JOC The Journal of Organic Chemistry

Article

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Transition-Metal-Catalyzed Arylation of Nitroimidazoles and Further Transformations of Manipulable Nitro Group

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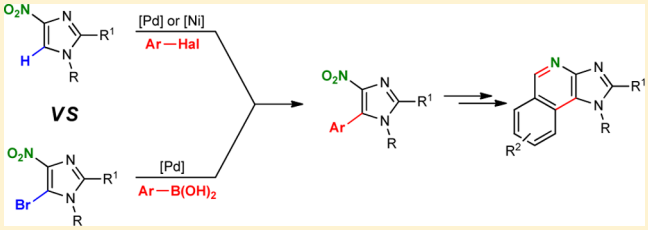
Supporting Information

ABSTRACT: Pd- or Ni-catalyzed C−H arylation of 4-nitroimidazole derivatives directed by a manipulable nitro group was developed. The reaction tolerates a wide range of substituted aryl halides and 4-nitroimidazoles. The experiments indicated that the nitro group has influence on regioselectivity of the reaction. In addition, we have shown that the efficiency of the Suzuki−Miyaura cross-coupling reaction of nitroimidazoles is slightly lower in comparison to the direct C−H arylation. The exploration of the chemical potential of the nitro group and a putative reaction mechanism are discussed.



INTRODUCTION

Substituted imidazoles are important heteroaromatic compounds which are known to exhibit a broad range of biological activities.[1] They are also important building blocks found in naturally occurring compounds,[2] and imidazoles are versatile precursors to *N*-heterocyclic carbenes useful as ligands in various catalytically active transition-metal complexes[3] and in organocatalysis.[4] Moreover, imidazolium salts can be used as environmentally friendly ionic solvents.[5] Accordingly, a number of methodologies for construction and/or substitution of various imidazoles have been intensively developed during the last few decades.[6] In this context, there are a number of established de novo methods for construction of imidazole ring with appropriate substituents via cyclocondensation reactions (for an example, see Figure 1 A).[6] Although these traditional approaches have been greatly improved, in most cases, the synthesis of each analogue of the library will require the entire de novo synthetic sequence, which usually results in complications in terms of formation of regioisomers, etc.[6c] On the other hand, the formation of a single C−C or C−X bond by catalytic cross-coupling reactions of imidazole derivatives eliminates most of the problems typical for de novo synthesis of imidazole derivatives (Figure 1 B).[6a,7] Though this approach has been greatly improved over the past decades,[7] the need for preparation of prefunctionalized starting materials along with the needs of "green chemistry" indicated its scope and efficiency limitations. However, during the past few years, direct transition-metal-catalyzed C−H activation reactions of privileged (hetero)arenes provides highly efficient means to synthesize functionalized (hetero)arenes[8] utilized extensively throughout the pharmaceutical and materials industries (Figure 1 C).[9,6]

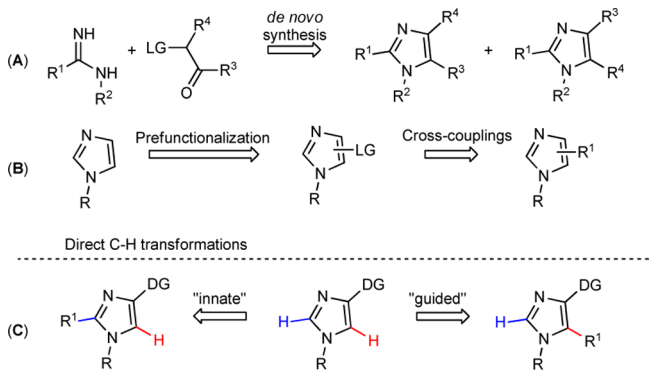


Figure 1. Common approaches for synthesis of functionalized imidazoles.

