, 2H), 7.89 (d, J = 8.0 Hz, 2H), 1.80 (s, 2H), 1.37 (s, 12H).

General Procedure for the Addition of 2-Chloropyridine Derivatives 11 to Activated 8a (Procedure D). 3-(4-Bromophenyl)-2*H*-azirine (**8a**, 100 mg, 0.512 mmol, 1.0 equiv), sodium sulfate (100 mg), and the 2-chloropyridine derivative (**11**) (1.02 mmol, 2.0 equiv) were loaded in a flame-dried, nitrogen-flushed 2−5 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous chloroform (2.6 mL, 0.2 M) was added, and the mixture was stirred until complete dissolution of the 2*H*-azirine. The solution was cooled to −20 °C in a water/isopropanol and dry ice bath (1:1). Trifluoromethanesulfonic anhydride (Tf_2O) (172.9 mg, 103 μL, 0.612 mmol, 1.2 equiv) was added dropwise to the solution, which became dark brown. The mixture was left to stir for an hour at −20 °C and then for another hour at room temperature. The reaction was then treated with anhydrous triethylamine (103.2 mg, 142 μL, 1.02 mmol, 2.0 equiv), and the course of the reaction was monitored by LCMS. Upon full conversion of the pyridinium salt to the desired product (for each example, reaction time with Et_3N is indicated in the characterization section), the mixture was then transferred to a 125 mL extraction funnel and extracted with DCM (2 × 40 mL) and aqueous sodium hydroxide (1 M, 10 mL). The organic extracts were combined, dried with sodium sulfate, and filtered over a sintered funnel, and the filtrate was evaporated under vacuo. The crude product was then purified by flash chromatography (heptanes/EtOAc, 25 g SNAP Ultra) to yield the desired compound **10**.

3-(4-Bromophenyl)imidazo[1,2-a]pyridine ***10a***.[9] The product was isolated following general procedure D using 2-chloropyridine **11a**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange oil (110 mg, 80% Yield). The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, J = 7.0 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 7.67−7.59 (m, 2H), 7.47−7.39 (m, 2H), 7.30−7.19 (m, 1H), 6.85 (td, J = 6.9, 1.0 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 146.0, 132.5, 132.3, 129.5, 128.0, 124.9, 124.6, 123.2, 122.2, 118.2, 113.1. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{13}H_{10}BrN_2$, 273.0022; found, 273.0024.

3-(4-Bromophenyl)-6-methylimidazo[1,2-a]pyridine ***10b***.[24] The product was isolated following general procedure D using 2-chloro-5-methylpyridine **11b**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown oil (111 mg, 76% Yield). The product corresponds to literature characterization. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.65 (d, J = 6.6 Hz, 2H), 7.64 (s, 1H) 7.59 (d, J = 9.2 Hz, 1H), 7.42 (d, J = 8.2 Hz, 2H), 7.09 (dd, J = 9.2, 1.6 Hz, 1H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 145.3, 132.5, 132.1, 129.5, 128.2, 128.0, 124.3, 122.7, 122.1, 120.8, 117.5, 18.4. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{14}H_{12}BrN_2$, 287.0179; found, 287.0178.

3-(4-Bromophenyl)-7-methylimidazo[1,2-a]pyridine ***10c***. The product was isolated following general procedure D using 2-chloro-4-methylpyridine **11c**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Red oil (113 mg, 77% Yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 7.1 Hz, 1H), 7.64 (s, 1H), 7.61 (d, J = 3.2 Hz, 2H), 7.50−7.41 (m, 3H), 6.71 (dd, J = 7.1, 1.5 Hz, 1H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 146.3, 136.6, 132.6, 131.4, 129.5, 128.1, 124.3, 122.7, 122.2, 116.3, 116.0, 21.4. IR ν: 3084, 2920, 2854, 1648, 1535, 1494, 1469, 1336, 1304, 1225, 1189, 1138 cm^{-1}. HRMS (ESI/

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Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}BrN_2$, 287.0179; found, 287.0178.

3-(4-Bromophenyl)-8-methylimidazo[1,2-a]pyridine ***10d***.[25] The product was isolated following general procedure D using 2-chloro-3-methylpyridine **11d**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Yellow solid (73.8 mg, 50% Yield). The product corresponds to literature characterization. ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, J = 6.9 Hz, 1H), 7.69 (s, 1H), 7.67−7.62 (m, 2H), 7.46−7.40 (m, 2H), 7.09−7.03 (m, 1H), 6.78 (t, J = 6.9 Hz, 1H), 2.65 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 146.5, 132.6, 131.6, 129.7, 128.3, 128.1, 125.2, 124.0, 122.3, 121.3, 113.3, 17.2. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_{12}BrN_2$, 287.0179; found, 287.0178.

3-(4-Bromophenyl)imidazo[1,2-a]pyridine-7-carbonitrile ***10e***. The product was isolated following general procedure D using 2-chloro-4-cyanopyridine **11e**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (72.2 mg, 47% Yield). ^1H NMR (500 MHz, $CDCl_3$): δ 8.33 (dd, J = 7.2, 0.8 Hz, 1H), 8.11−8.07 (m, 1H), 7.90 (s, 1H), 7.73−7.67 (m, 2H), 7.46−7.40 (m, 2H), 6.98 (dd, J = 7.2, 1.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.1, 135.8, 133.0, 129.8, 127.0, 126.8, 124.8, 124.1, 123.6, 117.6, 113.2, 107.2. IR ν: 3076, 3060, 2230, 1487, 1472, 1457, 1402, 1332, 1310, 1296, 1278, 1184 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_9BrN_3$, 297.9975; found, 297.9973.

