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Friedel–Crafts Reactions with *N*-Heterocyclic Alcohols

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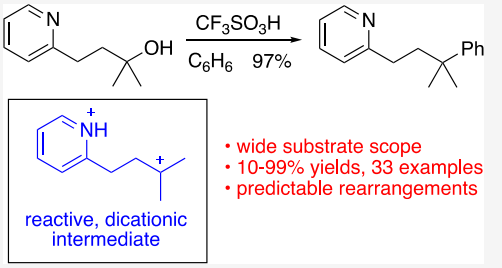
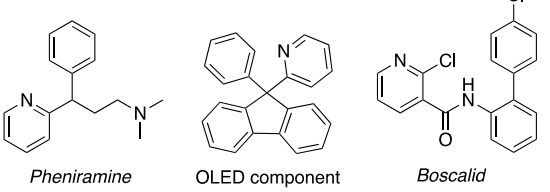
ABSTRACT: *N*-Heterocyclic alcohols are shown to be excellent substrates for superacid-promoted Friedel–Crafts reactions. The *N*-heterocyclic alcohols ionize to produce reactive, dicationic intermediates which provide good to excellent yields of arylation products.

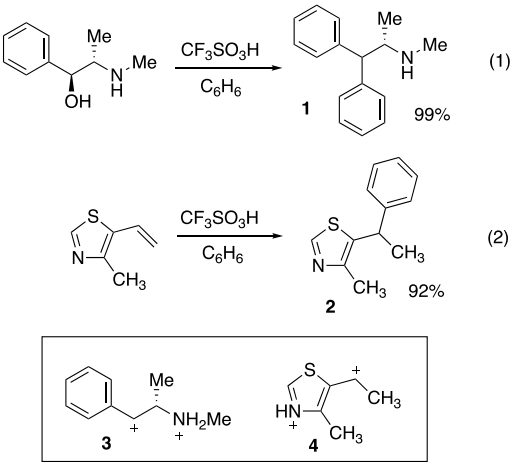


INTRODUCTION

Functionalized heterocyclic compounds are important synthetic targets. Roughly 70% of clinically useful pharmaceutical compounds contains one or more heterocyclic rings.[1] Improved access to heterocyclic scaffolds can lower the costs of pharmaceutical intermediates and provide routes to new chemical space for drug development. Heterocyclic compounds are also useful in numerous other applications, such as materials science,[2] agrochemicals,[3] and dyes/pigments.[4] Many important *N*-heterocyclic compounds contain aryl substituent groups—for example, *pheniramine* (an antihistamine drug), the fluorescent molecule used in an organic light-emitting diode, and *boscalid* (an antifungal agrochemical). While aryl substituents may be installed by a number of useful synthetic methods, our group has utilized dicationic electrophiles in the Friedel–Crafts reaction to prepare aryl-functionalized heterocycles and other products (1).[5] For example, amino alcohols and olefinic *N*-heterocycles provide the arylated products (**1** and **2**) in excellent yields by reaction in superacidic CF_3SO_3H (triflic acid).[5a,b]



These conversions involve the formation of the superelectrophilic intermediates (**3** and **4**) which react readily with arene nucleophiles. Similarly, we demonstrated that *N*-heterocyclic alcohols may be ionized in superacid to give aza-polycyclic aromatic compounds, presumably through dications.[5c] An $AlCl_3$-promoted transformation had been reported, giving phenylated products from an imidazole alcohol, and another arylation has been demonstrated with 2-hydroxymethylbenzimidazoles.[6,7] Nevertheless, the use of *N*-heterocyclic alcohols in Friedel–Crafts reactions has not been widely employed. In the following manuscript, we describe the use of this synthetic methodology to prepare aryl-functionalized *N*-heterocycles. Mechanisms are proposed involving dicationic electrophilic intermediates.



RESULTS AND DISCUSSION

Our initial studies examined the reactions of 2-(4-pyridyl)-2-propanol (**5**) in its reactions with triflic acid and arene nucleophiles (Scheme 1). When alcohol **5** is reacted with triflic acid (10 equiv) in the presence of benzene, a nearly quantitative yield of the Friedel–Crafts product (**6**) is

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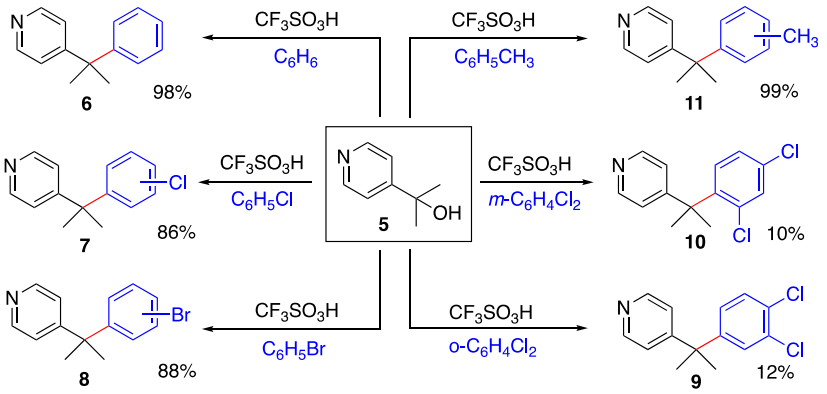
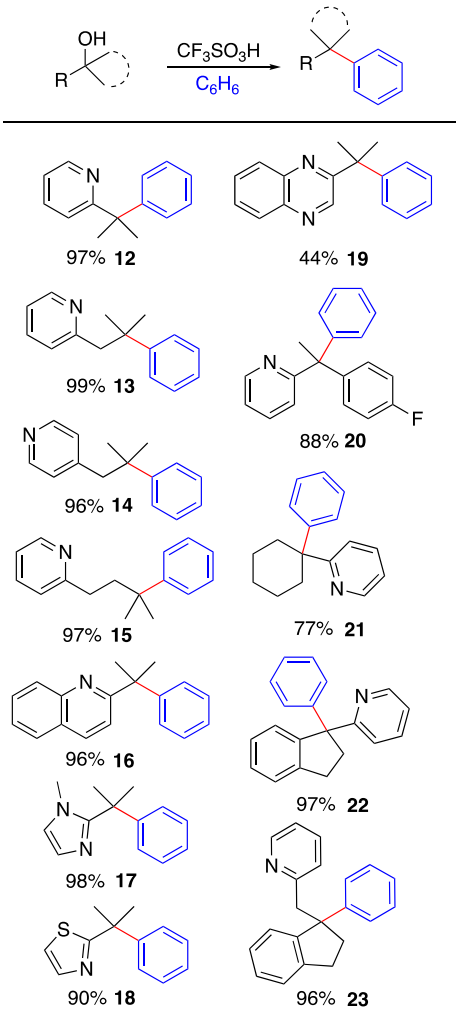
Scheme 1. Substrate Scope of Friedel–Craft Products[a]



[a]Isolated yields. [b]Reaction conditions: 1 mmol **5**, 10 mmol arene, and 10 mmol CF_3SO_3H, stirred at 25 °C for 15 h.

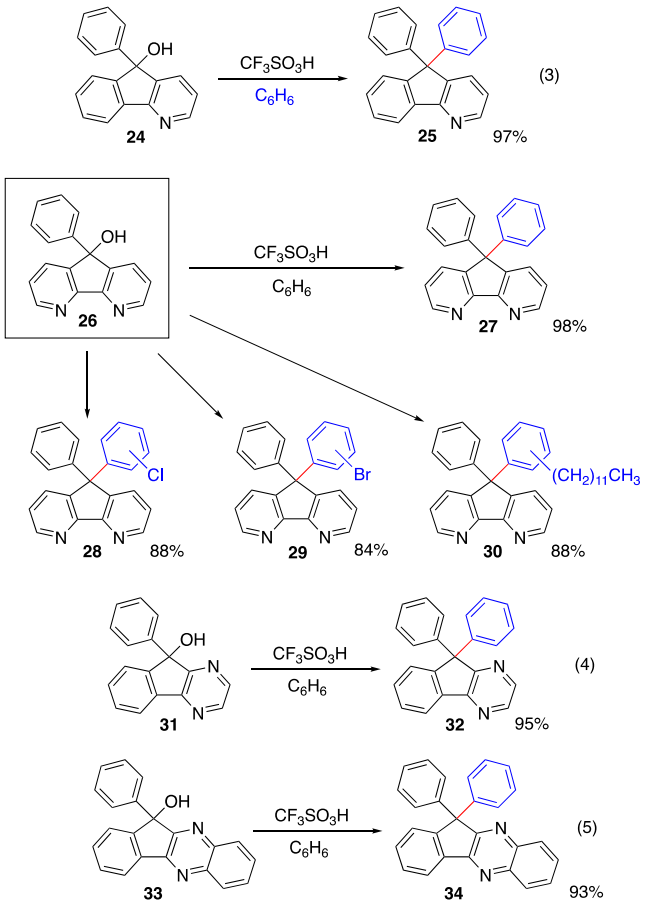
Table 1. Products (12–23) and Yields from the Reactions of *N*-Heterocyclic Alcohols with Benzene and Triflic Acid[a,b]



[a]Isolated yields. [b]Conditions: 1 mmol alcohol, 10 mmol C_6H_6, and 10 mmol CF_3SO_3H, 25 °C for 15 h.

obtained.[8] The conversion was not successful when weaker acids are used—H_2SO_4 or CF_3CO_2H—as there was no Friedel–Crafts reaction product detected at 25 °C. However, H_2SO_4 did provide a conversion to the elimination product, 4-(2-propenyl)pyridine. Using lower quantities of triflic acid likewise produced large amounts of 4-(2-propenyl)pyridine. With chloro- and bromobenzene, the arylated products (**7**–**8**) are obtained in good yields, while dichlorobenzenes lead to a significantly lower yield of the arylated products (**9**–**10**). Presumably, this is due to the deactivation of the aromatic ring by the chloro substituents. Although toluene provides the Friedel–Crafts product **11** in quantitative yield, it is formed as the mixture of regioisomers (like compounds **7** and **8**). The

Scheme 2. Substrate Scope of Aza- and Diazafluorenol Products[a]



[a]Isolated yields. Reaction conditions: 1 mmol **5**, 10 mmol arene, and 10 mmol CF_3SO_3H, stirred at 25 °C for 15 h.

