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Ligand-Controlled Synthesis of Azoles via Ir-Catalyzed Reactions of Sulfoxonium Ylides with 2-Amino Heterocycles

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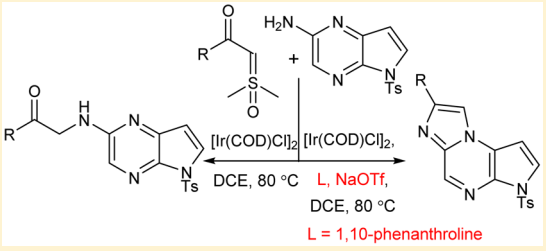
Supporting Information

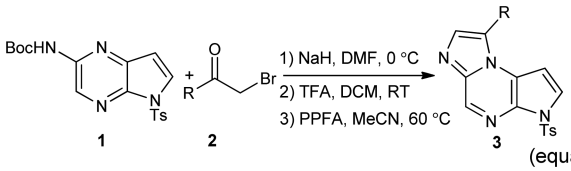
ABSTRACT: An iridium-catalyzed method was developed for the synthesis of imidazo-fused pyrrolopyrazines. The presence or absence of a nitrogenated ligand controlled the outcome of the reaction, leading to simple β-keto amine products in the absence of added ligand and the cyclized 7- and 8-substituted-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine products in the presence of ligand. This catalyst control was conserved across a variety of ylide and amine coupling partners. The substrate was shown to act as a ligand for the iridium catalyst in the absence of other ligands via NMR spectroscopy. Kinetic studies indicated that formation of the Ir-carbene was reversible and the slow step of the reaction. These mechanistic investigations suggest that the β-keto amine products form via an intramolecular carbene N−H insertion, and the imidazopyrrolopyrazines form via an intermolecular carbene N−H insertion.



INTRODUCTION

β-Keto sulfoxonium ylides are crystalline, bench-stable compounds that function as precursors to metal-carbene complexes.[1−9] These metal-carbene intermediates are known to insert into X−H bonds (X = N, O, S) to generate molecules of synthetic interest; however, only a limited number of examples have been reported.[1,2,10−14] In contrast, the insertion of metal carbenes generated from diazo compounds into X−H bonds has been well-documented.[15−18] In many cases, the use of diazo compounds on large scales is challenging, due to safety issues resulting from rapid exotherm upon reaction and the generation of stoichiometric nitrogen gas as a byproduct.[19−23] Sulfoxonium ylides are a more practical alternative to diazo compounds, as they are safer to synthesize and generate only nonvolatile dimethyl sulfoxide (DMSO) as the byproduct of metal-carbenoid formation.[3] In fact, sulfoxonium ylides have been employed on a manufacturing scale in the synthesis of the CRTH2 antagonist MK-7246.[12] We are interested in further exploring the chemistry of metal-carbenoids generated from sulfoxonium ylides for the syntheses of pharmaceutically relevant molecules.

Imidazo-fused pyrrolopyrazines act as kinase inhibitors and have been shown to be effective for treatment of oncological and immunological diseases.[24,25] In a previous report, our research group described the synthesis of azole **3** via reactions of **1** with a series of α-bromo ketones **2**, followed by Boc-deprotection and intramolecular cyclization under acidic conditions (eq 1).[26] Although **3** was obtained in good yields, many of the α-bromo ketones utilized were lachrymatory oils that were both challenging to purify and unstable under ambient conditions.[27−30]



(equation 1)

An alternative approach to access **3** from readily available, crystalline starting materials can be envisaged through insertion of a metal-carbenoid generated from β-keto sulfoxonium ylide **5** into the N−H bond of 5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-amine **4** (eq 2).

Indeed, the N−H insertion product **6** was obtained in moderate yields (40−50%) under conditions similar to that reported by Mangion and co-workers for reactions of aromatic amines with sulfoxonium ylides (eq 3).[2,10] In addition to the expected acyclic N−H insertion product **6**, the cyclized azole **7** (a regioisomer of **3**) was observed as a minor product in the Ir-catalyzed reaction.

Intrigued by the facile cyclization to **7** in the absence of a dehydrating agent, we wondered if the selectivity of the Ir-catalyzed reaction could be inverted to favor formation of **7** directly from **4** and **5**. We describe herein a general method for the regioselective synthesis of 7- and

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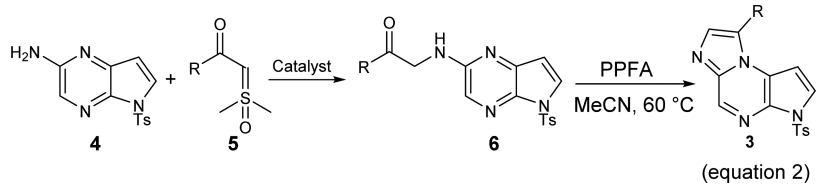
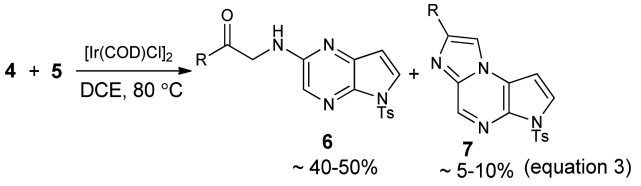


(equation 2)



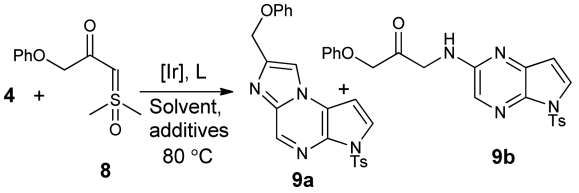
(equation 3)

8-substituted-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazines from Ir-catalyzed reactions of 5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-amine and *β*-keto sulfoxonium ylides. The nature of the ligand on Ir was found to significantly impact the selectivity of the reaction. In addition to imidazo-fused pyrrolopyrazines, a variety of azoles derived from other aryl amidines could also be easily accessed in high yields and selectivity.

RESULTS AND DISCUSSIONS

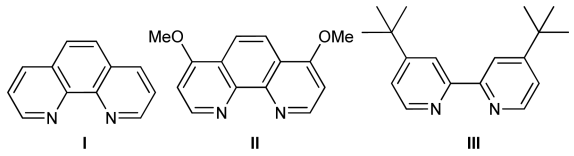
Amine **4** reacted with sulfoxonium ylide **8** in the presence of catalytic $[Ir(COD)Cl]_2$ (COD = 1,5-cyclooctadiene) to form **9b** in 42% yield along with 10% of **9a** (Table 1, entry 1).[2]

Table 1. Evaluation of Reaction Parameters for Ir-Catalyzed N−H Insertion Reaction To Favor Formation of Azole 9a[c]



entry	L	solvent	additive[a]	9a (%)	9b (%)	9a/9b
1	none	DCE	none	10	42	0.24
2	none	DCE	4 Å MS	9	57	0.16
3	none	DCE	4 Å MS, $NaBArF_{24}$	5	17	0.29
4	**I**	DCE	none	11	16	0.69
5	**I**	DCE	$NaBArF_{24}$	57	4	14
6	**I**	DCE	4 Å MS, $NaBArF_{24}$	60	5	12
7	**II**	DCE	4 Å MS, $NaBArF_{24}$	26	4	6.5
8	**III**	DCE	4 Å MS, $NaBArF_{24}$	52	6	8.7
9	**I**	DCE	4 Å MS, NaOTf	67	6	11
10[b]	**I**	DCE	4 Å MS, NaOTf	81	5	16

[a]5 mol %. [b]**4** (1.0 equiv) and **8** (1.5 equiv) were used. [c]All experiments were conducted with **4** (1.5 equiv), **8** (1 equiv), $[Ir(COD)Cl]_2$ (2.5 mol %), L (5 mol %), and 4 Å MS (240 wt % with respect to ylide) in DCE (0.25 M) at 80 °C unless stated otherwise. The yield and ratio of **9a** and **9b** were determined by HPLC analysis of the reaction mixture at 210 nm.