3-(4-Bromophenyl)-8-chloroimidazo[1,2-a]pyridine ***10f***. The product was isolated following general procedure D using 2,3-dichloropyridine **11f**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (119 mg, 76%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.20 (dd, J = 6.9, 1.0 Hz, 1H), 7.74 (s, 1H), 7.69−7.63 (m, 2H), 7.45−7.39 (m, 2H), 7.30 (dd, J = 7.3, 1.0 Hz, 1H), 6.79 (t, J = 7.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 143.7, 133.2, 132.7, 129.8, 127.8, 126.5, 124.3, 123.7, 122.9, 122.1, 112.7. IR ν: 3091, 3041, 3026, 1537, 1520, 1491, 1473, 1347, 1306, 1292, 1219 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C1_3H_9BrClN_2$, 306.9632; found, 306.9633.

8-Bromo-3-(4-bromophenyl)imidazo[1,2-a]pyridine ***10g***. The product was isolated following general procedure D using 3-bromo-2-chloropyridine **11g**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (153 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.24 (dd, J = 6.9, 0.9 Hz, 1H), 7.76 (s, 1H), 7.68−7.64 (m, 2H), 7.50 (dd, J = 7.2, 0.9 Hz, 1H), 7.45−7.40 (m, 2H), 6.73 (t, J = 7.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 144.2, 133.2, 132.8, 129.8, 127.9, 127.2, 126.6, 122.9, 122.7, 113.1, 112.6. IR ν: 3084, 3038, 1535, 1511, 1486, 1472, 1343, 1303, 1291 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_9Br_2N_2$, 350.9127; found, 350.9126.

3-(4-Bromophenyl)-8-iodoimidazo[1,2-a]pyridine ***10h***. The product was isolated following general procedure D using 2-chloro-3-iodopyridine **11h**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (167 mg, 82%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.25 (dd, J = 6.9, 1.0 Hz, 1H), 7.76 (s, 1H), 7.73 (dd, J = 7.1, 1.0 Hz, 1H), 7.67−7.64 (m, 2H), 7.43−7.40 (m, 2H), 6.60 (t, J = 7.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.5, 134.3, 132.8 (2), 129.8, 127.9, 126.7, 123.6, 122.9, 113.9, 85.0. IR ν: 3071, 3035, 2999, 1534, 1502, 1483, 1472, 1433, 1400, 1341, 1292, 1212 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_9BrIN_2$, 398.8989; found, 398.8990.

3-(4-Bromophenyl)-6-fluoro-8-methylimidazo[1,2-a]pyridine ***10i***. The product was isolated following general procedure D using 2-chloro-5-fluoro-3-picoline **11i**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown powder (109 mg, 70%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.00 (ddd, J = 4.2, 2.3, 0.6 Hz, 1H), 7.62 (s, 1H), 7.58−7.56 (m, 2H), 7.34−7.32 (m, 2H), 6.90 (ddd, J = 8.5, 2.2, 1.1 Hz, 1H), 2.59 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 153.7 (d, ^1J = 236.9 Hz, J_{C-F}), 144.4, 132.9 (d, ^3J = 2.5 Hz, J_{C-F}), 132.6, 129.4, 129.3, 128.0, 126.2 (d, ^4J = 2.0 Hz, J_{C-F}), 122.4, 115.5 (d, ^2J = 25.4 Hz, J_{C-F}), 107.7 (d, ^2J = 41.6 Hz, J_{C-F}), 17.2 (d, ^4J = 1.2 Hz, J_{C-F}). ^{19}F NMR (471 MHz, $CDCl_3$): δ −75.7 (s). IR ν: 3095, 3059, 2988, 2926, 1645, 1615, 1557, 1494, 1469, 1394, 1382, 1340, 1309, 1284, 1265 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_{11}BrFN_2$, 305.0084; found, 305.0083.

Ethyl 3-(4-Bromophenyl)imidazo[1,2-a]pyridine-8-carboxylate ***10j***. The product was isolated following general procedure D using ethyl 2-chloronicotinate **11j**. The reaction was stirred with Et_3N for 10 min. Brine was used instead of sodium hydroxide 1 M in the work-up procedure to avoid ester hydrolysis. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Dark orange solid (132 mg, 75%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.41 (dd, J = 8.0, 2.0 Hz, 1H), 7.98 (d, J = 2.0 Hz, 1H), 7.83 (s, 1H), 7.67 (d, J = 6.5 Hz, 2H), 7.42 (d, J = 6.5 Hz, 2H), 6.91 (t, J = 8.0 Hz, 1H), 4.55 (q, J = 7.0 Hz, 2H), 1.47 (t, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 164.4, 143.4, 133.8, 132.6, 129.9, 128.9, 127.7, 126.9, 125.1, 122.8, 120.9, 111.8, 61.8, 14.4. IR ν: 3050, 2984, 2929, 1721, 1531, 1489, 1472, 1265, 1201 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{16}H_{14}BrN_2O_2$, 345.0233; found, 345.0235.

3-(4-Bromophenyl)-7-(trifluoromethyl)imidazo[1,2-a]pyridine ***10k***. The product was isolated following general procedure D using 2-chloro-4-trifluoromethylpyridine **11k**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Light brown solid (78 mg, 55%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.36 (dt, J = 7.0, 1.0 Hz, 1H), 8.02 (dt, J = 1.9, 1.0 Hz, 1H), 7.84 (s, 1H), 7.71−7.67 (m, 2H), 7.46−7.42 (m, 2H), 7.02 (dd, J = 7.3, 1.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 144.2, 134.5, 132.8, 129.7, 127.2, 126.5 (q, ^2J = 34.0 Hz, J_{C-F}), 126.1, 124.0, 123.2 (q, ^1J = 272.2 Hz, J_{C-F}), 123.1, 116.4 (q, ^3J = 5.0 Hz, J_{C-F}), 108.9 (q, ^3J = 2.5 Hz, J_{C-F}). ^{19}F NMR (471 MHz, $CDCl_3$): δ −62.37 (s). IR ν: 3099, 3075, 1493, 1469, 1346, 1315, 1303, 1266, 1252 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_9BrF_3N_2$, 340.9896; found, 340.9897.

