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C−H Bond Functionalization Under Metalation−Deprotonation Process: Regioselective Direct Arylation of 3-Aminoimidazo[1,2-*a*]pyrazine

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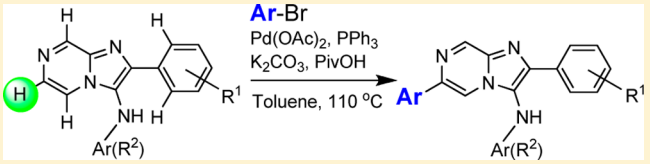
Supporting Information

ABSTRACT: Concerted metalation deprotonation (CMD) approach with appropriate proton shuttle precursor, base, and solvent (PivOH−K_2CO_3−toluene) has rendered a regioselective Pd-catalyzed C6-arylation of 3-aminoimidazo[1,2-*a*]pyrazine, a therapeutically relevant scaffold accessible by multicomponent reaction. The arylation of this heteroarene suffers from competing C5 and C2′-arylation reactions, while the developed process has virtually eliminated these competing arylations. Density functional calculations for CMD C−H activation at C6, C5, C8, and C2′ sites imply that the energy barrier with distortion energy penalty as major contributing component influences the regioselectivity.



Direct arylation of (hetero)arene has recently emerged as an appealing and valuable strategy in organic synthesis.[1] In contrast to conventional cross-coupling reactions,[2] this approach does not require additional prefunctionalization of arenes. It avoids especially the prior preparation and use of stoichiometric (hetero)arylmetal derivatives. Therefore, these reactions are atom-economical and produce less waste. However, regioselective C−H bond functionalization and the practicability of these processes for versatile (hetero)arenes are major constraints. Regioselective arylation becomes more problematic for heterocyclic scaffolds possessing multiple closely related nucleophilic centers and or acidic C−H (s), such as oxazole, thiazole, imidazole, pyrrole, and indole.[1a,3] In the context of versatility, π-nucleophilic aromatics as direct arylation coupling partners are common. For these arenes, the C−H bond functionalizations are often proposed to take place via electrophilic aromatic substitution (S_EAr) pathway,[4] although Heck-like[5] and oxidative C−H insertion[6] pathways also have been demonstrated. In contrast, electron-deficient arenes are less explored. The concerted metalation deprotonation (CMD) pathway, an excellent approach introduced by Fagnou[7] and a similar proton abstraction mechanism first proposed by Echavarren and Maseras,[8] has enabled various electron-deficient aromatics as valid arene coupling partners for direct arylation.[9] In this pathway, several electron-rich heterocycles have also been found later to be operative.[9a,b] Herein, we report a novel regioselective Pd-catalyzed direct C6-arylation reaction of 3-aryl/alkylamino and 2-aryl/alkyl substituted imidazo[1,2-*a*]pyrazine, a π-deficient heteroarene, with bromoarene via metalation−deprotonation process (Figure 1). Several ring nitrogen atoms and the substitution/functionality present in the scaffold contribute differently to the electronic and steric factors and can coordinate to Pd-catalyst. These cause competing arylations of the scaffold at other sites (such as C2′ and C5). Our developed CMD process with

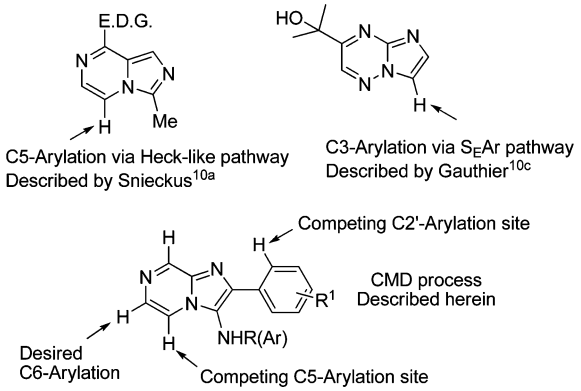


Figure 1. Arylations of N-fused imidazoles.

pivalate proton shuttle, in situ generated from PivOH−K_2CO_3, in toluene solvent has virtually eliminated these competing arylations. The computational studies indicate that the C−H activation energy barrier (distortion energy penalty as major governing component) favored the C6-CMD TS over C2′, C5, and C8. There are a few methods reported for arylation reactions of fused imidazo-heterocycles, including C5-arylation of imidazo[1,5-*a*]pyrazine via Heck-like pathway, and C3-arylations of imidazo[1,2-*b*][1,2,4]triazine and imidazo[1,2-*a*]-pyrimidine via S_EAr process.[10] The present work introduces CMD-mediated C6-arylation of 3-aminoimidazo[1,2-*a*]pyrazine, a therapeutically important motif.

Imidazo[1,2-*a*]pyrazines and their derivatives with 3-aryl/alkyl-amine, 2-aryl/alkyl and 6-aryl substitutions have been found to possess a wide range of bioactivities.[11,12] Analogues of

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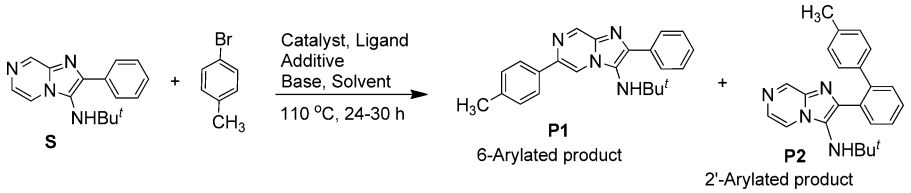
Table 1. Evaluation of Reagents and Conditions for C6-Arylation of 3-Aminoimidazo1,2-*a*]pyrazine (S)[a]



entry	catalyst	ligand	additive	base	solvent	**P1**:**P2**[b]	yield (%)[c] of **P1**
1	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$		Cs_2CO_3	DMF	1.1:1	**P1**:15 (**P2**:13)[d]
2	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	Cs_2CO_3	DMF	1.2:1	**P1**:18 (**P2**:15)
3	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	Cs_2CO_3	**toluene**	4.5:1	
4[e]	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	Cs_2CO_3	mesitylene	4:1	
5	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	**PivOH**	**K_2CO_3**	toluene	49:1	62
6[e]	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	K_2CO_3	mesitylene	19:1	
7	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	KOAc	toluene	7.3:1	
8	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$		CsOPiv	toluene	trace	
9	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH	Ag_2CO_3	toluene	32.3:1	46
10	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$		K_2CO_3	toluene	1.2:1	
11	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	PivOH		toluene	trace	
12	$Pd(OAc)_2$	$(t\text{-Bu})_2MeP{\cdot}HBF_4$	Mes CO_2H	K_2CO_3	toluene	44.4:1	47
13	**$Pd(OAc)_2$**	**PPh_3**	**PivOH**	**K_2CO_3**	**toluene**	**100:0**	**65**