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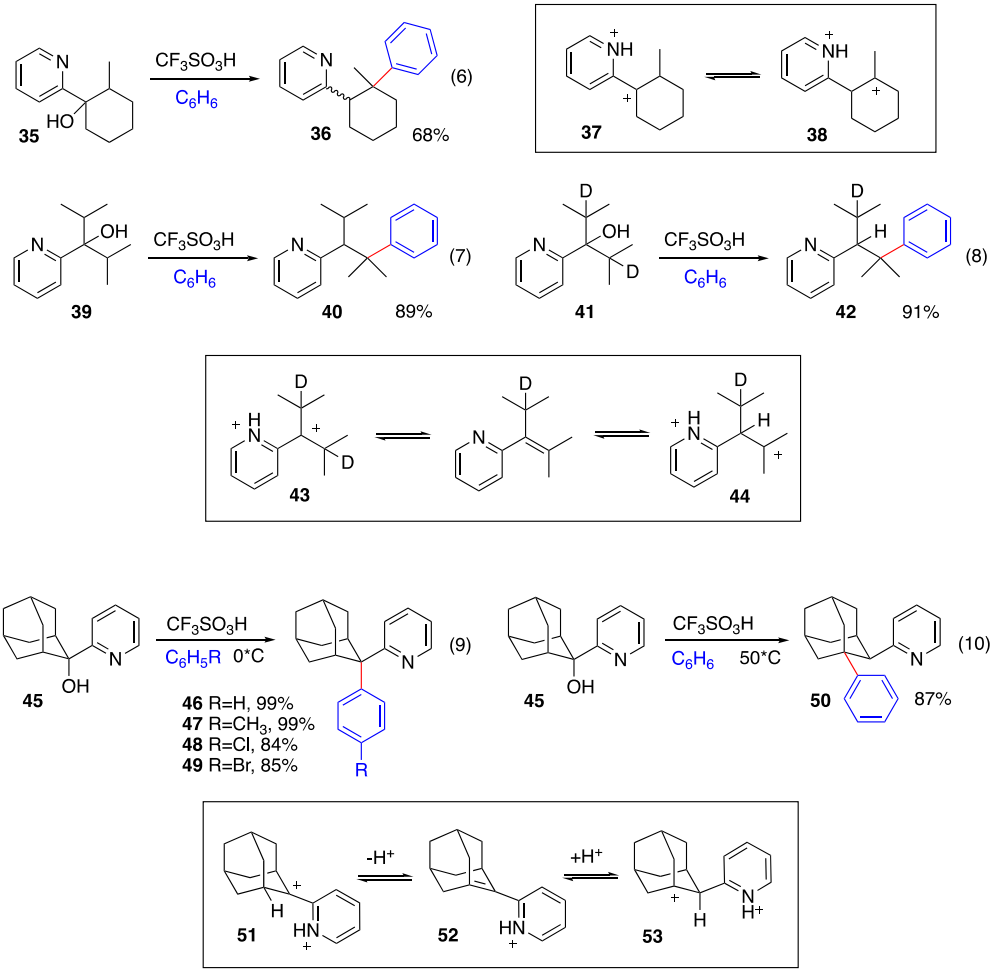
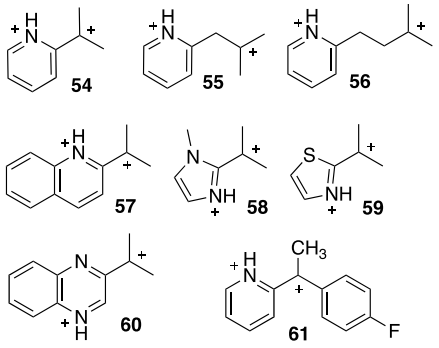
Scheme 3. Reactions Involving Charge Migration Processes



Scheme 4. Proposed Dicationic Intermediates



observed product yields are consistent with the formation of reactive electrophiles, ones that is capable of reacting with deactivated arenes such dichlorobenzene.

The Friedel–Crafts chemistry is found to be effective with a variety of *N*-heterocyclic alcohol substrates (Table 1). Like the 2-(4-pyridyl)-2-propanol (**5**), the isomeric 2-(2-pyridyl)-2-propanol gives the corresponding phenylation product **12** in high yield. With increasing distance between the two sites of ionization, the chemistry remains highly effective. Thus, ionization of 4-(2-pyridyl)-2-methyl-2-butanol provides the phenylated product **15** four carbons away from the pyridine nitrogen. Other *N*-heterocycles give conversions to the respective Friedel–Crafts products, including quinolyl (**16**), imidazolyl (**17**), thioazolyl (**18**), and quinoxalyl (**19**). The quinoxalyl product is produced in lower yield because of its tendency to form an elimination product. Although the Friedel–Crafts chemistry did not show good regioselectivity with halogen-substituted benzenes (Scheme 1), a single regioisomer of the triarylethane (**20**) was prepared in good yield by installation of the 4-fluorophenyl group in the starting *N*-heterocyclic alcohol. Structurally diverse products may be prepared starting from cyclic ketones. For example, cyclohexanone provides the heterocyclic alcohol from 2-lithiopyridine, and the subsequent Friedel–Crafts reaction gives product **21**. Similarly, 1-indanone gives products **22** and **23** from this reaction sequence.

Aza- and diazafluorenols also provide excellent yields of the Friedel–Crafts products (Scheme 2). When azafluorenol **24** is reacted with triflic acid and benzene, the substitution product **25** is obtained in nearly quantitative yield (eq 1). Likewise, the diazafluorenol **26** quantitatively gives the product from benzene (**27**). This compound was previously synthesized in 80% yield from 4,5-diazafluorene using a palladium-catalyzed procedure, as described in a patent related to its use in electroluminescent materials.[9] High yields are also obtained from chlorobenzene, bromobenzene, and 1-phenyldodecane, providing compounds **28** (o/p, 1:6), **29** (o/p, 1:6), and **30** (o/p, 1:3), respectively. As in the case of alcohol **5**, the diazafluorenol **26** does not react with good regioselectivity with monosubstituted benzenes. Diazafluorenols **31** and **33** are

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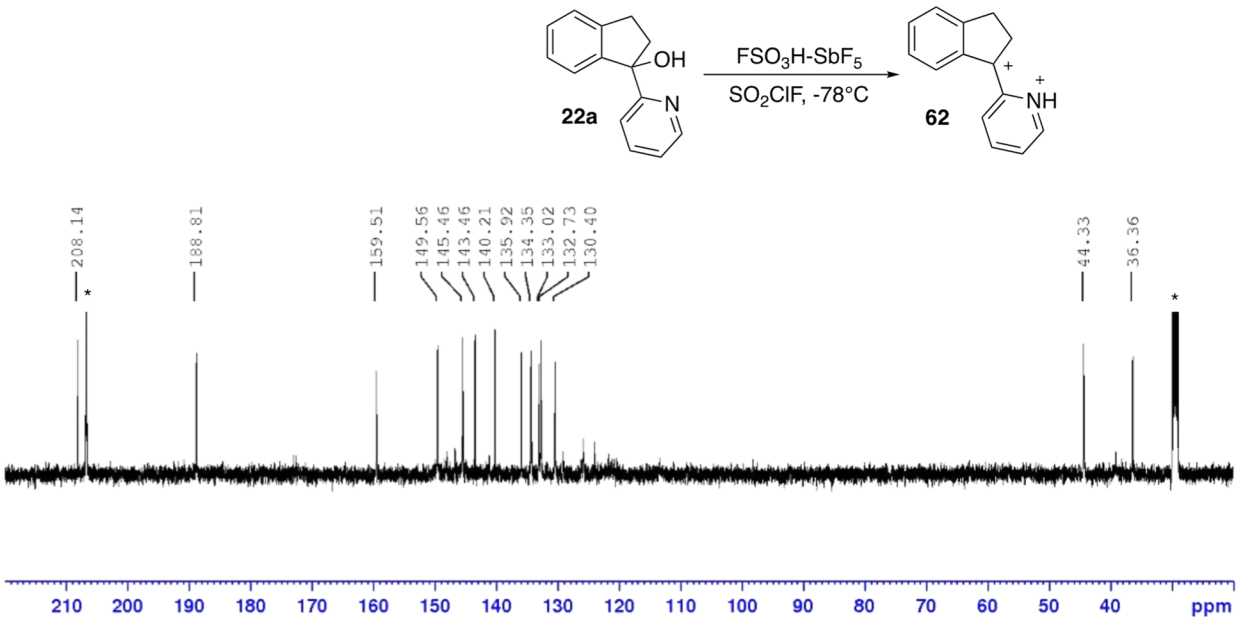

Figure 1. Ionization of alcohol **22a** to the dicationic species (**62**) in superacid and the resulting ^{13}C NMR (*d_6-acetone, external standard).

similarly found to give the Friedel–Crafts reaction products, **32** and **34**, in excellent yields (eqs 4–5).