3-(4-Bromophenyl)-6-(trifluoromethoxy)imidazo[1,2-a]pyridine ***10l***. The product was isolated following general procedure D using 2-chloro-5-trifluoromethoxypyridine **11l**. The reaction was stirred with Et_3N for 36 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Light brown solid (89 mg, 49%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.28 (dd, J = 1.5, 0.7 Hz, 1H), 7.77 (s, 1H), 7.72 (d, J = 0.8 Hz, 1H), 7.71−7.68 (m, 2H), 7.44−7.40 (m, 2H), 7.20 (ddd, J = 9.8, 2.1, 1.0 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 144.6, 138.7 (q, ^3J = 2.5 Hz, J_{C-F}), 134.2, 132.8, 129.4, 127.4, 126.0, 122.9, 120.6 (q, ^1J = 258.3 Hz, J_{C-F}), 120.4, 118.9, 116.9. ^{19}F NMR (471 MHz, $CDCl_3$): δ −58.35 (s). IR ν: 3100, 1536, 1501, 1476, 1243, 1201, 1159 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_9BrF_3N_2O$, 356.9845; found, 356.9846.

3-(4-Bromophenyl)-6-nitroimidazo[1,2-a]pyridine ***10m***. The product was isolated following general procedure D using 2-chloro-5-nitropyridine **11m**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (73.7 mg, 45%). ^1H NMR (500 MHz, $CDCl_3$): δ 9.33 (d, J = 2.1 Hz, 1H), 8.00 (dd, J = 9.8, 2.1 Hz, 1H), 7.86 (s, 1H), 7.77−7.73 (m, 3H), 7.45 (d, J = 8.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.0, 137.9, 135.8, 133.1, 129.8, 127.4, 126.3, 123.8, 123.6, 118.6, 118.1. IR ν: 3581, 3102, 2922, 2851, 1637, 1547, 1517, 1502, 1471, 1364, 1349, 1237, 1289 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_9BrN_3O_2$, 317.9873; found, 317.9854.

3-(4-Bromophenyl)-7-phenylimidazo[1,2-a]pyridine ***10n***. The product was isolated following general procedure D using 2-chloro-4-phenylpyridine **11n**. The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange solid (80.1 mg, 45%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 7.2 Hz, 1H), 7.90 (s, 1H), 7.73 (s, 1H), 7.69−7.66 (m, 4H), 7.52−7.46 (m, 4H), 7.42 (t, J = 7.3 Hz, 1H), 7.15 (dd, J = 7.2, 1.9 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 146.6, 145.5, 138.3, 137.9, 133.0, 132.5, 129.4, 129.1, 128.4, 128.0, 126.8, 123.1,

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122.3, 114.8, 113.0. IR ν: 3053, 2921, 1642, 1590, 1496, 1484, 1475, 1341, 1310, 1294, 1234, 1171 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{19}H_{14}BrN_2$, 349.0335; found, 349.0337.

3-(4-Bromophenyl)imidazo[1,2-b]isoquinoline ***10o.*** The product was isolated following general procedure D using 1-chloroisoquinoline **11o**. The reaction was stirred with Et_3N for 12 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange oil (51.7 mg, 31%). ^1H NMR (400 MHz, $CDCl_3$): δ 9.34 (s, 1H), 8.38 (s, 1H), 8.25 (d, J = 8.3 Hz, 1H), 8.14 (t, J = 7.2 Hz, 1H), 8.07 (d, J = 8.3 Hz, 1H), 7.91 (t, J = 7.6 Hz, 1H), 7.87 (s, 1H), 7.38 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 8.7 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 155.4, 139.9, 139.5, 139.2, 138.6, 133.7, 132.4, 131.7, 130.5, 127.0, 126.9, 126.8, 123.3, 120.2, 120.1. IR ν: 3075, 3030, 1618, 1593, 1491, 1396, 1289, 1235, 1192 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{17}H_{12}BrN_2$, 323.0179; found, 323.0177.

3-(4-Bromophenyl)imidazo[2,1-a]isoquinoline ***10p.*** The product was isolated following general procedure D using 3-chloroisoquinoline **11p**. The reaction was stirred with Et_3N for 12 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown oil (30.1 mg, 18%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.66 (d, J = 8.0 Hz, 1H), 8.02 (d, J = 7.4 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.70−7.63 (m, 4H), 7.60 (dd, J = 7.5, 1.1 Hz, 1H), 7.49−7.42 (m, 2H), 7.08 (d, J = 7.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 144.1, 132.6, 130.5, 130.0, 129.5, 128.6 (2), 128.3, 127.0, 126.9, 124.2, 123.6, 122.5, 120.9, 113.7. IR ν: 3048, 2924, 1625, 1477, 1449, 1329, 1290 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{17}H_{12}BrN_2$, 323.0179; found, 323.0179.

3-(4-Bromophenyl)imidazo[1,2-a]pyrimidine ***10q.*** The product was isolated following general procedure D using 2-chloropyrimidine **11q**. The reaction was stirred with Et_3N for 1 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (72 mg, 51%). ^1H NMR (500 MHz, $CDCl_3$): δ 8.61−8.57 (m, 2H), 7.89 (s, 1H), 7.69−7.65 (m, 2H), 7.44−7.40 (m, 2H), 6.93 (dd, J = 6.7, 4.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 149.9, 149.3, 134.2, 132.9, 131.1, 129.5, 127.3, 123.3, 122.9, 109.3. IR ν: 3082, 3062, 3049, 3035, 2928, 1613, 1513, 1490, 1465, 1422, 1280 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]+ calcd for $C_{12}H_9BrN_3$, 273.9975; found, 273.9975.

