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Ligandless Palladium-Catalyzed Regioselective Direct C−H Arylation of Imidazo[1,2-*a*]imidazole Derivatives

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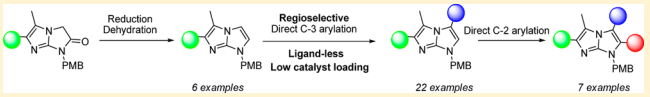
Supporting Information

ABSTRACT: Herein a novel access to functionalizable 6-substituted imidazo[1,2-*a*]imidazole scaffolds is described. The reactivity of this heterobicyclic unit toward direct C−H arylation was studied, and conditions allowing regioselective arylation at position 3 were successfully developed. The practicability of this method is manifested by the ligandless conditions and low catalyst loading. The strategy is functional group tolerant and provides rapid access to a large variety of 3,6-di(hetero)arylated imidazo[1,2-*a*]imidazole derivatives. A second arylation at position 2 was then carried out, and a library of diversified 2,3,6-tri(hetero)arylated imidazo[1,2-*a*]imidazoles was generated in good yields. A one-pot, two-step procedure was finally developed.



INTRODUCTION

Lately, nitrogen bridgehead heterocycles have received considerable attention in the field of drug discovery due to their interesting biological properties.[1] Recently, our group made significant efforts to discover a new synthetic route and study the chemical reactivity of [5−5]fused ring systems.[2] In particular, the imidazo[1,2-*a*]imidazole unit has been studied as a CRF_1R antagonist involved in diseases such as depression and anxiety.[3]

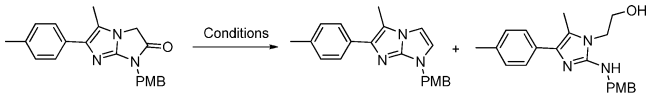
However, current strategies to access this biheterocyclic system are limited and generally consist of constructing the 5−5 fused ring with the desired substituents in appropriate positions.[2d,4] A careful literature survey revealed that only a few functionalization methods (bromination, nitration, and formylation) have been reported to date.[5]

We therefore focused on developing a new synthetic pathway allowing subsequent functionalization of the imidazo-[1,2-*a*]imidazole skeleton in order to generate a diversified library of this structurally relevant motif.

RESULTS AND DISCUSSION

We first sought to prepare some imidazo[1,2-*a*]imidazole synthons. For this purpose, a reduction−dehydration sequence of the imidazoimidazolinone compound **1**, previously prepared,[2d] was considered. By using sodium borohydride in ethanol, the expected compound **2** was not obtained. At room temperature, no reaction occurred while under reflux, product **3** resulting in ring opening was generated in 68% yield (Table 1, entries 1 and 2).

Table 1. Access to the Imidazo[1,2-*a*]imidazole Core



entry	reducing agent (equiv)	solvent	*T* (°C)	time (h)	yield (%)[a]
1	$NaBH_4$ (2.2)	ethanol	rt	48	98 (**1**) + traces (**3**)
2	$NaBH_4$ (2.2)	ethanol	reflux	2	68 (**3**)
3	$LiAlH_4$ (2.2)	THF	0 to rt	12	*b*
4	DIBAL-H (1.5)	THF	0 to rt	12	74 (**2**)

[a]Yield of isolated product after column chromatography. [b]Degradation of the reaction mixture. PMB = *p*-methoxybenzyl.

This type of reactivity has already been reported.[6] By using $LiAlH_4$ as reducing agent, degradation of the reaction mixture was observed (Table 1, entry 3), but treatment of compound **1** with 1.5 equiv of diisobutylaluminium hydride in THF at room temperature provided the desired imidazo[1,2-*a*]-imidazole derivative **2** in a good yield of 74% (Table 1, entry 4).

In order to explore the scope of these optimized conditions, we applied this methodology to several 1-(4-methoxybenzyl)-5-methyl-1*H*-imidazo[1,2-*a*]imidazol-2(3*H*)-ones bearing different substituents at position 6. It was noticed that aryl

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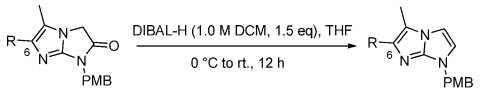
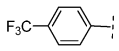
groups bearing methyl or trifluoromethyl substituents were well tolerated, as the corresponding imidazomidazoles were generated in 74 and 80% yields, respectively (Table 2, entries 1 and 2). With the 3-methoxy substituent, 3 equiv of DIBAL-H was necessary to complete the reaction and provide the imidazo[1,2-*a*]imidazole **10** in 83% yield (Table 2, entry 3). The 6-(thiophen-3-yl)-imidazo[1,2-*a*]imidazole **11** was also isolated with a good yield (Table 2, entry 4). However, when 3- or 4-pyridinyl groups are present a subsequent reaction under acidic conditions was needed to allow the dehydration step (Table 2, entries 5 and 6).

Table 2. Scope of the Reduction/Dehydration Sequence



1, 4-8 2, 9-13

Entry	R	Product	Yield (%)[a]
1	 1	2	74
2	 4	9	80
3	 5	10	82[b]
4	 6	11	58
5	 7	12	55[c]
6	 8	13	32[d]

[a]Yield of isolated product after column chromatography. [b]Reaction was performed with 3 equiv of DIBAL-H instead of 1.5 equiv. [c]Additional step: HCl, 1,4-dioxane, rt, 1h. [d]Additional step; HCl, 1,4-dioxane, reflux, 1h.

Regarding the six compounds synthesized, two positions remain potentially functionalizable (positions 2 and 3), enlarging the potential molecular diversity offered by this synthon.

Based on our domain of expertise,[7] we proceeded to study the reactivity of this skeleton toward direct C−H arylation. Our main concern was obviously to control the regioselectivity of this type of reaction.

Pd-catalyzed direct C−H arylation of heteroarenes using aryl halides as coupling partners has proven to be a powerful method to access a wide variety of arylated or heteroarylated heterocycles.[8] By avoiding the preliminary preparation of an organometallic species, which is mandatory for more classical cross-coupling procedures such as Suzuki, Stille, or Negishi coupling, direct C−H arylation appears as a method of choice. In addition, instead of releasing metallic salts, the main byproducts of direct C−H arylation are a base associated with HX which is an additional advantage from an environmental point of view.

So far, to our knowledge, there has been no reported example of direct arylation of the imidazo[1,2-*a*]imidazole core. Our study was initiated by applying standard conditions widely used in our laboratory: 4-bromotoluene (1.0 equiv), palladium acetate (0.1 equiv), tricyclohexylphosphine (0.2 equiv), and potassium carbonate (1.5 equiv) in 1,4-dioxane. After reflux for 72 h, the conversion was incomplete, and a mixture of monoarylated and diarylated products was obtained (Table 3, entry 1).

In order to reach full conversion and to better control the regioselectivity of this reaction, the parameters were varied. First, by using toluene as solvent, both conversion and selectivity were slightly better. On the other hand, performing the reaction in *N*-methyl-2-pyrrolidinone (NMP) allowed complete regioselectivity, but conversion was limited to 50% regardless of the temperature, reaction time, or amount of 4-bromotoluene involved (Table 3, entries 4−6).

We then examined the influence of the nature of the ligand. Thanks to these assays, we demonstrated that the regioselectivity of the reaction is directly linked to the ligand. When the reaction was performed using 0.2 equiv of tri-*o*-tolylphosphine (P(*o*-tolyl)$_3$) the diarylated compound **15** was not detected, but conversion was limited to 36% (Table 3, entry 7). The use of 0.2 equiv of (2-furyl)phosphine (P(2-furyl)$_3$) improved conversion, but traces of the unwanted compound **15** were observed (Table 3, entry 8). A similar result was obtained with tri-*tert*-butylphosphine (P(^{t}Bu)$_3$) (Table 3, entry 9). Unfortunately, carrying out the reaction in the presence of Xantphos enhanced the diarylation reaction (Table 3, entry 10).

Using an electron-poor phosphine such as (P(OCH-(CF$_3$)$_2$)$_3$) or employing 2,2′-bipyridine afforded interesting results as conversion was almost complete, and the amount of 15 was low (Table 5, entries 11 and 12). These results were improved in the presence of 1,10-phenanthroline (Table 3, entry 13). The monoarylated product **14** was isolated in 72% yield.

The crystal structure of compound **14** was determined by single-crystal X-ray diffraction and demonstrated that the C−H arylation happened regioselectively at position 3 (see the Supporting Information).

We finally established that the reaction was efficient and selective even without the use of ligand (Table 3, entry 14). Such an experimental protocol constituted a significant advancement as it is operationally simpler, cheaper, and eco-friendlier. Some examples of ligandless direct C−H arylation have already been reported.[9]

We then extended the methodology to 4-chloro- and 4-iodotoluene. Similar results were obtained with the iodoaryl, whereas a lower conversion was observed with the corresponding chloro-coupling partner (Table 3, entries 15 and 16). To complete the optimization, we finally evaluated the impact of the amount of palladium acetate.

We were pleased to observe that the catalyst loading could be drastically reduced to 2 mol % without impacting either the yield or the reaction time (Table 3, entries 17 and 18).

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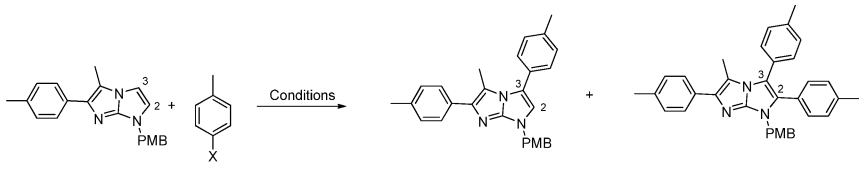
Table 3. Pd-Catalyzed Regioselective C-3 Arylation of 2



2 14 15

entry	$Pd(OAc)_2$ (eq)	ligand (0.2 equiv)	X (equiv)	solvent	T (°C)	time (h)	ratio (%)[a] **1/14/15**	yield[b] (%)
1	0.1	PCy_3	Br (1.0)	1,4-dioxane	101	72	52/40/8	
2	0.1	PCy_3	Br (1.0)	1,4-dioxane	150	15	20/60/20	
3	0.1.	PCy_3	Br (1.0)	toluene	150	15	19/65/16	
4	0.1	PCy_3	Br (1.0)	NMP	150	15	50/50/0	
5	0.1	PCy_3	Br (1.0)	NMP	180	72	50/50/0	
6	0.1	PCy_3	Br (2.0)	NMP	180	72	50/50/0	
7	0.1	P(*o*-tolyl)$_3$	Br (1.0)	toluene	150	15	64/36/0	
8	0.1	P(2-furyl)$_3$	Br (1.0)	toluene	150	15	28/66/6	
9	0.1	P(^{t}Bu)$_3$	Br (1.0)	toluene	150	15	31/62/7	
10	0.1	Xantphos	Br (1.0)	toluene	150	15	32/41/27	
11	0.1	P(OCH(CF_3)$_2$)$_3$	Br (1.0)	toluene	150	15	8/82/10	
12	0.1	2,2-bipyridine	Br (1.0)	toluene	150	15	3/87/10	70 (**14**)
13	0.1	1,10-phenantroline	Br (1.0)	toluene	150	15	0/100/0	72 (**14**)
14	0.1		Br (1.0)	toluene	150	15	0/100/0	73 (**14**)
15	0.1		Cl (1.0)	toluene	150	15	85/15/0	
16	0.1		I (1.0)	toluene	150	15	0/100/0	72 (**14**)
17	0.05		Br (1.0)	toluene	150	15	0/100/0	71 (**14**)
18	0.02		Br (1.0)	toluene	150	15	0/100/0	73 (**14**)

[a]Conversion determined by integration in ^{1}HNMR [b]Yield of isolated product after column chromatography

This reduction in the quantity of catalyst is again a significant result from an economic and sustainability point of view. We then tried to understand the origin of this reactivity. The best ligands in terms of selectivity appeared to be 2,2′-bipyridine and 1,10-phenanthroline. Similar results were obtained in the absence of ligand. It is also likely that the imidazo[1,2-*a*]imidazole core which is also rich in nitrogen atoms plays the role of ligand. However, additional studies are required to confirm this hypothesis.