Significant amounts of the unreacted starting materials **4** and **8** remained after 24 h at 80 °C; no further conversion was observed by allowing the reaction to proceed for a longer time. A slightly improved yield of **9b** was observed upon addition of 4 Å molecular sieves to the reaction mixture (entry 2). A cationic Ir-complex generated *in situ* by addition of sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate ($NaBArF_{24}$) formed an inferior catalyst and afforded **9b** in only 17% yield (entry 3). We speculated that the moderate yield of **9b** was due to the inhibition of the Ir-catalyst by the reaction byproduct, DMSO.[31] In addition, **4**, **9a**, and **9b** could bind to Ir and inhibit reaction.[2]

Our approach to improving the yield of **9b** was to overcome the suspected catalytic inhibition by introducing a ligand onto Ir that would form a more robust catalyst. The use of 1,10-phenanthroline (**I**) formed **9b** in a disappointing yield; however, **9a** was formed in a noticeably higher ratio (compare entries 1 and 4). To our surprise, the addition of substoichiometric amounts of $NaBArF_{24}$ to a mixture of $[Ir(COD)Cl]_2$ and **I** formed a catalyst system that inverted the selectivity of the reaction and favored formation of the cyclized product **9a** over **9b** in 14:1 ratio (entry 5) providing **9a** in a synthetically useful yield. The beneficial effect of the tetra-arylborate counteranion on the overall yield of the reaction is in contrast to the much lower yield observed when $NaBArF_{24}$ was used with $[Ir(COD)Cl]_2$ in the absence of added ligand. As observed earlier, addition of molecular sieves to the reaction led to a slightly improved yield (entry 6). 4,7-Dimethoxy-1,10-phenanthroline (**II**) and 4,4′-*tert*-butylpyridine (**III**) also favored **9a** as the major product but were inferior to **I** (entries 7 and 8). Other nitrogen containing ligands and triphenylphosphine formed **9b** as the major product,[32] clearly indicating that the nature of ligand on Ir impacts both the selectivity and yield of the reaction. Of the noncoordinating counteranion additives explored, the highest yield of **9a** was observed in the presence of NaOTf (entry 9), and further improvement in the yield was observed by using 1.5 equiv of the sulfoxonium ylide **8** (entry 10).[33] No product formation was observed in the absence of $[Ir(COD)Cl]_2$.

Having established optimal reaction conditions to selectively form **9a**, the scope of the sulfoxonium ylide was explored. Reactions of ylides containing either alkyl (Table 2, entries 1 and 2) or electron-poor aryl groups (Table 2, entries 3 and 4) adjacent to the carbonyl formed azoles in higher selectivity than reactions of sulfoxonium ylides containing electron-rich aryl groups (entries 8 and 9) adjacent to the carbonyl. Nitro, ester, bromo, ether, *N*,*N*-dimethylamino and thiophene functionalities were all well-tolerated under the reaction conditions providing azoles in synthetically useful yields. Moderate to good selectivity for the formation of **9**−**19a** over **9**−**19b** was observed utilizing a wide range of sterically and electronically varied *β*-keto sulfoxonium ylides. The selectivity could be reversed to favor *β*-keto amine products by conducting the Ir-catalyzed N−H insertion reaction in the absence of **I** and NaOTf (Condition B). Under these conditions, *β*-keto amines **9b**, **12b**, **14b**, and **18b** were prepared with high selectivity over the corresponding cyclic products **9a**, **12a**, **14a**, and **18a**.

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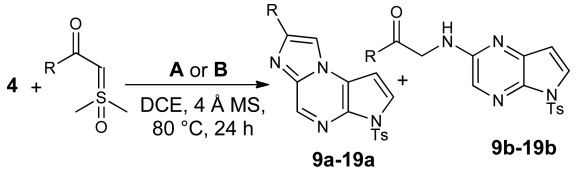
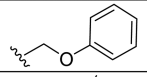
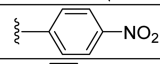
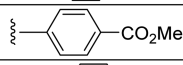
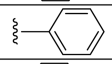
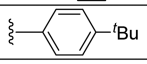
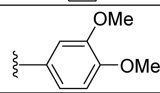
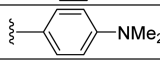
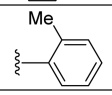
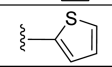
Table 2. Substrate Scope of Ir-Catalyzed Reaction of 2-Tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (4) with *β*-Keto Sulfoxonium Ylides[d]



A: $[Ir(COD)Cl]_2$ (2.5 mol%), **I** (5 mol%), NaOTf (5 mol%)
B: $[Ir(COD)Cl]_2$ (2.5 mol%)

entry	R =	Condition	yield[a]	ratio of products[b]
1		**A** **B**	65 42	**9a**/**9b** = 16:1 = 1:4
2		**A**	66	**10a**/**10b** = 16:1
3		**A**	37	**11a**/**11b** = NA[c]
4		**A** **B**	49 37	**12a**/**12b** = NA[c] = 1:19
5		**A**	64	**13a**/**13b** = 5:1
6		**A** **B**	60 31	**14a**/**14b** = 7:1 = 1:31
7		**A**	60	**15a**/**15b** = 5:1
8		**A**	49	**16a**/**16b** = 3:1
9		**A**	49	**17a**/**17b** = 4:1
10		**A** **B**	63 33	**18a**/**18b** = 4:1 = 1:48
11		**A**	41	**19a**/**19b** = 4:1

[a]Isolated yield. [b]Ratio was determined by ^{1}H NMR spectroscopy. [c]The *β*-keto amine was not detected in the ^{1}H NMR spectra of the crude reaction mixture. [d]All experiments were run with **4** (1 equiv) and ylide (1.5 equiv).

The scope of other aryl amidines (**21**–**24**) that could engage with ylide **20** was also explored (Table 3). Good to excellent selectivity for **25a**–**28a** over **25b**–**28b** was observed providing rapid access to pharmaceutically relevant heterocyclic compounds in high yields. The extent of selectivity for the formation of azole over *β*-keto amine depended on the nature of the aryl amidine. While azoles **26a** and **28a** were the only products observed in the reactions of quinolin-2-amine and pyrimidin-2-amine (entries 2 and 4), **25a** and **27a** were favored over **25b** and **27b** in 24:1 and 11:1 ratios, respectively (entries 1 and 3).

The underlying reasons for the influence of ligand and counteranion on the selectivity of Ir-catalyzed reactions of *β*-keto sulfoxonium ylides with **4** is not immediately obvious. As discussed above, while *β*-keto amines are the preferred product in the presence of $[(COD)IrCl]_2$, azoles are the preferred product in the presence of $[(COD)IrCl]_2$, **I**, and NaOTf. No conversion of the *β*-keto amines **9b** to azoles **9a** was observed when isolated **9b** was heated for 24 h at 80 °C in the presence of $[(COD)IrCl]_2$, **I**, and NaOTf, suggesting that **9b** and **9a** were formed via divergent pathways. The mechanism of generation of Ir-carbene intermediates from sulfoxonium ylides and the subsequent reaction of the carbene intermediate with amines have not been studied in detail.[34,35] We propose that **4** acts as a supporting ligand for Ir in the absence of added ligand to form the four-coordinate intermediate **A** (Figure 1, left). The Ir-amine complex **A** reacts with sulfoxonium ylide to form the Ir-carbene intermediate **B**, and intramolecular reaction of amine with Ir-carbenoid forms **C**. Protonation of Ir-enolate forms Ir complex **D**, which undergoes ligand exchange to release the product and reform complex **A**. In contrast, when 1,10-phenanthroline is introduced as a ligand in the presence of NaOTf, formation of the four-coordinate Ir-complex **E** from the reaction of $[(COD)IrCl]_2$ with 1,10-phenanthroline and NaOTf likely occurs before coordination of the amine substrate **4** to the metal (Figure 1, right). Complex **E** reacts with sulfoxonium ylide to form the Ir-carbene intermediate **F**. Intermolecular reaction of **4** with **F** generates intermediate **G**, which tautomerizes to form intermediate **H**. Protonation of Ir-enolate reforms complex **E** and generates imine **J** that cyclizes to form azole **9a**.

The hypothesis proposed in Figure 1 was supported by following the interaction of $[(COD)IrCl]_2$ with **4** and 1,10-phenanthroline by ^{1}H–^{15}N HMBC NMR spectroscopy (Figure 2). Consistent with literature reports,[36] ^{15}N signals for **b** and **c** were observed at −86 and −119.8 ppm, while **d** was observed at −207.9 ppm. The ^{15}N signal for **a** is expected between −300 to −330 ppm but was not observed. The broad ^{1}H signal observed for the $-NH_2$ protons most likely causes

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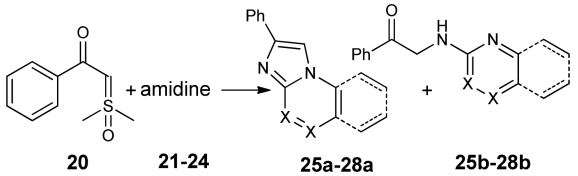
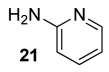
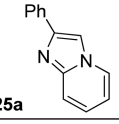
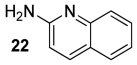
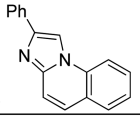
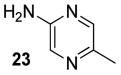
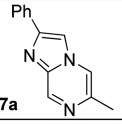
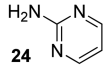
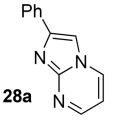
Table 3. Substrate Scope of Ir-Catalyzed Reaction of 20 with Aryl Amidines[d]



entry	amidine	desired product	yield[a]	ratio of products[b]
1	 21	 25a	92	**25a**/**25b** = 24:1
2	 22	 26a	66	**26a**/**26b** = NA[c]
3	 23	 27a	69	**27a**/**27b** = 11:1
4	 24	 28a	68	**28a**/**28b** = NA[c]

[a]Isolated yield. [b]Ratio was determined by ^{1}H NMR spectroscopy. [c]The acyclic product (β-keto amine) was not detected in the ^{1}H NMR spectra of the crude reaction mixture. [d]All reactions were run with $[Ir(COD)Cl]_2$ (2.5 mol %), **I** (5 mol %), NaOTf (5 mol %), 4 Å MS (240 wt %), amidine (1 equiv), and **20** (1.5 equiv) in 1,2-dichloroethane at 80 °C for 24 h.