3-(4-Bromophenyl)-6-chloroimidazo[1,2-a]pyrazine ***10r.*** The product was isolated following general procedure D using 2,5-dichloropyrazine **11r**. The reaction was stirred with Et_3N for 15 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid. (81.0 mg, 51%). ^1H NMR (400 MHz, $CDCl_3$): δ 8.98 (d, J = 1.3 Hz, 1H), 8.26 (d, J = 1.3 Hz, 1H), 7.92 (s, 1H), 7.75−7.70 (m, 2H), 7.46−7.42 (m, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 143.2, 140.6, 136.3, 135.9, 133.1, 129.5, 126.7, 126.3, 123.9, 114.1. IR ν: 3105, 3049, 2919, 2850, 1604, 1468, 1415, 1312, 1140 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{12}H_8BrClN_3$, 307.9585; found, 307.9586.

3-(4-Bromophenyl)-6-chloroimidazo[1,2-b]pyridazine ***10s.***[26] The product was isolated following general procedure D using 3-chloropyridazine **11s**. The reaction was stirred with Et_3N for 1 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Yellow solid. (40 mg, 28%). The product corresponds to literature characterization. ^1H NMR (500 MHz, $CDCl_3$): δ 8.06 (s, 1H), 7.97 (d, J = 9.4 Hz, 1H), 7.95−7.90 (m, 2H), 7.67−7.60 (m, 2H), 7.11 (d, J = 9.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 147.2, 139.0, 133.7, 132.2, 128.4, 127.6, 126.9 (2), 122.6, 118.6. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{12}H_8BrClN_3$, 307.9585; found, 307.9586.

1-(4-Bromophenyl)imidazo[1,2-a]quinoline ***10t.*** The product was isolated following general procedure D (on 0.25 mmol of **8a**) with 2-chloroquinoline **11t**, but after Et_3N (2.0 equiv.) was added, the reaction was heated in an oil bath at 80 °C for 16 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange solid (12.3 mg, 15%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.80 (dd, J = 7.8, 1.5 Hz, 1H), 7.68−7.64 (m, 2H), 7.61−7.53 (m, 3H), 7.49 (s, 1H), 7.43−7.38 (m, 3H), 7.32 (ddd, J = 8.6, 7.2, 1.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.3, 133.9, 133.5, 132.2, 131.7, 130.9, 129.5, 128.1, 127.6, 127.1, 124.9, 124.8, 123.3, 117.6, 117.0. IR ν: 3066, 2922, 2851, 1611, 1546, 1474, 1445, 1380, 1301 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{17}H_{12}BrN_2$, 323.0179; found, 323.0179.

General Procedure for the Addition of 2-Chloropyridine 11a to Various Activated 2*H*-Azirines 8 (Procedure E). 2*H*-azirine (**8**, 1.0 mmol, 1.0 equiv), sodium sulfate (100 mg for 100 mg of **8**), and 2-chloropyridine (**11a**) (227 mg, 189 μL, 2.0 mmol, 2.0 equiv) were loaded in a flame-dried, nitrogen-flushed 2−5 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous chloroform (5.0 mL, 0.2 M) was added, and the mixture was stirred until complete dissolution of the azirine. The solution was cooled to −20 °C in a water/isopropanol and dry ice bath. Trifluormethanesulfonic anhydride (338 mg, 202 μL, 1.2 mmol, 1.2 equiv) was added dropwise to the solution, which became dark brown. The mixture was left to stir for an hour at −20 °C and then for another hour at room temperature. The reaction was then treated with anhydrous triethylamine (202 mg, 278 μL, 2.0 mmol, 2.0 equiv), and the course of the reaction monitored by LCMS. Upon full conversion of the pyridinium salt to the desired product (for each example, reaction time with Et_3N is indicated in the characterization section), the mixture was then transferred to a 125 mL extraction funnel and extracted with DCM (2×) and aqueous sodium hydroxide (1 M). The organic extracts were combined and dried with sodium sulfate, filtered over a sintered funnel, and the filtrate was evaporated under vacuo. The crude product was then purified by flash chromatography (heptanes/EtOAc, 25 g SNAP Ultra) to yield the desired compound **14**.

3-(3-Bromophenyl)imidazo[1,2-a]pyridine ***14b.***[27] The product was isolated following general procedure E (on 1.0 mmol of **8b**). The reaction was stirred with Et_3N for 2 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange viscous liquid (191 mg, 70%). The product corresponds to literature characterization. ^1H NMR (500 MHz, $CDCl_3$): δ 8.32 (dt, J = 7.0, 1.2 Hz, 1H), 7.72−7.69 (m, 3H), 7.55 (ddd, J = 8.0, 2.0, 1.1 Hz, 1H), 7.50 (ddd, J = 7.7, 1.6, 1.1 Hz, 1H), 7.39 (t, J = 7.7 Hz, 1H), 7.27−7.22 (m, 1H), 6.87 (td, J = 6.8, 1.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.2, 132.8, 131.2 (2), 130.8 (2), 126.5, 124.9, 124.3, 123.3, 123.2, 118.3, 113.1. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_{10}BrN_2$, 273.0022; found, 273.0022.