[a]Conditions: Additive (30 mol %), base (2 equiv), ligand (20 mol %), imidazopyrazine (1 mmol), 4-bromotoluene (2.5 equiv), Pd catalyst (10 mol %) and anhydrous solvent were added sequentially to the reaction vessel under N_2, and the mixture was heated at 110 °C for 24−36 h. [b]Ratio was determined by RP-HPLC analysis. [c]Isolated yield. [d]It formed C5-arylated product in 3% yield. [e]Reaction temperature: 140 °C.

this scaffold represent various marketed drugs such as zolpidem and zolimidine. C6-Aryl derivatives of these compounds are normally prepared by a sequence of reactions.[11,13] It uses bromination of 2-aminopyrazine, condensation of 2-amino-5-bromopyrazine with α-haloketone or with aldehyde and isocyanide to produce 6-bromo-imidazopyrazine, and the Suzuki coupling with boronic acid. In addition, bromination of 2-aminopyrazine produces also unwanted regioisomeric brominated and polybromo derivatives.[11e] Therefore, inherent advantages of direct arylation chemistry and therapeutic importance signify 3-aminoimidazo[1,2-*a*]pyrazine as a useful direct arylation coupling partner.

In initial experiment, a model reaction of 3-*tert*-butylamino-2-phenylimidazopyrazine with bromotoluene was performed using Snieckus's method[10a] for C5-arylation of imidazo[1,5-*a*]-pyrazine (Table 1, entry 1). However, it provided 6-arylated product (**P1**), 2′-arylated product (**P2**), and 5-arylated product in 15, 13, and 3% yields, respectively. The reactions were then carried out following methods reported for arylation of other fused imidazo-heterocycles, imidazopyrimidine, imidazopyridazine, and imidazo-triazine.[10] All of them led to the formation of C6, C2′, and C5 arylated products in similar yields. These methods with a few variations of palladium sources and ligands could improve in neither regioselectivity nor synthetic conversion. CMD approach was then considered for investigation. In initial investigations, reactions were performed with additional use of PivOH as proton shuttle precursor in various solvents. Gratifyingly, in each reaction, the competing C5-arylation could be avoided. Although 2′-arylated product (**P2**) formed along with 6-arylated product (**P1**), the use of toluene as solvent significantly improved the regioselectivity for C6-arylation. Compared to polar solvents, apolar solvents were found to be more effective. Increasing the reaction temperature using mesitylene solvent was of no advantage. The competing C2′-arylation took place plausibly by directed C2′−H bond functionalization through 3-amino or imidazole ring nitrogen−palladium coordination.[1] Variation in base was then investigated. To our delight, the use of K_2CO_3 base replacing Cs_2CO_3 provided high regioselectivity and C6-arylated product in 62% isolated yield. K_2CO_3 was found to be superior to acetate. Use of CsOPiv (without PivOH) or the reaction performed in absence of base resulted in trace conversion. These imply that the choice of base is important. The CMD process was found to be essential. The reaction without PivOH resulted in almost loss of regioselectivity, less reaction conversion, and a complex mixture of products on prolonging the reaction (entry 10). 2-Mesitylenecarboxylate as proton shuttle was found to be inferior to pivalate. Various ligands and palladium sources were then evaluated. Interestingly, the combination of PPh_3−$Pd(OAc)_2$ with PivOH−K_2CO_3 afforded the formation of only 6-arylated product in 65% isolated yield and no 2′-arylated product (entry 13). Compared to aryl bromide, aryl iodide lowered the conversion. This might be due to poisoning of the catalyst by accumulated iodide in the reaction medium. With aryl iodide, the use of Ag_2CO_3 replacing K_2CO_3 enhanced desired arylation,[10a,14] but its use was found not imperative.

With the optimized protocol in hand, we next set out to explore its scope. Versatile 3-aryl/alkylamino and 2-aryl/alkyl substituted imidazo[1,2-*a*]pyrazines were prepared by Groebke−Blackburn−Bienaymé multicomponent reaction.[15,16] These imidazopyrazines in reaction with various aryl bromides provided C6-arylated products in moderate to good yields (Tables 2 and 3). In each case, the reaction provided the regioselective C6-arylation product with negligible or no (0−2%) 2′-arylated product, although the conversion was not complete. The 3-arylamine motifs of imidazopyrazine (products **9**−**11**, Table 3) remained intact, although they are susceptible toward possible direct arylation at 2′-position of 3-arylamine facilitated by electrophilic palladation or fused nitrogen coordination to

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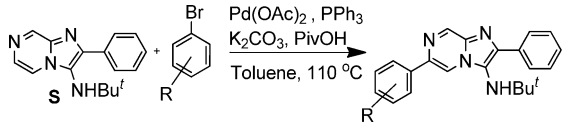
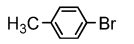
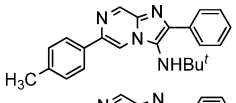
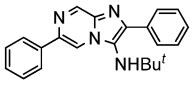
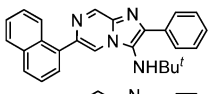
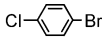
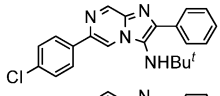
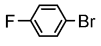
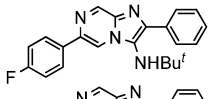
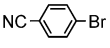
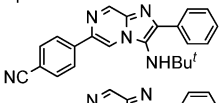
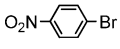
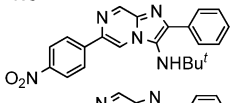
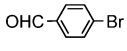
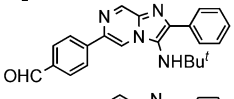
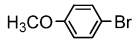
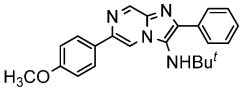
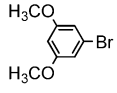
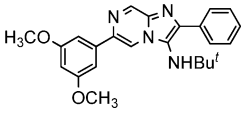
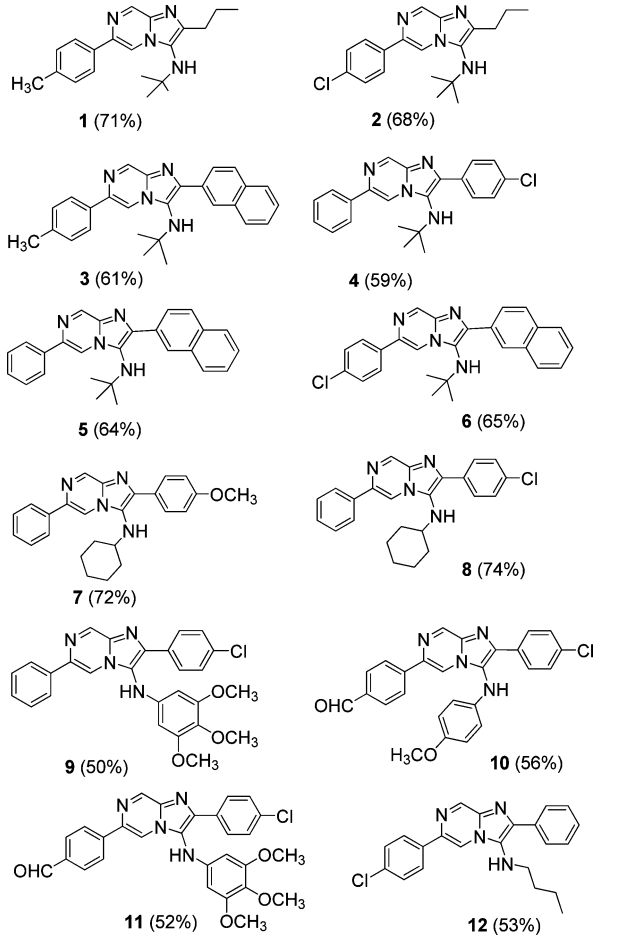
Table 2. C6-Arylation of 3-Aminoimidazopyrazine (S) with Various Bromoarenes[a]