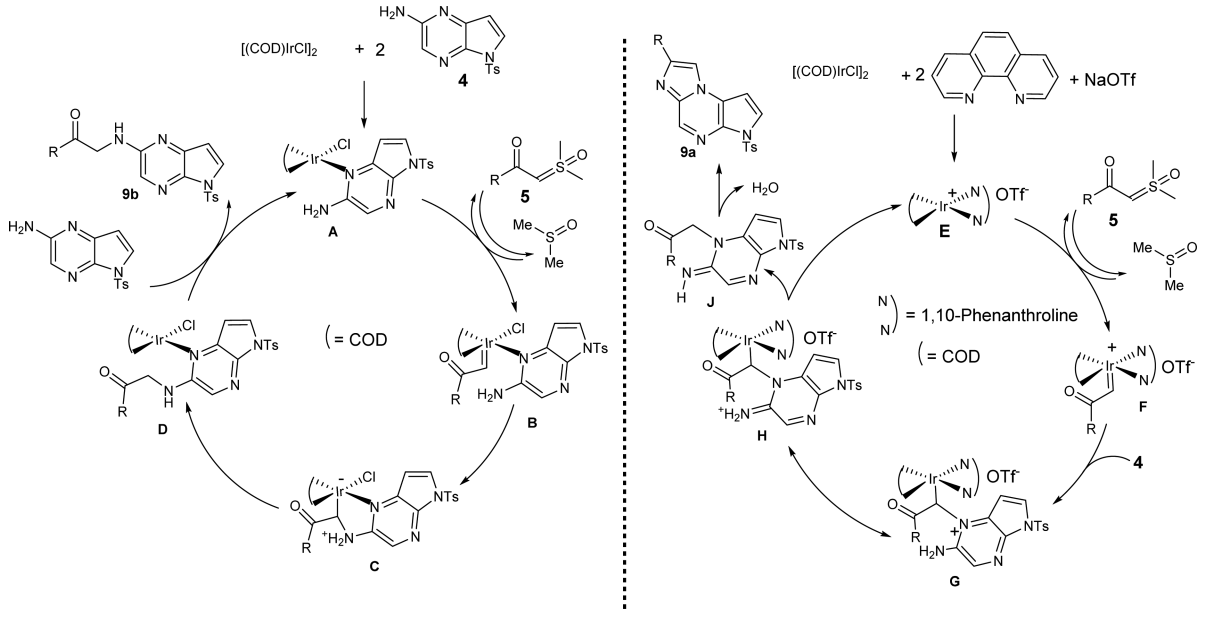


Figure 1. Proposed mechanisms for the formation of β-keto amine (left) or azole (right).

the absence of the ^{15}N signal for **a** in the ^{1}H−^{15}N HMBC NMR spectrum. When **4** and 0.5 equiv of $[(COD)IrCl]_2$ were mixed in CD_2Cl_2, the ^{15}N signal for **b** shifted to −176.6 ppm from −119.8 ppm. A clear signal for **a** was now observed at −308.0 ppm, and minimal change in the signals for **c** and **d** was observed. The significant chemical shift in the ^{15}N NMR peak for **b** is strong, albeit indirect, evidence for interaction of **4** with $[(COD)IrCl]_2$. In a similar experiment, the ^{15}N NMR signal for the nitrogen atoms in 1,10-phenanthroline (**e**) shifted from −72.9 ppm in the *absence* of $[(COD)IrCl]_2$ to −134.9 ppm in the *presence* of 0.5 equiv of $[(COD)IrCl]_2$ in CD_2Cl_2. When 1 equiv each of **4** and 1,10-phenathroline and 0.5 equiv of $[(COD)IrCl]_2$ were mixed together in CD_2Cl_2, the ^{15}N NMR signal for **e** was observed at −134.9 ppm, whereas the ^{15}N NMR signal for **b** was similar to that observed in the absence of $[(COD)IrCl]_2$.[37] These sets of ^{1}H−^{15}N HMBC NMR data suggest that 1,10-phenanthroline is a better ligand for Ir than **4**. This observation is consistent with our proposal of formation of

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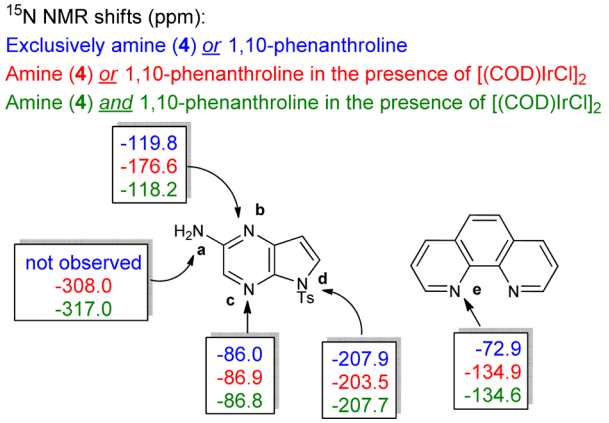

Figure 2. Interaction of $[(COD)IrCl]_2$ with amine (**4**) and 1,10-phenanthroline as studied by $^1H-^{15}N$ HMBC spectroscopy.

the Ir-complex **E** in the presence of 1,10-phenanthroline before **4** interacts with the metal (Figure 1). As proposed in Figure 1, the point of interaction of **4** with Ir determines the nature of the product formed in the reaction.

Further insight into the reaction mechanism was obtained by following the reactions by mass and ^1H NMR spectroscopy. Although no direct evidence for the generation of Ir-carbene intermediate **B** was obtained by ^1H NMR spectroscopy, formation of DMSO was observed in the reaction of **4** with **8** catalyzed by $[(COD)IrCl]_2$.[38] The insertion of Ir into **4** was determined to be reversible based on mass spectral studies with DMSO−$^{13}C_2$ (Table S2). When stoichiometric amounts of **4**, **8**, and $[(COD)IrCl]_2$ were reacted in DCE-d_4 at 40 °C, the rate of DMSO formation matched the rate of formation of **9b** (Figure 3). This suggests that the formation of Ir-carbene

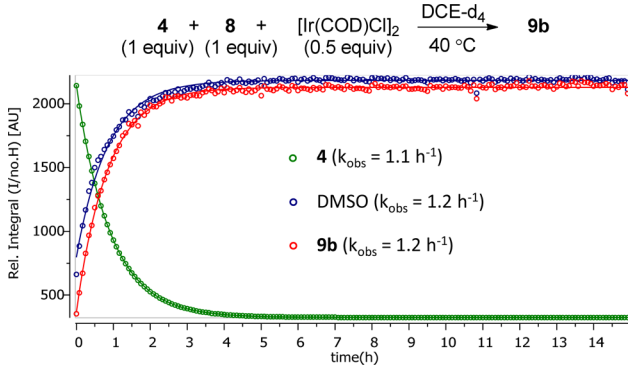

Figure 3. Formation of DMSO and **9b** in a stoichiometric reaction of **4** and **8** with $[Ir(COD)Cl]_2$.

intermediate **B** is the slow step of the reaction (Figure 1, left).[39] Fast, intramolecular reaction of the amine with Ir-carbene followed by protodemetalation likely generates the *β*-keto amine **9b**.

No evidence for the generation of Ir-carbene intermediate **F** was obtained by ^1H NMR spectroscopy during the reaction of **4** with **8** catalyzed by $[(COD)IrCl]_2$, 1,10-phenanthroline, and NaOTf. The rate of formation of DMSO was found to be similar to the rate of formation of azole **9a** when a reaction of **4** (1 equiv), **8** (10 equiv), $[(COD)IrCl]_2$ (0.5 equiv), 1,10-phenanthroline (1 equiv), and NaOTf (1 equiv) in DCE-d_4 was monitored by ^1H NMR spectroscopy at 80 °C (Figure 4), suggesting that the generation of Ir-carbene intermediate **F** is the rate-limiting step for azole formation. The reaction of

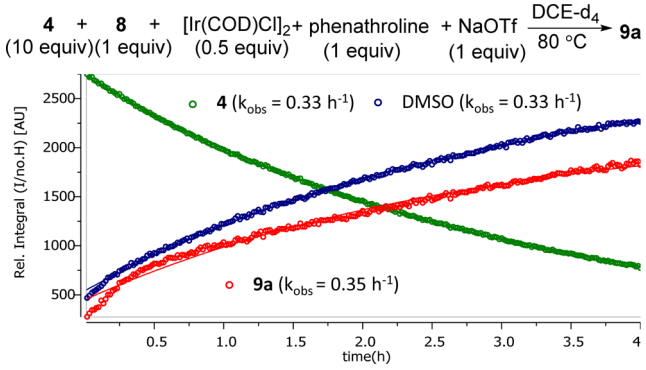

Figure 4. Formation of DMSO and **9a** in a stoichiometric reaction of **4** and **8** with $[Ir(COD)Cl]_2$, 1,10-phenathroline, and NaOTf.