This approach eliminates the need for the organometallic starting materials required in traditional cross-coupling methods;[7] in addition, these methods commonly reduce reaction byproducts, increase the number of available substrates, and decrease the synthetic effort required for formation of the desired C−C and/or C−X bonds. Nevertheless, despite the cutting edge innovations achieved in this field, a selective functionalization of a particular C−H bond of interest still remains a complex task. One of the possible solutions involves the employment of directing groups (DG).[10]

Received: November 15, 2014
Published: January 23, 2015

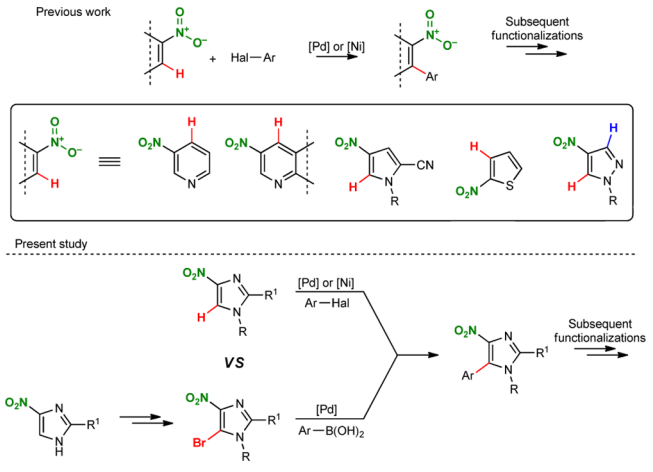
DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

However, in most of the cases these efficient moieties cannot be removed easily or they are not apt to undergo further functionalizations. Because of this, substantial effort has been directed toward the discovery of multifunctional directing groups for direct C−H activation of (hetero)arenes.[11] A clear example is the use of oxidizing directing groups that contains a covalent bond which is responsible for oxidation of the metal, eliminating the need of external oxidants which usually generates waste subproducts.[12] Another way to develop the multitasking character of the directing groups is the use of "removable" functional groups.[11,13]

In this context, the nitro group is almost the paradigm of what a manipulable directing group could be. It can behave as a classical directing group,[14] selecting the positions where the metal has to be incorporated and, typically, forming part of the target molecule via additional functionalizations after the C−H activation step. This two-step approach undoubtedly has a huge synthetic capacity.[15]

The use of the nitro group as a regiodirecting substituent in C−H activations has scarcely been reported to date.[16] Examples include the Pd-catalyzed *ortho* C−H arylation of nitrobenzene derivatives[16a] as well as the C−H arylation of positions 4 and 5 of 3-nitropyridine.[16b] In spite of this, the authors did not demonstrate the vast chemical potential of nitro group. In contrast to this, we recently communicated the selective and guided functionalization of 4-nitropyrazoles, fused 3-nitropyridines, 2-nitrothiophene, and 4-nitro-1*H*-pyrroles by Pd- and Ni-catalyzed C−H arylation, which was followed by demonstration of the multipurpose character of the nitro group as directing group (Scheme 1).[17] In our present study, we continue the amplification of this chemistry on the example of several *N*-substituted 4-nitroimidazoles (Scheme 1).

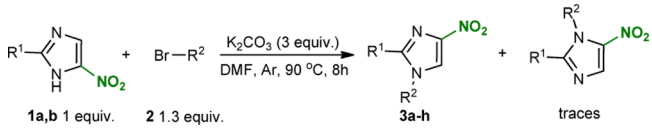
Scheme 1. Synthetic Potential of TM-Catalyzed Nitro Group Directed C−H Arylation of Heteroarenes



RESULTS AND DISCUSSION

Inspired by the tremendous chemical potential of the nitro group[15] and our recent successful results on C−H arylation of different nitro-substituted heteroarenes,[17] we began the present study on C−H arylation of nitroimidazoles. Accordingly, the starting *N*-substituted 4-nitroimidazoles **3a−h** were prepared using simple alkylation of commercially available 4(5)-nitroimidazole **1** with appropriate alkyl bromides as depicted in Table 1.