In order to explore the scope of the methodology and detect possible limitations, we next applied the most effective conditions to the different imidazoimidazole derivatives previously synthesized. Various aryl or heteroaryl bromides were employed. Gratifyingly, these optimized conditions proved to be quite efficient with a large variety of para-substituted aryl bromides bearing electron-donating (CH_3, CH_3O) or electron-withdrawing groups (CN, CF_3) groups (Table 4, entries 1−5). Notably, ortho- or meta-substitution did not disfavor arylation. In fact, compounds **20**−**24** were prepared in 66−75% yield (Table 4, entries 6−10). The 4-pyridinyl unit was also easily introduced (Table 4, entry 11), the pyrimidinyl derivative **26** was obtained in a good yield of 66%, and 10% of starting material was recovered (Table 4, entry 12). Increasing the reaction time did not lead to any improvement in terms of conversion. Similarly, the 1-(4-methoxybenzyl)-5-methyl-3-(thiophene-3-yl)-6-*p*-tolyl-1*H*-imidazo [1,2-*a*]imidazole **27** was prepared in a reasonable 59% yield (Table 4, entry 13).

We then examined the influence of the substitution at position 6 of the imidazoimidazole ring.

We were pleased to notice that when the 4-tolyl group (at position 6) was replaced by a 4-trifluoromethylphenyl or a 3-methoxyphenyl, direct C−H arylation at position 3 of the heterocyclic moiety was as efficient and selectivity was preserved (Table 4, entries 14−20).

We then extended the methodology to imidazo[1,2-*a*]imidazole derivatives bearing a heterocyclic unit at position 6.

When a 4-pyridinyl or 3- pyridinyl motif was present at position 6, the efficiency of the coupling was reduced. Whatever the aryl bromide involved, the reaction afforded a complex mixture of starting material, monoarylated product, and degradation compounds which did not enable us to isolate the expected imidazoimidazoles (Table 4, entries 21−24).

However, we were delighted to find that these conditions were compatible with the presence of a thienyl unit at position 6 as the 4-cyano and 4-methoxyphenyl groups were introduced in 69 and 62% yield, respectively (Table 4, entries 25 and 26).

In view of these encouraging results, we then turned our attention to the possible preparation of di(hetero)arylated compounds at positions 2 and 3. For this purpose, selected 3-(hetero)arylated scaffolds previously synthesized were submitted to the same conditions of C−H arylation (4-bromotoluene (1.0 equiv), palladium acetate (0.1 equiv), and potassium carbonate (1.5 equiv) in toluene.

First, we noticed that a 10%mol catalyst loading is mandatory to reach full conversion. Aryl substituents bearing an electron-rich or electron-poor group were easily introduced at position 2. Gratifyingly, the strategy proved to be highly effective regardless of the substitution at position 3 (Table 5, entries 1, 2, 4, 6, and 7). Moreover, 4-bromopyridine was also easily coupled, and the corresponding 3-aryl-2-(hetero)-arylimidazo[1,2-*a*]imidazoles **38** and **40** were cleanly obtained in 64 and 66% yield (Table 5, entries 3 and 5).

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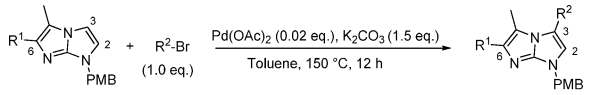
Table 4. Scope of the C-3 Regioselective Direct Arylation of Imidazo[1,2-*a*]imidazole Derivatives



2, 9-13 14, 16-36

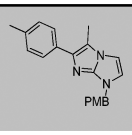
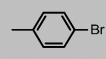
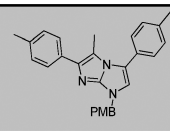
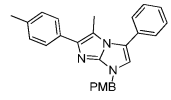
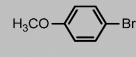
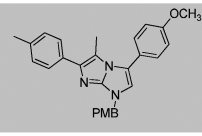
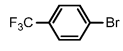
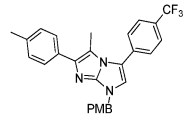
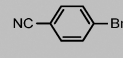
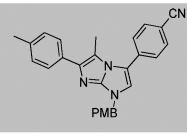
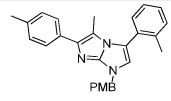
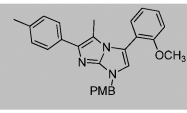
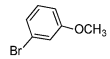
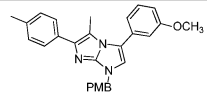
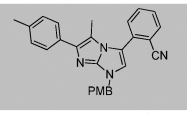
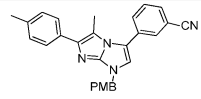
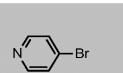
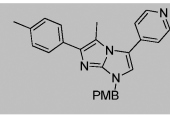
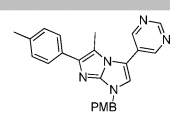
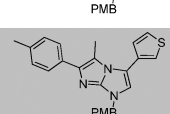
Entry	Starting material		R^2-Br	Product		Yield (%)[a](SM)[b]
1		2			14	73
2					16	75
3					17	72
4					18	71
5					19	78
6					20	73
7					21	75
8					22	72
9					23	71
10					24	66
11					25	71
12					26	66 (10)
13					27	59

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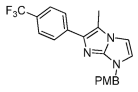
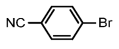
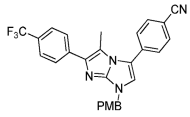
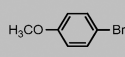
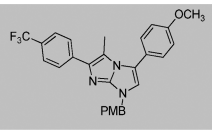
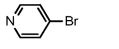
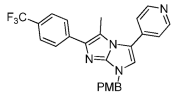
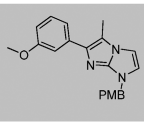
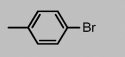
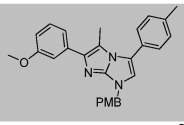
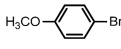
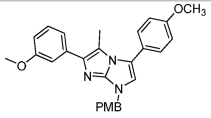
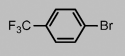
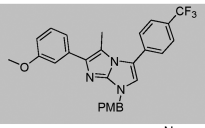
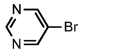
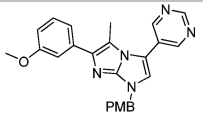
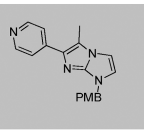
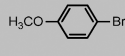
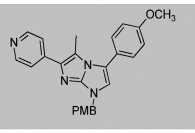
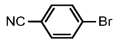
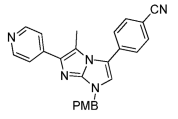
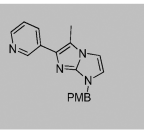
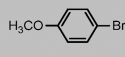
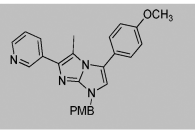
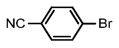
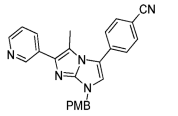
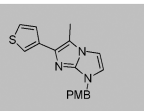
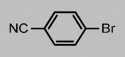
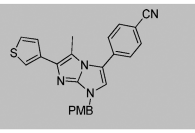
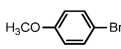
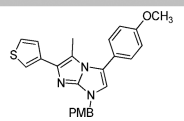
Table 4. continued

Entry	Starting material		R^2-Br	Product		Yield (%)[a](SM)[b]
14		9			28	74
15					29	80
16					30	60 (10)
17		10			31	60 (15)
18					32	55
19					33	46 (26)
20					34	50 (29)
21		12			-	-[c]
22					-	-[c]
23		13			-	-[c]
24					-	-[c]
25		11			35	69
26					36	62 (7)

[a]Yield of isolated product after column chromatography. [b]The starting material was recovered. [c]The reaction afforded a complex mixture of starting material, monoarylated compound, and degradation products inseparable by flash chromatography.