Entry	Bromoarene	Product	Yield (%)[b]
1			65
2			59
3			52
4			61
5			48
6			54
7			52
8			48
9			51
10			46

[a]Conditions: Imidazopyrazine (1 mmol), bromoarene (2.5 equiv), $Pd(OAc)_2$ (10 mol %), PPh_3 (20 mol %), PivOH (30 mol %), K_2CO_3 (2 equiv), 110 °C, N_2. [b]Isolated yield.

Table 3. Synthesis of Versatile C6-Aryl Derivatives of 3-Aminoimidazopyrazine with Diverse Substitutions



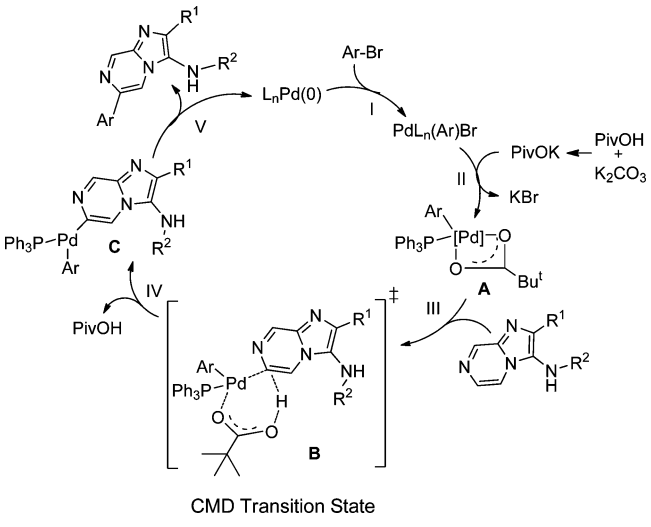


Figure 2. Proposed mechanism (CMD pathway).

catalyst. This direct arylation was also chemoselective with the fact that no C−N bond formation reaction (Buchwald−Hartwig coupling) was observed. Both electron-donating and -withdrawing groups on aryl bromides were compatible. The tolerance of functionalities such as chloro, cyano, nitro, methoxy, amine, and gratifyingly, even aldehyde in this protocol provides opportunity of their various further chemical manipulation in products.

The crucial role of pivalate as proton shuttle in this regioselective direct arylation implies that the arene C−H bond functionalization underwent plausibly via CMD mechanism (Figure 2). The lack of electronic effect (EWG vs EDG) of bromoarenes on the reactivity/regioselectivity in arylation rules out the possibility of sole electrophilic palladation. The oxidative addition of aryl bromide to Pd(0) forms ArPdBr, which in reaction with PivOK generates ArPd(OPiv) complex (**A**). This complex induces C6−H bond activation of imidazopyrazine and forms complex (**B**), which subsequently produces aryl-Pd-imidazopyrazine complex (**C**). Its reductive elimination produces C6-arylated imidazopyrazine and regenerates Pd(0).

To gain insight into the reasons for C6-selectivity, computational studies were performed for C−H activation energy barriers of CMD TSs (for details, see the Supporting Information). The energy barriers associated with C−H activations at different sites (C5, C6, C8 and C2′) were calculated by

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density functional theory (DFT) with the B3LYP exchange-correlation functional similar to that used by Fagnou and co-workers (see the Supporting Information). The lowest energy barrier (24.11 kcal mol^{-1}) was observed for C6-TS (Figure 3),

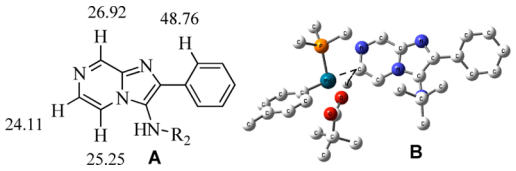


Figure 3. (A) Calculated energy barriers ($\Delta E^{\ddagger}_{gas}$) of activation (in kcal mol^{-1}) for CMD TSs. (B) C6-CMD TS structure.

which correlated with the experimental results. Computation considering implicit solvent conditions (toluene) using IEFPCM model also showed lowest barrier for C6-TS (27.06 kcal/mol) relative to other sites (C5, C8 and C2′). The range of barrier differences for C6, C5 and C8 ($\Delta E^{\ddagger}_{gas}$; 1.14−2.81 kcal mol^{-1} and $\Delta E^{\ddagger}_{solv}$; 1.07−2.60 kcal mol^{-1}) was found to be in accordance with the reported range of 0.7−6 kcal mol^{-1} for a variety of arenes.[7,9a]

