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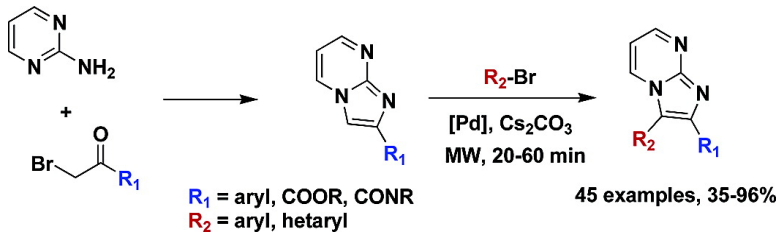

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Articles

Efficient Pd(0)-Mediated Microwave-Assisted Arylation of 2-Substituted Imidazo[1,2-*a*]pyrimidines

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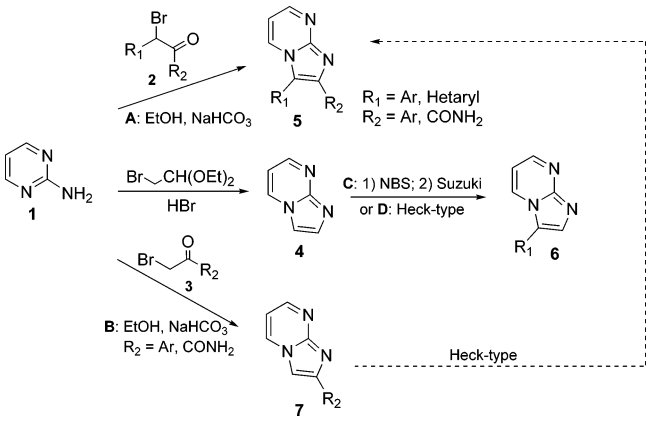
A short and practical synthesis of 2,3-substituted imidazo[1,2-*a*]pyrimidines, based on microwave-assisted Heck-type arylation of 2-substituted imidazo[1,2-*a*]pyrimidines, was developed. A 45-membered library of 2,3-substituted imidazo[1,2-*a*]pyrimidines was obtained with good yields and purities using this optimized protocol.

Introduction

Many 2,3-substituted imidazo[1,2-*a*]pyrimidines **5** (Scheme 1) are found to be biologically active.[1] For example, 2,3-diaryl imidazo[1,2-*a*]pyrimidines possess inhibitory activity against cyclooxigenase-2 (COX-2) with high selectivity in relation to COX-1.[2,3] Therefore, they could be useful for the treatment of inflammation and diseases mediated by COX-2 with a reduced ulcerogenic potential. Moreover, these compounds have been shown recently to express anti-cancer activity.[4] In addition, several 2-carboxamidoimidazo[1,2-*a*]-pyrimidines **5** (R_1 = Ar, R_2 = $CONH_2$) display analgesic, antipyretic, and anti-inflammatory activity[5] and might serve as potent glutamate antagonists for the treatment of cancer.[6] Differently substituted 2-carboxamidoimidazo[1,2-*a*]pyrimidines **5** were also reported to inhibit glycogen phosphorylase, making them useful in prophylactic and therapeutic treatment of diabetes, hyperglycemia, hypertension, and arteriosclerosis and as cardioprotectants.[7]

Within the framework of developing libraries of the aforementioned bioactive compounds, we are currently investigating the synthesis of various 2,3-substituted imidazo-[1,2-*a*]pyrimidines, bearing a phenyl, carboxamide, or carboxylate function at the 2-position and an aromatic substituent at the 3-position of scaffold **5**. To our knowledge, there is no general methodology described in the literature for the synthesis of such compounds. The main approach (Scheme 1, pathway A) starts from a suitable 1,2-diaryl-2-bromoethanone (**2**) which is reacted with 2-aminopyrimidine (**1**).[4] Unfortunately, variation of the substituents R_1 and R_2 is restricted because of the limited availability of the starting 1,2-diaryl-2-bromoketones (**2**) and the low overall yields.[3]

Scheme 1



Only 3-monosubstituted compounds **6** are accessible via an alternative approach (Scheme 1, pathway C) involving bromination of the 3-position[7] of the unsubstituted imidazo-[1,2-*a*]pyrimidine (**4**), followed by Suzuki coupling with a suitable arylboronic acid.[8] Although this sequence was successful, an additional step for the activation of the 3-position is required. It was recently reported that the 2-unsubstituted imidazo[1,2-*a*]pyrimidine scaffold **4** could be selectively arylated at the 3-position via a Heck-type reaction, which applies arylbromides in the presence of base and a catalytic amount of palladium (Scheme 1, pathway D).[9] This method provided an efficient synthesis of mono-substituted 3-arylimidazo[1,2-*a*]pyrimidines **6**, using commercially available aryl and heteroaryl bromides.