4 with $[(COD)IrCl]_2$ in the presence of 1,10-phenathroline was also found to be reversible (Table S2).

Although formation of both *β*-keto amine **9b** and azole **9a** proceeds via reversible, rate-limiting generation of putative Ir-carbene intermediates, the preference for formation of **9a** or **9b** from Ir-catalyzed reactions of **4** with **8** is controlled by the nature of ligand. Insertion of the reaction byproduct, DMSO, into the Ir-carbene intermediate likely inhibits the reaction. Our future efforts will focus on studying the reactivity of sulfoxonium ylides containing leaving groups other than DMSO (such as diaryl sulfoxide) that will be capable of irreversibly generating the metal-carbene intermediate. We expect that identification of appropriate sulfoxonium ylide will further expand the efficiency and utility of the reported methodology.

CONCLUSIONS

In summary, a novel method for the synthesis of a variety of azoles from Ir-catalyzed reactions of *β*-ketosulfoxonium ylides with aryl amidines has been developed. This method uses bench stable sulfoxonium ylide precursors in place of diazo compounds, making preparation more practical and scalable. Two distinct products, *β*-keto amines or azoles, can form from the Ir-catalyzed reactions of *β*-ketosulfoxonium ylides with aryl amidines. Azole is formed in preference to *β*-keto amine when 1,10-phenanthroline is used as the ligand for $[Ir(COD)Cl]_2$ in conjunction with a noncoordinating anion, such as triflate. *β*-Keto amine is the preferred product in the absence of any additional ligand or counteranion for $[Ir(COD)Cl]_2$. Mechanistic insight was provided based on NMR and mass spectral studies.

EXPERIMENTAL SECTION

General Information. All glassware was either oven-dried overnight at 130 °C or flame-dried under a stream of dry nitrogen prior to use. Unless otherwise specified, reagents were used as obtained from the vendor without further purification. Tetrahydrofuran and diethyl ether were freshly distilled from purple Na/benzophenone ketyl. Dichloromethane, acetonitrile, and toluene were dried over CaH_2 and freshly distilled prior to use. All other solvents were purified in accordance with "Purification of Laboratory Chemicals".[40] Air- and moisture-sensitive reactions were performed using standard Schlenk techniques under an atmosphere of nitrogen. Analytical thin layer chromatography (TLC) was performed utilizing precoated silica gel 60 F_{254} plates containing a fluorescent indicator, while preparative chromatography was performed using SilicaFlash P60 silica gel (230−400 mesh) via Still's method.[41] Unless otherwise stated, the mobile phases for column chromatography were mixtures of

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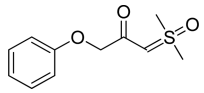
dichloromethane/ethyl acetate. Columns were typically run using a gradient method, beginning with 100% dichloromethane and gradually increasing the polarity using ethyl acetate. Various stains were used to visualize reaction products, including *p*-anisaldehyde, $KMnO_4$, ceric ammonium molybdate (CAM stain), and iodine powder.

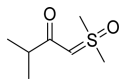
Routine NMR experiments were recorded in $CDCl_3$ at room temperature. Chemical shifts are reported in parts-per-million (ppm) relative to TMS (δ 0.00 ppm) for ^1H and to the solvent signal (δ 77.0 ppm) for ^{13}C. Scalar coupling constants are reported in hertz (Hz). Conventional 2D NMR experiments (COSY, HSQC, and HMBC) were recorded using standard pulse programs. In those cases where severe resonance overlap occurred, proton assignments were obtained by means of computer-assisted ^1H iterative full spin analysis (HiFSA).[42] High-pressure liquid chromatography (HPLC) analyses were performed at 210 nm. Accurate mass measurements were acquired using electrospray ionization, time-of-flight analyzer, or electron impact methods.

General Procedure for Synthesis of Sulfoxonium Ylides. A 250 mL round-bottom flask equipped with a magnetic stir bar and reflux condenser was charged with 9.9 g (45 mmol) of trimethylsulfoxonium iodide and 150 mL of THF under nitrogen. NaO^{t}Bu (4.5 g, 47.25 mmol) was added, heated to reflux, and allowed to stir for 2 h. After 2 h, the reaction mixture was cooled to room temperature, followed by dropwise addition of ester or acid chloride (15 mmol). The reaction mixture was stirred for 18 h and then quenched with 250 mL of water. The layers were separated, and the aqueous layer was extracted with 3 x 150 mL EtOAc, washed with 150 mL of saturated NaCl solution, stirred over Na_2SO_4, filtered, and then concentrated *in vacuo*. The resulting solid was charged to a 50 mL round-bottom flask, and 16 mL of EtOAc was added. Reaction was heated to 50 °C for 1 h and then allowed to cool to room temperature with constant stirring. The resulting slurry was filtered through a Buchner funnel under vacuum, and the solid was washed with ice-cold EtOAc to yield pure product, which was dried under vacuum for 12 h to remove residual solvents.

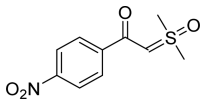


1-(Dimethyl(oxo)-λ^6-sulfanylidene)-3-phenoxypropan-2-one. Following the general procedure methyl phenoxyacetate (2.53 g, 15 mmol) was converted to 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3-phenoxypropan-2-one (1.86 g, 55%). The product was isolated as crystalline, white solid.

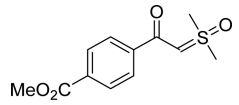
^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.29 (m, 2H), 6.97 (m, 1H), 6.92 (m, 2H), 4.91 (s, 1H), 4.41 (s, 2H), 3.44 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 185.7, 158.2, 129.5, 121.2, 114.6, 71.2, 68.9, 42.2. HRMS (ESI) *m*/*z* calculated for $C_{11}H_{14}O_3S$ $[M + H]^+$ 227.0737, found 227.0737. mp 118−120 °C.



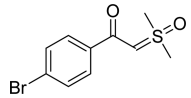
1-(Dimethyl(oxo)-λ^6-sulfanylidene)-3-methylbutan-2-one. Following the general procedure isobutyryl chloride (1.60 g, 15 mmol) was converted to 1-(dimethyl(oxo)-λ^6-sulfanylidene)-3-methylbutan-2-one (290 mg, 12%). The product was isolated as crystalline white solid. ^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 4.36 (s, 1H), 3.39 (s, 6H), 2.35 (hept, *J* = 6.9 Hz, 1H), 1.09 (d, *J* = 7.0 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 195.6, 67.0, 42.3, 38.8, 19.9. HRMS (ESI) *m*/*z* calculated for $C_7H_{14}O_2S$ $[M + H]^+$ 163.0788, found 163.0789. mp 135−137 °C.



2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-nitrophenyl)ethan-1-one. Following the general procedure 4-nitrobenzoyl chloride (2.78 g, 15 mmol) was converted to 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-nitrophenyl)ethan-1-one (1.95 g, 54%). The product was isolated as crystalline yellow solid.^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.24 (m, 2H), 7.93 (m, 2H), 5.03 (s, 1H), 3.55 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 179.3, 149.1, 144.5, 127.5, 123.5, 70.2, 42.3. HRMS (ESI) *m*/*z* calculated for $C_{10}H_{11}NO_4S$ $[M + H]^+$ 242.0482, found 242.0477. mp 175−178 °C

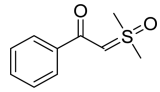


Methyl-4-(2-dimethyl(oxo)-λ^6-sulfanylidene)acetyl)benzoate. Following the general procedure, methyl 4-(chlorocarbonyl)benzoate (2.98 g, 15 mmol) was converted to methyl-4-(2-dimethyl(oxo)-λ^6-sulfanylidene)-acetyl)benzoate (1.03 g, 27%). The product was isolated as crystalline yellow solid.^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.06 (m, 2H), 7.85 (m, 2H), 5.02 (s, 1H), 3.93 (s, 3H), 3.53 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$),: 181.0, 166.7, 142.8, 131.8, 129.5, 126.5, 69.3, 52.2, 42.4. HRMS (ESI) *m*/*z* calculated for $C_{12}H_{14}O_4S$ $[M + H]^+$ 255.0686, found 255.0685. mp 158−160 °C.

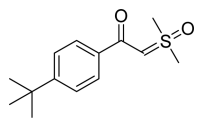


1-(4-Bromophenyl)-2-(2-dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one. Following the general procedure, 4-bromobenzoyl chloride (3.29 g, 15 mmol) was converted to 1-(4-bromophenyl)-2-(2-dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one (3.75 g, 86%). The product was isolated as crystalline yellow solid.

^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.66 (m, 2H), 7.52 (m, 2H), 4.94 (s, 1H), 3.51 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 180.9, 137.7, 131.3, 128.2, 125.2, 68.4, 42.5. HRMS (ESI) *m*/*z* calculated for $C_{10}H_{11}BrO_2S$ $[M + H]^+$ 274.9736, found 274.9735. mp 149−150 °C.