The analysis of distortion−interaction energy was studied (Table 4). The distortion energy (E_{dist}) is the energy associated with distortion of arene and Pd-catalyst from their ground states to form corresponding CMD TS geometries. The interaction energy (E_{int}) is the energy associated with interaction between arene and Pd-catalyst in the TS. Wiberg bond index (B_{Pd-C}) shows covalent bond interaction. The lower E_{dist} was observed for C6-CMD TS as compared to C5, C8, and C2′. The more facile distortions in arene and Pd-complex for C6 TS could be attributed to ring nitrogen atoms and substitutions of the scaffold favoring to C6-site (Figure 3B). The gain due to small E_{dist} penalty for C6 was higher than the loss from less negative E_{int} value. The C_{Ar}−Pd covalent interaction, quantified by the Pd−C_{Ar} bond order (B_{Pd-C6}), was higher for C6 than C5, C8 and C2′. In contrast, higher E_{dist} were observed in case of C5 and C8, which offsets the gain due to larger E_{int} values. These signify the lower energy barrier for C6−H activation, which is in correlation with the experimental regioselectivity. The C2′−H TS is favored by neither E_{dist} cost nor E_{int} gain. The arylation at C2′ as competing side reaction took place plausibly by directed C2′−H bond functionalization through 3-amino or imidazole ring nitrogen−palladium coordination.[1] We next set out to gain insight into superior efficiency of pivalate as proton shuttle to mesitylenecarboxylate and carbonate. The energy barriers of activation for CMD TSs with corresponding proton shuttles were evaluated. The relatively higher energies ($\Delta E^{\ddagger}_{gas}$) of activation for mesitylenecarboxylate (28.60 kcal mol^{-1}) and carbonate (36.70 kcal mol^{-1}) compared to pivalate correlated with the experimental results.

In conclusion, we have discovered a novel regioselective Pd-catalyzed direct C6-arylation of versatile substituted 3-aminoimidazo[1,2-*a*]pyrazines with various bromoarenes. CMD process was found to be crucial in accomplishing the site selectivity and synthetically useful conversion. The studies of distortion and interaction energies and bond index for CMD process were in agreement with experimental results. This work has rendered for the first time the inclusion of 3-aminoimidazo[1,2-*a*]pyrazine, a therapeutically relevant scaffold accessible by multicomponent reaction, in the array of (hetero)arene direct arylation coupling partners, and will potentially replace the usually followed multistep synthesis of 6-aryl derivatives of 3-aminoimidazo[1,2-*a*]pyrazines via bromo-intermediates.

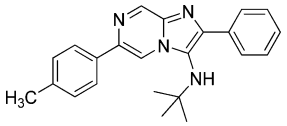
EXPERIMENTAL SECTION

General Considerations. The ^{1}H and ^{13}C spectra were recorded in $CDCl_3$/DMSO-d_6/CD_3OD solvents on 400/500 MHz spectrometer using TMS as internal standard. HRMS was measured using TOF analyzer. Melting points determined are uncorrected.

Representative Experimental Procedure for Synthesis of *N*-(*tert*-Butyl)-2-phenyl-6-(4-tolyl)imidazo[1,2-*a*]pyrazin-3-amine (Table 2, entry 1). PivOH (30 mg, 30 mol %), K_2CO_3 (276 mg, 2 mmol), PPh_3 (52 mg, 20 mol %), and *N*-*tert*-butyl-2-phenylimidazo-[1,2-*a*]pyrazin-3-amine (266 mg, 1 mmol) were taken subsequently in a round-bottom flask under N_2. To this mixture were added 4-bromotoluene (427 mg, 2.5 mmol), $Pd(OAc)_2$ (22 mg, 10 mol %) and anhydrous toluene (3 mL). The mixture was then stirred at 110 °C for 24 h (monitored by TLC). The resultant mixture was taken in EtOAc and washed with water. The organic solution was dried with anhydrous Na_2SO_4 and concentrated in rotatory evaporator under a vacuum. The column chromatographic purification of crude mixture on silica gel eluting with hexane−EtOAc (4:1) provided *N*-(*tert*-butyl)-2-phenyl-6-(4-tolyl)imidazo[1,2-*a*]pyrazin-3-amine (231 mg, 65% yield).

All arylation reactions (Table 2 and 3) were carried out following this experimental procedure.

1. N-tert-Butyl-2-phenyl-6-4-(tolyl)imidazo[1,2-a]pyrazin-3-amine (Table 2, Entry 1). Yellow semisolid: 231 mg, 65% yield; IR



(neat) ν_{max} = 3449, 2922, 1580, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.99 (s, 1H), 8.13 (d, J = 7.28 Hz, 2H), 7.65 (s, 1H), 7.43−7.38 (m, 6H), 7.34−7.32 (m, 1H), 2.48 (s, 3H), 2.47 (brs, NH), 0.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.7, 142.3, 139.7, 138.1, 134.6, 131.3, 131.2, 129.5, 129.4 (2CH), 129.0 (2CH), 128.6 (2CH), 128.2 (2CH), 128.0, 127.1, 57.0, 29.3 ($3CH_3$), 21.4; MS (APCI) m/z 357 (MH^+); HRMS (ESI) calcd for $C_{23}H_{24}N_4Na$ [M + Na]$^+$ 379.1893, found m/z 379.1903.

2. N-tert-Butyl-2-(4′-methylbiphenyl-2-yl)imidazo[1,2-a]pyrazin-3-amine (Side Product, P2). White semisolid: IR (neat) ν_{max} = 3338, 2918, 1607, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.02 (d, J = 1.4 Hz, 1H), 7.97 (dd, J = 4.6 Hz, 1.4 Hz, 1H), 7.82−7.78 (m, 2H), 7.48−7.43 (m, 3H), 7.07 (m, 4H), 2.33 (s, 3H), 0.73 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.0, 142.9, 140.5, 138.2, 137.6, 137.2, 132.8, 131.9, 129.8, 129.5 (2CH), 128.8, 128.7 (2CH), 128.6, 127.7, 125.8, 116.4, 55.8, 29.4, 21.2; MS (APCI) m/z 357 (MH^+); HRMS (ESI) calcd for $C_{23}H_{24}N_4Na$ [M + Na]$^+$ 379.1893, found m/z 379.1882.

Table 4. Analysis of Distortion/Interaction Energies for CMD TSs with Pivalate

site	$\Delta E^{\ddagger}_{gas}$	$\Delta E^{\ddagger}_{solv}$	$\Delta G^{\ddagger}_{gas}$	$\Delta G^{\ddagger}_{solv}$	$E_{dist(ArH)}$	$E_{dist(PdL}$	E_{int}	B_{Pd-C}
C5	25.25	28.13	40.52	43.41	48.56	22.76	−46.06	0.357
C6	24.11	27.06	40.31	43.26	40.89	18.29	−35.08	0.369
C8	26.92	29.66	41.01	43.75	53.09	23.08	−49.26	0.169
C2′	48.76	51.06	65.71	68.01	2.79	34.30	11.65	0.201

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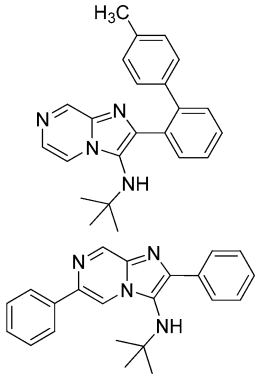
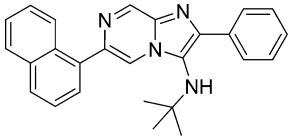