Table 1. Synthesis of Starting *N*-Substituted 4-Nitroimidazoles 3a−h



3	R^1	R^2	yield (%)
a	Me	ethyl	82
b	Me	*n*-butyl	88
c	Me	$(CH_2)_2Ph$	93
d	H	$(CH_2)_2Ph$	80
e	Me	$(CH_2)_3Ph$	78
f	Me	$(CH_2)_2OPh$	89
g	Me	CH_2-4-Tol	83
h	Me	2-BrC_6H_4	83

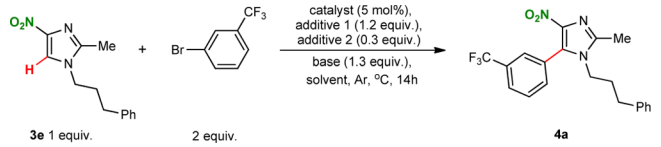
On the basis of our experience and following the general movements in the field, in order to achieve the desired highly efficient C−H arylation, a number of decisive challenges had to be overcome: (1) the first challenge is the optimizing reaction conditions, so that only the stoichiometric amounts of coupling partners can be used; (2) the second challenge is the investigation of regioselectivity in three potential active positions in the imidazole ring (positions 2, 4 and 5); and (3) in this context interrelation between "guided" and "innate" C−H arylation reactions should be investigated (Figure 1). Subsequently, the following criteria for design of an ideal directing group for C−H transformations should be fulfilled: (1) corresponding directing group should be capable of coordinating the catalyst; (2) the directing group should be sufficiently stable under typical transition-metal-catalyzed C−H activation reaction conditions; (3) and finally the directing group should be prone to undergo some further transformations, thereby allowing the synthesis of multifunctionalized target compounds.

With the set of *N*-substituted 4-nitroimidazoles **3a−h** in hand, we focused next on setting up optimal reaction conditions. Toward this end, in order to avoid further complications, we decided to use as a model compound 2-methyl-4-nitro-1-(3-phenylpropyl)-1*H*-imidazole **3e**. Based on our previous results, we considered the Pd catalysts with CuI as additives to be the starting point in this study.[17,18] To our delight, pilot experiments have indicated that, indeed, the Pd/CuI system is rather efficient in order to activate the C(5)−H bond of 4-nitroimidazole **3e** (Table 2, entries 1−5); namely, the best catalyst for the model compound **3e** is $PdCl_2(PPh_3)_2$. We obtained the desired product with 96% yield (entry 4). We found that addition of phosphine ligands has no real impact on overall yields of the reaction (entries 1, 2, and 4). Notably, the copper salt such as CuI in stoichiometric amounts provides desired product in almost quantitative yield (entry 4). Although, absence or use of substoichiometric amounts of CuI did not stop the reaction, the product was obtained with reduced yield (entry 5).

Interestingly, the use of Lewis acids like CuCl or Ag_2CO_3 still provides the formation of desired product, but with reduced yields (entries 6 and 7). The best base for the reaction was found to be the K_2CO_3/PivOH system; any change in the system decreased the yields (entries 8−11). Use of different solvents and temperatures has shown that the reaction runs effectively in DMF, DMA, and NMP without any notable

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

Table 2. Optimization of Reaction Conditions for the Synthesis of Compound 4a



entry	catalyst	ligand	additive 1	additive 2	base	solvent	temp (°C)	% yield[a]
1	$Pd(OAc)_2$	Cy_3PxHBF_4	CuI	PivOH	K_2CO_3	DMA	130	78
2	$Pd(OAc)_2$		CuI	PivOH	K_2CO_3	DMA	130	76
3			CuI	PivOH	K_2CO_3	DMA	130	
4	**$PdCl_2(PPh_3)_2$**		**CuI**	**PivOH**	**K_2CO_3**	**DMA**	**130**	**96**
5	$PdCl_2(PPh_3)_2$			PivOH	K_2CO_3	DMA	130	71
6	$PdCl_2(PPh_3)_2$		CuCl	PivOH	K_2CO_3	DMA	130	83
7	$PdCl_2(PPh_3)_2$		Ag_2CO_3	PivOH	K_2CO_3	DMA	130	63
8	$PdCl_2(PPh_3)_2$		CuI		K_2CO_3	DMA	130	25
9	$PdCl_2(PPh_3)_2$		CuI	Ph_3CCO_2H	K_2CO_3	DMA	130	22
10	$PdCl_2(PPh_3)_2$		CuI	PivOH	K_3PO_4	DMA	130	46
11	$PdCl_2(PPh_3)_2$		CuI		KOAc	DMA	130	80
12	$PdCl_2(PPh_3)_2$		CuI	PivOH	K_2CO_3	DMF	130	94
13	$PdCl_2(PPh_3)_2$		CuI	PivOH	K_2CO_3	NMP	130	90
14	$PdCl_2(PPh_3)_2$		CuI	PivOH	K_2CO_3	1,4-dioxane	100	
15	$PdCl_2(PPh_3)_2$		CuI	PivOH	K_2CO_3	toluene	100	15
16	**$NiCl_2(PPh_3)_2$**		**CuI**	**PivOH**	**K_2CO_3**	**DMA**	**130**	**64**