Some *N*-heterocyclic alcohols are found to undergo rearrangement reactions in the superacid promoted conversions (Scheme 3). When the cyclohexanol derivative **35** was reacted with triflic acid and benzene, phenylation occurs at the adjacent carbon to give **36** (eq 6). This transformation may be understood by assuming that compound **35** ionizes to the 1,3-dication **37**. Migration of charge generates the 1,4-dication **38**, a process driven by charge–charge repulsion, and this leads to the observed product **36**. In a similar conversion, alcohol **39** gives product **40** in good yield (eq 7)—a conversion that is also explained by charge migration in the dication. Migration of charge may occur by either direct 1,2-hydride shift or by a deprotonation–reprotonation sequence. In order to determine which process is occurring, we prepared deuterium-labeled substrate **41** and the superacid-promoted reaction gave product **42** with the loss of deuterium (eq. 8). This conversion is the result of an equilibrium between the initially formed 1,3-dication **43**, the intermediate from dedeuteration, and the 1,4-dication **44** from reprotonation. With a 2-adamantanol derivative (**45**), the Friedel–Crafts products **46-49** are formed in good yields and regioselectivities (eq 9). Upon heating to 50 °C with benzene, substrate **45** gives the Friedel–Crafts products (**50**) from reaction at the bridgehead carbon (eq 10). The analogous rearrangement products from chloro- and bromobenzene or toluene could not be obtained at 50 °C. The need for heating suggests a charge migration process involving a high energy intermediate. Assuming that the 1,3-dication **51** is the initially formed intermediate, charge migration by loss of a proton would give the strained bridgehead olefin **52** and reprotonation provides the 1,4-dication **53**, which then gives product **50**.

The previously described Friedel–Crafts reactions also involve dicationic electrophiles (Scheme 4). For the 2-pyridyl system, the 1,3-dication (**55**), 1,4-dication (**56**), and 1,5-dication (**57**) were all capable of reacting with benzene—giving products **12–13** and **15** in nearly quantitative yields. Other *N*-heterocycles generated dicationic intermediates, including the quinolyl (**57**), imidazolyl (**58**), thiazolyl (**59**), and quinoxalyl (**60**) systems. In the synthetic reactions, 10 equiv of superacid was used. While it is assumed that the quinoxalyl system reacts through dication **60**, the involvement of a tricationic intermediate cannot be excluded.

The indanyl dication **62** was observed directly using low-temperature NMR and stable ion conditions. Thus, ionization of alcohol **22a** in $FSO_3H–SbF_5–SO_2ClF$ at −78 °C provides a ^{13}C NMR spectrum in which dication **62** is clearly visible (Figure 1). The carbocation ^{13}C resonance is observed at δ 208.1, which suggests extensive delocalization of the positive charge into the adjacent aryl ring. This has been observed in other di- and tricationic systems.[5a,h] Charge–charge repulsive effects lead to strong resonance interactions with the π-electrons of the aryl ring. Efforts to observe the dicationic intermediate from 2-(4-pyridyl)-2-propanol (**5**) were not successful. Ionization of this substrate in $FSO_3H–SbF_5–SO_2ClF$ at −78 °C gave a complex NMR spectrum. Unlike the indanyl system, ionization of 2-(4-pyridyl)-2-propanol (**5**) does not benefit from stabilization of a benzylic carbocation center. Thus, a long-lived carbocation is not generated from **5**. During the CF_3SO_3H-promoted Friedel–Crafts transformation (leading to products **6–11**), a reactive dication is likely formed as a low-concentration transient species.

CONCLUSIONS

In this study, we have found that *N*-heterocyclic alcohols react in excess superacid to generate reactive electrophilic intermediates capable of undergoing Friedel–Crafts reactions with arenes. The yields of these conversions are often nearly quantitative. The chemistry encompasses a wide variety of *N*-heterocycles and alcohol structures. Mechanisms are proposed which involve dicationic, superelectrophilic intermediates. These dicationic intermediates are likely in equilibrium with monoprotonated, olefinic *N*-heterocycles.

EXPERIMENTAL SECTION

General Considerations. Condensation reactions were performed under an inert atmosphere using a thoroughly dried glassware.

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Products were isolated by flash chromatography using 60 Å silica gel. ^{1}H and ^{13}C NMR were carried out using either a 300 or 500 MHz spectrometer. High-resolution mass spectra were obtained from a commercial analytical laboratory with a time-of-flight (TOF) mass analyzer used for data collection. Reagents and solvents were purchased from commercial suppliers and used as received. Triflic acid was distilled prior to use and stored under a dry inert atmosphere. Structural assignments were made with additional information from gCOSY, gHSQC, and gHMBC experiments.

SAFETY: triflic acid is highly corrosive—it should be handled in an efficient fume hood by appropriately trained individuals utilizing a personal protective gear.

General Procedure A: Synthesis of Alcohols. The nitrogen heterocycle (1 mmol) was dissolved in tetrahydrofuran (10 mL) at −78 °C, and *n*-butyllithium (0.44 mL, 2.5 M in hexanes, 1.76 mmol) was added dropwise using a syringe. After stirring for 1 h at −78 °C, 1.2 mmol ketone dissolved in tetrahydrofuran (5 mL, 0.24 M) was added slowly over a period of 30 min. The resulting mixture was stirred for 1 h at −78 °C, and the mixture was gradually warmed to room temperature overnight. The reaction was quenched with ammonium chloride, and the product was extracted with chloroform (3 × 20 mL). The mixture was washed with brine, and the organic layer was separated and dried over sodium sulfate (Na_2SO_4). Flash column was performed with silica gel.

General Procedure B: Synthesis of Alcohols. The *N*-heterocyclic carbonyl compound (1 mmol, 0.067 M) was dissolved in tetrahydrofuran (15 mL) at −78 °C, and 1.2 equiv of Grignard or organolithium reagent (1.2 mmol) was added dropwise using a syringe. The resulting mixture was stirred for 1 h at −78 °C, and the mixture was gradually warmed to room temperature overnight. The reaction was quenched with 1.0 M ammonium chloride, and the product was extracted with chloroform (3 × 20 mL). The mixture was washed with brine, and the organic layer was separated and dried over sodium sulfate (Na_2SO_4). Flash column is performed with silica gel.

General Procedure C: Friedel–Crafts Reaction. The alcohol (0.5 mmol) was dissolved in 5 mL (0.1 M) of chloroform and added to the arene (5 mmol). Triflic acid (0.5 mL, 5.47 mmol, 11 equiv) was then added dropwise. After stirring for 15 h at room temperature, the product mixture was then quenched by pouring over 20 g of ice. The resulting mixture was adjusted to a pH of 10−11 using 10 M sodium hydroxide. After the mixture is transferred to a separatory funnel, the mixture was extracted twice with chloroform. The combined organic extracts were subsequently washed with water and then with brine, dried over anhydrous sodium sulfate, and concentrated under vacuum. Flash chromatography was performed with silica gel.

*4-(2-Phenylpropan-2-yl)pyridine (**6**).* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (1.02 g, 7.5 mmol), benzene (6.75 mL, 75 mmol), and triflic acid (6.75 mL, 75 mmol) gave 4-(2-phenylpropan-2-yl)pyridine **6** (1.44 g, 7.4 mmol, 98%) as an essentially pure oil. R_f = 0.12 (1:9, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.51 (d, J = 3.7 Hz, 2H), 7.33−7.29 (m, 2H), 7.25−7.21 (m, 3H), 7.17−7.16 (m, 2H), 1.70 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 163.8, 147.7, 146.7, 128.5, 126.7, 126.5, 123.4, 43.4, 29.7.[10]

*4-(2-(4-Chlorophenyl)propan-2-yl)pyridine (**7**) as a Mixture of Isomers (o/p, 9:10).* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (68.5 mg, 0.5 mmol), chlorobenzene (0.5 mL, 5 mmol), and triflic acid (0.44 mL, 5 mmol) produced 4-(2-(4-chlorophenyl)propan-2-yl)pyridine **7** (99 mg, 0.43 mmol, 86%) as an oil. The product was purified using silica gel chromatography (1:4, EtOAc/hexanes). R_f = 0.28 (1:4, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, J = 5.8 Hz, 2H), 8.49 (d, J = 5.5 Hz, 2H), 7.64 (dd, J = 6.4, 1.5 Hz, 1H), 7.37−7.24 (m, 6H), 7.15−7.12 (m, 4H), 7.09−7.08 (m , 2H), 1.75 (s, 5H), 1.68 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.2, 159.0, 149.7, 149.4, 147.3, 144.5, 134.1, 132.1, 131.8, 128.4, 128.3, 128.2, 127.9, 126.9, 122.0, 121.3, 43.8, 42.7, 29.9, 29.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{15}ClN$, 232.0888; observed, 232.0897.

*4-(2-(4-Bromophenyl)propan-2-yl)pyridine (**8**) as a Mixture of Isomers (o/p, 2:3).* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (68.5 mg, 0.5 mmol), bromobenzene (0.52 mL, 5 mmol), and triflic acid (0.44 mL, 5 mmol) produced 4-(2-(4-bromophenyl)propan-2-yl)pyridine **8** (121 mg, 0.44 mmol, 88%) as an oil. The product was purified using silica gel chromatography (3:7 EtOAc/hexanes). R_f = 0.21 (3:7, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, J = 5.7 Hz, 2H), δ 8.49 (d, J = 5.4 Hz, 1H), 7.66 (dd, J = 6.3, 1.6 Hz, 1H), 7.54 (dd, J = 6.4, 1.4 Hz, 1H), 7.44−7.38 (m, 3H), 7.17−7.12 (m, 3H), 7.10−7.08 (m, 4H), 1.77 (s, 4H), 1.67 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.1, 158.9, 149.7, 149.4, 147.8, 145.8, 135.6, 131.4, 128.6, 128.5, 128.3,127.4, 123.9, 122.0, 121.7, 120.2, 44.9, 42.7, 29.9, 29.7. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{15}BrN$, 276.0382; observed, 276.0394.