2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-phenylethan-1-one. Following the general procedure, benzoyl chloride (2.11 g, 15 mmol) was converted to 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-phenylethan-1-one (1.32 g, 34%). The product was isolated as crystalline white solid.^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.80 (m, 2H), 7.43 (m, 1H), 7.39 (m, 2H), 4.98 (s, 1H), 3.52 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 182.3, 138.8, 130.7, 128.1, 126.5, 68.1, 42.5. HRMS (ESI) *m*/*z* calculated for $C_{10}H_{12}O_2S$ $[M + H]^+$ 197.0631, found 197.0626. mp 114−116 °C.



1-(4-(tert-Butyl)phenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one. Following the general procedure, 4-*tert*-butylbenzoyl chloride (2.95 g, 15 mmol) was converted to 1-(4-(*tert*-butyl)phenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one (2.81 g, 74%). The product was isolated as crystalline tan solid.^1H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.74 (m, 2H), 7.41 (m, 2H), 4.95 (s, 1H), 3.51 (s, 6H), 1.33 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 182.2, 154.1, 136.1, 126.3, 125.1, 67.6, 42.6, 34.8, 31.2. HRMS (ESI) *m*/*z* calculated for $C_{14}H_{20}O_2S$ $[M + H]^+$ 253.1257, found 253.1259. mp 168−170 °C.

1-(3,4-Dimethoxyphenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one. Following the general procedure, methyl 3,4-dimethoxybenzoate

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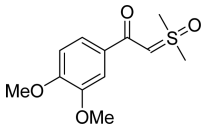
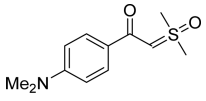
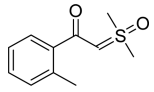


(2.94 g, 15 mmol) was converted to 1-(3,4-dimethoxyphenyl)-2-(dimethyl(oxo)-λ^6-sulfanylidene)ethan-1-one (696 mg, 18%). The product was isolated as crystalline light yellow solid. ^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.44 (d, J = 2.0 Hz), 7.36 (dd, J = 8.3, 2.0 Hz, 1H), 6.85 (d, J = 8.3 Hz, 1H), 4.92 (s, 1H), 3.94 (s, 3H), 3.92 (s, 3H), 3.51 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 181.7, 151.2, 148.6, 131.8, 119.8, 110.1, 109.3, 67.2, 55.9, 55.9, 42.7. HRMS (ESI) m/z calculated for $C_{12}H_{16}O_4S$ $[M + H]^+$ 257.0843, found 257.0844. mp 131−133 °C.

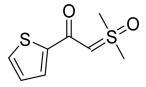


2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-(dimethylamino)-phenyl)ethan-1-one. Following the general procedure, 4-(dimethylamino)benzoyl chloride (2.75 g, 15 mmol) was converted to 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(4-(dimethylamino)phenyl)-ethan-1-one (1.52 g, 42%). The product was isolated as crystalline yellow solid.^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.77 (m, 2H), 6.72 (m, 2H), 4.91 (s, 1H), 3.56 (s, 6H), 3.07 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 182.3, 152.2, 128.0, 126.5, 110.9, 65.7, 42.9, 40.2. HRMS (ESI) m/z calculated for $C_{12}H_{17}NO_2S$ $[M + H]^+$ 240.1053, found 240.1051. mp 166−168 °C.



2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(o-tolyl)ethan-1-one. Following the general procedure, *o*-toluoyl chloride (2.30 g, 15 mmol) was converted to 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(*o*-tolyl)ethan-1-one (1.08 g, 34%). The product was isolated as crystalline white solid.

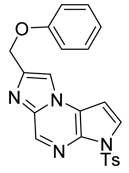
^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.41 (m, 1H), 7.24 (m, 1H), 7.18 (m, 1H), 7.15 (m, 1H), 4.64 (s, 1H), 3.52 (s, 6H) 2.47 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 186.8, 140.9, 135.5, 130.8, 128.9, 127.2, 125.3, 71.0, 42.3, 20.1. HRMS (ESI) m/z calculated for $C_{11}H_{14}O_2S$ $[M + H]^+$ 211.0788, found 211.0787. mp 104−106 °C.



2-(Dimethyl(oxo)-λ^6-sulfanylidene)-1-(thiophen-2-yl)ethan-1-one. Following the general procedure, methyl 2-thiophene carboxylate (2.13 g, 15 mmol) was converted to 2-(dimethyl(oxo)-λ^6-sulfanylidene)-1-(thiophen-2-yl)ethan-1-one (1.64 g, 54%). The product was isolated as crystalline tan solid.

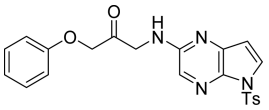
^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.44 (dd, J = 3.7, 1.2 Hz, 1H), 7.41 (dd, J = 5.0, 1.2 Hz, 1H), 7.04 (dd, J = 5.0, 3.7 Hz, 1H), 4.88 (s, 1H), 3.51 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 175.6, 145.6, 129.0, 127.5, 127.0, 67.0, 42.8. HRMS (ESI) m/z calculated for $C_8H_{10}O_2S_2$ $[M + H]^+$ 203.0195, found 203.0191. mp 165−167 °C.

General Procedure for Ir-Catalyzed N−H Insertion Reaction. To a thick-walled pressure tube in an inert atmosphere glovebox was added ylide (1.72 mmol, 1.5 equiv) and amine (1.15 mmol, 1 equiv), followed by $[Ir(COD)Cl]_2$ (0.029 mmol, 0.025 equiv), 1,10-phenanthroline (0.058 mmol, 0.05 equiv), NaOTf (0.058 mmol, 0.05 equiv), and powdered 4 Å molecular sieves (1.15 g). 1,2-Dichloroethane (4.6 mL) was added, rinsing down the sides of the pressure tube, the tube was capped and removed from the glovebox. The reaction was heated to 80 °C for 24 h, then cooled to room temperature, vacuum filtered through medium fritted funnel, washed with CH_2Cl_2, and concentrated under reduced pressure. The resulting mixture was purified via column chromatography using CH_2Cl_2/EtOAc gradient unless otherwise specified.



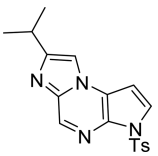
*7-(Phenoxymethyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine (**9a**).* Following the general procedure, 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 7-(phenoxymethyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (72 mg, 68%). The resulting crystalline yellow solid was isolated after column chromatography using a 5 to 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.81 (s, 1H), 8.08 (m, 2H), 7.86 (s, 1H), 7.73 (d, J = 4.0 Hz, 1H), 7.30 (m, 2H), 7.29 (m, 1H), 7.28 (m, 1H), 7.02 (m, 2H), 6.97 (m, 1H), 6.72 (d, J = 4.0 Hz, 1H), 5.35 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 158.3, 145.8, 145.6, 139.4, 136.6, 134.9, 132.9, 129.9, 129.5, 128.2, 123.8, 121.3, 118.4, 114.7, 109.8, 98.4, 64.9, 21.7. HRMS (ESI) m/z calculated for $C_{22}H_{18}N_4O_3S$ $[M + H]^+$ 419.1173, found 419.1165. mp 153−155 °C.



*1-Phenoxy-3-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)-propan-2-one (**9b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 1-phenoxy-3-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)amino)propan-2-one (11 mg, 10%). The resulting amorphous orange solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.98 (m, 2H), 7.80 (s, 1H), 7.75 (d, J = 4.0 Hz, 1H), 7.33 (m, 2H), 7.25 (m, 2H), 7.02 (m, 1H), 6.94 (m, 2H), 6.54 (d, J = 4.0 Hz, 1H), 5.29 (t, J = 4.9 Hz, 1H), 4.73 (s, 2H), 4.55 (d, J = 4.9 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 204.1, 157.5, 151.8, 145.3, 138.6, 135.3, 135.0, 129.8, 128.7, 128.2, 127.7, 122.0, 114.5, 105.8, 72.0, 49.1, 21.6. HRMS (ESI) m/z calculated for $C_{22}H_{20}N_4O_4S$ $[M + H]^+$ 437.1279, found 437.1277.



*7-Isopropyl-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazine (**10a**).* Following the general procedure 5-tosyl-5H-pyrrolo[2,3-*b*]-pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 7-isopropyl-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (270 mg, 66%). The resulting crystalline white solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.77 (s, 1H), 8.06 (m, 2H), 7.70 (d, J = 4.0 Hz, 1H), 7.57 (s, 1H), 7.28 (m, 2H), 6.71 (d, J = 4.0 Hz, 1H), 3.18 (hept, J = 6.9 Hz, 1H), 2.37 (s, 3H), 1.39 (d, J = 7.0 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 156.5, 145.9, 139.3, 136.2, 134.9, 132.9, 129.8, 128.0, 123.5, 118.3, 107.2, 98.4, 28.7, 22.5, 21.6. HRMS (ESI) m/z calculated for $C_{18}H_{18}N_4O_2S$ $[M + H]^+$ 355.1224, found 355.1224. mp 197−199 °C.