However, our attempts to arylate the corresponding 2-substituted analogues, following the same Heck-type procedure, failed. To find proper arylation conditions, we started to investigate this reaction in more detail. Here, we report a hitherto unprecedented protocol for the arylation of the 3-position of 2-substituted imidazo[1,2-*a*]pyrimidines **7** using microwave irradiation (Scheme 1, pathway B).

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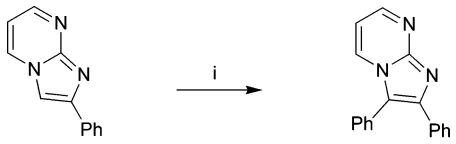
Scheme 2[a]



7a **5{1}**

[a] Reaction conditions: (i) bromobenzene (1.35 equiv), Pd catalyst (8 mol %)/ligand (16 mol %), Cs_2CO_3 (1.1 equiv), 1,4-dioxane, and heating or MW-irradiation.

Table 1. Optimization of the Conditions for the Arylation of **7a** with Bromobenzene[a]

entry	conditions	catalyst/ligand	temp (°C)	time (h)	yield (%)
1	Δ	$Pd(OAc)_2/Ph_3P$	100	72	24
2		$Pd(OAc)_2/Ph_3P$	120	72	42
3		$Pd(OAc)_2/Ph_3P$	145	72	56
4		$Pd(PPh_3)_2Cl_2/Ph_3P$	145	72	4
5		$Pd(PPh_3)_4$	145	72	15
6	MW[b]	$Pd(OAc)_2/Ph_3P$	100	4	32
7		$Pd(OAc)_2/Ph_3P$	120	1	70
8		$Pd(OAc)_2/Ph_3P$	145	0.5	96
9		$Pd(PPh_3)_2Cl_2/Ph_3P$	145	0.5	0
10		$Pd(PPh_3)_4$	145	0.5	20

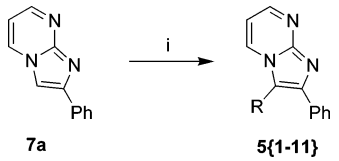
[a] All reactions were performed on a 0.5 mmol scale in 6 mL of 1,4-dioxane with 1.35 equiv of bromobenzene, 1.35 equiv of Cs_2CO_3, 8 mol % of the catalyst, and 16 mol % PPh_3 (if necessary). [b] All the MW experiments were performed at 150 W maximum power.

Results and Discussion

We started to reinvestigate the arylation of 2-phenylimidazo[1,2-*a*]pyrimidine (**7a**) with bromobenzene by exploiting the previously described procedure[9] for 2-unsubstituted imidazo[1,2-*a*]pyrimidines (Scheme 2). However, with the literature conditions, even after 3 days of conventional heating at 100 °C in 1,4-dioxane and application of $Pd(AcO)_2/PPh_3$ as the catalyst system and cesium carbonate as the base, a yield of only 24% was obtained for the desired arylated product **5**{**1**} (Table 1, entry 1). The best conditions were found when the temperature was increased to 145 °C, which resulted in a moderate yield of 56% (Table 1, entry 3). Increasing the temperature of the reaction up to 180 °C led to a number of unidentified side products and to decomposition of the catalyst in a few hours. Switching the catalyst system to $Pd(PPh_3)_2Cl_2/PPh_3$ (Table 1, entry 4) or $Pd(PPh_3)_4$ (Table 1, entry 5) seemed to be deleterious for the reaction. As we have previously demonstrated the beneficial effects of the application of microwave irradiation for transition metal-catalyzed reactions,[10,11] we decided to investigate the use of this technique for this arylation procedure.