[a]Isolated yields.

differences in yields (entries 4 and 12−15). Finally, the use of the other catalysts was ineffective. Among these, perhaps unsurprisingly, the reaction catalyzed by $NiCl_2(PPh_3)_2$ occurred uneventfully and furnished the desired product, although the conversion of reactants was not very high (entry 16).

Next, the generality of this protocol toward coupling partners was examined (Scheme 2). To our delight, it was found that this transformation worked well for both electron-rich and electron-deficient arenes. Notably, a broad number of functionalities, such as F (**4p**), Cl (**4h**), CF_3 (**4a,e,h,m**), and OMe (**4d,i,o,r,t**), and a variety of other functional groups, such as ketone (**4s**), NO_2 (**4b**), and even aldehyde (**4c,d,g,i,j,l,t**), as well as heterocycles (**4f,n,q**) were perfectly tolerated under these reaction conditions, providing target arylated nitroimidazoles in high to quantitative yields. Expectedly, the functional group tolerance was equal in a wide range of substituted 4-nitroimidazoles with no changes in the reaction conditions. The use of aryl iodides resulted in formation of a great amount of biphenyles via homocoupling induced by CuI: this demanded a large excess of the aryl halide, and the overall yields were visibly lower than with aryl bromides (**4a,b,e,o**). Together with this, aryl chlorides, in general, were not active enough under these reaction conditions (**4h**). Subsequently, the scope of the Ni-catalyzed C−H arylation reaction of the corresponding 4-nitroimidazoles was examined. We have found that the reaction has general character allowing an efficient introduction of an aryl group into the imidazole ring in moderate yields (**4b,e,f,g,k,m,n,r**).