*3-Methyl-1-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)-butan-2-one (**10b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 3-methyl-1-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)amino)butan-2-one (24 mg, 6%). The resulting crystalline white solid was isolated

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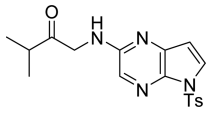
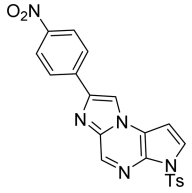


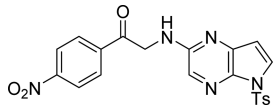
after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.97 (m, 2H), 7.78 (s, 1H), 7.74 (d, J = 4.0 Hz, 1H), 7.26 (m, 2H), 6.54 (d, J = 4.0 Hz, 1H), 5.40 (t, J = 4.3 Hz, 1H), 4.32 (d, J = 4.2 Hz, 2H), 2.74 (hept, J = 6.9 Hz, 1H), 2.37 (s, 3H), 1.19 (d, J = 6.9 Hz, 7H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 210.0, 151.9, 145.2, 138.6, 135.3, 134.8, 129.7, 128.5, 128.4, 127.7, 105.8, 49.3, 39.0, 21.6, 18.3. HRMS (ESI) m/z calculated for $C_{18}H_{20}N_4O_3S$ $[M + H]^+$ 373.1251, found 373.1255. mp 134−137 °C.



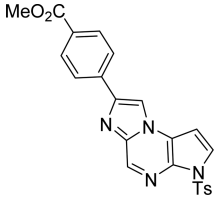
*7-(4-Nitrophenyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine (**11a**).* Following the general procedure 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 7-(4-nitrophenyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (148 mg, 34%). The resulting crystalline orange solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.87 (s, 1H), 8.33 (m, 2H), 8.19 (s, 1H), 8.16 (m, 2H), 8.11 (m, 2H), 7.78 (d, J = 4.0 Hz, 1H), 7.33 (m, 2H), 6.79 (d, J = 3.9 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 147.7, 146.0, 145.2, 140.2, 139.2, 137.0, 134.8, 133.1, 129.9, 128.3, 126.8, 124.3, 124.1, 118.2, 108.8, 98.2, 21.7. HRMS (ESI) m/z calculated for $C_{21}H_{15}N_5O_4S$ $[M + H]^+$ 434.0918, found 434.0919. mp 250 °C (decomp).



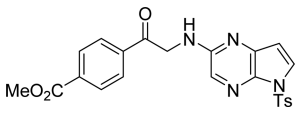
*1-(4-Nitrophenyl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)-amino)ethan-1-one (**11b**).* Following the general procedure 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 1-(4-nitrophenyl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]-pyrazine-2-yl)amino)ethan-1-one (126 mg, 28%). The resulting crystalline yellow solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.37 (m, 2H), 8.23 (m, 2H), 7.99 (m, 2H), 7.88 (s, 1H), 7.77 (d, J = 3.9 Hz, 1H), 7.28 (d, m, 2H), 6.56 (d, J = 4.0 Hz, 1H), 5.60 (t, J = 4.3 Hz, 1H), 4.95 (d, J = 4.3 Hz, 2H), 2.38 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 194.0, 151.6, 150.8(, 145.3, 139.1, 138.5, 135.3, 135.0, 129.8, 129.1, 128.7, 128.4, 127.8, 124.1, 105.7, 48.8, 21.6. HRMS (ESI) m/z calculated for $C_{21}H_{17}N_5O_5S$ $[M + H]^+$ 452.1024, found 452.1026. mp 195−197 °C.



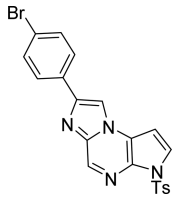
*Methyl 4-(3-Tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazine-7-yl)-benzoate (**12a**).* Following the general procedure, 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to methyl 4-(3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine-7-yl)benzoate (250 mg, 48%). The resulting crystalline orange solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.86 (s, 1H), 8.15 (s, 1H), 8.13 (m, 2H), 8.10 (m, 2H), 8.06 (m, 2H), 7.76 (d, J = 4.0 Hz, 1H), 7.32 (m, 2H), 6.78 (d, J = 4.0 Hz, 1H), 3.94 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 166.7, 146.5, 145.9, 140.1, 137.2, 136.8, 134.8, 133.0, 130.2, 129.9, 129.9, 128.2, 126.1, 123.9, 118.2, 108.3, 98.4, 52.2, 21.7. HRMS (ESI) m/z calculated for $C_{23}H_{18}N_4O_4S$ $[M + H]^+$ 447.1122, found 447.1123. mp 263 °C (decomp).



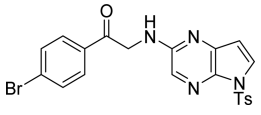
*Methyl 4-((5-Tosyl-5H-pyrrolo[2,3-b]pyrazin-2-yl)glycyl)benzoate (**12b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to methyl 4-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)glycyl)benzoate (59 mg, 11%). The resulting crystalline yellow solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.17 (m, 2H), 8.11 (m, 2H), 7.98 (m, 2H), 7.87 (s, 1H), 7.75 (d, J = 4.0 Hz, 1H), 7.27 (m, 2H), 6.56 (d, J = 4.0 Hz, 1H), 5.68 (t, J = 4.4 Hz, 1H), 4.92 (d, J = 4.3 Hz, 2H), 3.97 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 194.8, 166.0, 151.8, 145.3, 138.6, 137.8, 135.3, 134.9, 134.7, 130.0, 129.7, 128.6, 128.5, 127.9, 127.76, 105.8, 52.6, 48.6, 21.6. HRMS (ESI) m/z calculated for $C_{23}H_{20}N_4O_5S$ $[M + H]^+$ 465.1228, found 465.1227. mp 200−203 °C.



*7-(4-Bromophenyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine (**13a**).* Following the general procedure 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 7-(4-bromophenyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (74 mg, 64%). The resulting crystalline orange solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 8.83 (s, 1H), 8.09 (m, 2H), 8.06 (s, 1H), 7.85 (m, 2H), 7.75 (d, J = 4.1 Hz, 1H), 7.59 (m, 2H), 7.33 (m, 2H), 6.77 (d, J = 4.1 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 146.7, 145.9, 140.0, 136.6, 134.9, 133.1, 132.0, 131.9, 129.9, 128.2, 127.8, 123.9, 122.7, 118.2, 107.5, 98.4, 21.7. HRMS (ESI) m/z calculated for $C_{21}H_{15}N_4O_2SBr$ $[M + H]^+$ 467.0172, found 467.0170. mp 245 °C (decomp).



*1-(4-Bromophenyl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)-amino)ethan-1-one (**13b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 1-(4-bromophenyl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)-amino)ethan-1-one (14 mg, 13%). The resulting crystalline yellow solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., J, nH): 7.98 (m, 2H), 7.92 (m, 2H), 7.86 (s, 1H), 7.75 (d, J = 4.0 Hz, 1H), 7.66 (m, 2H), 7.27 (m, 2H), 6.56 (d, J = 4.0 Hz, 1H), 5.66 (t, J = 4.3 Hz, 1H), 4.86 (d, J = 4.4 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): 194.2, 151.9,

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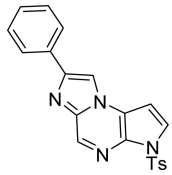
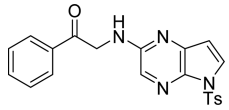
145.3, 138.6, 135.3, 134.9, 133.3, 132.3, 129.8, 129.4, 129.3, 128.6, 128.5, 127.8, 105.8, 48.2, 21.6. HRMS (ESI) m/z calculated for $C_{21}H_{17}N_4O_3SBr$ $[M + H]^+$ 485.0278, found 485.0276. mp 212−214 °C.



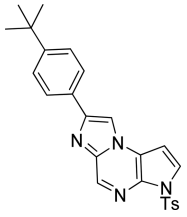
*7-Phenyl-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazine (**14a**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 7-phenyl-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (58 mg, 60%). The resulting crystalline off-white solid was isolated after column chromatography using a 1 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.84 (s, 1H), 8.09 (m, 2H), 8.07 (s, 1H), 7.98 (m, 2H), 7.73 (d, *J* = 4.0, 1H), 7.45 (m, 2H), 7.37 (m, 1H), 7.31 (m, 2H), 6.77 (d, *J* = 4.0 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): 147.9, 145.8, 139.9, 136.6, 134.9, 133.0, 132.9, 129.9, 128.9, 128.7, 128.1, 126.3, 123.7, 118.2, 107.4, 98.4, 21.7. HRMS (ESI) m/z calculated for $C_{21}H_{16}N_4O_2S$ $[M + H]^+$ 389.1067, found 389.1069. mp 233−235 °C.