*4-(2-(3,4-Dichlorophenyl)propan-2-yl)pyridine (**9**).* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (137 mg, 1 mmol), o-dichlorobenzene (1.02 mL, 10 mmol), and triflic acid (0.88 mL, 10 mmol) produced 4-(2-(3,4-dichlorophenyl)propan-2-yl)-pyridine **9** (32 mg, 0.12 mmol, 12%) as an oil. The product was purified using silica gel chromatography (1:4, EtOAc/hexanes). R_f = 0.32 (1:4, EtOAc/hexanes).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (d, J = 4.8 Hz, 2H), 7.37 (d, J = 8.45 Hz, 1H), 7.32 (d, J = 2.3 Hz, 1H), 7.14−7.13 (m, 2H), 7.01 (dd, J = 6.1, 2.3 Hz, 1H), 1.67 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 158.3, 149.8, 149.1, 132.4, 130.4, 130.3, 128.8, 126.5, 121.9, 42.7, 29.8. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{14}Cl_2N$, 266.0498; observed, 266.0510.

*4-(2-(2,4-Dichlorophenyl)propan-2-yl)pyridine (**10**).* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (137 mg, 1 mmol), *o*-dichlorobenzene (1.15 mL, 10 mmol), and triflic acid (0.88 mL, 10 mmol) produced 4-(2-(2,4-dichlorophenyl)propan-2-yl)-pyridine **10** (26 mg, 0.1 mmol, 10%) as an oil. The product was purified using silica gel chromatography (1:4, EtOAc/hexanes). R_f = 0.30 (1:4, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.50 (br s, 2H), 7.57 (d, J = 9.1 Hz, 1H7.34−7.33 (m, 2H), 7.06 (d, J = 6.0 Hz, 1H), 1.73 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 158.4, 149.6, 143.2, 134.9, 133.4, 131.5, 128.9, 127.0, 121.1, 43.6, 29.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{14}H_{14}Cl_2N$, 266.0498; found, 266.0498.

*4-(2-(p-Tolyl)propan-2-yl)pyridine (**11**) as a Mixture of Isomers.* Following general procedure C, 2-(pyridin-4-yl)propan-2-ol **5** (137 mg, 1 mmol), toluene (1.06 mL, 10 mmol), and triflic acid (0.88 mL, 10 mmol) produced 4-(2-(tolyl)propan-2-yl)pyridine **11** (208 mg, 0.99 mmol, 99%) as an oil containing the three regioisomeric products. R_f = 0.84 (1:4, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.50−8.48 (m, 2H), 7.57−7.56 (m, 1H), 7.28−7.14 (m, 2H), 7.10−7.09 (m, 2H), 7.05−7.02 (m, 1H), 2.33−3.32 (m, 3H), 1.68−1.67 (m, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.1, 159.7, 159.6, 149.9, 149.6, 148.6, 145.8, 145.4, 137.7, 136.5, 135.7, 132.6, 129.0, 128.1, 127.4, 127.0, 126.9, 126.6, 126.1, 125.9, 123.8, 122.11, 122.07, 121.2, 43.8, 42.8, 42.5, 30.2, 30.0, 21.8, 21.6, 20.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{15}H_{18}N$, 212.1434; observed, 212.1439.

*2-(2-Phenylpropan-2-yl)pyridine (**12**).* Following general procedure C, 2-(pyridin-2-yl)propan-2-ol[11] (**12a**, 68 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol, 10 eq), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-phenylpropan-2-yl)pyridine **12** (95 mg, 0.44 mmol, 97%) as an essentially pure oil. R_f = 0.11 (1:9 EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.60 (d, J = 4.1 Hz, 1H), 7.56 (td, J = 5.8, 1.8 Hz, 1H), 7.33−7.27 (m, 4H), 7.23−7.20 (m, 1H), 7.13−7.10 (m, 2H), 1.78 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 168.7, 149.6, 148.4, 136.1, 128.2, 126.7, 125.9, 121.7, 120.8, 45.6, 29.6.[10]

*2-(2-Methyl-2-phenylpropyl)pyridine (**13**).* Following standard procedure A, 2-methylpyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and acetone (0.09 mL, 1.2 mmol) provided 2-methyl-1-(pyridin-2-yl)propan-2-ol[12] (119 mg, 79%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f = 0.53 (1:1, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.49 (dd, J = 4.2, 0.6 Hz, 1H), 7.62 (td, J = 5.9, 1.8 Hz, 1H), 7.19−7.11 (m, 2H), 5.57 (br s, 1H), 2.90 (s, 2H), 1.21 (2, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 159.9, 148.3, 136.8, 124.4, 121.5, 70.7, 68.6, 29.5.

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Following general procedure C, 2-methyl-1-(pyridin-2-yl)propan-2-ol (**13a**, 76 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-methyl-2-phenylpropyl)pyridine **13** (105 mg, 99%) as an essentially pure oil. R_f = 0.29 (1:4, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (dd, J = 4.3, 0.9 Hz, 1H), 7.60 (td, J = 6.0, 1.8 Hz, 1H), 7.33−7.23 (m, 6H), 6.64 (d, J = 7.9 Hz, 1H), 3.20 (s, 2H), 1.43 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 158.0, 147.7, 146.2, 138.2, 128.3, 126.1, 126.0, 125.5, 122.2, 51.4, 39.3, 28.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{15}H_{18}N$, 212.1434; found, 212.1434.

*4-(2-Methyl-2-phenylpropyl)pyridine (**14**).* Following standard procedure A, 4-methylpyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and acetone (0.09 mL, 1.2 mmol) provided 2-methyl-1-(pyridin-4-yl)propan-2-ol (**14a**, 110 mg, 0.73 mmol, 73%) as an oil. The product was purified using silica gel chromatography (1:4, EtOAc: hexanes). R_f = 0.39 (1:4, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.41 (d, J = 5.8 Hz, 2H), 7.15 (d, J = 5.9 Hz, 2H), 2.74 (s, 2H), 1.22 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 149.0, 147.5, 126.0, 70.3, 49.2, 29.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_9H_{14}NO$, 152.1070; found, 152.1074. Following general procedure C, 2-methyl-1-(pyridin-4-yl)propan-2-ol **14a** (76 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 4-(2-methyl-2-phenylpropyl)pyridine **14** (101 mg, 96%) as an essentially pure oil. R_f = 0.30 (50% ethyl acetate: hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.48 (d, J = 3.8 Hz, 2H), 7.33−7.24 (m, 5H), 6.78 (d, J = 5.3 Hz, 2H), 2.93 (s, 2H), 1.38 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 150.1, 147.3, 147.2, 128.2, 126.2, 126.1, 50.7, 38.9, 28.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{15}H_{18}N$, 212.1434; found, 212.1440.

*2-(3-Methyl-3-phenylbutyl)pyridine (**15**).* Following standard procedure A, 2-methylpyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 1,2-epoxy-2-methylpropane (0.11 mL, 1.2 mmol) provided 2-methyl-4-(pyridin-2-yl)butan-2-ol (**15a**, 148 mg, 0.9 mmol, 90%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f = 0.62 (1:1, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.35 (dd, J = 4.1, 0.8 Hz, 1H), 7.45 (td, J = 5.9, 1.8 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 6.98−6.94 (m, 1H), 4.52 (s, 1H), 2.84 (t, J = 8.0 Hz, 2H), 1.81 (t, J = 8.0 Hz, 2H), 1.18 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 162.2, 148.5, 136.5, 122.9, 120.9, 69.7, 42.9, 32.9, 29.5. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{10}H_{16}NO$, 166.1226; found, 166.1229. Following general procedure C, 2-methyl-4-(pyridin-2-yl)butan-2-ol (**15a**, 83 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(3-methyl-3-phenylbutyl)pyridine **15** (109 mg, 0.49 mmol, 97%) as an essentially pure oil. R_f = 0.59 (1:4 EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (d, J = 4.7 Hz, 1H), 7.65 (td, J = 5.9, 1.7 Hz, 1H), 7.41−7.28 (m, 4H), 7.21−7.09 (m, 3H), 2.64−2.58 (m, 2H), 2.11−2.05 (m, 2H), 1.41 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 161.7, 148.6, 147.6, 138.2, 128.34, 128.27, 125.8, 123.5, 121.6, 44.4, 37.8, 33.1, 28.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{16}H_{19}N$, 226.1590; found, 226.1593.

*2-(2-Phenylpropan-2-yl)quinoline (**16**).* Following general procedure B, quinaldoyl chloride (191 mg, 1 mmol) and methyllithium 1.6 M in Et_2O (3.6 mL, 2.2 mmol) produced 2-(quinolin-2-yl)propan-2-ol (**16a**, 118 mg, 0.63 mmol, 63%) as an oil. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f = 0.43 (3:7, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.84 (d, J = 8.1 Hz, 1H), 7.77−7.72 (m, 1H), 7.59−7.53 (m, 1H), 7.48 (d, J = 8.6 Hz, 1H), 5.93 (br s, 1H), 1.64 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$) δ 165.7, 145.8, 137.4, 129.9, 128.8, 127.4, 127.1, 126.4, 117.1, 71.8, 30.5. Following general procedure C, 2-(quinolin-2-yl)propan-2-ol (**16a**, 93 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-phenylpropan-2-yl)quinoline **16** (119 mg, 0.48 mmol, 96%) as an essentially pure oil. R_f = 0.87 (5% E/H). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8.7 Hz,˙1H), 7.78−7.71 (m, 2H), 7.56−7.50 (m, 1H), 7.34 (d, J = 4.2 Hz, 4H), 7.28−7.22 (m, 1H), 7.10 (d, J = 8.7 Hz, 1H), 1.88 (S, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 168.3, 149.4, 147.0, 135.7, 129.5, 129.1, 128.2, 127.3, 126.8, 126.5, 126.0, 121.0, 4.4, 29.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{18}N$, 248.1434; found, 248.1439.