3-(2-Bromophenyl)imidazo[1,2-a]pyridine ***14c.***[28] The product was isolated following general procedure E (on 1.0 mmol of **8c**). The reaction was stirred with Et_3N for 5 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Orange solid (136 mg, 50%). The product corresponds to literature characterization. ^1H NMR (500 MHz, $CDCl_3$): δ 7.81 (dt, J = 6.9, 1.2 Hz, 1H), 7.78−7.75 (m, 1H), 7.73−7.70 (m, 2H), 7.47−7.43 (m, 2H), 7.38−7.33 (m, 1H), 7.25 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.82 (td, J = 6.8, 1.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.7, 133.6, 133.5, 133.3, 130.8, 130.3, 127.9, 125.2, 124.8, 124.6, 124.5, 118.1, 112.4. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_{10}BrN_2$, 273.0022; found, 273.0023.

3-(3-Chlorophenyl)imidazo[1,2-a]pyridine ***14d.***[28b,29] The product was isolated following general procedure E (on 1.0 mmol of **8d**). The reaction was stirred with Et_3N for 2 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Dark orange viscous liquid (165 mg, 69%). The product corresponds to literature characterization. ^1H NMR (500 MHz, $CDCl_3$): δ 8.31 (dt, J = 7.0, 1.2 Hz, 1H), 7.71 (s, 1H), 7.68 (dt, J = 9.1, 1.1 Hz, 1H), 7.55 (ddd, J = 2.1, 1.3, 0.8 Hz, 1H), 7.45−7.43 (m, 2H), 7.41−7.36 (m, 1H), 7.23 (ddd, J = 9.1, 6.7, 1.2 Hz, 1H), 6.85 (td, J = 6.8, 1.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.4, 135.2, 133.0, 131.1, 130.5, 128.2, 127.8, 126.0, 124.7, 124.4, 123.2, 118.4, 113.0. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{13}H_{10}ClN_2$, 229.0527; found, 229.0527.

3-(2-Chlorophenyl)imidazo[1,2-a]pyridine ***14e.***[28,29] The product was isolated following general procedure E (on 1.0 mmol of **8e**). The reaction was stirred with Et_3N for 4 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid

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(170 mg, 74%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (dt, J = 6.9, 1.2 Hz, 1H), 7.72−7.69 (m, 2H), 7.59−7.56 (m, 1H), 7.49−7.46 (m, 1H), 7.41 (dd, J = 7.5, 1.8 Hz, 2H), 7.24 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.82 (td, J = 6.8, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 145.9, 134.7, 133.7, 132.8, 130.3, 130.2, 128.2, 127.2, 124.5, 124.4, 122.9, 118.0, 112.3. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{13}H_{10}ClN_2$, 229.0527; found, 229.0527.

3-(2-Fluorophenyl)imidazo[1,2-a]pyridine ***14f***.[28a,b,29a,b,30] The product was isolated following general procedure E (on 1.0 mmol of **8f**). The reaction was stirred with Et_3N for 10 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (154 mg, 73%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03 (ddt, J = 6.9, 3.1, 1.1 Hz, 1H), 7.76 (s, 1H), 7.73 (dt, J = 9.1, 1.1 Hz, 1H), 7.52 (td, J = 7.4, 1.7 Hz, 1H), 7.49−7.43 (m, 1H), 7.32−7.29 (m, 1H), 7.29−7.27 (m, 1H), 7.27−7.24 (m, 1H), 6.87 (td, J = 6.8, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.9 (d, ^1J = 249.5 Hz, J_{C-F}), 146.0, 133.2, 131.4 (d, ^4J = 3.2 Hz, J_{C-F}), 130.6 (d, ^3J = 8.2 Hz, J_{C-F}), 125.0, 124.9 (d, ^3J = 3.5 Hz, J_{C-F}), 124.5 (d, ^3J = 4.5 Hz, J_{C-F}), 120.3, 117.9, 116.9 (d, ^2J = 15.2 Hz, J_{C-F}), 116.3 (d, ^2J = 21.5 Hz, J_{C-F}), 112.7. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{13}H_{10}FN_2$, 213.0823; found, 213.0820.

3-(4-Methoxyphenyl)imidazo[1,2-a]pyridine ***14g***.[27] The product was isolated following general procedure E (on 1.0 mmol of **8g**). The reaction was stirred with Et_3N for 1 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (120 mg, 54%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (dt, J = 7.0, 1.2 Hz, 1H), 7.68 (dt, J = 9.1, 1.1 Hz, 1H), 7.63 (s, 1H), 7.49−7.45 (m, 2H), 7.19 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 7.08−7.03 (m, 2H), 6.80 (td, J = 6.8, 1.2 Hz, 1H), 3.88 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 159.7, 145.6, 131.7, 129.7, 125.6, 124.2, 123.3, 121.4, 118.1, 114.7, 112.5, 55.4. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{14}H_{13}N_2O$, 225.1023; found, 225.1020.

Methyl 4-(Imidazo[1,2-a]pyridin-3-yl)benzoate ***14h***.[29b,31] The product was isolated following general procedure E (on 1.0 mmol of **8h**). The reaction was stirred with Et_3N for 16 h. Brine was used instead of sodium hydroxide 1 M in the work-up procedure to avoid ester hydrolysis. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Beige solid (140 mg, 55%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dt, J = 7.0, 1.1 Hz, 1H), 8.21−8.15 (m, 2H), 7.79 (s, 1H), 7.71 (dt, J = 9.1, 1.1 Hz, 1H), 7.67−7.64 (m, 2H), 7.25 (ddd, J = 9.1, 6.7, 1.2 Hz, 1H), 6.88 (td, J = 6.8, 1.2 Hz, 1H), 3.96 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 166.7, 146.8, 133.9, 133.6, 130.7, 129.6, 127.4, 125.1, 125.0, 123.5, 118.6, 113.3, 52.4. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}N_2O_2$, 253.0972; found, 253.0969.