As the last part of this work, we extended the methodology to a double and one-pot C-2 and C-3 direct arylation of the imidazo[1,2-*a*]imidazole **2**. Such one-pot sequential multiple C−H arylations have already been described for some azoles[10]

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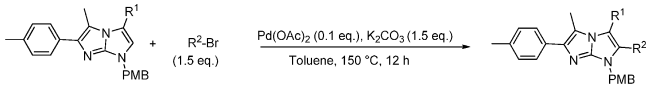
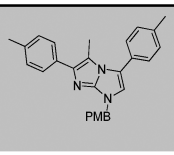
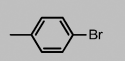
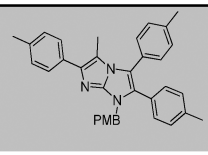
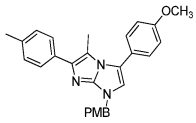
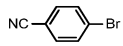
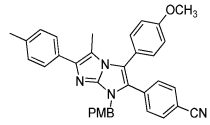
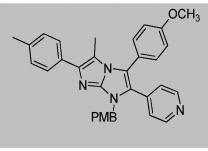
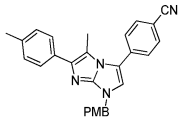
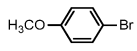
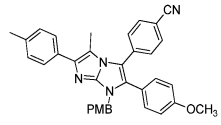
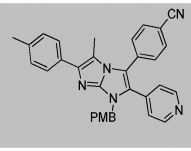
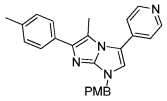
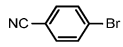
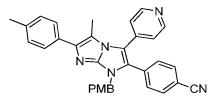
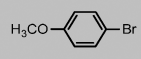
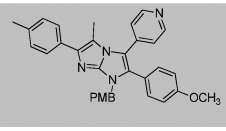
Table 5. C-2 Direct C−H Arylation of 3-(Hetero)arylated Imidazo[1,2-*a*]imidazoles

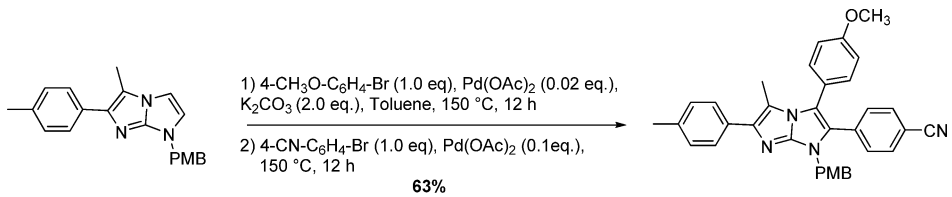


14, 17, 19, 25 15, 37-42

Entry	Starting Material		R^2-Br	Product		Yield (%)[a]
1		14			15	73
2		17			37	62
3					38	64
4		19			39	50
5					40	66
6		25			41	60
7					42	61

[a]Yield of isolated product after column chromatography.

Scheme 1. One-Pot, Two-Step Sequence of C-2 and C-3 Direct C−H Arylation of the Imidazo[1,2-*a*]imidazole 2



2 37

but never for the imidazo[1,2-*a*]imidazole core. After 12 h of heating in the presence of 4-bromoanisole (1.0 equiv), palladium acetate (0.02 equiv), and potassium carbonate (2.0 equiv), 0.1 extra equiv of catalyst, and 4-bromobenzonitrile (1.5 equiv) were added. After an additional 12 h at 150 °C, the diarylated compound **37** was isolated, after purification, in 63% yield (Scheme 1). This "sequential one-pot two-step procedure" enabled the preparation of product **37** with a higher yield compared to the successive double C−H arylation sequence (63% instead of 45%).

CONCLUSION

In conclusion, we have reported here a novel and efficient method to access the imidazomimidazole core. The first C-3 pallado-catalyzed functionalization of this heterocyclic unit was developed. The methodology described is original, ligand-free, totally C-3 regioselective, and performed with a low catalyst loading. A wide range of (hetero)aryl coupling partners with both electron-rich and electron-poor substituents were introduced with good to excellent yields giving access to a library of diverse 3,6-di(hetero)arylated imidazo[1,2-*a*]-

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imidazole derivatives. Further investigations involving a second arylation at position 2 were successfully carried out and several 2,3,6-tri(hetero)arylated imidazo[1,2-*a*]imidazole derivatives have been obtained successfully. Finally, a "sequential one-pot two-step" procedure was also developed.

EXPERIMENTAL SECTION

General Information. The reactions were monitored by thin-layer chromatography (TLC) using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed using silica gel 60 (230−400 mesh, 0.040−0.063 mm) or, when specified, using neutral alumina (58 Å pore size, Brockmann I, pH = 7.0 ± 0.5 in H_2O). All reagents were purchased from commercial suppliers and were used without further purification. Melting points were measured on samples in open capillary tubes and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on two spectrometers at 250 or 400 MHzfor the proton (^{1}H) and 63.5 or 101 MHz for the carbon (^{13}C). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard in $CDCl_3$ and the residual pic of DMSO for DMSO-d_6. The following abbreviations are used for the proton spectra multiplicities: s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; bs, broad signal. Coupling constants (*J*) are reported in hertz (Hz). C_{IV} is the abbreviation for quaternary carbons.The infrared spectra of compounds were recorded on an ATR (attenuated total reflectance) equipped with a crystal diamond. Absorption bands are given in cm^{-1}. HRMS were performed on a Q-TOF mass spectrometer.

Preparation of Compounds 1, 4, and 6−8. These compounds were synthesized as described previously.[2d]

General Procedure A. To a solution of imidazo[1,2-*a*]-imidazolin-2-one **1** and **4**−**8** in dry THF at 0 °C and under argon was added dropwise DIBAL-H (1.5 equiv). After being stirred at room temperature for 12 h, the reaction mixture was quenched with an aqueous solution of HCl (1.0 M) and extracted with ethyl acetate. The combined organic layers were washed with an aqueous saturated solution of Na_2CO_3, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired products **2** and **9**−**13**.

General Procedure B. A sealed tube containing a stirring bar was charged with imidazo[1,2-*a*]imidazole **2**, **9**, **10**, or **11** (hetero)aryl bromide (1.0 equiv) and potassium carbonate (1.5 equiv) in toluene. The tube was evacuated and backfilled with dry argon twice. Palladium acetate (0.02 equiv) was added, and the mixture was heated at 150 °C for 12 h. After the mixture was cooled to room temperature, the solvent was removed under reduced pressure and the residue was purified by flash chromatography to provide the desired products **4** and **16**−**36**.

General Procedure C. A sealed tube containing a stirring bar was charged with imidazo[1,2-*a*]imidazole **14**, **17**, **19**, or **25**, (hetero)aryl bromide (1.0 equiv), and potassium carbonate (1.5 equiv) in toluene. The tube was evacuated and backfilled with dry argon twice. Palladium acetate (0.1 equiv) was added, and the mixture was heated at 150 °C for 12 h. After cooling, the solvent was removed under reduced pressure, and the residue was purified by flash chromatography to provide the desired products **15** and **37**−**42**.

*1-(4-Methoxybenzyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]-imidazole (**2**).* The reaction was carried out as described in general procedure A using imidazo[1,2-*a*]imidazole **1** (100 mg, 0.287 mmol) and DIBAL-H (1 M in DCM, 430 μL, 0.431 mmol) in 3 mL of THF. Standard workup followed by flash chromatography (dichloromethane/ethyl acetate 100/0 to 95/5) afforded **2** as a beige solid (70 mg, 75%). Mp: 153−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 2.4 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 5.12 (s, 2H), 3.79 (s, 3H), 2.50 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.4 (C_{IV}), 146.4 (C_{IV}), 139.5 (C_{IV}), 135.6 (C_{IV}), 133.4 (C_{IV}), 129.6 (CH), 129.0 (CH), 128.4 (C_{IV}), 127.3 (CH), 118.1 (CH), 114.2 (CH), 110.8 (C_{IV}), 103.0 (CH), 55.3 (CH_3), 48.6 (CH_2), 21.2 (CH_3), 10.3 (CH_3). IR ν (neat, cm^{-1}): 1599, 1513, 1248, 1229, 1770, 1036, 820. HRMS (ESI+): exact mass calcd for $C_{21}H_{22}N_3O$ 332.17574 [M + H]$^+$, found 332.17597 [M + H]$^+$.

*2-(2-((4-Methoxybenzyl)amino)-5-methyl-4-p-tolyl-1H-imidazol-1-yl)ethanol (**3**).* To a solution of imidazo[1,2-*a*]imidazolin-2-one **1** (100 mg, 0.288 mmol) in 3 mL of ethanol was added $NaBH_4$ (24 mg, 0.633 mmol, 2.2 equiv). The reaction mixture was refluxed for 2 h before being quenched with HCl (37%, 400 μL). After dilution with water (10.0 mL), the reaction mixture was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with a saturated solution of Na_2CO_3 (1 × 20 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford **3** as a yellow solid (69 mg, **68%**). Mp: 108−110 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.7 Hz, 2H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 4.87 (bs, 1H), 4.37 (d, *J* = 5.4 Hz, 2H), 3.79 (s, 3H), 3.59 (t, *J* = 4.4 Hz, 2H), 3.38 (t, *J* = 4.4 Hz, 2H), 2.37 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.7 (C_{IV}), 149.6 (C_{IV}), 135.1 (C_{IV}), 132.9 (C_{IV}), 131.8 (C_{IV}), 131.5 (C_{IV}), 129.1 (CH), 129.0 (CH), 126.7 (CH), 118.0 (C_{IV}), 113.8 (CH), 61.3 (CH_2), 55.3 (OCH_3), 47.1 (CH_2), 45.1 (CH_2), 21.2 (CH_3), 10.1 (CH_3). IR ν (neat, cm^{-1}): 2913 (bs), 1596, 1511, 1245, 1034, 820. HRMS (ESI+): exact mass calcd for $C_{21}H_{26}N_3O_2$ 352.20195 [M + H]$^+$, found 352.201176 [M + H]$^+$.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-5-methyl-1H-imidazo[1,2-a]imidazol-2(3H)-one (**5**).* A flask containing a stirring bar was charged with 6-bromo-1-(4-methoxybenzyl)-5-methyl-1*H*-imidazo[1,2-*a*]imidazol-2(3*H*)-one[2d] (0.400 g, 1.190 mmol) in a mixture of toluene/ethanol [2:1, v/v, 11.5 mL), 3-methoxyphenylboronic acid (0.271 g, 1.5 equiv) and potassium carbonate (0.246 g, 1.5 equiv). The flask was evacuated and backfilled with dry argon twice. 1,1-Bis(diphenylphosphanyl)ferrocenedichloropalladium(II)−chloroform (1/1) [Pd(dppf)Cl$_2$·CH$_2$Cl$_2$] (0.097 g, 0.10 equiv) was added, and the mixture was refluxed for 4 h. The mixture was cooled to room temperature, and the solvents were removed under reduced pressure. The residu was purified by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 95/5) to provide the **5** as a beige solid (264 mg, 61%). Mp: 151−153 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 7.8 Hz, 2H), 7.35−7.14 (m, 3H), 6.85 (d, *J* = 7.8 Hz, 2H), 6.80 (d, *J* = 8.3 Hz, 1H), 4.87 (s, 2H), 4.32 (s, 2H), 3.96 (s, 3H), 3.77 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.0 (C_{IV}), 159.9 (C_{IV}), 159.6 (C_{IV}), 148.0 (C_{IV}), 136.6 (C_{IV}), 136.4 (C_{IV}), 130.6 (CH), 129.5 (CH), 127.9 (2 × C_{IV}), 119.3 (CH), 114.2 (CH), 112.5 (CH), 111.9 (CH), 55.4 (2 × CH_3), 47.9 (CH_2), 43.7 (CH_2), 10.6 (CH_3). IR ν (neat, cm^{-1}): 1732, 1609, 1507, 1165, 1034. HRMS (ESI+): exact mass calcd for $C_{21}H_{22}N_3O_3$ 220.10805 [M + H]$^+$, found 220.10785 [M + H]$^+$.