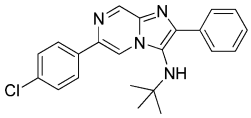
3. N-tert-Butyl-2,6-diphenylimidazo[1,2-a]pyrazin-3-amine (Table 2, Entry 2). Yellow semisolid: 201 mg, 59% yield; IR (neat) ν_{max} = 3435, 2924, 1606, 1459 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.01 (s, 1H), 8.11 (d, J = 7.04 Hz, 2H), 7.68 (s, 1H), 7.59−7.53 (m, 5H), 7.44−7.40 (m, 2H), 7.35−7.33 (m, 1H), 2.43 (brs, NH), 0.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.0, 142.6, 138.1, 134.6, 132.5, 131.5, 131.1, 129.5, 129.2 (2CH), 128.7 (2CH), 128.6 (2CH), 128.2 (2CH), 128.1, 127.1, 57.0, 29.7 ($3CH_3$); MS (APCI) m/z 343 (MH^+); HRMS (ESI) calcd for $C_{22}H_{22}N_4Na$ [M + Na]$^+$ 365.1737, found m/z 365.1745.

4. N-tert-Butyl-6-(naphthalen-1-yl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 3). Yellow semisolid: 204 mg, 52%



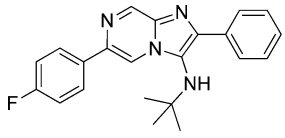
yield; IR (neat) ν_{max} = 3313, 2926, 1610, 1472 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.10 (s, 1H), 8.06 (d, J = 8.44 Hz, 1H), 8.02−7.98 (m, 3H), 7.83 (s, 1H), 7.73−7.65 (m, 2H), 7.59−7.57 (m, 1H), 7.47 (t, J = 7.2 Hz, 1H), 7.38 (m, 2H), 7.31 (d, J = 7.3 Hz, 1H), 7.21 (d, J = 8.4 Hz, 1H), 0.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.3, 143.0, 137.8, 134.6, 133.0, 132.2, 132.0, 130.3, 130.0, 129.7, 129.1, 128.9, 128.7 (2CH), 128.2, 128.1 (2CH), 127.8, 127.1, 126.9, 125.3, 124.2, 56.0, 29.3 ($3CH_3$), MS (APCI) m/z 393 (MH^+); HRMS (ESI) calcd for $C_{26}H_{24}N_4Na$ [M + Na]$^+$ 415.1893, found m/z 415.1896.

5. N-tert-Butyl-6-(4-chlorophenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 4). Yellow semisolid: 229 mg, 61%



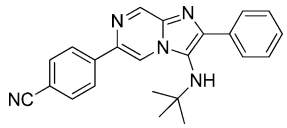
yield; IR (neat) ν_{max} = 3390, 2967, 1533, 1478 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.93 (s, 1H), 7.93 (d, J = 7.12 Hz, 2H), 7.59 (s, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.40 (d, J = 8.6 Hz, 2H), 7.37−7.34 (m, 2H), 7.29−7.27 (m, 1H), 2.43 (brs, NH), 0.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.5, 142.8, 138.0, 135.4, 134.4, 131.8, 130.8, 130.7 (2CH), 130.3, 128.6 (2CH), 128.5 (2CH), 128.3 (2CH), 128.2, 126.9, 57.0, 29.5 ($3CH_3$); MS (APCI) m/z 377 (MH^+); HRMS (ESI) calcd for $C_{22}H_{21}ClN_4Na$ [M + Na]$^+$ 399.1347, found m/z 399.1366.

6. N-(tert-Butyl)-6-(4-fluorophenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 5). Yellow semisolid: 172 mg, 48%



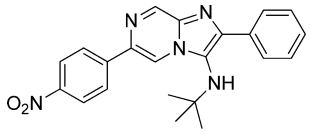
yield; IR (neat) ν_{max} = 3442, 2923, 1613, 1472, 1275 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.96 (s, 1H), 8.08 (d, J = 6.84 Hz, 2H), 7.71−7.66 (m, 3H), 7.43 (t, J = 6.9 Hz, 2H), 7.36−7.32 (m, 3H), 3.86 (brs, NH), 0.34 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 161.1, 143.1, 141.7 (2CH), 137.2, 134.3, 132.3 (d, J = 8 Hz), 131.2 (d, J = 25 Hz), 128.6, 128.5 (2CH), 128.1 (d, J = 3 Hz), 128.0 (2CH), 127.9, 126.9, 115.5 (d, J = 22 Hz), 114.2 (d, J = 21 Hz), 55.5. 28.9 ($3CH_3$); MS (APCI) m/z 361 (MH^+); HRMS (ESI) calcd for $C_{22}H_{21}FN_4Na$ [M + Na] $^+$ 383.1642, found m/z 383.1634.

7. N-(tert-Butyl)-6-(4-cyanophenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 6). Yellow semisolid: 198 mg, 54%



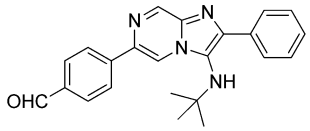
yield; IR (neat) ν_{max} = 3420, 2935, 2257, 1645, 1432 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.01 (s, 1H), 8.07 (d, J = 7.44 Hz, 2H), 7.95 (d, J = 7.56 Hz, 2H), 7.85 (d, J = 7.52 Hz, 2H), 7.79 (s, 1H), 7.43 (t, J = 7.0 Hz, 2H), 7.37−7.34 (m, 1H), 4.08 (brs, NH), 0.31 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ = 143.6, 142.4, 136.9, 136.4, 134.1, 131.9, 131.1 (2CH), 130.9 (2CH), 130.3, 128.6 (2CH), 128.1 (2CH), 128.0, 127.1, 118.7, 111.0, 55.4, 28.8 ($3CH_3$); MS (APCI) m/z 368 (MH^+); HRMS (ESI) calcd for $C_{23}H_{21}N_5Na$ [M + Na]$^+$ 390.1689, found m/z 390.1693.