*1-Methyl-2-(2-phenylpropan-2-yl)-1H-imidazole (**17**).* Following standard procedure A, *n*-methylimidazole (0.08 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and acetone (0.09 mL, 1.2 mmol) provided 2-(1-methyl-1*H*-imidazole-2-yl)propan-2-ol (**17a**, 73 mg, 0.52 mmol, 52%) as a white solid. mp 112−115 °C. The product was purified using silica gel chromatography (100% EtOAc). R_f 0.30 (100% EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.72 (d, J = 1.1 Hz, 1H), 6.65 (d, J = 1.2 Hz, 1H), 4.33 (br s, 1H), 3.81 (s, 3H), 1.57 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 151.4, 125.4, 122.7, 69.9, 34.8, 29.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_7H_{13}N_2O$, 141.1022; found, 141.1023. Following general procedure C, 2-(1-methyl-1*H*-imidazole-2-yl)propan-2-ol (**17a**, 70 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 1-methyl-2-(2-phenylpropan-2-yl)-1*H*-imidazole **17** (98 mg, 0.49 mmol, 98%) as an essentially pure oil. R_f = 0.31 (100% EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32−7.28 (m, 2H), 7.25−7.14 (m, 3H), 7.00 (d, J = 1.2 Hz, 1H), 6.76 (d, J = 1.2 Hz, 1H), 3.06 (s, 3H), 1.77 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 153.5, 147.3, 128.7, 126.3, 125.9, 125.6, 122.4, 40.8, 34.2, 29.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{13}H_{17}N_2$, 201.1386; found, 201.1391.

*2-(2-Phenylpropan-2-yl)thiazole (**18**).* Following general procedure B, 2-acetylthiazole (0.1 mL, 1 mmol) and methyllithium 1.6 M in Et_2O (1.8 mL, 1.1 mmol) produced 2-(thiazol-2-yl)propan-2-ol (**18a**, 110 mg, 0.78 mmol, 78%) as an oil. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f = 0.43 (3:7, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 3.3 Hz, 1H), 7.2 (d, J = 3.3 Hz, 1H), 4.00 (s, 1H), 1.67 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 179.8, 142.1, 118.8, 73.1, 30.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_6H_{10}NOS$, 144.0478; observed, 144.0473. Following general procedure C, 2-(thiazol-2-yl)propan-2-ol (**18a**, 72 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-phenylpropan-2-yl)thiazole **18** (91 mg, 0.45 mmol, 90%) as a white solid (melting point > 260 °C). The product was purified using silica gel chromatography (1:9, EtOAc/hexanes) R_f = 0.60 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73 (d, J = 3.3 Hz, 1H), 7.40−7.22 (m, 6H), 1.89 (s, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 180.4, 147.7, 141.9, 128.3, 126.6, 126.2, 118.6, 44.5, 30.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{12}H_{14}NS$, 204.0842; observed, 204.0842.

*2-(2-Phenylpropan-2-yl)quinoxaline (**19**).* Following general procedure B, 2-quinoxaloyl chloride (192 mg, 1 mmol) and methyllithium 1.6 M in Et_2O (3.6 mL, 2.2 mmol) produced 2-(quinoxalin-2-yl)propan-2-ol (**19a**, 102 mg, 0.54 mmol, 54%) as an oil. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f = 0.31 (3:7, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.05 (s, 1H), 8.16−8.14 (m, 1H), 8.10−8.09 (m, 1H), 7.81−7.78 (m, 2H), 1.72 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 160.5, 142.5, 141.6, 140.2, 130.4, 129.6, 129.1, 128.8, 71.6, 30.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{11}H_{13}N_2O$, 189.1022; found, 189.1026. Following general procedure C, 2-(quinoxalin-2-yl)propan-2-ol (**19a**, 94 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-phenylpropan-2-yl)quinoxaline **19** (55 mg, 0.22 mmol, 44%) as an oil. The product was purified using silica gel chromatography (1:19, EtOAc/hexanes). R_f = 0.87 (1:19, EtOAc/hexanes).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.53 (s, 1H), 8.14 (d, J = 8.2 Hz, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.78−7.74 (m, 2H), 7.35−7.28 (m, 4H), 7.27−7.25 (m, 1H), 1.89 (s, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ163.0, 147.8, 145.9, 140.6, 129.7, 129.4, 129.1, 128.9, 128.6, 126.7, 126.5, 45.1, 28.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{17}H_{17}N_2$, 249.1386; found, 249.1388.

*2-(1-(4-Fluorophenyl)-1-phenylethyl)pyridine (**20**).* Following standard procedure A, 2-bromopyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 4-fluoroacetophenone (0.15 mL, 1.2 mmol) provided 1-(4-fluorophenyl)-1-(pyridin-2-yl)ethanol (**20a**, 191 mg, 0.69 mmol, 69%) as a white solid. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f 0.56 (3:7,

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EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[14] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (d, J = 4.3 Hz, 1H), δ 7.63 (td, J = 6.0 Hz, 1.7), 1H), δ 7.49−7.44 (m, 2H), δ 7.28 (d, J = 8.0 Hz, 1H), δ 7.16 (dd, J = 3.9, 1.0 Hz, 1H), 6.98 (t, J = 8.7 Hz, 2H), δ 5.94, (br s, 1H), 1.92 (s, 3H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 164.6, 163.4, 160.2, 147.5, 143.1 (d, J = 3.2 Hz), 137.1, 127.8, 127.7 (d, J = 8.0 Hz), 122.2, 120.2, 114.9 (d, J = 21.3 Hz), 74.8, 29.4. ^{19}F {^{13}C} NMR (471 MHz, $CDCl_3$): δ −116.2. Following general procedure C, 1-(4-fluorophenyl)-1-(pyridin-2-yl)ethanol (**20a**, 108 mg, 0.5 mmol) benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(1-(4-fluorophenyl)-1-phenylethyl)pyridine **20** (122 mg, 95.0 mmol, 88%) as an oil. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). R_f = 0.54 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, J = 4.8 Hz, 1H), δ 7.59 (td J = 5.9, 1.9 Hz, 1H), δ 7.34−7.25 (m, 3H), 7.19−6.96 (m, 8H), 2.26 (s, 3H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.9, 162.8, 159.6, 148.9, 148.1, 144.0 (d, J = 13.2 Hz), 136.1, 130.3 (d, J = 31 Hz), 128.3 (d, J = 129 Hz), 126.3, 123.5, 121.2, 114.6 (d, J = 83 Hz), 54.6, 29.6. ^{19}F {^{13}C} NMR (471 MHz, $CDCl_3$): δ −117.2. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{19}H_{17}FN$, 278.1340; observed, 278.1347.

*2-(1-Phenylcyclohexyl)pyridine (**21**).* Following standard procedure A, 2-bromopyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and cyclohexanone (0.12 mL, 1.2 mmol) provided 1-(pyridin-2-yl)cyclohexanol (**21a**, 120 mg, 0.68 mmol, 68%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f 0.81 (1:1, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, J = 3.9 Hz, 1H), 7.55 (td J = 6.1, 1.8 Hz, 1H), 7.38−7.25 (m, 5H), 7.16 (t, J = 9.3 Hz, 2H), 7.06 (dd J = 4.9 Hz, 0.7, 1H), 2.62−2.21 (m, 2H), 2.28−2.21 (m, 2H), 1.59−1.51 (m, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.7, 148.5, 147.6, 136.4, 128.3, 127.0, 125.7, 122.2, 120.6, 48.7, 36.1, 29.7, 26.2, 22.9. Following general procedure C, 1-(pyridin-2-yl)cyclohexanol (**21a**, 88 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(1-phenylcyclohexyl)pyridine **21** (91 mg, 0.38 mmol, 77%) as an oil. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). R_f = 0.78 (1:9, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[10] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, J = 3.9 Hz, 1H), 7.6 (td, J = 15.5, 1.8 Hz, 1H), 7.39−7.27 (m, 5H), 7.16 (t, J = 8.4 Hz, 2H), 7.07 (dd J = 4.9, 3.9 Hz, 1H), 2.62−2.55 (m, 2H), 2.28−2.21 (m, 2H), 1.60−1.51 (m, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.7, 148.5, 147.6, 136.4, 128.3, 127.0, 125.7, 122.2, 120.6, 48.7, 36.1, 29.7, 26.2, 22.9.

*2-(1-Phenyl-2,3-dihydro-1H-inden-1-yl)pyridine (**22**).* Following general procedure A, 2-bromopyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 1-indanone (152 mg, 1.2 mmol) provided 1-(pyridin-2-yl)-2,3-dihydro-1*H*-inden-1-ol (**22a**, 175 mg, 0.83 mmol, 83%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f 0.67 (1:1, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[15] ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd J = 3.9, 0.87 Hz, 1H), 7.58 (td, 6.1, 1.7 Hz, 1H), 7.33−7.29 (m, 2H), 7.20−7.16 (m, 2H), 7.06 (dd, J = 6.9, 0.9 Hz, 2H), 6.02 (br s, 1H), 3.30−3.22 (m, 1H), 3.12−3.04 (m, 1H), 2.56 (td, J = 4.2, 2.3 Hz, 2H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 164, 147.6, 147.3, 143.9, 137.1, 128.4, 127.1, 124.9, 124.2, 122.2, 120.3, 84.4, 42.9, 30.4. Following general procedure C, 1-(pyridin-2-yl)-2,3-dihydro-1*H*-inden-1-ol (**22a**, 105 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(1-phenyl-2,3-dihydro-1*H*-inden-1-yl)pyridine **22** (131 mg, 0.48 mmol, 97%) as an oil. The product was purified using silica gel chromatography (1:9, ethyl acetate/hexanes). R_f = 0.56 (1:9, ethyl acetate/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, J = 3.9 Hz, 1H), δ 7.59 (td J = 5.8, 1.8 Hz 1H), 7.35−7.09 (m, 11H), 3.60−3.54 (m, 1H), 3.03−2.95 (m, 2H), 2.70−2.64 (m, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 165.3, 148.8, 148.0, 147.5, 144.6, 136.1, 128.3, 128.1, 127.2, 126.3, 126.2, 124.9, 123.5, 121.2, 64.3, 42.0, 30.8. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{20}H_{18}N$, 272.1434; observed, 272.1437.