*1-(4-Methoxybenzyl)-5-methyl-6-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-a]imidazole (**9**).* The reaction was carried out as described in general procedure A using imidazo[1,2-*a*]imidazole **4** (1.05 g, 2.62 mmol) and DIBAL-H (1 M in DCM, 3.9 mL, 3.92 mmol) in 40 mL of THF. Standard workup followed by flash chromatography (dichloromethane to dichloromethane/ethyl acetate 95/5) afforded **9** as a white solid (800 mg, 80%). Mp: 90−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 8.2 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 2.4 Hz, 1H), 6.59 (d, *J* = 2.4 Hz, 1H), 5.11 (s, 2H), 3.79 (s, 3H), 2.53 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 146.5 (C_{IV}), 139.9 (2 × C_{IV}), 138.1 (C_{IV}), 129.6, 128.2 (CH), 127.6 (q, J^2_{C-F} = 32.3 Hz, C_{IV}), 127.1 (CH), 125.3 (q, J^3_{C-F} = 3.86 Hz, C_{IV}), 124.6 (q, J^1_{C-F} = 273 Hz, CH), 118.9 (CH), 114.2 (CH), 112.1 (C_{IV}), 103.1 (CH), 55.3 (CH_3), 48.7 (CH_2), 10.5 (CH_3). IR ν (neat, cm^{-1}): 1613, 1513, 1321, 1246, 1157, 1065, 845. HRMS (ESI+): exact mass calcd for $C_{21}H_{19}F_3N_3O$: 386.14747 [M + H]$^+$, found 386.14769 [M + H]$^+$.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-5-methyl-1H-imidazo[1,2-a]imidazole (**10**).* The reaction was carried out as described in general procedure A using imidazo[1,2-*a*]imidazole **5** (300 mg, 0.826 mmol) and DIBAL-H (1 M in DCM, 2.48 mL, 2.478 mmol) in 9 mL of THF. Standard workup followed by flash

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chromatography (dichloromethane/ethyl acetate 9/1 to 7/3) afforded **10** as a yellow oil (234 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30−7.28 (m, 5H), 6.87 (d, J = 7.6 Hz, 2H), 6.81−6.78 (m, 2H), 6.55 (s, 1H), 5.11 (s, 2H), 3.87 (s, 3H), 3.79 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.8 (C_{IV}), 159.6 (C_{IV}), 146.4 (C_{IV}), 139.4 (C_{IV}), 137.8 (C_{IV}), 129.7 (CH), 129.4 (CH), 128.5 (C_{IV}), 120.1 (CH), 118.5 (CH), 114.3 (CH), 112.8 (CH), 112.2 (CH), 111.5 (C_{IV}), 103.2 (CH), 55.5 (CH_3), 55.4 (CH_3), 48.8 (CH_2), 10.5 (CH_3). IR ν (neat, cm^{-1}): 1607, 1511, 1284, 1175, 1029. HRMS (ESI+): exact mass calcd for $C_{21}H_{22}N_3O_2$ 348.17065 $[M + H]^+$, found 348.17070 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-6-(thiophene-3-yl)-1H-imidazo-[1,2-a]imidazole (**11**).* The reaction was carried out as described in general procedure A using imidazo[1,2-*a*]imidazole **6** (960 mg, 0.280 mmol), DIBAL-H (1 M in DCM, 4.2 mL, 0.420 mmol), in 35 mL of THF. Standard workup followed by flash chromatography (dichloromethane) afforded **11** as a white solid (510 mg, 56%). Mp: 125−127 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (dd, J = 1.2, 5.0 Hz, 1H), 7.44 (dd, J = 1.2, 3.0 Hz, 1H), 7.34 (dd, J = 3.0, 5.0 Hz, 1H), 7.27 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.77 (d, J = 2.4 Hz, 1H), 6.53 (d, J = 2.4 Hz, 1H), 5.10 (s, 2H), 3.78 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 146.3 (C_{IV}), 137.5 (C_{IV}), 135.7 (C_{IV}), 129.6, 128.3 (CH), 127.1 (C_{IV}), 125.1 (CH), 119.7 (CH) 118.3 (CH), 114.2 (CH), 110.9 (CH), 103.1 (CH), 55.0 (CH_3), 48.6 (CH_2), 10.1 (CH_3). IR ν (neat, cm^{-1}): 1605, 1509, 1240, 1167, 1025, 861. HRMS (ESI+): exact mass calcd for $C_{18}H_{18}N_3OS$ 324.11682 $[M + H]^+$, found 324.11651 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-6-(pyridin-4-yl)-1H-imidazo[1,2-a]imidazole (**12**).* The reaction was carried out as described in general procedure A using imidazo[1,2-*a*]imidazolin-2-one **7** (820 mg, 2.45 mmol) and DIBAL-H (1 M in DCM, 3.2 mL, 3.18 mmol), in 30 mL of THF. Standard workup followed by precipitation in a mixture of pentane/ethyl acetate 1/1 afforded the 2-nondeshydrated derivative. To a suspension of this compound (80 mg, 0.237 mmol) in 3 mL of 1,4-dioxane were added a few drops of a solution of an aqueous solution of HCl (6 M). After the mixture was stirred for 1 h, a white solid appeared. The reaction mixture was quenched with a saturated solution of Na_2CO_3 (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with water (2 × 20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography (dichloromethane/ethyl acetate 8/2 to 5/5) to afford **12** as a beige solid (63.0 mg, 55%). Mp: 121−123 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, J = 6.2 Hz, 2H), 7.63 (d, J = 6.2 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 2.5 Hz, 1H), 6.60 (d, J = 2.4 Hz, 1H), 5.10 (s, 2H), 3.78 (s, 3H), 2.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6 (C_{IV}), 149.8 (CH), 146.6 (C_{IV}), 143.8 (C_{IV}), 136.6 (C_{IV}), 129.6 (CH), 128.0 (C_{IV}), 121.2 (CH), 119.3 (CH), 114.3 (CH), 113.8 (C_{IV}), 103.0 (CH), 55.3 (OCH_3), 48.7 (CH_2), 10.7 (CH_3). IR ν (neat, cm^{-1}): 1609, 1596, 1512, 1273, 1248, 1775, 1028, 842. HRMS (ESI +): exact mass calcd for $C_{19}H_{19}N_4O$ 319.15534 $[M + H]^+$, found 319.15557 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-6-(pyridin-3-yl)-1H-imidazo[1,2-a]imidazole (**13**).* To a solution of imidazo[1,2-*a*]imidazolin-2-one (941 mg, 2.89 mmol) **8** in 34 mL of dry THF at 0 °C and under argon was added dropwise DIBAL-H (1.0 M in DCM, 3.7 mL, 1.30 equiv). After being stirred at room temperature for 12 h, the reaction mixture was quenched with an aqueous solution of HCl (1.0 M, 20 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with an aqueous saturated solution of Na_2CO_3, dried over $MgSO_4$, filtered, and concentated under reduced pressure. The residue was disolved in 1,4-dioxane, and a few drops of a solution of HCl 6 M were added. After 1 h of refluxing, the reaction mixture was quenched with an aqueous saturated solution of Na_2CO_3 and extracted with ethyl acetate. The combined organic layers were washed with water, dried over $MgSO_4$, filtered,and concentated under reduced pressure. The residue was purified by flash chromatography (dichloromethane/ethyl acetate 8/2 to 5/5) to afford compound **13** as a white solid (302 mg, 32%). Mp: 97−99 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.94 (d, J = 2.3 Hz, 1H), 8.48 (dd, J = 4.8, 1.7 Hz, 1H), 8.07 (dt, J = 3.8, 1.9 Hz, 1H), 7.36−7.27 (m, 3H), 6.89 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 2.4 Hz, 1H), 6.60 (d, J = 2.4 Hz, 1H), 5.12 (s, 2H), 3.80 (s, 3H), 2.54 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 160.9 (C_{IV}), 149.7 (CH), 148.5 (CH), 148.1 (C_{IV}), 137.7 (C_{IV}), 135.9 (CH), 133.6 (C_{IV}), 131.0 (CH), 129.5 (C_{IV}), 124.8 (CH), 120.2 (CH), 115.7 (CH), 113.6 (C_{IV}), 104.5 (CH), 56.7 (CH_3), 50.2 (CH), 11.7 (CH_3). IR ν (neat, cm^{-1}): 1611, 1511, 1458, 1247, 1176, 1024, 852. HRMS (ESI+): exact mass calcd for $C_{19}H_{19}N_4O$ 319.15534 $[M + H]^+$, found 319.15581 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3,6-di-p-tolyl-1H-imidazo[1,2-a]-imidazole (**14**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (220 mg, 0.664 mmol), palladium acetate (3.00 mg, 13.28 μmol), potassium carbonate (137 mg, 0.996 mmol), and 4-bromotoluene (81.0 μL, 0.664 mmol) in 6.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **14** as a yellow solid (201 mg, 73%). Mp: 153−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.1 Hz, 2H), 7.37−7.31 (m, 4H), 7.25−7.19 (m, 4H), 6.88 (d, J = 8.7 Hz, 2H), 6.44 (s, 1H), 5.14 (s, 2H), 3.79 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 147.0 (C_{IV}), 140.4 (C_{IV}), 137.9 (C_{IV}), 135.7 (C_{IV}), 133.3 (C_{IV}), 129.8 (C_{11}), 129.0 (CH), 129.0 (CH), 128.74 (CH), 128.3 (C_{IV}), 127.8 (CH), 126.29 (C_{IV}), 120.6 (C_{IV}), 115.4 (CH), 114.2 (CH), 112.2 (C_{IV}), 55.3 (CH_3), 48.7 (CH_2), 21.3 (CH_3), 21.2 (CH_3), 12.1 (CH_3). IR ν (neat, cm^{-1}): 1067, 1512, 1246, 1174, 1031, 821. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O$ 422.22269 $[M + H]^+$, found 422.22259 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-phenyl-6-p-tolyl-1H-imidazo-[1,2-a]imidazole (**16**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.452 mmol), and 4-bromobenzene (32 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **16** as a yellow foam (91 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 8.0 Hz, 2H), 7.48−7.31 (m, 7H), 7.23 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H), 6.49 (s, 1H), 5.16 (s, 2H), 3.79 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.35 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 146.9 (C_{IV}), 140.4 (C_{IV}), 135.9 (C_{IV}), 133.1 (C_{IV}), 129.8 (CH), 129.2 (C_{IV}), 129.0 (CH), 128.7 (CH), 128.4 (CH), 128.2 (C_{IV}), 128.0 (CH), 127.9 (CH), 120.6 (C_{IV}), 115.7 (CH), 114.3 (CH), 112.2 (C_{IV}), 55.3 (CH_3), 48.8 (CH_2), 21.2 (CH_3), 12.1 (CH_3). IR ν (neat, cm^{-1}): 1601, 1511, 1246, 1166, 1031, 819. HRMS (ESI+): exact mass calcd for $C_{27}H_{26}N_3O$ 408.20734 $[M + H]^+$, found 408.20739 $[M + H]^+$.