8. N-(tert-Butyl)-6-(4-nitrophenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 7). Yellow semisolid: 201 mg, 52%



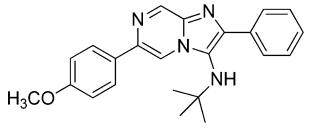
yield; IR (neat) ν_{max} = 3451, 2925, 1592, 1443 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.07 (s, 1H), 8.40 (dd, J = 6.92 Hz, 1.8 Hz, 2H), 7.90 (d, J = 7.16 Hz, 2H), 7.78 (s, 1H), 7.74 (dd, J = 6.84 Hz, 1.92 Hz, 2H), 7.49−7.45 (m, 2H), 7.41−7.39 (m, 1H), 2.70 (brs, NH), 0.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 147.8, 144.5, 143.5, 138.5, 137.6, 134.0, 132.5, 130.6 (2CH), 129.6, 128.6 (4CH), 128.5, 127.0, 122.9 (2CH), 57.2, 29.2 ($3CH_3$); MS (APCI) m/z 388 (MH^+); HRMS (ESI) calcd for $C_{22}H_{21}N_5NaO_2$ [M + Na]$^+$ 410.1587, found m/z 410.1576.

9. N-(tert-Butyl)-6-(4-formylphenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 8). Yellow semisolid: 177 mg, 48%



yield; IR (neat) ν_{max} = 3391, 2920, 1702, 1601, 1444 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 10.14 (s, 1H), 9.05 (s, 1H), 8.07 (d, J = 7.92 Hz, 2H), 7.99 (d, J = 7.32 Hz, 2H), 7.77 (s, 1H), 7.73 (d, J = 7.92 Hz, 2H), 7.47−7.44 (m, 2H), 7.39−7.37 (m, 1H), 2.56 (brs, NH), 0.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 191.3, 144.0, 143.2, 138.1, 137.8, 136.4, 134.1, 132.2, 130.3, 130.1 (2CH), 129.3 (2CH), 128.6 (2CH), 128.4 (2CH), 128.2, 127.0, 57.0, 29.3 ($3CH_3$); MS (APCI) m/z 371 (MH^+); HRMS (ESI) calcd for $C_{23}H_{22}N_4NaO$ [M + Na]$^+$ 393.1686, found m/z 393.1704.

10. N-(tert-Butyl)-6-(4-methoxyphenyl)-2-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 2, Entry 9). Yellow semisolid: 189 mg, 51%



yield; IR (neat) ν_{max} = 3438, 2924, 1633, 1468 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.98 (s, 1H), 8.11 (d, J = 7.48 Hz, 2H), 7.63 (s, 1H), 7.47−7.40 (m, 4H), 7.34−7.32 (m, 1H), 7.11 (d, J = 8.56 Hz, 2H), 3.91 (s, 3H), 2.52 (brs, NH), 0.50 (s, 9H); ^{13}C NMR (100 MHz,

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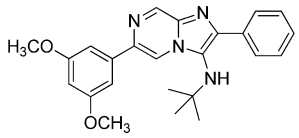
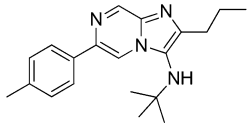
$CDCl_3$) δ = 160.5, 142.7, 142.2, 138.2, 134.6, 131.3, 131.1, 130.5 (2CH), 128.6 (2CH), 128.2 (2CH), 128.0, 127.1, 124.6, 114.1 (2CH), 57.1, 55.6, 29.4 ($3CH_3$); MS (APCI) m/z 373 (MH^+); HRMS (ESI) calcd for $C_{23}H_{24}N_4NaO$ [M + Na]$^+$ 395.1842, found m/z 395.1857.

11. N-(tert-Butyl)-6-(3,5-dimethoxyphenyl)-2-phenylimidazo[1,2-a]pyrazin-3-amine (Table 2, Entry 10). Yellow semisolid: 185 mg,



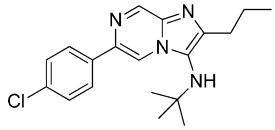
46% yield; IR (neat) ν_{max} = 3438, 2927, 1629, 1345 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.99 (s, 1H), 8.15 (d, J = 7.08 Hz, 2H), 7.70 (s, 1H), 7.43−7.40 (m, 2H), 7.34−7.32 (m, 1H), 6.66−6.62 (m, 3H), 3.87 (s, 6H), 2.64 (brs, NH), 0.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.2 (2C), 142.7, 142.6, 138.1, 134.6, 134.1, 131.1, 130.7, 128.6 (2CH), 128.2 (2CH), 128.1, 127.3, 107.3 (2CH), 101.1, 56.9, 55.8 ($2CH_3$), 29.5 ($3CH_3$); MS (APCI) m/z 403(MH^+); HRMS (ESI) calcd for $C_{24}H_{26}N_4NaO_2$ [M + Na]$^+$ 425.1948, found m/z 425.1968.

Table 3. *1. N-tert-Butyl-2-propyl-6-(p-tolyl)imidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 1).* Yellow semisolid: 228 mg, 71% yield; IR



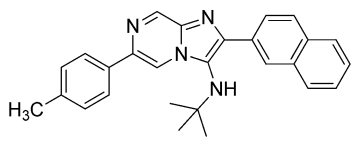
(neat) ν_{max} = 3380, 2961, 1613,1482 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.89 (s, 1H), 7.62 (s, 1H), 7.34 (m, 4H), 2.79 (t, J = 7.8 Hz, 2H), 2.46 (s, 3H), 2.35 (brs, NH), 1.90−1.84 (m, 2H), 1.04−1.01 (t, J = 7.36 Hz, 3H), 0.63 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 145.9, 141.4, 139.4, 138.1, 131.2, 131.1, 129.5, 129.3 (2CH), 128.9 (2CH), 126.7, 55.9, 30.1, 29.3 ($3CH_3$), 22.6, 21.3, 14.3; MS (APCI) m/z 323 (MH^+); HRMS (ESI) calcd for $C_{20}H_{26}N_4Na$ [M + Na]$^+$ 345.2050, found m/z 345.2055.

2. N-(tert-Butyl)-6-(4-chlorophenyl)-2-propylimidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 2). Yellow semisolid: 232 mg, 68%



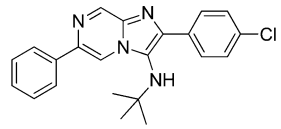
yield; IR (neat) ν_{max} = 3389, 2962, 1533, 1478 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.91 (s, 1H), 7.64 (s, 1H), 7.48 (dd, J = 8.30 Hz, 1.12 Hz, 2H), 7.42 (d, J = 8.28 Hz, 2H), 2.81−2.77 (m, 2H), 2.36 (brs, NH), 1.90−1.84 (m, 2H), 1.03 (t, J = 7.24 Hz, 3H), 0.66 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.1, 141.7, 137.9, 135.1, 131.6, 131.1 (2CH), 130.6, 130.3, 128.0 (2CH), 126.7, 55.9, 30.0, 29.5 ($3CH_3$), 22.6, 14.3; MS (APCI) m/z 343 (MH^+); HRMS (ESI) calcd for $C_{19}H_{23}ClN_4Na$ [M + Na]$^+$ 365.1503, found m/z 365.1512.