The reaction of 2-phenylimidazo[1,2-*a*]pyrimidine (**7a**) was tested under microwave irradiation at 100 °C in 1,4-dioxane with $Pd(OAc)_2/PPh_3$ as the catalyst system and cesium carbonate as the base. However, after 4 h, the desired product **5**{**1**} was obtained in only a 32% yield (Table 1, entry 6). When the ceiling temperature was increased to 120 °C, the reaction time could be shortened to 1 h and a good yield of 70% was obtained (Table 1, entry 7). A further increase of the temperature to 145 °C produced the product in an excellent 96% yield, and the irradiation time could be shortened to a mere 30 min (Table 1, entry 8). In all cases, a slight excess of bromobenzene (1.35 equiv) was used to drive the arylation to completion. The use of more than 1.5 equiv of bromobenzene resulted in the formation of a significant amount of unidentified side products.

Scheme 3[a]



7a **5{1-11}**

[a] Reaction conditions: (i) RBr (1.35 equiv), $Pd(AcO)_2$ (8 mol %), PPh_3 (16 mol %), Cs_2CO_3 (1.1 equiv), 1,4-dioxane, MW 150 W, 20−60 min, 145 °C.

Table 2. Arylation of 2-Phenylimidazo[1,2-*a*]pyrimidine (**7a**) with Various Aryl Bromides[a]

entry	product	R	time (min)	yield (%)
1	**5**{**1**}	phenyl	30	96
2	**5**{**2**}	4′-fluorophenyl	20	95
3	**5**{**3**}	4′-chlorophenyl	35	82
4	**5**{**4**}	4′-trifluoromethylphenyl	25	84
5	**5**{**5**}	2′-fluorophenyl	60	86
6	**5**{**6**}	3′,5′-difluorophenyl	50	65
7	**5**{**7**}	4′-methoxyphenyl	60	54
8	**5**{**8**}	4′-methanesulfonylphenyl	25	80
9	**5**{**9**}	isoquinol-4-yl	60	67
10	**5**{**10**}	pyridin-2-yl	50	55
11	**5**{**11**}	4′-*tert*-butylphenyl	55	46

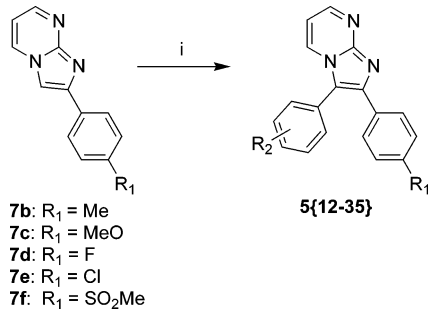
[a] All reactions were performed on a 0.5 mmol scale in 6 mL of 1,4-dioxane with 1.35 equiv of aryl bromide, 1.35 equiv of Cs_2CO_3, 8 mol % $Pd(OAc)_2$, and 16 mol % PPh_3; all experiments were performed at 150 W maximum power and a ceiling temperature of 145 °C.

To determine the scope and limitations of our microwave-assisted protocol, we investigated the arylation procedure with several aryl bromides (Scheme 3, Table 2). In agreement with the arylation mechanism proposed by Larsen et al.,[9] we noticed that in almost all cases the more-reactive electron-poor aryl bromides resulted in high yields (80−96%) (Table 2, entries 1−5 and 8). The less-reactive aryl bromides such as 4′-*tert*-butyl- (Table 2, entry 11) and 4′-methoxyphenyl bromide (Table 2, entry 7) resulted in lower yields. The procedure could also be applied successfully for hetaryl bromides (Table 2, entries 9 and 10), although lower yields were obtained.

Unexpectedly, 3′,5′-difluorobromobenzene was quite unreactive despite the two electron-withdrawing groups (Table 2, entry 6). An increase of the temperature to 160 °C during microwave irradiation did not improve the yield and resulted in decomposition.

To further evaluate the applicability of our microwave-enhanced arylation procedure, we investigated different combinations of 2-arylimidazo[1,2-*a*]pyrimidines **7b**−**f**, which were prepared according to standard procedures,[12] with various arylbromides (Scheme 4, Table 3). To circumvent the problem of the poor solubility of several of the 2-arylimidazo[1,2-*a*]pyrimidines in 1,4-dioxane, the temperature was increased irradiation to 160 °C. The changeof 1,4-dioxane for DMF resulted in the formation of large amounts of

Scheme 4[a]



[a] Reaction conditions: (i) aryl bromide (1.35 equiv), $Pd(AcO)_2$ (8 mol %), PPh_3 (16 mol %), Cs_2CO_3 (1.1 equiv), 1,4-dioxane, MW 150 W, 20−60 min, 160 °C.