*1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**17**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.301 mmol), and 4-bromoanisole (38 μL, 0.452 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **17** as a yellow foam (95 mg, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ δ 7.59 (d, J = 7.8 Hz, 2H), 7.40−7.32 (m, 4H), 7.24 (d, J = 7.8 Hz, 2H, 2H), 6.98−6.81 (m, 4H), 6.42 (s, 1H), 5.15 (s, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 2.37 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 161.0 (C_{IV}), 160.9 (C_{IV}), 148.1 (C_{IV}), 141.5 (C_{IV}), 137.2 (C_{IV}), 134.5 (C_{IV}), 131.8 (CH), 131.2 (CH), 130.4 (CH), 129.8 (C_{IV}), 129.2 (CH), 122.9 (C_{IV}), 121.7 (C_{IV}), 116.6 (CH), 115.6 (CH), 115.2 (CH), 113.5 (C_{IV}), 56.8 (CH_3), 56.7 (CH_3), 50.1 (CH_2), 22.7 (CH_3), 13.3 (CH_3). IR ν (neat, cm^{-1}): 1607, 1511, 1455, 1244, 1173, 1029, 823. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O_2$ 438.21760 $[M + H]^+$, found 438.21782 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-6-p-tolyl-3-(4-(trifluoromethyl)-phenyl)-1H-imidazo[1,2-a]imidazole (**18**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.415 mmol), and 4-

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bromobenzotrifluoride (42 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **18** as a yellow oil (101 mg, 71%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.70−7.52 (m, 6H), 7.36 (d, J = 8.7 Hz, 2H), 7.24 (d, J = 8.2 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 6.57 (s, 1H), 5.17 (s, 2H), 3.80 (s, 3H), 2.38 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.6 (C_{IV}), 146.9 (C_{IV}), 140.9 (C_{IV}), 136.1 (C_{IV}), 132.8 (C_{IV}), 129.9 (CH), 129.7 (q, J^2_{C-F} = 31.0 Hz, C_{IV}), 129.1 (CH), 128.9 (C_{IV}), 128.3 (CH), 127.9 (CH + C_{IV}), 125.5 (q, J^3_{C-F} = 3.88 Hz, CH) 124.0 (q, J^1_{C-F} = 275 Hz, CF_3) 119.3 (C_{IV}), 116.7 (CH), 114.3 (CH), 112.2 (C_{IV}), 55.3 (OCH_3), 48.9 (CH_2), 21.3 (CH_3), 12.4 (CH_3). IR ν (neat, cm^{-1}): 1607, 1513, 1321, 1247, 1163, 1118, 1107, 1066, 845. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}F_3N_3O$ 476.19442 $[M + H]^+$, found 476.19462 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]-imidazol-3-yl)benzonitrile (**19**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.452 mmol), and 4-bromobenzonitrile (54.9 mg, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **19** as a yellow solid (101 mg, 78%). Mp: 173−175 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 7.9 Hz, 2H), 7.51 (d, J = 7.7 Hz, 2H), 7.46 (d, J = 7.9 Hz, 2H), 7.27 (d, J = 8.2 Hz, 2H), 7.16 (d, J = 7.7 Hz, 2H), 6.82 (d, J = 8.2 Hz, 2H), 6.53 (s, 1H), 5.09 (s, 2H), 3.72 (s, 3H), 2.31 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7 (C_{IV}), 147.0 (C_{IV}), 141.4 (C_{IV}), 136.2 (C_{IV}), 133.85 (C_{IV}), 132.8 (C_{IV}), 132.3 (CH), 129.9 (CH), 129.1 (CH), 128.2 (CH), 127.9 (CH), 127.7 (C_{IV}), 118.97 (C_{IV}), 118.6 (C_{IV}), 117.3 (CH), 114.3 (CH), 112.2 (C_{IV}), 110.9 (C_{IV}), 55.3 (CH_3), 48.9 (CH_2), 21.3 (CH_3), 12.6 (CH_3). IR ν (neat, cm^{-1}): 2223 (CN), 1600, 1510, 1345, 1243, 1171, 1026, 836. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}N_4O$ 433.20229 $[M + H]^+$, found 433.20238 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-o-tolyl-6-p-tolyl-1H-imidazo-[1,2-a]imidazole (**20**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.415 mmol), and 2-bromotoluene (36 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **20** as a yellow oil (92 mg, 73%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.58 (d, J = 8.1 Hz, 2H), 7.37−7.27 (m, 5H), 7.24−7.18 (m, 3H), 6.89 (d, J = 8.7 Hz, 2H), 6.41 (s, 1H), 5.17 (s, 2H), 3.80 (s, 3H), 2.36 (s, 3H), 2.24 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 146.4 (C_{IV}), 139.8 (C_{IV}), 138.6 (C_{IV}), 135.7 (C_{IV}), 133.1 (C_{IV}), 131.7 (CH), 130.0 (CH), 129.7 (CH), 129.1 (CH), 129.0 (CH), 128.5 (C_{IV}), 128.4 (C_{IV}), 127.6 (CH), 125.5 (CH), 118.6 (C_{IV}), 116.1 (CH), 114.2 (CH), 110.0 (C_{IV}), 55.3 (CH_3), 48.7 (CH_2), 21.2 (CH_3), 20.3 (CH_3), 10.3 (CH_3). IR ν (neat, cm^{-1}): 1607, 1513, 1246, 1174, 1032, 822. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O$ 422.22269 $[M + H]^+$, found 422.22289 $[M + H]^+$.

*1-(4-Methoxybenzyl)-3-(2-methoxyphenyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**21**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.415 mmol), and 2-bromoanisole (36 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **21** as a yellow oil (99 mg, 75%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.60 (d, J = 8.1 Hz, 2H), 7.40−7.26 (m, 4H), 7.20 (d, J = 8.3 Hz, 2H), 6.99−6.85 (m, 4H), 6.47 (s, 1H), 5.16 (s, 2H), 3.79 (s, 6H), 2.37 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.5 (C_{IV}), 158.0 (C_{IV}), 146.6 (C_{IV}), 139.5 (C_{IV}), 135.6 (C_{IV}), 133.5 (C_{IV}), 132.2 (CH), 130.3 (CH), 130.0 (CH), 129.1 (CH), 128.5 (C_{IV}), 127.8 (CH), 120.4 (CH), 118.3 (C_{IV}), 116.7 (C_{IV}), 116.6 (CH), 114.3 (CH), 113.0 (C_{IV}), 110.5 (CH), 55.4 (CH_3), 55.3 (CH_3), 48.8 (CH_2), 21.3 (CH_3), 10.3 (CH_3). IR ν (neat, cm^{-1}): 1607, 1512, 1244, 1175, 1024, 822. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O_2$ 438.21760 $[M + H]^+$, found 438.21783 $[M + H]^+$.

*1-(4-Methoxybenzyl)-3-(3-methoxyphenyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**22**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.602 mmol), and 3-bromoanisole (38 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **22** as a yellow oil (95 mg, 72%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.60 (d, J = 8.1 Hz, 2H), 7.36−7.21 (m, 5H), 7.04−6.86 (s, 5H,), 6.50 (s, 1H), 5.15 (s, 2H), 3.82 (s, 3H), 3.78 (s, 3H), 2.38 (s, 6H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.4 (C_{IV}), 159.3 (C_{IV}), 146.7 (C_{IV}), 140.3 (C_{IV}), 135.7 (C_{IV}), 133.0 (C_{IV}), 130.3 (C_{IV}), 129.7 (CH), 129.3 (CH), 128.9 (CH), 128.1 (C_{IV}), 127.7 (CH), 121.0 (CH), 120.4 (C_{IV}), 115.7 (CH), 114.1 (CH), 114.0 (CH), 113.5 (CH), 112.1 (C_{IV}), 55.2 (CH_3), 48.62 (CH_2), 21.1 (CH_3), 12.1 (CH_3). IR ν (neat, cm^{-1}): 1606, 1512, 1462, 1246, 1160, 1033, 821. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O_2$ 438.21761 $[M + H]^+$, found 438.21748 $[M + H]^+$.

*2-(1-(4-Methoxybenzyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]-imidazol-3-yl)benzonitrile (**23**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.452 mmol), and 2-bromobenzonitrile (54.9 mg, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **23** as a yellow foam (92 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (dd, J = 7.7, 1.3 Hz, 1H), 7.67 (td, J = 7.7, 1.4 Hz, 1H), 7.58−7.63 (m, 3H), 7.47 (td, J = 7.6, 1.3 Hz, 1H), 7.40 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.8 Hz, 2H), 6.87 (s, 1H), 5.24 (s, 2H), 3.82 (s, 3H), 2.41 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.6 (C_{IV}), 146.5 (C_{IV}), 140.9 (C_{IV}), 136.1 (C_{IV}), 133.5 (CH), 132.8 (C_{IV}), 132.4 (C_{IV}), 132.2 (CH), 130.7 (CH), 129.8 (CH), 129.1 (CH), 128.3 (CH_{Ar}), 127.9 (CH), 127.7 (C_{IV}), 118.7 (CH), 117.9 (C_{IV}), 115.4 (C_{IV}), 114.3 (CH), 112.2 (C_{IV}), 112.1 (C_{IV}), 55.3 (CH_3), 49.0 (CH_2), 21.2 (CH_3), 11.9 (CH_3). IR ν (neat, cm^{-1}): 1603, 1513, 1246, 1173, 1030, 822. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}N_4O$: 433.20229 $[M + H]^+$, found 433.20247 $[M + H]^+$.