3-(4-(tert-Butyl)phenyl)imidazo[1,2-a]pyridine ***14i***.[27,32] The product was isolated following general procedure E (on 1.0 mmol of **8i**). The reaction was stirred with Et_3N for 16 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid. (135 mg, 54%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.35 (dt, J = 7.0, 1.2 Hz, 1H), 7.69 (dt, J = 9.1, 1.1 Hz, 1H), 7.68 (s, 1H), 7.56−7.53 (m, 2H), 7.51−7.48 (m, 2H), 7.21 (ddd, J = 9.1, 6.7, 1.3 Hz, 1H), 6.81 (td, J = 6.8, 1.2 Hz, 1H), 1.38 (s, 9H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 151.6, 145.9, 132.0, 128.0, 126.3 (2), 125.9, 124.5, 123.7, 118.2, 112.7, 34.9, 31.4. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{17}H_{19}N_2$, 251.1543; found, 251.1540.

3-(3-(Trifluoromethyl)phenyl)imidazo[1,2-a]pyridine ***14j***.[29,33] The product was isolated following general procedure E (on 1.0 mmol of **8j**). The reaction was stirred with Et_3N for 16 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown viscous liquid (158 mg, 60%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.30 (dt, J = 7.0, 1.1 Hz, 1H), 7.82 (s, 1H), 7.77 (s, 1H), 7.76−7.72 (m, 2H), 7.70−7.63 (m, 2H), 7.28−7.24 (m, 1H), 6.88 (td, J = 6.8, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 146.6, 133.1, 132.0 (q, ^2J = 32.6 Hz, J_{C-F}), 131.3 (q, ^4J = 1.2 Hz, J_{C-F}), 130.3, 130.0, 125.1, 125.0 (q, ^3J = 7.7 Hz, J_{C-F}), 124.7 (q, ^3J = 3.8 Hz, J_{C-F}), 124.4, 123.9 (q, ^1J = 273.0 Hz, J_{C-F}), 123.2, 118.6, 113.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ −63.28 (s). HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{14}H_{10}F_3N_2$, 263.0791; found, 263.0787.

3-(Naphthalen-2-yl)imidazo[1,2-a]pyridine ***14k***.[27] The product was isolated following general procedure E (on 0.6 mmol of **8k**). The reaction was stirred with Et_3N for 1 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown viscous oil (110 mg, 75%). The product corresponds to literature characterization. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (dt, J = 7.0, 1.2 Hz, 1H), 8.03 (d, J = 1.2 Hz, 1H), 7.98 (d, J = 8.5 Hz, 1H), 7.92−7.88 (m, 2H), 7.81 (s, 1H), 7.73 (dt, J = 9.1, 1.1 Hz, 1H), 7.66 (dd, J = 8.4, 1.8 Hz, 1H), 7.58−7.52 (m, 2H), 7.24 (ddd, J = 8.6, 6.7, 1.2 Hz, 1H), 6.86 (td, J = 6.8, 1.2 Hz, 1H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 146.2, 133.7, 133.0, 132.7, 129.2, 128.1, 128.0, 127.0 (2), 126.7, 126.6, 125.9 (2), 124.8, 123.6, 118.3, 113.0. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{17}H_{13}N_2$, 245.1073; found, 245.1071.

4-(Imidazo[1,2-a]pyridin-3-yl)phenyl Acetate ***14l***. The product was isolated following general procedure E (on 1.0 mmol of **8l**). The reaction was stirred with Et_3N for 16 h. Brine was used instead of sodium hydroxide 1 M in the work-up procedure to avoid ester hydrolysis. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Yellow solid (167 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 7.0 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.72 (s, 1H), 7.58 (d, J = 8.6 Hz, 2H), 7.35 (dd, J = 8.9, 7.0 Hz, 1H), 7.31−7.27 (m, 2H), 6.94 (app t, J = 6.7 Hz, 1H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 169.5, 151.0, 145.3, 130.8, 129.6, 126.3, 125.9, 125.3, 123.7, 122.8, 117.8, 113.6, 21.3. IR ν: 3097, 2805, 2670, 1613, 1527, 1498, 1438, 1363, 1265, 1225 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{15}H_{13}N_2O_2$, 253.0972; found, 253.0968.

3-(4-(Azidomethyl)phenyl)imidazo[1,2-a]pyridine ***14m***. The product was isolated following general procedure E (on 0.283 mmol of **8m**). The reaction was stirred with Et_3N for 16 h. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. Brown solid (50 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (dt, J = 7.0, 1.2 Hz, 1H), 7.72 (s, 1H), 7.70 (dt, J = 9.1, 1.1 Hz, 1H), 7.61−7.57 (m, 2H), 7.50−7.46 (m, 2H), 7.24 (ddd, J = 9.2, 6.7, 1.2 Hz, 1H), 6.85 (td, J = 6.8, 1.2 Hz, 1H), 4.43 (s, 2H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 146.2, 135.7, 132.4, 129.3, 129.2, 128.6, 125.3, 124.9, 123.5, 118.3, 113.1, 54.6. IR ν: 2941, 2885, 2090, 1610, 1500, 1353, 1313, 1274 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{14}H_{12}N_5$, 250.1087; found, 250.1083.

3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-imidazo[1,2-a]pyridine ***14n***. The product was isolated following general procedure E (on 1.0 mmol of **8n**). The reaction was stirred with Et_3N for 1 h 30 min. Purified using a gradient of 30% EtOAc in 70% heptanes to 100% EtOAc. White solid. (165 mg, 52%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.38 (dt, J = 7.0, 1.2 Hz, 1H), 7.97−7.94 (m, 2H), 7.74 (s, 1H), 7.70 (dt, J = 9.1, 1.1 Hz, 1H), 7.60−7.57 (m, 2H), 7.23 (ddd, J = 9.1, 6.7, 1.2 Hz, 1H), 6.84 (td, J = 6.8, 1.2 Hz, 1H), 1.37 (s, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 146.3, 135.8 (2), 132.7, 132.0, 127.1, 125.9, 124.8, 123.6, 118.4, 113.0, 84.2, 25.0. IR ν: 2980, 2928, 1607, 1485, 1359, 1324, 1290 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: [M + H]$^+$ calcd for $C_{19}H_{22}BN_2O_2$, 321.1769; found, 321.1761.