3. N-tert-Butyl-2-(naphthalen-2-yl)-6-(p-tolyl)imidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 3). Yellow semisolid: 247 mg, 61%



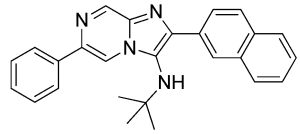
yield; IR (neat) ν_{max} = 3391, 2969, 1598, 1479 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.04 (s, 1H), 8.67 (s, 1H), 8.35 (dd, J = 8.7 Hz, 1.64 Hz, 1H), 7.93−7.91 (m, 1H), 7.87 (d, J = 8.7 Hz, 1H), 7.84−7.81 (m, 1H), 7.66 (s, 1H), 7.47−7.46 (m, 2H), 7.44−7.39 (m, 4H), 2.54 (brs, NH), 2.48 (s, 3H), 0.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.4, 142.3, 139.8, 138.3, 133.4, 133.1, 132.2, 131.4, 131.2, 129.52 (2CH), 129.49, 128.9 (2CH), 128.4, 127.64, 127.58 (2CH), 127.5, 126.5, 126.1, 126.0, 57.2, 29.4 ($3CH_3$), 21.4; MS (APCI) m/z 407 (MH^+); HRMS (ESI) calcd for $C_{27}H_{26}N_4Na$ [M + Na]$^+$ 429.2050, found m/z 429.2064.

4. N-(tert-Butyl)-2-(4-chlorophenyl)-6-phenylimidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 4). Yellow semisolid: 221 mg, 59%



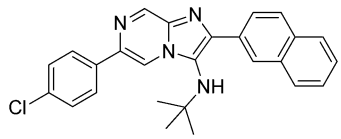
yield; IR (neat) ν_{max} = 3438, 2925, 1620, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.0 (s, 1H), 8.13 (dd, J = 6.8 Hz, 1.8 Hz, 2H), 7.69 (s, 1H), 7.60−7.56 (m, 3H), 7.54−7.52 (m, 2H), 7.39 (dd, J = 6.8 Hz, 1.8 Hz, 2H), 2.38 (brs, NH), 0.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.7, 141.6, 138.2, 133.9, 133.1, 132.4, 131.6, 131.0, 129.8 (2CH), 129.6, 129.0 (2CH), 128.9 (2CH), 128.4 (2CH), 127.1, 57.2, 29.4 ($3CH_3$); MS (APCI) m/z 377 (MH^+); HRMS (ESI) calcd for $C_{22}H_{21}ClN_4Na$ [M + Na]$^+$ 399.1347, found m/z 399.1341.

5. N-(tert-Butyl)-2-(naphthalen-2-yl)-6-phenylimidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 5). Yellow semisolid: 250 mg, 64%



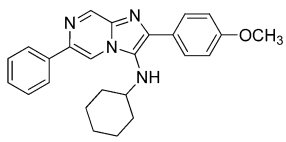
yield; IR (neat) ν_{max} = 3390, 2926,1611, 1415 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.05 (s, 1H), 8.65 (s, 1H), 8.32 (dd, J = 8.6 Hz, 1.48 Hz, 1H), 7.93−7.91 (m, 1H), 7.88 (d, J = 8.6 Hz, 1H), 7.85−7.82 (m, 1H), 7.70 (s, 1H), 7.61−7.55 (m, 5H), 7.49−7.46 (m, 2H), 2.50 (brs, NH), 0.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.64, 142.6, 138.3, 133.4, 133.1, 132.5, 132.1, 131.6, 131.1, 129.6, 129.1 (2CH), 128.9 (2CH), 128.4, 127.66, 127.63, 127.62, 127.4, 126.5, 126.1, 126.0, 57.2, 29.3 ($3CH_3$); MS (APCI) m/z 393 (MH^+); HRMS (ESI) calcd for $C_{26}H_{24}N_4Na$ [M + Na]$^+$ 415.1893, found m/z 415.1882.

6. N-(tert-Butyl)-6-(4-chlorophenyl)-2-(naphthalen-2-yl)imidazo-[1,2-a]pyrazin-3-amine (Table 3, Entry 6). Yellow semisolid: 277 mg,



65% yield; IR (neat) ν_{max} = 3437, 2925, 1605, 1461 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.06 (s, 1H), 8.56 (s, 1H), 8.22 (dd, J = 8.52 Hz, 1.6 Hz, 1H), 7.94−7.89 (m, 2H), 7.86−7.84 (m, 1H), 7.69 (s, 1H), 7.59−7.57 (m, 2H), 7.52−7.48 (m, 4H), 2.54 (brs, NH), 0.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 143.3, 142.8, 138.1, 135.6, 133.4, 133.2, 131.8, 131.7, 130.8, 130.6 (2CH), 130.3, 128.7 (3CH), 128.4, 127.8, 127.7 (2CH), 127.2, 126.3, 126.2, 57.2, 29.4 ($3CH_3$); MS (APCI) m/z 427(MH^+); HRMS (ESI) calcd for $C_{26}H_{23}ClN_4Na$ [M + Na]$^+$ 449.1503, found m/z 449.1503.

7. N-Cyclohexyl-2-(4-methoxyphenyl)-6-phenylimidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 7). Yellow semisolid: 286 mg, 72%



yield; IR (neat) ν_{max} = 3380, 2927, 1610, 1448, 1250 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.96 (s, 1H), 8.12 (d, J = 8.72 Hz, 2H), 7.61 (s, 1H), 7.55 (m, 5H), 6.96 (d, J = 8.68 Hz, 2H), 3.85 (s, 3H), 2.51 (d, J = 6.08 Hz, NH), 2.26−2.21 (m, 1H), 1.37−1.34 (m, 3H), 1.02−0.99 (m, 2H), 0.84−0.79(m, 3H), 0.59−0.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 159.4, 142.2, 139.3, 137.5, 131.8, 130.6, 130.3, 129.6, 129.4 (2CH), 129.1(2CH), 128.4 (2CH), 127.5, 126.5, 113.7

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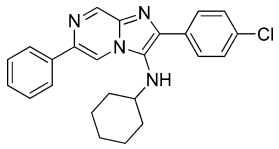
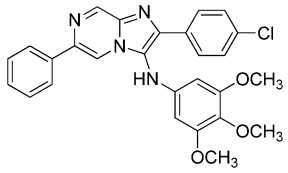
(2CH), 57.3, 55.2, 33.7 ($2CH_2$), 25.5, 24.6 ($2CH_2$); MS (APCI) m/z 399 (MH^+); HRMS (ESI) calcd for $C_{25}H_{26}N_4NaO$ $[M + Na]^+$ 421.1999, found m/z 421.1998.