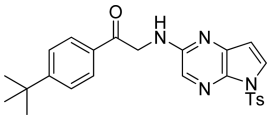
*1-Phenyl-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)-ethan-1-one (**14b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 1-phenyl-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)amino)ethan-1-one (9 mg, 9%). The resulting amorphous orange solid was isolated column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.05 (m, 2H), 7.98 (m, 2H), 7.85 (s, 1H, H3), 7.74 (d, *J* = 4.0 Hz, 1H), 7.63 (m, 1H), 7.51 (m, 2H), 7.26 (m, 2H), 6.56 (d, *J* = 4.0 Hz, 1H), 5.73 (t, *J* = 4.4 Hz, 1H), 4.89 (d, *J* = 4.4 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): 195.0, 152.0, 145.2, 138.6, 135.3, 134.8, 134.6, 134.0, 129.7, 128.9, 128.6, 128.4, 127.9, 127.7, 105.8, 48.2, 21.6. HRMS (ESI) m/z calculated for $C_{21}H_{18}N_4O_3S$ $[M + H]^+$ 407.1173, found 407.1175.



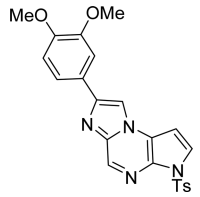
*7-(4-(tert-Butyl)phenyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine (**15a**).* Following the general procedure, 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 7-(4-(*tert*-butyl)phenyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (67 mg, 60%). The resulting crystalline orange solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.84 (s, 1H), 8.09 (m, 2H), 8.05 (s, 1H), 7.91 (m, 2H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.49 (m, 2H), 7.30 (m, 2H), 6.77 (d, *J* = 4.0 Hz, 1H), 2.38 (s, 3H), 1.36 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 151.9, 148.0, 145.8, 139.9, 136.5, 134.9, 133.0, 130.1, 129.9, 128.1, 126.0, 125.8, 123.6, 118.2, 107.2, 98.5, 34.7, 31.3, 21.6. HRMS (ESI) m/z calculated for $C_{25}H_{24}N_4O_2S$ $[M + H]^+$ 445.1693, found 445.1692. mp 235 °C (decomp).



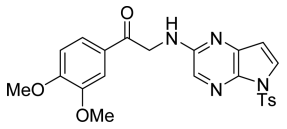
*1-(4-(tert-Butyl)phenyl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)ethan-1-one (**15b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 1-(4-(*tert*-butyl)phenyl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]-pyrazine-2-yl)amino)ethan-1-one (14 mg, 12%). The resulting crystalline brown solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*): 8.06 (m, 2H), 8.04 (m, 2H), 7.92 (s, 1H), 7.81 (d, *J* = 4.0 Hz, 1H), 7.59 (m, 2H), 7.33 (m, 2H), 6.64 (d, *J* = 4.0 Hz, 1H), 5.80 (t, *J* = 4.3 Hz, 1H), 4.93 (d, *J* = 4.3 Hz, 2H), 2.43 (s, 3H), 1.42 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 194.6, 158.1, 152.2, 145.3, 138.7, 135.4, 134.8, 132.1, 129.8, 128.7, 128.5, 128.0, 127.8, 125.9, 105.9, 48.4, 35.5, 31.3, 21.9. HRMS (ESI) m/z calculated for $C_{25}H_{26}N_4O_3S$ $[M + H]^+$ 463.1799, found 463.1797. mp 157−159 °C.



*7-(3,4-Dimethoxyphenyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazine (**16a**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 7-(3,4-dimethoxyphenyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]-pyrazine (196 mg, 38%). The resulting crystalline orange solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.83 (s, 1H), 8.10 (m, 2H), 8.01 (s, 1H), 7.74 (d, *J* = 3.9 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.49 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.34−7.29 (m, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.77 (d, *J* = 3.9 Hz, 1H), 4.01 (s, 3H), 3.94 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 149.6, 149.4, 148.0, 145.8, 139.9, 136.3, 134.9, 133.1, 129.9, 128.2, 126.0, 123.7, 118.9, 118.2, 111.3, 109.4, 106.8, 98.4, 56.1, 56.0, 21.68. HRMS (ESI) m/z calculated for $C_{23}H_{20}N_4O_4S$ $[M + H]^+$ 449.1279, found 449.1277. mp 173−175 °C.



*1-(3,4-Dimethoxyphenyl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)ethan-1-one (**16b**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 1-(3,4-dimethoxyphenyl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]-pyrazine-2-yl)amino)ethan-1-one (102 mg, 19%). The resulting amorphous yellow solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.98 (m, 2H), 7.86 (s, 1H), 7.75 (d, *J* = 4.0 Hz, 1H), 7.71 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.57 (d, *J* = 2.0 Hz, 1H), 7.27 (m, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 4.0 Hz, 1H), 5.75 (t, *J* = 4.2 Hz, 1H), 4.85 (d, *J* = 4.2 Hz, 2H), 3.97 (s, 3H), 3.96 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 193.5, 154.0, 152.1, 149.3, 145.2, 138.6, 135.3, 134.8, 129.7, 128.7, 128.4, 127.8, 127.7, 122.6, 110.2, 110.0, 105.8, 56.1, 56.1, 47.7, 21.6. HRMS (ESI) m/z calculated for $C_{23}H_{22}N_4O_5S$ $[M + H]^+$ 467.1384, found 467.1387.

*N,N-Dimethyl-4-(3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine-7-yl)aniline (**17a**).* Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was

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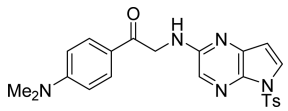
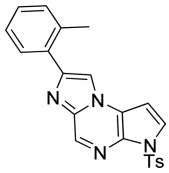
converted to *N*,*N*-dimethyl-4-(3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine-7-yl)aniline (287 mg, 58%). The resulting crystalline yellow solid was isolated after column chromatography using a 5 → 30% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.80 (s, 1H), 8.08 (m, 2H), 7.94 (s, 1H), 7.86 (m, 2H), 7.71 (d, *J* = 4.0 Hz, 1H), 7.30 (m, 2H), 6.79 (m, 2H), 6.75 (d, *J* = 4.0 Hz, 1H), 3.02 (s, 6H), 2.38 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 150.8, 148.7, 145.7, 139.9, 136.0, 135.0, 133.1, 129.8, 128.1, 127.3, 123.5, 120.9, 118.1, 112.3, 106.0, 98.5, 40.4, 21.7. HRMS (ESI) *m*/*z* calculated for $C_{23}H_{21}N_5O_2S$ $[M + H]^+$ 432.1489, found 432.1489. mp 229−231 °C.



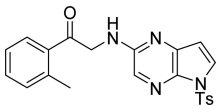
1-(4-(Dimethylamino)phenyl)-2-((5-tosyl)-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)ethan-1-one (**17b**). Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 1-(4-(dimethylamino)phenyl)-2-((5-tosyl)-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)amino)ethan-1-one (16 mg, 3%). The resulting crystalline orange solid was isolated after column chromatography using a 5 → 30% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.97 (m, 2H), 7.95 (m, 1H), 7.84 (s, 1H), 7.73 (d, *J* = 3.9 Hz, 2H), 7.26 (d, m, 2H), 6.68 (m, 2H), 6.57 (d, *J* = 4.0 Hz, 1H), 5.87 (t, *J* = 4.1 Hz, 1H), 4.77 (d, *J* = 4.1 Hz, 2H), 3.08 (s, 6H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ 192.3, 153.9, 152.3, 145.2, 138.7, 135.4, 134.6, 130.1, 129.7, 128.8, 128.2, 127.7, 122.3, 110.7, 105.9, 47.3, 40.0, 21.6. HRMS (ESI) *m*/*z* calculated for $C_{23}H_{23}N_5O_3S$ $[M + H]^+$ 450.1595, found 450.1604. mp 222 °C (decomp).



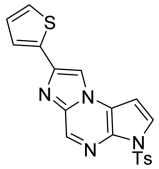
7-(o-Tolyl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]pyrazine (**18a**). Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 7-(*o*-tolyl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (282 mg, 61%). The resulting crystalline white solid was isolated after column chromatography using a 5 → 30% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH,): 8.86 (s, 1H), 8.09 (m, 2H), 7.91 (s, 1H), 7.81 (m, 1H), 7.74 (d, *J* = 4.0 Hz, 1H), 7.31 (m, 2H), 7.297* (m, 1H), 7.293* (m, 1H), 7.292* (m, 1H), 6.78 (d, *J* = 4.0 Hz, 1H), 2.56 (s, 3H), 2.38 (s, 3H). *Indicates proton assignments obtained by ^{1}H iterative full spin analysis. ^{13}C NMR (176 MHz, $CDCl_3$) δ: 147.7, 145.8, 139.1, 136.7, 135.9, 134.9, 132.9, 132.5, 131.0, 129.8, 129.8, 128.4, 128.1, 126.1, 123.6, 118.2, 109.9, 98.5, 21.7, 21.4. HRMS (ESI) *m*/*z* calculated for $C_{22}H_{18}N_4O_2S$ $[M + H]^+$ 403.1224, found 403.1232. mp 194−196 °C.