*3-(1-(4-Methoxybenzyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]-imidazol-3-yl)benzonitrile (**24**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.452 mmol), and 3-bromobenzonitrile (54.9 mg, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **24** as a yellow foam (86 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (t, J = 1.7 Hz, 1H), 7.69 (dt, J = 7.8, 1.5 Hz, 1H), 7.63 (dt, J = 7.8, 1.5 Hz, 1H), 7.60 (d, J = 7.8 Hz, 2H), 7.53 (t, J = 7.7 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 6.57 (s, 1H), 5.17 (s, 2H), 3.80 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7 (C_{IV}), 146.8 (C_{IV}), 141.1 (C_{IV}), 136.2 (C_{IV}), 132.7 (C_{IV}), 132.4 (CH), 131.5 (CH), 131.1 (CH), 130.7 (C_{IV}), 129.9 (CH), 129.3 (CH + C_{IV}), 129.1 (CH), 127.9 (CH), 127.7 (C_{IV}), 118.3 (2 × C_{IV}), 116.8 (CH), 114.3 (CH), 112.9 (C_{IV}), 111.9 (C_{IV}), 55.3 (CH_3), 48.9 (CH_2), 21.2 (CH_3), 12.3 (CH_3). IR ν (neat, cm^{-1}): 2229, 1604, 1513, 1246, 1190, 1190, 1031, 823. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}N_4O$ 433.20229 $[M + H]^+$, found 433.20239 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-(pyridin-4-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**25**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.302 mmol), palladium acetate (1.4 mg, 6.04 μmol), potassium carbonate (62 mg, 0.453 mmol), and 4-bromopyridine (48.0 mg, 0.302 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 5/5) afforded **25** as a brown foam (87 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (d, J = 6.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.38−7.33 (m, 4H), 7.23 (d, J = 8.0 Hz, 2H), 6.90 (d, J = 8.6 Hz,

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2H), 6.68 (s, 1H), 5.18 (s, 2H), 3.81 (s, 3H), 2.45 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7 (C_{IV}), 149.9 (CH), 146.9 (C_{IV}), 141.2 (C_{IV}), 136.9 (C_{IV}), 136.3 (C_{IV}), 132.6 (C_{IV}), 129.9 (CH), 129.1 (CH), 127.9 (CH), 127.6 (C_{IV}), 121.9 (CH), 118. Three (C_{IV}), 117.8 (CH), 114.4 (CH), 112.4 (C_{IV}), 55.3 (CH_3), 49.0 (CH_2), 21.2 (CH_3), 12.7 (CH_3). IR ν (neat, cm^{-1}): 1594, 1512, 1246, 1172, 1031, 822. HRMS (ESI+): exact mass calcd for $C_{26}H_{25}N_4O$ 409.20229 $[M + H]^+$, found 409.20232 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-(pyrimidin-5-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**26**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.452 mmol), and 4-bromopyrimidine (47.8 mg, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **26** as a yellow solid (81 mg, 66%, 10% of starting material were recovered). Mp: 154−156 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.19 (s, 1H), 8.86 (s, 2H), 7.58 (d, J = 7.9 Hz, 2H), 7.37 (d, J = 8.6 Hz, 2H), 7.23 (d, J = 7.9 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 6.65 (s, 1H), 5.20 (s, 2H), 3.81 (s, 3H), 2.39 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.8 (C_{IV}), 157.6 (CH), 155.6 (CH), 146.8 (C_{IV}), 141.3 (C_{IV}), 136.3 (C_{IV}), 132.6 (C_{IV}), 130.0 (CH), 129.1 (CH), 127.9 (CH), 127.5 (C_{IV}), 124.1 (C_{IV}), 117.5 (CH), 114.4 (CH), 113.4 (C_{IV}), 111.9 (C_{IV}), 55.3 (CH_3), 49.1 (CH_2), 21.2 (CH_3), 12.1 (CH_3). IR ν (neat, cm^{-1}): 1607, 1509, 1244, 1174, 1029, 823. HRMS (ESI+): exact mass calcd for $C_{25}H_{24}N_5O$ 410.19754 $[M + H]^+$, found 410.19769 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-(thiophene-3-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**27**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **2** (100 mg, 0.301 mmol), palladium acetate (1.4 mg, 6.02 μmol), potassium carbonate (62 mg, 0.662 mmol), and 3-bromothiophene (28 μL, 0.301 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **27** as a yellow oil (73 mg, 59%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.58 (d, J = 8.2 Hz, 2H), 7.39−7.31 (m, 4H), 7.25−7.16 (m, 3H), 6.88 (d, J = 8.7 Hz, 2H), 6.51 (s, 1H), 5.15 (s, 2H), 3.80 (s, 3H), 2.38 (s, 6H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.4 (C_{IV}), 146.4 (C_{IV}), 140.0 (C_{IV}), 135.7 (C_{IV}), 132.8 (C_{IV}), 129.6 (CH), 129.1 (C_{IV}), 128.9 (CH), 128.3 (CH), 128.0 (C_{IV}), 127.7 (CH), 125.7 (CH), 123.5 (CH), 115.8 (CH), 115.5 (C_{IV}), 114.1 (CH), 112.0 (C_{IV}), 55.2 (CH_3), 48.6 (CH_2), 21.1 (CH_3), 11.5 (CH_3). IR ν (neat, cm^{-1}): 1604, 1514, 1254, 1174, 1030, 846. HRMS (ESI+): exact mass calcd for $C_{25}H_{24}N_3OS$ 414.16346 $[M + H]^+$, found 414.16370 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-5-methyl-6-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-a]imidazol-3-yl)benzonitrile (**28**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **9** (100 mg, 0.259 mmol), palladium acetate (1.2 mg, 5.18 μmol), potassium carbonate (54 mg, 0.259 mmol), and 4-bromobenzonitrile (47.0 mg, 0.388 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1) afforded **28** as a yellow foam (93 mg, 74%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.83 (d, J = 7.9 Hz, 2H), 7.73−7.65 (m, 4H), 7.54 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 6.67 (s, 1H), 5.18 (s, 2H), 3.81 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 161.2 (C_{IV}), 148.5 (C_{IV}), 141.3 (C_{IV}), 140.7 (C_{IV}), 134.9 (C_{IV}), 133.8 (CH), 131.3 (CH), 129.8 (q, J^2_{C-F} = 32.5 Hz, C_{IV}), 129.7 (CH), 129.3 (CH), 128.8 (C_{IV}), 126.8 (q, J^3_{C-F} = 3.90 Hz, CH), 125.9 (q, J^1_{C-F} = 274 Hz, CF_3), 120.4 (C_{IV}), 119.9 (C_{IV}), 119.3 (CH), 115.8 (CH), 115.0 (C_{IV}), 112.7 (C_{IV}), 56.7 (CH_3), 50.5 (CH_2), 14.0 (CH_3). IR ν (neat, cm^{-1}): 2225, 1618, 1603, 1321, 1280, 1102, 1064, 850. HRMS (ESI +): exact mass calcd for $C_{28}H_{22}F_3N_4O$ 487.17402 $[M + H]^+$, found 487.17421 $[M + H]^+$.

*1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-5-methyl-6-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-a]imidazole (**29**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **9** (100 mg, 0.259 mmol), palladium acetate (1.2 mg, 5.18 μmol), potassium carbonate (54 mg, 0.259 mmol), and 4-bromoanisole (33 μL, 0.388 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **29** as a yellow foam (101 mg, 80%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.82 (d, J = 8.1 Hz, 2H, H_{Ar}), 7.65 (d, J = 8.2 Hz, 2H, H_{Ar}), 7.41−7.31 (m, 4H, H_{Ar}), 6.97−6.86 (m, 4H, H_{12} + H_{18}), 6.47 (s, 1H, H_2), 5.15 (s, 2H, H_9), 3.85 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.34 (s, 3H, CH_3). The ^{13}C NMR analysis of compound **29** has been performed but a degradation of this product during the time of the analysis was observed. IR ν (neat, cm^{-1}): 1615, 1512, 1321, 1245, 1103, 1066, 1028, 846. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}F_3N_3O_2$ 492.18934 $[M + H]^+$, found 492.18922 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-3-(pyridin-4-yl)-6-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-a]imidazole (**30**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **9** (100 mg, 0.259 mmol), palladium acetate (1.2 mg, 5.18 μmol), potassium carbonate (54 mg, 0.259 mmol), and 4-bromopyridine (41.0 mg, 0.259 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 9/1 to 7/3) afforded **30** as a beige solid (72 mg, 60%, 10% of starting material were recovered). Mp: 180−182 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.65 (d, J = 6.1 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H), 7.39−7.33 (m, 4H), 6.92 (d, J = 8.6 Hz, 2H), 6.72 (s, 1H), 5.18 (s, 2H), 3.81 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.9 (C_{IV}), 150.1 (CH), 147.3 (C_{IV}), 140.0 (C_{IV}), 139.40 (C_{IV}), 136.8 (2 × C_{IV}), 129.3 (CH), 128.4 (q, J^2_{C-F} = 32.6 Hz, C_{IV}), 127.9 (CH), 127.5 (C_{IV}), 125.4 (q, J^3_{C-F} = 3.90 Hz, CH), 124.6 (q, J^1_{C-F} = 274 Hz, CF_3), 122.1 (CH), 118.3 (CH), 114.5 (CH), 113.9 (C_{IV}), 55.4 (CH_3), 49.1 (CH_2), 12.8 (CH_3). IR ν (neat, cm^{-1}): 1618, 1593, 1509, 1320, 1152, 1240, 1103, 826. HRMS (ESI+): exact mass calcd for $C_{26}H_{22}F_3N_4O$ 463.17402 $[M + H]^+$, found 463.17394 $[M + H]^+$.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-5-methyl-3-p-tolyl-1H-imidazo[1,2-a]imidazole (**31**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **10** (100 mg, 0.288 mmol), palladium acetate (1.3 mg, 5.76 μmol), potassium carbonate (60 mg, 0.432 mmol), and 4-bromotoluene (35 μL, 0.288 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 7/3 to 5/5) afforded **31** as a yellow oil (76 mg, 60%, 15% of starting material were recovered). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.25 (m, 7H), 7.21 (d, J = 7.6 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.0 Hz, 1H), 6.46 (s, 1H), 5.14 (s, 2H), 3.87 (s, 3H), 3.79 (s, 3H), 2.38 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.7 (C_{IV}), 159.6 (C_{IV}), 147.0 (C_{IV}), 140.3 (C_{IV}), 138.1 (C_{IV}), 137.7 (C_{IV}), 129.9 (CH), 129.3 (CH), 129.2 (CH), 128.9 (CH), 128.4 (C_{IV}), 126.3 (C_{IV}), 120.7 (C_{IV}), 120.6 (CH), 115.7 (CH), 114.3 (CH), 113.3 (CH), 112.8 (C_{IV}), 112.3 (CH), 55.4 (CH_3), 55.3 (CH_3), 48.8 (CH_2), 21.4 (CH_3), 12.2 (CH_3). IR ν (neat, cm^{-1}): 1609, 1512, 1245, 1173, 1033. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O_2$ 438.21760 $[M + H]^+$, found 438.21753 $[M + H]^+$.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-3-(4-methoxyphenyl)-5-methyl-1H-imidazo[1,2-a]imidazole (**32**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **10** (100 mg, 0.288 mmol), palladium acetate (1.3 mg, 5.76 μmol), potassium carbonate (60 mg, 0.432 mmol) and 4-bromoanisole (36 μL, 0.288 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (dichloromethane/ethyl acetate 10/0 to 9/1) afforded **32** as a yellow oil (72.7 mg, 55%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.39−7.25 (m, 7H), 6.95−6.78 (m, 5H), 6.43 (s, 1H), 5.14 (s, 2H), 3.87 (s, 3H), 3.84 (s, 3H), 3.79 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.8 (C_{IV}), 159.7 (C_{IV}), 159.6 (C_{IV}), 146.9 (C_{IV}), 140.1 (C_{IV}), 137.6 (C_{IV}), 130.5 (CH), 129.9 (CH), 129.3 (CH), 128.5 (C_{IV}), 121.6 (C_{IV}), 120.6 (CH), 120.4 (C_{IV}), 115.5 (CH), 114.3 (CH), 113.9 (CH), 113.3 (CH), 112.7 (C_{IV}), 112.3 (CH), 55.5 (CH_3), 55.4 (2 × CH_3), 48.8 (CH_2), 12.0 (CH_3). IR ν (neat, cm^{-1}): 1610, 1512, 1245, 1173, 1030. HRMS (ESI+): exact mass calcd for $C_{28}H_{28}N_3O_3$ 454.21252 $[M + H]^+$, found 454.21221 $[M + H]^+$.