*2-((1-Phenyl-2,3-dihydro-1H-inden-1-yl)methyl)pyridine (**23**).* Following standard procedure A, 2-methylpyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 1-indanone (158 mg, 1.2 mmol) provided 1-(pyridin-2-ylmethyl)-2,3-dihydro-1*H*-inden-1-ol (**23a**, 202 mg, 0.9 mmol, 90%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes) R_f = 0.62 (1:1, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (d, J = 4.3 Hz, 1H), 7.64 (td, J = 6.0, 1.7 Hz, 1H), 7.28−7.22 (m, 3H), 7.16−7.11 (m, 1H), 7.04 (t, J = 7.0 Hz, 2H), 3.29−3.10 (m, 2H), 3.05−2.98 (m, 1H), 2.90−2.82 (m, 1H), 2.23−2.19 (m, 2H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 159.5, 148.3, 147.6, 142.4, 137.0, 127.9, 126.4, 124.8, 124.6, 123.2, 121.9, 83.2, 46.0, 40.4, 29.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{15}H_{16}NO$, 226.1226; found, 226.1231. Following general procedure C, 1-(pyridin-2-ylmethyl)-2,3-dihydro-1*H*-inden-1-ol (**23a**, 112 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-((1-phenyl-2,3-dihydro-1*H*-inden-1-yl)methyl)pyridine **23** (133 mg, 0.48 mmol, 96%) as an essentially pure oil. R_f = 0.22 (1:9, EtOAc/hexanes).^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54 (dd, J = 4.2, 0.9 Hz, 1H), 7.49 (td, J = 6.0, 1.8 Hz, 1H), 7.37−7.27 (m, 6H), 7.25−7.14 (m, 4H) 6.61 (d, J = 7.9 Hz, 1H), 3,81 (d, J = 13.1 Hz, 1H), 3.54 9d, J = 13.1 Hz, 1H), 2.78−2.57 (m, 2H), 2.49−2.30 (m, 2H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 157.9, 147.3, 146.8, 144.6, 137.7, 128.3, 127.2, 127.1, 126.3, 126.2, 125.6, 125.2, 124.8, 122.2, 57.1, 47.9, 39.6, 30.5. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{20}N$, 286.1590; found, 286.1596.

*5,5-Diphenyl-5H-indeno[1,2-b]pyridine (**25**).* Following general procedure B, 5*H*-indeno[1,2-*b*]pyridin-5-one (181 mg, 1 mmol) and PhLi 1.9 M in dibutyl ether (2.3 mL, 1.2 mmol) produced 5-phenyl-5*H*-indeno[1,2-*b*]pyridin-5-ol **24** (212 mg, 0.82 mmol, 82%) as a white solid. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f 0.39 (3:7, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[16] Following general procedure C, 5-phenyl-5*H*-indeno[1,2-*b*]pyridin-5-ol **24** (130 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 5,5-diphenyl-5*H*-indeno[1,2-*b*]pyridine **25** (160 mg, 0.49 mmol, 97%) as a white solid (mp 206−207 °C) as an essentially pure product. R_f = 0.44 (1:4, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d, J = 4.8 Hz, 1H), 8.12 (d, J = 7.4 Hz, 1H), 7.73 (d, J = 7.7 Hz, 1H) 7.49−7,41 (m, 3H), 7.28−7.22 (m, 11H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.3, 151.5, 149.0, 145.0, 144.8, 139.3, 133.5, 129.7, 128.4, 128.1, 128.0, 127.0, 126.2, 122.0, 121.2, 63.5. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{24}H_{18}N$, 320.1434; observed, 320.1437.

*5,5-Diphenyl-5H-cyclopenta[1,2-b:5,4-b′]dipyridine (**27**).* Following general procedure B, 5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridin-5-one (180 mg, 1 mmol) and PhLi 1.9 M in dibutyl ether (2.3 mL, 1.2 mmol) produced 5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridin-5-ol **26** (156 mg, 0.6 mmol, 60%) as a white solid. The product was purified using silica gel chromatography (3:1, EtOAc/hexanes). R_f 0.44 (3:1, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[17] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.53 (d, J = 4.0 Hz, 2H), 7.68 (d, J = 7.4 Hz, 2H), 7.38−7.37 (m, 2H), 7.31−7.16 (m, 3H), 7.18−7.14 (m, 2H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 156.9, 150.8, 145.5, 141.0, 132.9, 128.5, 127.9, 125.3, 124.1, 79.8. Following general procedure C, 5-phenyl-5*H*-cyclopenta-[1,2-*b*:5,4-*b*′]dipyridin-5-ol **26** (129 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 5,5-diphenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridine **27** (157 mg, 0.49 mmol, 98%) as an essentially pure, white solid (mp > 260 °C). R_f = 0.47 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.76 (dd, J = 3.6,1.1 Hz, 2H), 7.80 (dd, J = 6.4, 1.4 hz, 2H), 7.33−7.25 (m, 8H), 7.20−7.17 (m, 4H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 157.3, 150.1, 145.8, 133.9, 128.7, 127.8, 127.5, 123.6, 61.7. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{23}H_{17}N_2$, 321.1386; found, 321.1394.

*5-(4-Chlorophenyl)-5-phenyl-5H-cyclopenta[1,2-b:5,4-b′]-dipyridine (**28**) as a Mixture of Isomers (1:6, o/p).* Following general procedure C, 5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridin-5-ol **26** (129 mg, 0.5 mmol), chlorobenzene (0.5 mL, 5 mmol), and triflic

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acid (0.45 mL, 5 mmol) produced 5-(4-chlorophenyl)-5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridine **28** (156 mg, 0.44 mmol, 88%) as a white solid (mp 205−207 °C). The product was purified using silica gel chromatography (1:9, MeOH/EtOAc). R_f 0.57 (1:9, MeOH/EtOAc). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.67 (d, J = 4.7 Hz, 1H), 7.9 (d, J-7.8 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.23−7.14 (m, 4H), 7.07−7.14 (m, 1H), 7.03 (d, J = 8.6 Hz, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 157.7, 157.6, 150.5, 150.4, 145.2, 145.2, 140.1, 133.8, 133.5, 133.4, 132.5, 130.6, 129.2, 129.1,128.8, 127.8, 127.2, 126.8, 123.5, 123.5, 61.8, 61.1. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{23}H_{16}ClN_2$, 355.0997; found, 355.1000.

*5-(4-Bromophenyl)-5-phenyl-5H-cyclopenta[1,2-b:5,4-b′]-dipyridine (**29**) as a Mixture of Isomers (1:3, o/p).* Following general procedure C, 5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridin-5-ol **26** (129 mg, 0.5 mmol), bromobenzene (0.52 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 5-(4-bromophenyl)-5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridine **28** (92 mg, 0.42 mmol, 84%) as a white solid. The product was purified using silica gel chromatography (10% MeOH/EtOAc). R_f = 0.52 (10% MeOH/EtOAc). mp 220−222 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.78 (d, J = 4.0 Hz, 2H), 8.05 (d, J = 7.9 Hz, 1H), 7.78 (dd, J-6.5, 1.3 Hz, 2H), 7.41−7.37 (m, 2H), 7.35−7.31 (m, 2H), 7.29−7.26 (m, 5H), 7.18−7.15 (m, 3H), 7.07−7.04 (m, 2H): ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 156.8, 150.1, 145.4, 142.8, 142.6, 134.7, 134.0, 131.8, 129.5, 128.9, 128.8, 127.8, 127.7, 127.2, 123.8, 121.7, 61.3. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{23}H_{15}BrN_2Na$, 421.0311; found, 421.0309.

*5-(4-Dodecylphenyl)-5-phenyl-5H-cyclopenta[1,2-b:5,4-b′]-dipyridine(1:3-O:P) (**30**) as a Mixture of Isomers (1:3, o/p).* Following general procedure C, 5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridin-5-ol **26** (129 mg, 0.5 mmol), 1-dodecylbenzene (0.57 mL, 2 mmol), and triflic acid (0.45 mL, 5 mmol) produced 5-(4-dodecylphenyl)-5-phenyl-5*H*-cyclopenta[1,2-*b*:5,4-*b*′]dipyridine **30** (156 mg, 0.44 mmol, 88%) as a white solid. The product was purified using silica gel chromatography (1:9, MeOH/EtOAc). R_f = 0.83 (1:9, MeOH/EtOAc). mp 120−121 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.81−8.63 (m, 2H), 7.73 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 7.7 Hz, 1H), 7.24−7.10 (m, 9H), 6.68 (s, 2H), 2.47 (t, J = 8.0 Hz, 1H), 1.62−1.47 (m, 2H), 1.21−1.18 (m, 16H), 0.86−0.79 (m, 4H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 159.9, 149.8, 146.2, 143.6, 142.4, 140.4, 134.2, 128.8, 128.7, 128.6, 128.1, 127.8, 127.7, 126.9, 123.7, 61.5, 35.5, 31.9, 31.3, 29.7, 29.63, 29.57, 29.5, 29.4, 29.3, 23.7, 23.0, 22.7, 14.1. HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_{35}H_{40}N_2Na$, 511.3084; found, 511.3081.