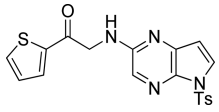
1-(o-Tolyl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)amino)-ethan-1-one (**18b**). Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (332 mg, 1.15 mmol) was converted to 1-(*o*-tolyl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)amino)-ethan-1-one (58 mg, 12%). The resulting amorphous white solid was isolated after column chromatography using a 5 → 30% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.98 (m, 2H), 7.85 (s, 1H), 7.83 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.74 (d, *J* = 4.0 Hz, 1H), 7.45 (td, *J* = 7.5, 1.3 Hz, 1H), 7.32 (td, *J* = 7.8, 1.3 Hz, 1H), 7.30 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.27 (m, 2H), 6.55 (d, *J* = 4.0 Hz, 1H), 5.69 (t, *J* = 4.5 Hz, 1H), 4.78 (d, *J* = 4.5 Hz, 2H), 2.56 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 198.1, 152.0, 145.2, 139.3, 138.6, 135.3, 134.8, 134.6, 132.4, 132.3, 129.7, 128.6, 128.6, 128.4, 127.7, 125.9, 105.8, 49.8, 21.6, 21.6. HRMS (ESI) *m*/*z* calculated for $C_{22}H_{20}N_4O_3S$ $[M + H]^+$ 421.1329, found 421.1332.



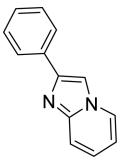
7-(Thiophen-2-yl)-3-tosyl-3H-imidazo[1,2-a]pyrrolo[2,3-e]-pyrazine (**19a**). Following the general procedure, 5-tosyl-5H-pyrrolo-[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 7-(thiophen-2-yl)-3-tosyl-3*H*-imidazo[1,2-*a*]pyrrolo[2,3-*e*]pyrazine (40 mg, 41%). The resulting crystalline orange solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.82 (s, 1H), 8.09 (m, 2H), 7.97 (s, 1H), 7.74 (d, *J* = 3.9, 1H), 7.52 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.35 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.31 (m, 2H), 7.11 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.75 (d, *J* = 3.9 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$), δ: 145.9, 142.8, 139.6, 136.5, 136.3, 134.8, 133.1, 129.9, 128.2, 127.9, 126.0, 124.7, 123.8, 118.1, 106.8, 98.4, 21.7. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{14}N_4O_2S_2$ $[M + H]^+$ 395.0631, found 395.0628. mp 205−207 °C.



1-(Thiophen-2-yl)-2-((5-tosyl-5H-pyrrolo[2,3-b]pyrazine-2-yl)-amino)ethan-1-one (**19b**). Following the general procedure, 5-tosyl-5H-pyrrolo[2,3-*b*]pyrazine-2-amine (72 mg, 0.25 mmol) was converted to 1-(thiophen-2-yl)-2-((5-tosyl-5*H*-pyrrolo[2,3-*b*]pyrazine-2-yl)-amino)ethan-1-one (10 mg, 10%). The resulting crystalline white solid was isolated after column chromatography using a 5 → 40% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 7.98 (m, 2H), 7.90 (dd, *J* = 3.8, 1.1 Hz, 1H), 7.84 (s, 1H), 7.75 (d, *J* = 4.0 Hz, 1H), 7.72 (dd, *J* = 4.9, 1.1 Hz), 7.27 (m, 2H), 7.19 (dd, *J* = 4.9, 3.8 Hz, 1H), 6.56 (d, *J* = 4.0 Hz, 1H), 5.57 (t, *J* = 4.5 Hz, 1H), 4.83 (d, *J* = 4.5 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 188.2, 151.9, 145.3, 141.1, 138.6, 135.3, 134.9, 134.4, 132.3, 129.7, 128.5, 128.5, 128.4, 127.7, 105.8, 48.3, 21.6. HRMS (ESI) *m*/*z* calculated for $C_{19}H_{16}N_4O_3S_2$ $[M + H]^+$ 413.0737, found 413.0737. mp 200 °C (decomp).



2-Phenylimidazo[1,2-a]pyridine (**25a**). Following the general procedure, 2-aminopyridine (108 mg, 1.15 mmol) was converted to 2-phenylimidazo[1,2-*a*]pyridine (179 mg, 92%). The resulting crystalline tan solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.09 (dt, *J* = 6.8, 1.2 Hz, 1H), 7.95 (m, 2H), 7.84 (s, 1H), 7.62 (dt, *J* = 9.1, 1.2 Hz, 1H), 7.43 (m, 2H), 7.33 (m, 1H), 7.15 (ddd, *J* = 9.1, 6.7, 1.2 Hz, 1H), 6.75 (td, *J* = 6.7, 1.2 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 145.7, 145.6, 133.7, 128.7, 128.0, 126.0, 125.6, 124.7, 117.5, 112.4, 108.1. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{10}N_2$ $[M + H]^+$ 195.0917, found 195.0919. mp 132−134 °C.

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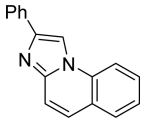
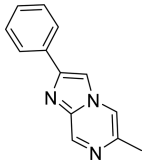


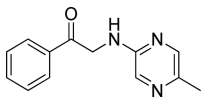
*2-Phenylimidazo[1,2-a]quinoline (**26a**).* Following the general procedure, 2-aminoquinoline (36 mg, 0.25 mmol) was converted to 2-phenylimidazo[1,2-*a*]quinoline (40 mg, 66%). The resulting crystalline yellow solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.33 (s, 1H), 8.01 (m, 2H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.82 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.66 (ddt, *J* = 8.4, 7.1, 1.3 Hz, 1H), 7.60 (d, *J* = 9.4 Hz, 1H), 7.53 (dd, *J* = 9.4, 1.1 Hz, 1H), 7.48 (m, 1H), 7.47 (m, 2H), 7.34 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 144.9, 144.2, 133.8, 132.5, 129.2, 128.8, 128.7, 127.8, 126.3, 125.8, 124.7, 123.4, 117.1, 115.1, 106.7. HRMS (ESI) *m*/*z* calculated for $C_{17}H_{12}N_2$ $[M + H]^+$ 245.1074, found 245.1077. mp 103−105 °C.



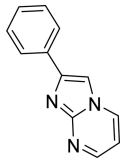
*6-Methyl-2-phenylimidazo[1,2-a]pyrazine (**27a**).* Following the general procedure, 2-amino-5-methylpyrazine (27 mg, 0.25 mmol) was converted to 6-methyl-2-phenylimidazo[1,2-*a*]pyrazine (33 mg, 63%).The resulting crystalline tan solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 9.03 (br s, 1H), 7.96 (m, 2H), 7.88 (t, *J* = 1.2 Hz, 1H), 7.86 (s, 1H), 7.46 (m, 2H), 7.38 (m, 1H), 2.52 (d, *J* = 1.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 147.7, 142.4, 139.9, 138.4, 132.9, 128.8, 128.7, 126.2, 115.6, 108.8, 20.8. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{11}N_3$ $[M + H]^+$ 210.1026, found 210.1025. mp 171−173 °C.



*2-((5-Methylpyrazin-2-yl)amino)-1-phenylethan-1-one (**27b**).* Following the general procedure, 2-amino-5-methylpyrazine (27 mg, 0.25 mmol) was converted to 2-((5-methylpyrazin-2-yl)amino)-1-phenylethan-1-one (4 mg, 6%). The resulting amorphous orange solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.07 (m, 2H), 8.02 (d, *J* = 1.5 Hz, 1H), 7.90 (br s, 1H), 7.63 (td, *J* = 7.3, 1.3 Hz, 1H), 7.52 (m, 2H), 5.58 (br t, *J* = 4.3 Hz, 1H), 4.87 (d, *J* = 4.3 Hz, 2H), 2.40 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 195.0, 151.8, 141.2, 140.4, 134.7, 134.0, 132.3, 128.9, 127.9, 48.1, 20.1. HRMS (ESI) *m*/*z* calculated for $C_{13}H_{13}N_3O$ $[M + H]^+$ 228.1132, found 228.1132.



*2-Phenylimidazo[1,2-a]pyrimidine (**28a**).* Following the general procedure, 2-aminopyrimidine (24 mg, 0.25 mmol) was converted to 2-phenylimidazo[1,2-*a*]pyrimidine (33 mg, 68%). The resulting crystalline orange solid was isolated after column chromatography using a 2 → 10% gradient of EtOAc in CH_2Cl_2.

^{1}H NMR (700 MHz, $CDCl_3$), δ (mult., *J*, nH): 8.53 (dd, *J* = 4.1, 2.0 Hz, 1H), 8.43 (dd, *J* = 6.7, 2.0 Hz, 1H), 8.04 (m, 2H), 7.83 (s, 1H), 7.46 (m, 2H), 7.37 (m, 1H), 6.86 (dd, *J* = 6.7, 4.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$) δ: 149.7, 149.0, 147.4, 133.1, 132.8, 128.7, 128.6, 126.3, 108.7, 106.0. HRMS (ESI) *m*/*z* calculated for $C_{12}H_9N_3$ $[M + H]^+$ 196.0870, found 196.0865. mp 187−190 °C.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00497.

^{1}H and ^{13}C spectra of all compounds reported in the manuscript, complete optimization of reaction conditions for the formation of **9a**, and investigation of insertion of Ir into **8** by mass spectroscopy (PDF)

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Notes

The authors declare no competing financial interest.

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