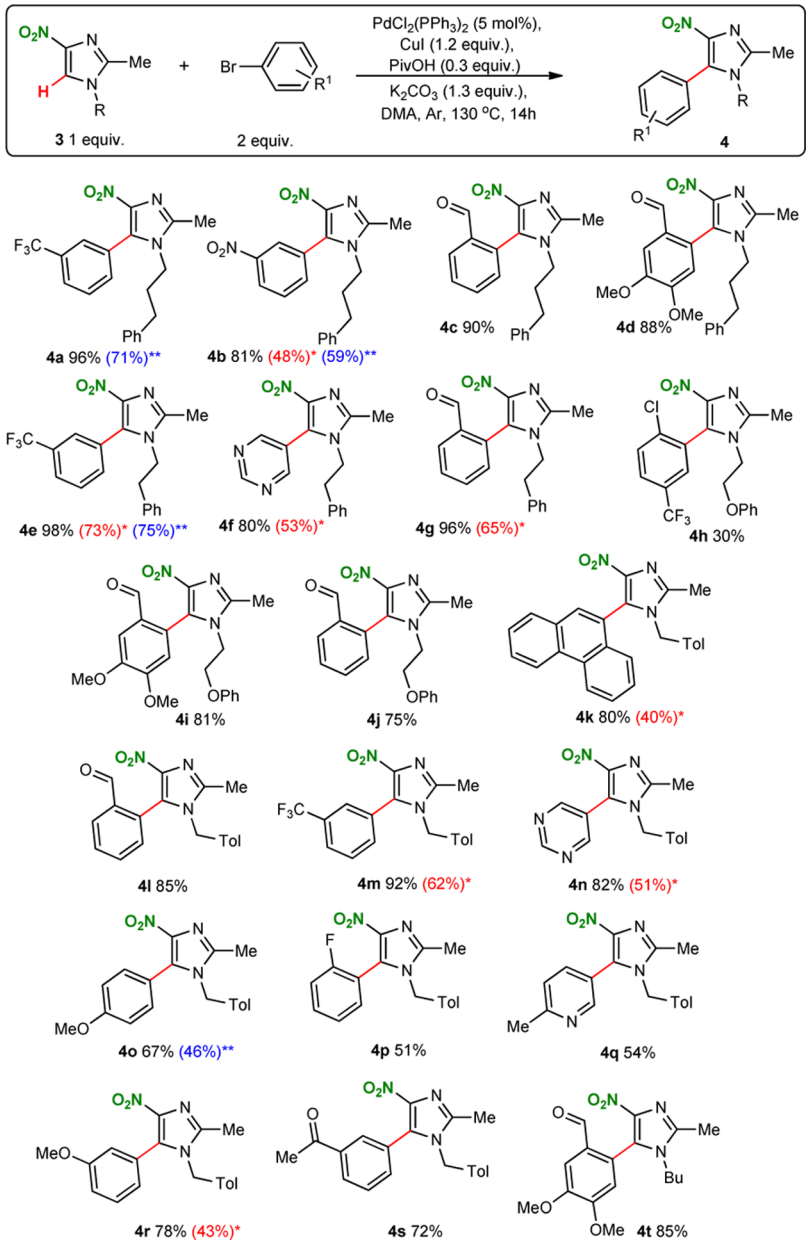
Surprisingly, during the course of the reaction conditions optimization, we observed another interesting process. Namely, when CuI was replaced by Ag_2CO_3 along with C−H arylation by aryl bromide (63%), a Pd-catalyzed intramolecular dehydrogenative 2-fold C−H cross-coupling occurred (Table 2, entry 7, Scheme 3).[18a,19] Initially, we observed traces of cyclization product **5a** (8%) together with C−H arylation product **4a** (63%); nevertheless, reducing the amount of aryl bromide dramatically increased the yield of intramolecular dehydrogenative 2-fold C−H cross-coupling reaction. In this context, this search found that in the absence of aryl halide presence of an oxidant (in this case Ag_2CO_3) can initiate an intramolecular dehydrogenative 2-fold C−H cross-coupling of 4-nitroimidazoles leading to different fused systems **5a−c** in good to excellent yields (Scheme 3).

Naturally, after the development of an efficient Pd- and Ni-catalyzed arylation of simple 4-nitroimidazoles, next we were interested in exploration of this reaction procedure for 2,5-unsubstituted 4-nitroimidazole **3d**. It is known from the literature that the regioselectivity of Pd-catalyzed C−H activation of imidazoles depends on the catalytic system used.[6a] Empirical studies indicated that the C-5 position of imidazoles exhibits higher reactivity than that at the C-2 position toward the Pd-catalyzed arylation in the presence of weak bases and phosphine ligands. The C-4 position is relatively less reactive in this respect. It was also demonstrated that the addition of Cu(I) salts alters the bias toward the C-2 position.[6a] This reactivity pattern is also consistent with theoretically calculated CMD barriers for *N*-methylimidazole.[20]

However, in our case, the situation is different due to the nitro group that can direct the reaction. Thus, when we performed the reaction of 4-nitroimidazole **3d** with 2.5 equiv of aryl bromide under standard reaction conditions, the corresponding 2,5-disubstituted products **6** were observed (Scheme 4). Nevertheless, when the amount of aryl bromide was decreased to 1.1 equiv, remarkably C-5 substituted 4-nitroimidazoles **7** were the only observed regioisomer (Scheme 4). When we performed the reaction in the absence of CuI the yield of reaction decreased without any changes in regioselectivity (see also Table 2, entries 4 and 5). This means that in 4-nitroimidazole **3d** the "guiding" effect of the nitro group dramatically changes the regioselectivity of the reaction, even though in the reaction medium stoichiometric amount of CuI was presented.[6a,20] Having these results in hand, further a stepwise synthesis of 2,5-diaryl-4-nitroimidazole with two different aryl groups was performed. Starting from