Table 3. Arylation of 2-Arylimidazo[1,2-*a*]pyrimidines **7b-f**[a]

entry	product	R_1	R_2	time (min)	yield (%)
1	**5**{**12**}	4′-Me	H	20	76
2	**5**{**13**}	4′-Me	4′-F	30	44
3	**5**{**14**}	4′-Me	4′-$MeSO_2$	30	70
4	**5**{**15**}	4′-Me	4′-CF_3	20	71
5	**5**{**16**}	4′-Me	Cl	60	79
6	**5**{**17**}	4′-Me	4′-MeO	60	48
7	**5**{**18**}	4′-MeO	H	30	65
8	**5**{**19**}	4′-MeO	4′-F	40	79
9	**5**{**20**}	4′-MeO	4′-Cl	30	70
10	**5**{**21**}	4′-MeO	4′-CF_3	30	74
11	**5**{**22**}	4′-MeO	2′-F	60	55
12	**5**{**23**}	4′-MeO	4′-$MeSO_2$	30	77
13	**5**{**24**}	4′-F	H	20	90
14	**5**{**25**}	4′-F	4′-F	20	89
15	**5**{**26**}	4′-F	4′-Cl	20	94
16	**5**{**27**}	4′-F	4′-CF_3	20	69
17	**5**{**28**}	4′-F	4′-COMe	40	35
18	**5**{**29**}	4′-F	2′-F	40	58
19	**5**{**30**}	4′-Cl	H	20	86
20	**5**{**31**}	4′-Cl	4′-F	40	56
21	**5**{**32**}	4′-Cl	4′-CF_3	40	72
22	**5**{**33**}	4′-Cl	4′- $MeSO_2$	50	65
23	**5**{**34**}	4′- $MeSO_2$	4′-F	30	84
24	**5**{**35**}	4′- $MeSO_2$	biphenyl-4-yl	40	67

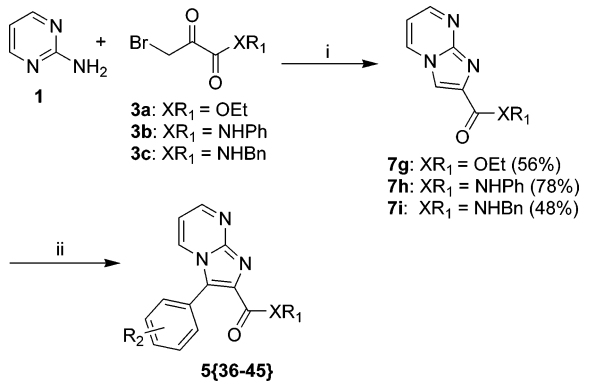
[a] All reactions were performed on a 0.5 mmol scale in 6 mL of 1,4-dioxane with 1.35 equiv of aryl bromide, 1.35 equiv of Cs_2CO_3, 8 mol % $Pd(OAc)_2$, and 16 mol % PPh_3; all experiments were performed at 150 W maximum power and a ceiling temperature of 160 °C.

resinous material. Consistently, most activated aryl bromides bearing electron-withdrawing groups, gave good to excellent yields (Table 3, entries 3−5, 8−10, 12, 14−16, 21, and 23). Aryl bromides bearing electron-donating groups gave lower yields (Table 3, entry 6). The lower yields for 3-(2′-fluoro)-imidazo[1,2-α]pyrimidines **5**{**22**} and **5**{**29**} could probably be attributed to steric hindrance (Table 3, entries 11 and 18).

Although 2-(4′-methylsulfonylphenyl)imidazo[1,2-*a*]pyrimidine (**7f**) is hardly soluble in 1,4-dioxane, moderate to good yields were obtained at the elevated temperature of 160 °C (Table 3, entries 23 and 24).

Finally, we turned our attention to the arylation of imidazo-[1,2-*a*]pyrimidines bearing an ethyl carboxylate or carboxamide function at the 2-position (Scheme 5, Table 4).[13] The starting imidazo[1,2-*a*]pyrimidines[14,15] **7g**−**i** were prepared from commercially available ethyl 3-bromopyruvate **3a** and 3-bromopyruvamides[16,17] **3b** and **c**.