*9,9-Diphenyl-9H-indeno[1,2-b]pyrazine (**32**).* Following general procedure B, 9*H*-indeno[1,2-*b*]pyrazin-9-one (232 mg, 1 mmol) and PhLi 1.9 M in dibutyl ether (2.3 mL, 1.2 mmol) produced 9-phenyl-9*H*-indeno[1,2-*b*]pyrazin-9-ol **31** (149 mg, 0.82 mmol, 82%) as a white solid. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f = 0.39 (3:7, EtOAc/hexanes). mp 210−211 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.45 (d, J = 2.8 Hz, 1H), 8.33 (d, J = 2.8 Hz, 1H), 8.04−8.02 (m, 1H), 7.55−7.50 (m, 2H), 7.46−7.39 (m, 3H), 7.34−7.31 (m, 3H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 149.2, 147.1, 144.1, 142.4, 140.7, 136.4, 131.7, 130.1, 128.6, 128.1, 126.8, 125.6, 125.3, 122.0, 80.5. High-resolution MS [M + H]$^+$ calcd for $C_{17}H_{12}N_2O$, 261.1022; found, 261.1027. Following general procedure C, phenyl-9*H*-indeno[1,2-*b*]pyrazin-9-ol **31** (130 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 9,9-diphenyl-9*H*-indeno[1,2-*b*]pyrazine **32** (152 mg, 0.47 mmol, 95%) as a white solid. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f = 0.93 (3:7, EtOAc/hexanes). mp > 260 °C ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51−8.47 (m, 2H), 8.18−8.15 (m, 1H), 7.55−7.51 (m, 3H), 7.39 (s, 2H), 7.28−7.22 (m, 8H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.9, 148.9, 148.8, 145.6, 140.3, 139.1, 131.4, 129.2, 128.7, 127.9, 127.1, 124.5, 123.0, 121.89, 121.86, 121.0, 66.1. High-resolution MS [M + H]$^+$ calcd for $C_{23}H_{16}N_2$, 321.1386; found, 321.1393.

*11,11-Diphenyl-11H-indeno[1,2-b]quinoxaline (**34**).* Following general procedure B, 11*H*-indeno[1,2-*b*]quinoxalin-11-one (182 mg, 1 mmol) and PhLi 1.9 M in dibutyl ether (2.3 mL, 1.2 mmol) produced 11-phenyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ol **33** (264 mg, 0.85 mmol, 85%) as a white solid. The product was purified using silica gel chromatography (1:4, EtOAc/hexanes). R_f = 0.22 (1:4, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[18] ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.15−8.10 (m, 2H), 8.03−8.01 (m, 1H), 7.76−7.64 (m, 3H), 7.54−7.50 (m, 3H), 7.44−7.42 (m, 2H), 7.31−7.29 (m, 2H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 143.0, 142.1, 130.9, 130.0, 129.2, 128.7, 128.4, 128.3, 127.5, 127.4, 63. High-resolution MS [M + H]$^+$ calcd for $C_{21}H_{14}N_2O$, 311.1179; observed, 311.1182. Following general procedure C, 11-phenyl-11*H*-indeno[1,2-*b*]quinoxalin-11-ol **33** (155 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 11,11-diphenyl-11*H*-indeno[1,2-*b*]quinoxaline **34** (172 mg, 0.47 mmol, 93%) as a white solid. The product was purified using silica gel chromatography (1:4, EtOAc/hexanes). R_f = 0.84 (1:4, EtOAc/hexanes). mp 205−206 °C. Spectroscopic data are consistent with those reported previously.[18] ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.92 (d, J = 7.7 Hz, 1H), 8.71 (dd, J = 7.5, 0.8 Hz, 1H), 8.35 (dd, J = 7.0, 1.3 Hz, 1H), 8.11−8.01 (m, 2H), 7.91−7.86 (m, 1H), 7.82−7.76 (m, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.35−7.33 (m, 6H), 7.28−7.25 (m, 4H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.8, 154.8, 146.8, 142.6, 140.9, 137.3, 134.6, 132.2, 130.8, 130.5, 128.8, 128.5, 128.3, 128.0, 127.8, 122.4, 118.2, 63.8. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{27}H_{19}N_2$, 371.1543; found, 371.1546.

*2-(2-Methyl-1-phenylcyclohexyl)pyridine (**36**) Formed as the Mixture of Diastereomers.* Following general procedure A, 2-bromopyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 2-methylcyclohexanone (0.134 mg, 1.2 mmol) provided 2-methyl-1-(pyridin-2-yl)cyclohexanol **35** (120 mg, 0.68 mmol, 68%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f = 0.81 (1:1, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.46 (d, J = 4.9 Hz, 1H), 7.66 (td J = 3.1,1.7 Hz, 1H), 7.32 (d, J = 2.9 Hz, 1H), 7.15−7.13 (m, 1H), 5.20 (s, 1H), 1.84−1.75 (m, 3H), 1.71−1.53 (m, 5H), 1.42−1.38 (m, 1H), 0.48 (d, J = 6.7 Hz, 3H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 165.0, 146.9, 136.9, 121.6, 119.1, 74.8, 40.4, 40.3, 30.6, 26.3, 22.0, 15.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{12}H_{18}NO$, 192.1383; observed, 192.1382. Following general procedure A, 2-methyl-1-(pyridin-2-yl)cyclohexanol **35** (96 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2-methyl-1-phenylcyclohexyl)pyridine **36** (170 mg, 0.34 mmol, 68%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f = 0.81 (1:1, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): 8.60 (d, J = 4.9 Hz, 1H), 8.53 (d, J = 4.9 Hz, 1H), 7.65−7.60 (m,1H), 7.59−7.56 (m, 1H), 7.43−7.41 (m, 2H), 7.37−7.73 (m, 4H), 7.30−7.28 (m 3H), 7.25−7.21 (m, 2H), 7.18−7.16 (m, 1H), 7.15−7.07 (m, 3H), 3.21−3.19 (m, 1H), 2.81−2,76 (m, 1H), 2.57−2.52 (m, 1H), 2.42−2.39 (m, 1H), 2.32−2.25 (m, 2H), 2.18−2.16 (m, 1H), 2.08−1.80 (m, 8H), 1.72−1.61 (m, 3H), 1.41−1.36 (m, 2H), 0.84 (d, J = 6.6 Hz, 3H), 0.76 (d, J = 6.5 Hz, 3H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 165.5, 165.4, 149.3, 149.1, 147.3, 145.3, 136.2, 136.1, 128.3, 128.3, 127.5, 127.5, 126.8, 125.9, 125.4, 122.5, 121.9, 121.1, 120.9, 53.7, 53.1, 48.4, 44.1, 43.1, 38.6, 37.0, 37.0, 36.8, 36.4, 36.0, 34.1, 34.1, 31.6, 30.1, 29.6, 28.7,20.6, 20.4, 20.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{22}N$, 252.1747; observed, 252.1753.

*2-(2,4-Dimethyl-2-phenylpentan-3-yl)pyridine (**40**).* Following general procedure A, 2-bromopyridine (0.1 mL, 1 mmol), *n*-BuLi (0.44 mL, 1.1 mmol), and 2,4-dimethylpentan-3-one (0.17 mL, 1.2 mmol) provided 2,4-dimethyl-3-(pyridin-2-yl)pentan-3-ol **39** (166 mg, 0.86 mmol, 86%) as an oil. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). R_f = 0.80 (1:9, EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.49 (d, J = 4.8 Hz, 1H), 7.63 (td J = 6.1, 1.4 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 7.15 (dd, J = 4.9, 2.4 Hz, 1H), 5.55 (s, 1H), 2.28 (sxt J = 6.8 Hz, 2H), 0.79 (d, J = 6.8 Hz, 6H), 0.75 (d, J = 7.0 Hz, 6H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.5, 146.8, 135.9, 121.6, 120.6, 79.6, 34.2, 17.5, 16.7. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{12}H_{20}NO$, 194.1539; observed, 194.1543. Following general procedure C, 2,4-dimethyl-3-(pyridin-2-yl)pentan-3-ol (97 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(2,4-dimethyl-

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2-phenylpentan-3-yl)pyridine **40** (113 mg, 0.45 mmol, 89%) as an oil. The product was purified using silica gel chromatography(1:9, EtOAc/hexanes). R_f = 0.40 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.61 (d J = 3.9 Hz, 1H), 7.56 (td, J = 5.8, 1.9 Hz, 1H), 7.52−7.49 (m, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.20−7.10 (m, 3H), 3.09 (d, J = 8.7 Hz, 1H), 2.30 (q, J = 4.4 Hz, 1H), 1.66 (s, 3H), 0.95 (s, 3H), 0.60 (dd, J = 12.9, 6.6 Hz, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 163.7, 151.7, 148.7, 135.2, 127.8, 126.2, 125.3, 125.2, 121.0, 64.0, 41.2, 32.3, 29.8, 23.3, 23.0, 22.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for$C_{18}H_{23}N$, 254.1903; observed, 254.1912.