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*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-5-methyl-3-(4-(trifluoromethyl)phenyl)-1H-imidazo[1,2-a]imidazole (**33**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **10** (100 mg, 0.288 mmol), palladium acetate (1.3 mg, 5.76 μmol), potassium carbonate (60 mg, 0.432 mmol), and 4-bromobenzotrifluoride (40 μL, 0.288 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 7/3 to 5/5) afforded **33** as a yellow oil (65 mg, 46%, 26% of starting material were recovered). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.25 Hz, 2H), 7.56 (d, *J* = 8.25 Hz, 2H), 7.35 (d, *J* = 8.25 Hz, 2H), 7.32−7.25 (m, 3H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.86−6.82 (m, 1H), 6.59 (s, 1H), 5.17 (s, 2H), 3.87 (s, 3H), 3.79 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.8 (C_{IV}), 159.5 (C_{IV}), 147.1 (C_{IV}), 140.9 (C_{IV}), 137.3 (C_{IV}) 132.9 (C_{IV}), 129.8 (q, J^2_{C-F} = 32.0 Hz, C_{IV}), 129.9 (CH), 129.4 (CH), 128.5 (CH), 128.0 (C_{IV}), 125.5 (q, J^3_{C-F} = 4.0 Hz, CH), 124.1 (q, J^1_{C-F} = 253 Hz, CF_3), 120.6 (CH), 119.4 (C_{IV}), 117.0 (CH), 114.4 (CH), 113.4 (CH), 112.8 (C_{IV}), 112.5 (CH), 55.4 (CH_3), 55.3 (CH_3), 49.0 (CH_2), 12.5 (CH_3). IR ν (neat, cm^{-1}): 1610, 1514, 1316, 1164, 1068. HRMS (ESI+): exact mass calcd for $C_{28}H_{25}F_3N_3O_2$ 492.18934 $[M + H]^+$, found 492.18949 $[M + H]^+$.

*1-(4-Methoxybenzyl)-6-(3-methoxyphenyl)-5-methyl-3-(pyrimidin-5-yl)-1H-imidazo[1,2-a]imidazole (**34**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **10** (100 mg, 0.288 mmol), palladium acetate (1.3 mg, 5.76 μmol), potassium carbonate (60 mg, 0.432 mmol) and 5-bromopyrimidine (46 mg, 0.288 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 5/5 to ethyl acetate) afforded **34** as a yellow oil (61 mg, 50%, 29% of starting material were recovered). ^{1}H NMR (250 MHz, $CDCl_3$): δ 9.19 (s, 1H), 8.86 (s, 2H), 7.38−7.24 (m, 5H), 6.93−6.83 (m, 3H), 6.66 (s, 1H), 5.19 (s, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.9 (C_{IV}), 159.8 (C_{IV}), 157.8 (CH), 155.7 (CH), 147.0 (C_{IV}), 141.3 (C_{IV}), 137.0 (C_{IV}), 130.1 (CH), 129.5 (CH), 127.6 (C_{IV}), 124.2 (C_{IV}), 120.7 (CH), 117.8 (CH), 114.5 (CH), 113.5 (CH), 112.7 (CH), 112.5 (C_{IV}), 55.5 (CH_3), 55.4 (CH_3), 49.2 (CH_2), 12.2 (CH_3). IR ν (neat, cm^{-1}): 1610, 1513, 1246, 1231, 1173. HRMS (ESI+): exact mass calcd for $C_{25}H_{24}N_5O_2$ 426.19245 $[M + H]^+$, found 426.19240 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-5-methyl-6-(thiophene-3-yl)-1H-imidazo[1,2-a]imidazol-3-yl)benzonitrile (**35**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **11** (100 mg, 0.309 mmol), palladium acetate (1.4 mg, 6.18 μmol), potassium carbonate (64 mg, 0.309 mmol), and 4-bromobenzonitrile (56.0 mg, 0.309 mmol) in 3.00 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyal acetate 8/2 to 9/1) afforded **35** as a yellow oil (90 mg, **69%**). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.49−7.43 (m, 2H), 7.41−7.30 (m, 3H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.61 (s, 1H), 5.14 (s, 2H), 3.80 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 159.7 (C_{IV}), 146.9 (C_{IV}), 137.2 (C_{IV}), 136.7 (C_{IV}), 133.7 (C_{IV}), 132.3 (CH), 129.9 (C_{11}), 128.2 (CH), 127.6 (C_{IV}), 127.5 (CH), 125.3 (CH), 120.8 (CH), 119.0 (C_{IV}), 18.6 (C_{IV}), 117.5 (CH), 114.4 (CH), 112.3 (C_{IV}), 111.0 (C_{IV}), 55.3 (CH_3), 49.0 (CH_2), 12.4 (CH_3). IR ν (neat, cm^{-1}): 2223, 1602, 1654, 1513, 1247, 1173, 1030, 842. HRMS (ESI +): exact mass calcd for $C_{25}H_{21}N_4OS$ 425.14306 $[M + H]^+$, found 425.143314 $[M + H]^+$.

*1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-5-methyl-6-(thiophene-3-yl)-1H-imidazo[1,2-a]imidazole (**36**).* The reaction was carried out as described in general procedure B using imidazo[1,2-*a*]imidazole **11** (100 mg, 0.309 mmol), palladium acetate (1.4 mg, 6.18 μmol), potassium carbonate (64 mg, 0.463 mmol) and 4-bromoanisole (39 μL, 0.309 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyal acetate 9/1 to 8/2) afforded **36** as a yellow oil (82 mg, 62%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.51−7.34 (m, 7H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.97 (d, *J* = 8.6 Hz, 2H) 6.44 (s, 1H), 5.16 (s, 2H), 3.87 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 161.0 (C_{IV}), 160.9 (C_{IV}), 148.1 (C_{IV}), 138.7 (C_{IV}), 137.6 (C_{IV}), 131.8 (CH), 131.2 (CH), 130.5 (C_{IV}), 129.7 (C_{IV}), 129.0 (CH), 126.5 (CH), 122.8 (C_{IV}), 121.7 (CH), 116.7 (CH), 115.6 (CH), 115.2 (CH), 113.6 (C_{IV}), 56.8 (CH_3), 56.7 (CH_3), 50.1 (CH_2), 13.1 (CH_3). IR ν (neat, cm^{-1}): 1609, 1589, 1511, 1243, 1173, 1029, 834. HRMS (ESI+): exact mass calcd for $C_{25}H_{24}N_3O_2S$ 430.15837 $[M + H]^+$, found 430.15872 $[M + H]^+$.

*1-(4-Methoxybenzyl)-5-methyl-2,3,6-tri-p-tolyl-1H-imidazo[1,2-a]imidazole (**15**).* A sealed tube containing a stirring bar was charged with imidazo[1,2-*a*]imidazole **2** (100 mg, 0.302 mmol), 4-bromotoluene (112 μL, 0.905 mmol, 3 equiv), and potassium carbonate (126 mg, 0.905 mmol, 3 equiv) in 3 mL of toluene. The tube was evacuated and backfilled with dry argon twice. Palladium acetate (6.8 mg, 0.0302 mmol, 0.10 equiv) was added and the reaction mixture heated at 150 °C for 15 h. After the mixture was cooled, the solvent was removed under reduced pressure and the residue was purified by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) to afford **15** as a yellow solid (111 mg, **72%**). ***or*** the reaction was carried out as described in general procedure C using the imidazo[1,2-*a*]imidazole **14** (100 mg, 0.237 mmol), palladium acetate (5.3 mg, 0.0237 mmol), potassium carbonate (47 mg, 0.342 mmol), and 4-bromotoluene (44 μL, 0.356 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 8/2) afforded **15** as a yellow foam (121 mg, 73%). Mp: 169−171 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 8.1 Hz, 2H), 7.23−7.18 (m, 4H), 7.127.06 (m, 6H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 2H), 5.09 (s, 2H), 3.74 (s, 3H), 2.37 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 158.9 (C_{IV}), 146.8 (C_{IV}), 139.8 (C_{IV}), 138.3 (C_{IV}), 137.7 (C_{IV}), 135.6 (C_{IV}), 133.4 (C_{IV}), 130.9 (CH), 130.7 (CH), 129.8 (C_{IV}), 129.2 (CH), 129.1 (CH), 129.0 (CH + C_{IV}), 128.7 (CH), 127.9 (CH), 126.1 (C_{IV}), 125.9 (C_{IV}), 117.1 (C_{IV}), 113.7 (CH), 112.0 (C_{IV}), 55.2 (CH_3), 46.7 (CH_2), 21.4 (CH_3), 21.3 (CH_3), 21.2 (CH_3), 11.7 (CH_3). IR ν (neat, cm^{-1}): 1605, 1511, 1434, 1244, 1178, 1030, 819. HRMS (ESI+): exact mass calcd for $C_{35}H_{34}N_3O$ 512.26964 $[M + H]^+$, found 512.26979 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]imidazol-2-yl)benzonitrile (**37**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **17** (100 mg, 0.229 mmol), palladium acetate (5.1 mg, 0.023 mmol), potassium carbonate (47 mg, 0.342 mmol) and 4-bromobenzonitrile (62 mg, 0.342 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 8/2) afforded **37** as a yellow foam (76 mg, 62%) or a sealed tube containing a stirring bar was charged with the imidazo[1,2-*a*]imidazole **2** (97 mg, 0.292 mmol), 4-bromoanisole (37 μL, 0.292 mmol, 1.0 equiv), and potassium carbonate (81 mg, 0.584 mmol, 2.0 equiv) in 3 mL of toluene. The tube was evacuated and backfilled with dry argon twice. Palladium acetate (1.3 mg, 5.84 μmol, 0.02 equiv) was added, the reaction mixture was heated at 150 °C for 12 h, and 4-bromobenzonitrile (80 mg, 0.438 mmol, 1.5 equiv) was added. Then palladium acetate (6.5 mg, 0.0292 mmol, 0.10 equiv) were added, and the reaction mixture was heated at 150 °C for 12 h. After cooling down, toluene was removed under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate 9/1 to 8/2) afforded **37** as a yellow solid (99 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.0 Hz, 2H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.22 (m, 6H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 5.15 (s, 2H), 3.82 (s, 3H), 3.75 (s, 3H), 2.38 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.9 (C_{IV}), 159.1 (C_{IV}), 147.3 (C_{IV}), 140.5 (C_{IV}), 136.0 (C_{IV}), 134.2 (C_{IV}), 133.0 (C_{IV}), 132.3 (CH), 132.1 (CH), 131.0 (CH), 129.2 (C_{IV}), 129.0 (CH), 128.9 (CH), 127.8 (CH), 127.1 (C_{IV}), 120.0 (C_{IV}), 118.5 (2 × C_{IV}), 113.9 (2 × CH_{12}), 112.2 (C_{IV}), 111.6 (C_{IV}), 55.3 (CH_3), 55. Two (CH_3), 47.4 (CH_2), 21.2 (CH_3), 11.4 (CH_3). IR ν (neat, cm^{-1}): 2226, 1606, 1513, 1455, 1246, 1174, 1029, 862. HRMS (ESI+): exact mass calcd for $C_{35}H_{31}N_4O_2$ 539.24415 $[M + H]^+$, found 539.24383 $[M + H]^+$.