Scheme 5[a]



[a] Reaction conditions: (i) (1) acetone, reflux, 45 min, (2) $NaHCO_3$ (4 equiv), $EtOH/H_2O$ (3:2), 65 °C, 1 h; (ii) aryl bromide (1.35 equiv), $Pd(AcO)_2$ (8 mol %), PPh_3 (16 mol %), Cs_2CO_3 (1.1 equiv), 1,4-dioxane, MW 150 W, 25−40 min, 145 °C.

Table 4. Arylation of Imidazo[1,2-*a*]pyrimidine-2-carboxylic Acid Derivatives **7** g−**i**[a]

entry	product	XR_1	R_2	time (min)	yield (%)
1	**5**{**36**}	OEt	4′-CF_3	30	64
2	**5**{**37**}	OEt	H	45	47
3	**5**{**38**}	NHPh	H	25	80
4	**5**{**39**}	NHPh	4′-F	25	67
5	**5**{**40**}	NHPh	4′-Cl	30	86
6	**5**{**41**}	NHPh	4′-CF_3	45	67
7	**5**{**42**}	NHPh	3′,5′-diF	60	54
8	**5**{**43**}	NHBn	H	20	92
9	**5**{**44**}	NHBn	4′-CF_3	20	86
10	**5**{**45**}	NHBn	4′-$MeSO_2$	30	55

[a] All reactions were performed on a 0.5 mmol scale in 6 mL of 1,4-dioxane with 1.35 equiv of aryl bromide, 1.35 equiv of Cs_2CO_3, 8 mol % $Pd(OAc)_2$, and 16 mol % PPh_3; all experiments were performed at 150 W maximum power and a ceiling temperature of 145 °C.

The reaction of ethyl imidazo[1,2-*a*]pyrimidine-2-carboxylate (**7g**) resulted in a considerable amount of decomposition products (Table 4, entries 1 and 2). The coupling of 1-bromo-4-(methylsulfonyl)benzene with **7i** unexpectedly resulted in the formation a lot of homo-coupled products, together with the desired compound (Table 4, entry 10). 1-Bromo-3′,5′-difluorobenzene appeared to be quite unreactive and required 1 h of microwave irradiation to give the arylated product **5**{**42**} in a 54% yield (Table 4, entry 7). In all other cases, the desired compounds were formed in good yields.

In conclusion, we have developed a short and efficient microwave-enhanced protocol for the Pd(0)-mediated arylation of 2-substituted imidazo[1,2-*a*]pyrimidines at their 3-position. The general applicability of this procedure was proven by the synthesis of a small combinatorial library of various 2,3-substituted imidazo[1,2-*a*]pyrimidines. Moreover, we have demonstrated that this procedure could be applied for the synthesis of difficult to obtain imidazo[1,2-*a*]-pyrimidines with 2-carboxamide or 2-carboxylate functions.

Experimental Section

General Methods. Melting points were determined using a Reichert−Jung Thermovar apparatus or an Electrothermal 9200 digital melting point apparatus and are uncorrected. ^1H NMR spectra were recorded on a Bruker Avance 300

instrument using $CDCl_3$ as the solvent unless otherwise stated. The ^1H and ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane using the residual solvent signal as an internal reference. Mass spectra were recorded by using a Kratos MS50TC and a Kratos Mach III system. The ion source temperature was 150−250 °C, as required. High-resolution electrospray ionization mass spectra were performed with a resolution of 10 000. The low-resolution spectra were obtained with a HP5989A MS instrument. For thin-layer chromatography, analytical TLC plates (Alugram SIL G/UV_{254}) and 70−230 mesh silica gel (E. M. Merck) were used.

Microwave Irradiation Experiments. A monomode CEM-Discover microwave reactor (CEM Corporation, P.O. Box 200, Matthews, NC 28106) was used in the standard configuration as delivered, including proprietary software. All experiments were carried out in sealed microwave-process vials (10 mL) at the maximum power and temperature, as indicated in the tables. After completion of the reaction, the vial was cooled to 50 °C via air-jet cooling before it was opened.

General Procedure for the Arylation of 2-Substituted Imidazo[1,2-*a*]pyrimidines. Imidazo[1,2-*a*]pyrimidine (0.5 mmol), cesium carbonate (180 mg, 0.55 mmol, 1.1 equiv), palladium acetate (9 mg, 8 mol %), and triphenylphosphine (21 mg, 16 mol %) were placed in a 10 mL MW vial . Then 1,4-dioxane (6 mL) and arylbromide (0.68 mmol, 1.35 equiv) were added. The mixture was degassed by the bubbling of argon gas through it for 5 min. The vial was sealed and exposed to microwave irradiation at 150 W maximum power and a ceiling temperature as indicated. The reaction mixture was diluted with 200 mL of dichloromethane and washed with water (3 × 300 mL), and then the organic phase was dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo, and the crude mixture was purified by column chromatography on silica gel using ethyl acetate−methanol (9:1) as the eluent.