*2-(4-Deutero-2,4-dimethyl-2-phenylpentan-3-yl)pyridine (**42**).* 2,4-Dimethyl-3-pentanone (224 mg, 2 mmol) was placed in a nitrogen flushed flask, and 1 mL of 37% DCl in D_2O was added. The mixture was stirred for 6 h at room temperature. The mixture was then quenched with sodium bicarbonate and extracted with chloroform, washed with brine, and dried over sodium sulfate. Removal of the solvent provided 2,4-dideutero-2,4-dimethyl-3-pentanone as an oil (+99% deuterium incorporation). ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.02 (br s, 12H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 38.3 (C-D, t, J = 19.5 Hz), 18.3 (carbonyl ^{13}C resonance not visible). HRMS (ESI-TOF): m/z [M + Na]$^+$ calcd for $C_7H_{12}D_2ONa$, 139.1062; observed, 139.1059. Following general procedure A, 2-bromopyridine (0.1 mL, 1 mmol), n-BuLi (0.44 mL, 1.1 mmol), and 2,4-dideutero-2,4-dimethyl-3-pentanone (140 mg, 1.2 mmol) provided 2,4-dideutero-2,4-dimethyl-3-(pyridin-2-yl)pentan-3-ol **41** (171 mg, 1.06 mmol, 88%) as an oil. The product was purified using silica gel chromatography (1:1, EtOAc/hexanes). R_f 0.80 (1:1, EtOAc/hexanes).^{1}H NMR (500 MHz, $CDCl_3$): δ 8.52 (d, J = 4.9 Hz 1H), 7.66 (td, J = 5.8, 1.7 Hz, 1H), δ 7.26 (d, J = 8.0 Hz, 1H), 7.20−7.17 (m, 1H), 5.55 (s, 1H), 0.79 (d, J = 21.7 Hz, 12H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 161.6, 146.8, 135.9, 121.6, 120.6, 79.6, 33.8 (C-D, t, J = 19.4 Hz), 17.4, 16.6. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{12}H_{18}D_2NO$, 196.1665; observed, 196.1664. Following general procedure C, 2,4-dideutero-2,4-dimethyl-3-(pyridin-2-yl)-pentan-3-ol (98 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) produced 2-(4-deutero-2,4-dimethyl-2-phenylpentan-3-yl)pyridine **42** (116 mg, 0.46 mmol, 91%) as an oil. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). R_f = 0.4 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d J = 3.9 Hz, 1H), 7.57 (td J = 5.8, 1.9 1H), 7.52−7.49 (m, 2H), 7.34−7.28 (m, 2H), 7.20−7.10 (m, 3H), 3.09 (s, 1H), 1.66 (s, 3H), 0.95 (s, 3H), 0.59 (d, J = 12.9 Hz, 6H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 163.7, 151.7, 148.6, 135.2, 127.8, 126.2, 125.3, 125.2, 121.0, 63.9, 41.2, 32.3, 29.4 (C-D, t, J = 19.5 Hz), 23.2, 22.9, 22.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{18}H_{23}DNO$, 255.1966; observed, 255.1974.

*2-(2-Phenyladamantan-2-yl)pyridine (**46**).* Following general procedure A, 2-bromopyridine (0.5 mL, 5 mmol), n-BuLi (2.2 mL, 5.5 mmol), and 2-adamantanone (900 mg, 6 mmol) provided 2-(pyridin-2-yl)adamantan-2-ol **45** (625 mg, 55%) as a white solid. The product was purified using silica gel chromatography (3:7, EtOAc/hexanes). R_f 0.45 (3:7, EtOAc/hexanes). Spectroscopic data are consistent with those reported previously.[19] ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.55 (d, J = 2.4 Hz, 1H), 7.69 (t, J = 1.0 Hz, 1H), 7.49 (dd, J = 4.8, 0.4 Hz, 1H), 7.14−7.17 (m, 1H), 2.69 (br s, 1H), 2.44 (d, J = 5.1 Hz, 3H), 1.92 (s, 1H), 1.80−1.65 (m, 9H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 164.1, 149.2, 136.6, 122.0, 120.1, 37.7, 35.1, 34.8, 32.0, 27.3, 27.0. Similar to general procedure C, 2-(pyridin-2-yl)adamantan-2-ol (114 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) reacted at 0 °C using a ice bath for 1 h, which provided 2-(2-phenyladamantan-2-yl)pyridine **46** (143 mg, 0.49 mmol, 99%) as a white solid. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). mp 154−156 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.56−8.53 (m, 1H), 7.58−7.48 (m, 3H), 7.40−7.37 (m, 1H), 7.28 (t, J = 7.4 Hz, 1H), 7.11−7.06 (m, 1H), 6.92 (dd, 4.8, 1.0 Hz, 1H), 3.48 (s, 2H), 2.10−1.96 (m, 4H), 1.86−1.76 (m, 8H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.8, 148.9, 146.8, 136.2, 128.4, 126.5, 125.2, 120.8, 119.9, 53.4, 38.0, 33.8, 33.3, 32.0, 27.7, 27.6. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{24}N$, 290.1915; found, 290.1903.

*2-(2-(p-Tolyl)adamantan-2-yl)pyridine (**47**) Formed as a Mixture of Isomers (1:13, o/p).* Similar to general procedure C, 2-(pyridin-2-yl)adamantan-2-ol (**45**, 114 mg, 0.5 mmol), toluene (0.53 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) reacted at 0 °C using an ice bath for 1 h, which provided 2-(2-(*p*-tolyl)adamantan-2-yl)pyridine **47** (150 mg, 0.49 mmol, 99%) as a white solid. The product was purified using silica gel chromatography (1:9 EtOAc/hexanes). R_f = 0.69 (1:9 EtOAc/hexanes). mp 172−174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.63 (d, J = 4.8 Hz, 1H), 8.04 (7.7 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.28 (t, J = 4.4 Hz, 1H), 7.11 (d, J = 8.1 Hz, 2H), 3.48 (br s, 2H), 2.21 (s, 3H), 2.04−1.73 (m, 12H). ^{13}C {^{1}H} NMR (125 MHz, $CDCl_3$): δ 167.1, 148.9, 143.8, 136.2, 134.5, 129.2, 126.4, 120.7, 119.9, 53.1, 38.1, 33.8, 33.4, 32.0, 27.7, 27.6, 20.9. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{22}H_{26}N$, 304.2060; found, 304.2071.

*2-(2-(4-Chlorophenyl)adamantan-2-yl)pyridine (**48**).* Following general procedure C, 2-(pyridin-2-yl)adamantan-2-ol (**45**, 114 mg, 0.5 mmol), chlorobenzene (0.5 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) provided 2-(2-(4-chlorophenyl)adamantan-2-yl)pyridine **48** (136 mg, 0.42 mmol, 84%) as a white solid. mp 132−133 °C. The product was purified using silica gel chromatography (1:9, EtOAc/hexanes). R_f = 0.51 (1:9, EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.54−8.51 (m, 1H), 7.54 (td, J = 5.6, 1.9 Hz, 1H), 7.47−7.43 (m, 2H), 7.35−7.33 (d, J = 8.1 Hz, 1H), 7.23−7.20 (m, 2H), 6.96 (dd, J = 4.8, 1.0 Hz), 3.39 (br s, 2H), 1.97 (t, J = 13.0 Hz, 4H), 1.83−1.74 (m, 8H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.3, 149.1, 145.4, 136.3, 130.8, 128.5, 128.0, 120.7, 120.1, 53.1, 37.9, 33.7, 33.1, 31.9, 27.6, 27.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{23}ClN$, 324.1514; found, 324.1519.

*2-(2-(4-Bromophenyl)adamantan-2-yl)pyridine (**49**).* Following general procedure C, 2-(pyridin-2-yl)adamantan-2-ol (114 mg, 0.5 mmol), bromobenzene (0.52 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) provided 2-(2-(4-bromophenyl)adamantan-2-yl)pyridine **49** (156 mg, 0.43 mmol, 85%) as a white solid (mp 135−136 °C). The product was purified using silica gel chromatography(1:9, ethyl acetate/hexanes). R_f = 0.84 (1:9, ethyl acetate/hexanes).^{1}H NMR (300 MHz, $CDCl_3$ with TMS): δ 8.53 (4.8, 1.0 Hz, 1H), 7.51 (td, 8.0, 1.9 Hz, 1H_, 7.43−7.32 (m, 5H), 6.96−6.92 (m, 1H), 3.40 (br s, 2H), 2.00 (t, J = 13.1 Hz, 4H), 1.83−1.74 (8H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 166.2, 149.1, 145.9, 136.3, 131.4, 128.5, 120.7, 120.2, 119.0, 53.2, 37.9, 33.7, 33.2, 31.9, 27.6, 27.4. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{24}BrN$, 368.1008; found, 368.1016.

*2-(1-Phenyladamantan-2-yl)pyridine (**50**).* Similar to general procedure C, 2-(pyridin-2-yl)adamantan-2-ol (114 mg, 0.5 mmol), benzene (0.45 mL, 5 mmol), and triflic acid (0.45 mL, 5 mmol) reacted at 50 °C using a sand bath for 15 h, provided 2-(1-phenyladamantan-2-yl)pyridine **50** (126 mg, 0.44 mmol, 87%) as a white solid. mp 121−123 °C. The product was purified using silica gel chromatography (1:9, ethyl acetate/hexanes). R_f = 0.56 (1:9, ethyl acetate/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.51 (d, J = 4.8 Hz, 1H), 7.46 (td J = 5.9, 1.9 Hz, 1H), 7.20−7.16 (m, 3H), 7.11−7.06 (m, 2H), 7.03−6.93 (m, 2H), 3.78 (s, 1H), 2.86 (d, J = 12.9 Hz, 1H), 2.36−2.17 (m, 6H), 2.07−2.01 (m,1H), 1.90−1.77 (m, 4H), 1.61−1.56 (m, 1H). ^{13}C {^{1}H} NMR (75 MHz, $CDCl_3$): δ 167.6, 148.7, 144.4, 135.9, 129.3, 127.5, 124.9, 120.5, 119.8, 53.2,48.1, 42.2, 39.6, 37.5, 36.5, 35.4, 30.7, 29.3, 28.3. HRMS (ESI-TOF): m/z [M + H]$^+$ calcd for $C_{21}H_{24}N$, 290.1903; observed, 290.1913.

■ 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.3c00403.

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Literature references for known compounds and NMR spectra of new compounds (PDF)

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Author Contributions

Preliminary studies were done by M.V.A. The experimental work was done largely by J.C.H. The project was conceived by D.A.K.. The low temperature NMR studies were done by D.A.K. and J.C.H. The manuscript was written by D.A.K. and J.C.H.

Notes

The authors declare no competing financial interest.

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