Experimental Procedure for the Formation of *N*-(2-(4-Bromophenyl)-2-oxoethyl)-1,1,1-trifluoromethane Sulfonamide (18) (Scheme 3). 3-(4-Bromophenyl)-2*H*-azirine (**8a**, 100 mg, 0.512 mmol, 1.0 equiv) and sodium sulfate (100 mg) were charged in a flame-dried, nitrogen-flushed 2−5 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous deuterated chloroform-*d* (2.6 mL, 0.2 M) was added, and the mixture was stirred until complete dissolution of the 2*H*-azirine. The solution was cooled to −20 °C in a water/isopropanol and dry ice bath (1:1). Trifluoromethanesulfonic anhydride (Tf_2O) (172.9 mg, 103 μL, 0.612 mmol, 1.2 equiv) was added dropwise to the solution, which became dark brown. The reaction was immediately quenched by

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addition of water (1 mL), and the reaction was warmed to rt over 30 min. The mixture was then transferred to a 60 mL extraction funnel and extracted with DCM (2 × 30 mL) and brine (20 mL). The organic extracts were combined, dried with sodium sulfate, and filtered over a sintered funnel, and the filtrate was evaporated under vacuo. The crude product was then purified by flash chromatography using a 50 g SNAP Ultra column (100% heptanes to 30% EtOAc in 70% heptanes over 30 CV) to yield the desired compound **18**[14] (125 mg, 71%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82−7.79 (m, 2H), 7.71−7.67 (m, 2H), 6.01 (br s, 1H), 4.73 (d, J = 1.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 190.3, 132.7, 131.9, 130.5, 129.4, 119.6 (q, ^1J = 321.3 Hz, J_{C-F}), 49.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ −76.64 (s). IR ν: 3240, 1691, 1589, 1397, 1368, 1318 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_9H_8BrF_3NO_3S$, 345.9355; found, 345.9351.

Experimental Procedure for the Formation of 3-Bromo-1-(2-(4-bromophenyl)-1-((trifluoromethyl)sulfonyl)aziridin-2-yl)-2-chloropyridin-1-ium (19g) (Scheme 4). 3-(4-Bromophenyl)-2*H*-azirine (**8a**, 100 mg, 0.512 mmol, 1.0 equiv) and 3-bromo-2-chloropyridine (195 mg, 1.024 mmol, 2.0 equiv) were charged in a flame-dried, nitrogen-flushed 2−5 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous deuterated chloroform-*d* (2.6 mL, 0.2 M) was added, and the mixture was stirred until complete dissolution of the azirine. The solution was cooled to −20 °C in a water/isopropanol and dry ice bath. Trifluoromethanesulfonic anhydride (Tf_2O) (172.9 mg, 103 μL, 0.612 mmol, 1.2 equiv) was added dropwise to the solution, which became dark brown. The solution was stirred at −20 °C for 1 h and at room temperature for 1 h. During that time, a light brown solid precipitated out of the reaction. The solid was then filtered on a Buchner funnel, and the solid was washed with $CDCl_3$ (2 × 2 mL). The solid was recuperated and dried under vacuo to obtain the desired pyridinium salt **19g** as a beige solid (328 mg, 96%). The product was characterized in THF-d_8 as it is poorly soluble in $CDCl_3$. ^{1}H NMR (400 MHz, THF-d_8): δ 9.36 (d, J = 6.8 Hz, 1H), 9.09 (d, J = 8.4 Hz, 1H), 8.27 (dd, J = 6.8, 8.4 Hz, 1H), 7.75−7.70 (m, 4H), 4.71 (br d, J = 1.5 Hz, 1H), 4.51 (br d, J = 1.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, THF-d_8): δ 154.3, 147.8, 146.0, 143.5, 133.6, 133.1, 128.7, 127.9, 127.0 (q, ^1J = 272.2 Hz, J_{C-F}), 124.9, 122.1 (q, ^1J = 323.8 Hz, J_{C-F}), 71.6, 42.8. ^{19}F NMR (471 MHz, THF-d_8): δ −74.47 (s), −75.57 (s). IR ν: 3098, 1593, 1426, 1396, 1269, 1251 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M - OTf]^+$ calcd for $C_{14}H_9Br_2ClF_3N_2O_2S$, 520.8359; found, 520.8366.

Experimental Procedure for the Reaction between 3-Bromo-1-(2-(4-bromophenyl)-1-((trifluoromethyl)sulfonyl)-aziridin-2-yl)-2-chloropyridin-1-ium (19g) and Et_3N (Scheme 4). 3-Bromo-1-(2-(4-bromophenyl)-1-((trifluoromethyl)sulfonyl)-aziridin-2-yl)-2-chloropyridin-1-ium (**19g**) (30 mg, 0.045 mmol, 1.0 equiv) was charged in a flame-dried, nitrogen-flushed 2−5 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous chloroform (0.23 mL, 0.2 M) was added, and the suspension was stirred for 2 min. Triethylamine (9.1 mg, 13 μL, 0.090 mmol, 2.0 equiv) was added in one portion. The solid gradually solubilized, and the reaction was stirred at room temperature for 1 h. LCMS indicated full conversion of the pyridinium salt to the desired imidazo[1,2-*a*]pyridine **10g**. The solvent was evaporated under vacuo, and the crude product was then purified by flash chromatography using a 25 g SNAP Ultra column (100% heptanes to 50% EtOAc in 50% heptanes over 20 CV) to yield the desired compound **10g** (13 mg, 77%) as a red oil. ^{1}H NMR spectra match the characterization data previously reported.