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*1-(4-Methoxybenzyl)-3-(4-methoxyphenyl)-5-methyl-2-(pyridin-4-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**38**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **17** (100 mg, 0.229 mmol), palladium acetate (5.1 mg, 22.9 μmol), potassium carbonate (47 mg, 0.342 mmol), and 4-bromopyridine (54 mg, 0.342 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 8/2 to 7/3) afforded **38** as a yellow oil (76 mg, 64%). ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.50 (d, *J* = 6.1 Hz, 2H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.25−7.18 (m, 4H), 7.09 (d, *J* = 8.6 Hz, 2H), 7.09 (d, *J* = 6.1 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.6 Hz, 2H), 5.18 (s, 2H), 3.83 (s, 3H), 3.76 (s, 3H), 2.38 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 160.0 (C_{IV}), 159.1 (C_{IV}), 149.9 (C_{18}), 147.3 (C_{IV}), 140.6 (C_{IV}), 137.5 (C_{IV}), 136.0 (C_{IV}), 133.0 (C_{IV}), 132.3 (CH), 129.2 (CH), 129.0 (CH), 128.9 (C_{IV}), 127.8 (CH), 126.2 (C_{IV}), 124.6 (CH), 120.0 (C_{IV}), 118.8 (C_{IV}), 113.9 (2 × CH), 112.2 (C_{IV}), 55.3 (CH_3), 55.2 (CH_3), 47.4 (CH_2), 21.2 (CH_3), 11.3 (CH_3). IR ν (neat, cm^{-1}): 1607, 1513, 1442, 1246, 1176, 1029, 826. HRMS (ESI+): exact mass calcd for $C_{33}H_{31}N_4O_2$ 515.24415 $[M + H]^+$, found 515.24391 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-2-(4-methoxyphenyl)-5-methyl-6-p-tolyl-1H-imidazo[1,2-a]imidazol-3-yl)benzonitrile (**39**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **19** (94 mg, 0.217 mmol), palladium acetate (4.9 mg, 21.7 μmol), potassium carbonate (45 mg, 0.326 mmol), and 4-bromoanisole (41 μL, 0.326 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 8/2) afforded **39** as a yellow solid (59.0 mg, 50%). Mp: 139−141 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ 7.62−7.54 (m, 4H), 7.36 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.11−7.00 (m, 4H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.75 (d, *J* = 8.7 Hz, 2H), 5.09 (s, 2H), 3.83 (s, 3H), 3.75 (s, 3H), 2.39 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (63.5 MHz, $CDCl_3$): δ 161.6 (C_{IV}), 160.5 (C_{IV}), 148.1 (C_{IV}), 142.2 (C_{IV}), 137.5 (C_{IV}), 135.3 (C_{IV}), 134.4 (C_{IV}), 133.9 (CH), 133.2 (CH), 131.9 (C_{IV}), 131.8 (CH), 130.7 (C_{IV} + CH), 130.5 (CH), 129.3 (CH), 121.6 (C_{IV}), 120.1 (C_{IV}), 116.8 (C_{IV}), 115.6 (CH), 115.2 (CH), 113.3 (C_{IV}), 112.2 (C_{IV}), 56.7 (CH_3), 56.6 (CH_3), 48.2 (CH_9), 22.7 (CH_3), 13.8 (CH_3). IR ν (neat, cm^{-1}): 2225, 1598, 1513, 1247, 1027, 828. HRMS (ESI+): exact mass calcd for $C_{35}H_{31}N_4O_2$ 539.24415 $[M + H]^+$, found 539.24414 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-5-methyl-2-(pyridin-4-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazol-3-yl)benzonitrile (**40**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **19** (88 mg, 0.217 mmol), palladium acetate (4.6 mg, 20.3 μmol), potassium carbonate (42 mg, 0.305 mmol), and 4-bromopyridine (48 mg, 0.305 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 6/4 to 4/6) afforded **40** as a beige solid (68 mg, 66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 5.9 Hz, 2H), 7.64−7.57 (m, 4H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 2H), 7.05−6.98 (m, 4H), 6.75 (d, *J* = 8.6 Hz, 2H), 5.17 (s, 2H), 3.75 (s, 3H), 2.39 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.3 (C_{IV}), 150.3 (CH), 147.2 (C_{IV}), 141.5 (C_{IV}), 136.5 (C_{IV}), 136.4 (C_{IV}), 132.7 (C_{IV}), 132.6 (C_{IV}), 132.1 (CH), 130.9 (CH), 129.1 (CH), 129.0 (C_{11}), 128.6 (C_{IV}), 127.9 (CH), 127.5 (C_{IV}), 124.9 (CH), 118.2 (C_{IV}), 116.7 (C_{IV}), 114.0 (CH), 112.1 (C_{IV}), 112.0 (C_{IV}), 55.2 (CH_3), 47.4 (CH_9), 21.3 (CH_3), 12.0 (CH_3). IR ν (neat, cm^{-1}): 2229 (CN), 1610, 1513, 1443, 1249, 1172, 824. HRMS (ESI+): exact mass calcd for $C_{33}H_{28}N_5O$ 510.22884 $[M + H]^+$, found 510.22892 $[M + H]^+$.

*4-(1-(4-Methoxybenzyl)-5-methyl-3-(pyridin-4-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazol-2-yl)benzonitrile (**41**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **25** (88 mg, 0.220 mmol), palladium acetate (4.9 mg, 22.0 μmol), potassium carbonate (46 mg, 0.331 mmol), and 4-bromobenzonitrile (60 mg, 0.331 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 7/3 to 6/4) afforded **41** as a beige solid (69 mg, 60%). Mp: 234−236 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 6.0 Hz, 2H), 7.62−7.58 (m, 4H), 7.27−7.20 (m, 4H), 7.16 (d, *J* = 6.0 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 6.74 (d, *J* = 8.7 Hz, 2H), 5.13 (s, 2H), 3.75 (s, 3H), 2.39 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 159.3 (C_{IV}), 149.9 (CH), 147.1 (C_{IV}), 141.4 (C_{IV}), 136.4 (C_{IV}), 136.1 (C_{IV}), 133.1 (C_{IV}), 132.7 (C_{IV}), 132.4 (CH), 131.5 (CH), 129.1 (CH), 128.9 (CH), 128.6 (C_{IV}), 128.5 (C_{IV}), 127.9 (CH), 124.5 (CH), 118.1 (C_{IV}), 115.7 (C_{IV}), 114.0 (CH), 112.9 (C_{IV}), 112.2 (C_{IV}), 55.2 (CH_3), 47.3 (CH_9), 21.2 (CH_3), 12.2 (CH_3). IR ν (neat, cm^{-1}): 2229, 1597, 1513, 1441, 1246, 1033, 829. HRMS (ESI+): exact mass calcd for $C_{33}H_{28}N_5O$ 510.22884 $[M + H]^+$, found 510.22882 $[M + H]^+$.

*1-(4-Methoxybenzyl)-2-(4-methoxyphenyl)-5-methyl-3-(pyridin-4-yl)-6-p-tolyl-1H-imidazo[1,2-a]imidazole (**42**).* The reaction was carried out as described in general procedure C using imidazo[1,2-*a*]imidazole **25** (90 mg, 0.220 mmol), palladium acetate (4.9 mg, 22.0 μmol), potassium carbonate (46 mg, 0.331 mmol), and 4-bromoanisole (42 μL, 0.331 mmol) in 3 mL of toluene. Standard workup followed by flash chromatography (petroleum ether/ethyl acetate 7/3 to 6/4) afforded **42** as a beige solid (68 mg, **61%**). Mp: 202−204 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (d, *J* = 6.1 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 7.9 Hz, 2H), 7.19 (d, *J* = 6.1 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.6 Hz, 2H), 5.11 (s, 2H), 3.86 (s, 3H), 3.78 (s, 3H), 2.42 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 160.3 (C_{IV}), 159.0 (C_{IV}), 149.5 (CH), 146.7 (C_{IV}), 140.8 (C_{IV}), 137.0 (C_{IV}), 136.0 (C_{IV}), 133.0 (C_{IV}), 132.5 (CH), 130.8 (C_{IV}), 129.3 (CH), 129.1 (CH), 127.9 (CH), 124.2 (CH), 120.1 (C_{IV}), 114.6 (C_{IV}), 114.2 (CH), 113.8 (CH), 112.0 (C_{IV}), 55.3 (CH_3), 55.2 (CH_3), 46.74 (CH_2), 21.2 (CH_3), 12.5 (CH_3). (1 C_{IV} is not observed). IR ν (neat, cm^{-1}): 1604, 1513, 1254, 1177, 1031, 841. HRMS (ESI+): exact mass calcd for $C_{33}H_{31}N_4O_2$ 515.24415 $[M + H]^+$, found 515.24402 $[M + H]^+$.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00534.

^{1}H and ^{13}C NMR for all new compounds (PDF)

Crystallographic data for compound **14** (CIF)

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Notes

The authors declare no competing financial interest.

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