2,3-Diphenylimidazo[1,2-*a*]pyrimidine 5{1}. Yield: 138 mg (96%). mp: 147−149 °C. ^1H NMR ($CDCl_3$): δ 8.55 (m, 1H), 8.23 (m, 1H), 7.78 (m, 2H), 7.53 (m, 5H), 7.28 (m, 3H), 6.82 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 150.2, 148.3, 144.2, 133.9, 131.1, 130.9 (×2), 130.2 (×2), 129.8, 129.2, 128.7 (×4), 128.4, 119.8, 109.0. HR-MS (EI): $C_{18}H_{13}N_3$ calcd 271.1109, found 271.1100.

3-(4-Fluorophenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{2}. Yield: 145 mg (95%). mp: 174−176 °C. ^1H NMR ($CDCl_3$): δ 8.58 (m, 1H), 8.19 (m, 1H), 7.73 (m, 2H), 7.45 (m, 3H), 7.29 (m, 4H), 6.83 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 165.2, 150.3, 148.3, 144.3, 133.9, 132.5, 130.9, 129.7 (×2), 128.8 (×2), 128.7 (×2), 128.6 (×2), 117.6, 109.2, 109.0. HR-MS (EI): $C_{18}H_{12}FN_3$ calcd 289.1015, found 289.1007.

3-(4-Chlorophenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{3}. Yield: 132 mg (82%). mp: 178−180 °C. ^1H NMR ($CDCl_3$): δ 8.57 (m, 1H), 8.22 (m, 1H), 7.75 (m, 2H), 7.53 (d, 2H, J = 7.3 Hz), 7.40 (d, 2H, J = 7.3 Hz), 7.30 (m, 3H), 6.83 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 150.4, 148.4, 144.5, 135.8, 132.5 (×2), 132.4, 132.3 (×2), 130.9 (×2), 130.5 (×2), 130.2, 128.6, 127.7, 118.5, 109.2. HR-MS (EI): $C_{18}H_{12}N_3Cl$ calcd 305.0720, found 305.0711.

3-[4-(Trifluoromethyl)phenyl]-2-phenylimidazo[1,2-*a*]-pyrimidine 5{4}. Yield: 142 mg (84%). mp: 164−167 °C. ^1H NMR ($CDCl_3$): δ 8.57 (m, 1H), 8.28 (m, 1H), 7.80 (d, 2H, J = 7.8 Hz), 7.67 (m, 2H), 7.60 (d, 2H, J = 7.7 Hz), 7.30 (m, 3H), 6.85 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 150.7, 148.6, 145.1, 133.4, 131.8 (×2), 131.3, 130.9, 130.9 (×2), 128.9, 128.8(×4), 128.7, 127.1, 118.2, 109.4. HR-MS (EI): $C_{19}H_{12}N_3F_3$ calcd 339.0983, found 339.0980.

3-(2-Fluorophenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{5}. Yield: 121 mg (84%). mp: 177−179 °C. ^1H NMR ($CDCl_3$): δ 8.60 (s, 1H), 8.08 (m, 1H), 7.77 (m, 2H), 7.58 (m, 1H), 7.36 (m, 6H), 6.87 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 162.3, 150.8, 148.3, 145.6, 144.9, 133.5, 132.8, 131.1, 128.5, 128.2 (×2), 128.5 (×2), 128.2, 117.4, 114.1, 109.9, 105.2. HR-MS (EI): $C_{18}H_{12}N_3F$ calcd 289.1015, found 289.1014.

3-(3,5-Difluorophenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{6}. Yield: 47 mg (65%). mp: 183−186 °C. ^1H NMR ($CDCl_3$): δ 8.64 (m, 2H), 7.65 (m, 2H), 7.35 (m, 6H), 7.07 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 165.6, 162.5, 150.7, 148.5, 125.3, 144.9, 133.2, 132.3, 128.9, 128.9 (×2), 128.8 (×2), 117.2, 109.7, 105.7. HR-MS (EI): $C_{18}H_{11}F_2N_3$ calcd 307.0921, found 307.0910.