8. N-Cyclohexyl-2-(4-chlorophenyl)-6-phenylimidazo[1,2-a]-pyrazin-3-amine (Table 3, Entry 8). Yellow semisolid: 297 mg, 74%



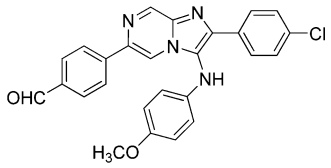
yield; IR (neat) ν_{max} = 3336, 2927, 1631, 1488 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 8.98 (s, 1H), 8.16 (dd, J = 6.76 Hz, 1.92 Hz, 2H), 7.64 (s, 1H), 7.63−7.53 (m, 5H), 7.40 (dd, J = 6.76 Hz, 1.92 Hz, 2H), 2.48 (d, J = 5.84 Hz, NH), 2.28−2.21 (m, 1H), 1.38−1.34 (m, 3H), 1.01−0.98 (m, 2H), 0.84−0.76 (m, 3H), 0.59−0.50 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 142.7, 138.1, 137.6, 133.7, 132.4, 131.6, 130.7, 130.4, 129.9, 129.4 (2CH), 129.0 (2CH), 128.6 (2CH), 128.5 (2CH), 128.1, 57.5, 32.7 ($2CH_2$), 25.4, 24.6 ($2CH_2$); MS (APCI) m/z 403 (MH^+); HRMS (ESI) calcd for $C_{24}H_{23}ClN_4Na$ $[M + Na]^+$ 425.1503, found m/z 425.1504.

9. 2-(4-Chlorophenyl)-6-phenyl-N-(3,4,5-trimethoxyphenyl)-imidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 9). Yellow semisolid:



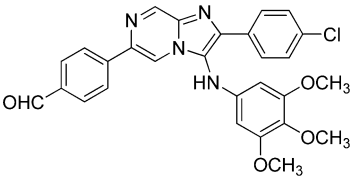
243 mg, 50% yield; IR (neat) ν_{max} = 3420, 2923, 1607, 1445, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.10 (s, 1H), 8.04 (d, J = 7.76 Hz, 2H), 7.66 (s, 1H), 7.42−7.40 (m, 1H), 7.36−7.32 (m, 4H), 7.25−7.23 (m, 2H), 5.06 (s, 2H), 4.70 (brs, NH), 3.71 (s, 3H), 3.51 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 153.7 (2C), 142.9, 141.7, 140.2, 138.5, 134.6, 131.8, 131.3, 131.0, 130.9, 130.8, 129.3 (2CH), 129.2, 128.9 (2CH), 128.7 (2CH), 128.0 (2CH), 120.5, 91.0 (2CH), 61.0 (OCH_3), 55.8 ($2OCH_3$); MS (APCI) m/z 487 (MH^+); HRMS (ESI) calcd for $C_{27}H_{23}ClN_4NaO_3$ $[M + Na]^+$ 509.1356, found m/z 509.1357.

10. 2-(4-Chlorophenyl)-N-(4-methoxyphenyl)-6-(4-formylphenyl)imidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 9).



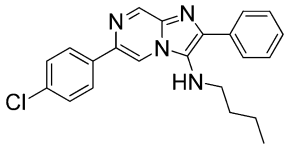
Yellow semisolid: 254 mg, 56% yield; IR (neat) ν_{max} = 3392, 2917, 1701, 1604, 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 10.03 (s, 1H), 9.13 (s, 1H), 7.98 (d, J = 8.28 Hz, 2H), 7.75 (d, J = 7.78 Hz, 2H), 7.67 (s, 1H), 7.38 (d, J = 7.78 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 6.49 (d, J = 8.52 Hz, 2H), 5.79 (d, J = 8.52 Hz, 2H), 4.71 (brs, NH), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 191.3, 153.8, 143.5, 141.9, 138.4, 137.2, 136.6, 136.4, 134.7, 130.9 (1CH, 1C), 130.2, 130.0 (2CH), 128.9 (2CH), 128.7 (2CH), 128.5(2CH), 120.9, 114.7 (2CH), 114.1(2CH), 55.6; MS (APCI) m/z 455 (MH^+); HRMS (ESI) calcd for $C_{26}H_{19}ClN_4NaO_2$ $[M + Na]^+$ 477.1094, found m/z 477.1079.

11. 2-(4-Chlorophenyl)-6-(4-formylphenyl)-N-(3,4,5-trimethoxyphenyl)imidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 11). Yellow semisolid: 267 mg, 52% yield; IR (neat) ν_{max} = 3401, 2928, 1698, 1599, 1431 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ = 10.03 (s, 1H), 9.15 (s, 1H), 8.00 (d, J = 7.76 Hz, 2H), 7.79 (d, J = 7.12 Hz, 2H), 7.71 (s, 1H), 7.41−7.37 (m, 4H), 5.03 (s, 2H), 4.80 (brs, NH), 3.72 (s, 3H), 3.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 191.2, 153.9 (2C), 143.6, 142.3, 139.9, 138.5, 136.6, 136.4, 134.9, 132.0, 131.0, 130.8, 130.2, 130.1 (2CH), 129.0 (2CH), 128.7 (2CH), 128.6 (2CH),



120.1, 90.8 (2CH), 61.1 (OCH_3), 55.9 ($2OCH_3$); MS (APCI) m/z 515 (MH^+); HRMS (ESI) calcd for $C_{28}H_{23}ClN_4NaO_4$ $[M + Na]^+$ 537.1306, found m/z 537.1318.

12. N-Butyl-6-(4-chlorophenyl)-2-phenylimidazo[1,2-a]pyrazin-3-amine (Table 3, Entry 12). Yellow oil: 199 mg, 53% yield; IR (neat)



ν_{max} = 3402, 2967, 1653, 1275 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.97 (s, 1H), 8.00 (d, J = 8.0 Hz, 2H), 7.60 (s, 1H), 7.55−7.51 (m, 4H), 7.46−7.43 (m, 2H), 7.36−7.34 (m, 1H), 2.41 (m, 2H), 1.74 (brs, NH), 0.96−0.92 (m, 4H), 0.72−0.69 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 143.0, 137.9, 137.1, 136.1, 133.5, 131.0 (2CH), 130.6, 130.0, 129.7, 129.4, 128.8 (2CH), 128.5 (2CH), 128.2, 127.5 (2CH), 49.1, 31.8, 19.8, 13.8; MS (APCI) m/z 377 (MH^+); HRMS (ESI) calcd for $C_{22}H_{21}ClN_4Na$ $[M + Na]^+$ 399.1347, found m/z 399.1340.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details of computational studies and ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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