Synthesis of Highly Potent Mnk_1/Mnk_2 Inhibitor (Scheme 6). *Formation of 4-(6-Chloroimidazo[1,2-a]pyrazin-3-yl)phenyl Acetate (23) via Optimized Conditions.* The azirine (**8l**, 516 mg, 2.95 mmol, 1.0 equiv), sodium sulfate (516 mg), and 2,5-dichloropyrazine (878 mg, 5.89 mmol, 2.0 equiv) were loaded in a flame-dried, nitrogen-flushed 20 mL Biotage microwave tube under a nitrogen atmosphere. Anhydrous chloroform (14.7 mL, 0.2 M) was added, and the mixture was stirred until complete dissolution of the azirine. The solution was cooled to −20 °C in a water/isopropanol and dry ice bath. Freshly distilled trifluormethanesulfonic anhydride (997 mg, 595 μL, 3.53 mmol, 1.2 equiv) was added dropwise to the solution, which became dark brown. The mixture was left to stir for an hour at −20 °C and then for another hour at room temperature. The reaction was then treated with anhydrous triethylamine (599 mg, 0.825 mL, 5.89 mmol, 2.0 equiv), and the course of the reaction was monitored by LCMS. Upon full conversion of the pyridinium salt to the desired product (1 h), the mixture was then transferred to a 125 mL extraction funnel and extracted with DCM (2 × 30 mL) and brine (20 mL). The organic extracts were combined, dried with sodium sulfate, and filtered over a sintered funnel, and the filtrate was evaporated under vacuo. The crude product was then purified by flash chromatography using a 50 g SNAP Ultra column (100% heptanes to 50% EtOAc in 50% heptanes over 30 CV) to yield the desired compound **23** (475 mg, 56%) as a dark brown solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.98 (d, J = 1.2 Hz, 1H), 8.29 (d, J = 1.2 Hz, 1H), 7.90 (s, 1H), 7.57 (d, J = 8.8 Hz, 2H), 7.31 (d, J = 8.8 Hz, 2H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.2, 151.4, 142.8, 140.1, 135.9, 135.7, 129.2, 126.8, 124.7, 123.1, 114.0, 21.1. IR ν: 3120, 3048, 1745, 1604, 1490, 1476, 1365, 1326, 1220 cm^{-1}. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{14}H_{11}ClN_3O_2$, 288.0535; found, 288.0532.

*Suzuki Coupling between **23** and 4-(4-Methylpiperazine-1-carbonyl)phenylboronic Acid Pinacol Ester (**24**).* 4-(6-Chloroimidazo[1,2-*a*]pyrazin-3-yl)phenyl acetate (**23**, 30 mg, 0.104 mmol, 1.0 equiv), 4-(4-methylpiperazine-1-carbonyl)phenylboronic acid pinacol ester (**24**, 51.7 mg, 0.156 mmol, 1.5 equiv), and sodium carbonate (44.7 mg, 0.417 mmol, 4.0 equiv) were charged in a nitrogen-flushed 0.5−2.0 mL Biotage vial with a magnetic stir bar. The solids were dissolved in a 5:1 mixture of DME (521 μL) and water (100 μL), and the solution was then sparged with a flow of nitrogen for 5 min. The mixture was treated with 1,1′-bis-(diphenylphosphino)ferrocene dichloropalladium(II) (7.63 mg, 10 mol %, 0.0104 mmol, 0.1 equiv), and the vial was capped with a microwave cap. The reaction was then heated to 120 °C under microwave irradiation (Biotage Initiator, 300 W, high absorption) for 1 h and 30 min. The reaction was cooled to rt and transferred to a 50 mL round bottom flask. The vial was rinsed with DCM, and silica gel was added (2 g). The suspension was evaporated to dryness to obtain a brown solid residue. The crude product was then purified by flash chromatography using a 25 g SNAP Ultra column (100% EtOAc to 50% MeOH in 50% EtOAc over 25 CV) to yield the desired compound **25**. The solid was then purified again using reverse-phase chromatography on a 12 g SNAP C18 Ultra column. A gradient of 100% 10 mM ammonium formate-buffered solution in water (AMF) to 50% MeCN in 50% AMF over 25 CV was used. The fractions containing pure compound were lyophilized overnight. Compound **25** was isolated as a white free-flowing solid as a formate salt (34 mg, 77%). Product **25** corresponds to literature characterization.[19] ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (d, J = 1.2 Hz, 1H), 8.54 (d, J = 1.2 Hz, 1H), 8.25 (s, 1H (formate)), 7.96 (d, J = 8.4 Hz, 2H), 7.83 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 3.93 (br s, 2H), 3.73 (br s, 2H), 2.79 (br s, 4H), 2.54 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, DMSO-d_6): δ 168.1, 165.2 (formate), 158.2, 142.2, 139.2, 137.1, 136.9, 135.1, 133.8, 128.8, 127.2, 126.8, 125.6, 116.8, 115.8, 113.1, 53.9, 46.5, 45.0, 43.6, 40.9. HRMS (ESI/Q-Exactive Orbitrap) m/z: $[M + H]^+$ calcd for $C_{24}H_{24}N_5O_2$, 414.1925; found, 414.1917.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02148.

General information and reagents, control reactions, isolation and characterization of reaction intermediates, optimization tables, and copies of ^{1}H NMR, $^{13}C\{^1H\}$ NMR, ^{19}F NMR, and FTIR spectra (PDF)

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FAIR data and the primary NMR FID files for compounds: **8a−8n**, **10a−10t**, **14b−14n**, **18**, **19g**, **23**, **25**, and **S1** (ZIP)

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Notes

The authors declare no competing financial interest.

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