3-(4-Methoxyphenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{7}. Yield: 81 mg (54%). mp: 181−183 °C. ^1H NMR ($CDCl_3$): δ 8.53 (m, 1H), 8.19 (m, 1H), 7.75 (m, 2H), 7.54 (d, 2H, J = 7.3 Hz), 7.33 (m, 3H), 7.06 (d, 2H, J = 7.3 Hz), 6.79 (m, 3H), 3.91 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 160.4, 148.6, 143.5, 132.4, 132.0, 130.9, 128.9 (×2), 128.7 (×2), 127.7 (×2), 127.3 (×2), 126.1, 119.7, 114.6, 108.5, 55.9. HR-MS (EI): $C_{19}H_{15}N_3O$ calcd 301.1215, found 301.1211.

3-(4-Methanesulfonylphenyl)-2-phenylimidazo[1,2-*a*]-pyrimidine 5{8}. Yield: 140 mg (80%). mp: 204−206 °C. ^1H NMR ($CDCl_3$): δ 8.64 (s, 1H), 8.35 (d, 1H, J = 6.4 Hz), 8.12 (d, 2H, J = 8.2 Hz), 7.70 (m, 3H), 7.35 (m, 2H), 6.90 (m, 1H), 3.21 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 151.0, 148.7, 145.4, 141.1, 134.9, 133.2, 131.6 (×2), 131.1, 129.0 (×4), 128.9, 117.8, 109.7, 44.7. HR-MS (EI): $C_{19}H_{15}N_3O_2S$ calcd 349.0885, found 349.0879.

4-(2-Phenylimidazo[1,2-*a*]pyrimidin-3-yl)-isoquinoline 5{9}. Yield: 108 mg (67%). mp: 202−205 °C. ^1H NMR ($CDCl_3$): δ 9.47 (s, 1H), 8.66 (br, 1H), 8.19 (d, 1H, J = 8.0 Hz), 7.82 (d, 1H, J = 8.1 Hz), 7.70 (m, 3H), 7.42 (d, 1H, J = 7.8 Hz), 7.23 (m, 3H), 6.79 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 154.93, 150.74, 149.08, 146.48, 146.39, 133.16, 133.41, 132.47, 131.48, 129.13 (×2), 129.10 (×2), 128.84 (×2), 128.76 (×2), 128.27, 124.23, 114.32, 109.28. HR-MS (EI): $C_{21}H_{14}N_4$ calcd 322.1218, found 322.1218.

2-Phenyl-3-(pyridin-2-yl)imidazo[1,2-*a*]pyrimidine 5{10}. Yield: 75 mg (55%). mp: 156−158 °C. ^1H NMR ($CDCl_3$): δ 8.50 (m, 2H), 8.42 (m, 1H), 8.02 (d, 2H, J = 7.3 Hz), 7.82 (m, 1H), 7.44 (m, 5H), 6.84 (m, 1H). ^{13}C NMR ($CDCl_3$): δ 151.2, 150.2, 149.8, 147.4, 133.7, 133.5, 132.5, 132.4, 129.7 (×2), 129.1, 128.9, 128.8 (×2), 109.1, 106.8. HR-MS (EI): $C_{17}H_{12}N_4$ calcd 272.1062, found 272.1057.

3-(4-*tert*-Butylphenyl)-2-phenylimidazo[1,2-*a*]pyrimidine 5{11}. Yield: 80 mg (49%). mp: 156−158 °C. ^1H NMR ($CDCl_3$): δ 8.63 (s, 1H), 8.25 (m, 1H), 7.77 (m, 2H), 7.55 (d, 2H, J = 7.2 Hz), 7.36 (d, 2H, J = 7.2 Hz), 7.32 (m, 3H), 6.78 (m, 1H), 1.40 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 153.6,

149.8, 147.4, 139.1, 133.1, 130.2, 129.3 (×2), 127.7 (×2), 127.1 (×2), 125.6 (×2), 109.3, 107.8, 32.7, 30.3 (×3). HR-MS (EI): $C_{22}H_{21}N_3$ calcd 327.1735, found 327.1732.

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Supporting Information Available. Experimental procedures and spectroscopic data for compounds **5**{**12**−**35**}, **7g**−**i**, and **5**{**36**−**45**}. This material is available free of charge via the Internet at http://pubs.acs.org.

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