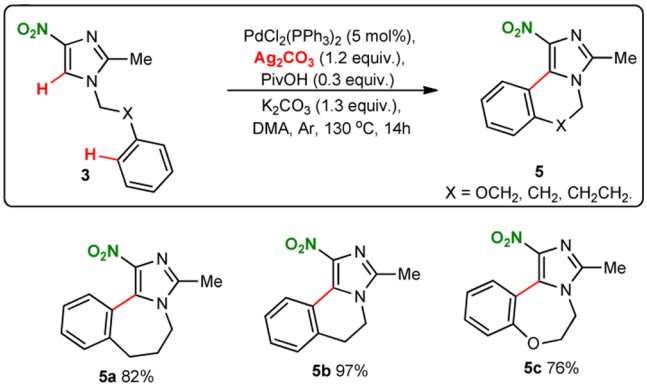
DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

Scheme 2. Scope of the Reaction with Respect to Aryl Bromides and *N*-Substituted 4-Nitroimidazoles.[a]



[a]Key: ** In the parentheses in blue are mentioned the yields of C−H arylation with appropriate aryl iodides.

Scheme 3. Synthesis of Fused Systems 5a−c



compound **7c** using standard reaction conditions, the corresponding 2,5-disubstituted imidazole **8a** was successfully isolated in 78% yield (Scheme 4).

Inspired by the successful results on regioselective C−H arylation of positions 2 and 5 of 4-nitroimidazoles, we next envisioned that the C−H arylation of position 4 in 5-nitroimidazole can be an excellent extension of the scope of the reaction. Toward this end, we designed and tested a number of reaction conditions; nevertheless, the reactions failed; in spite of the partial conversion of reactants, only an inseparable mixture of compounds was observed. Further, we tried to overcome this problem by finding another suitable procedure toward 4-arylated 5-nitroimidazoles. For this purpose, the Suzuki−Miyaura cross-coupling reaction of 5(4)-bromo-4(5)-nitroimidazoles **10** and **11** was tested (Table 3). To this end, 5(4)-bromo-4(5)-nitro-1*H*-imidazole **9** was

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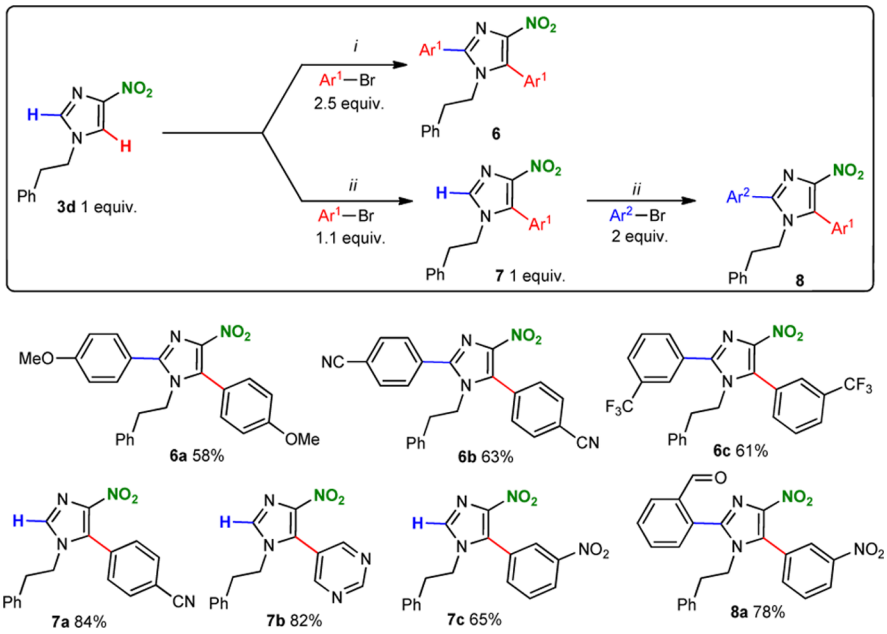
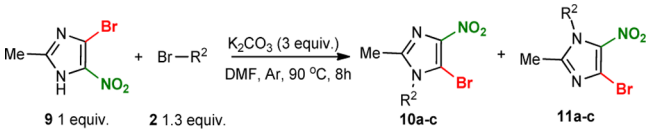
Scheme 4. Regioselective C−H Arylation of 4-Nitroimidazoles[a]



[a]Key: (i) $PdCl_2(PPh_3)_2$ (5 mol %), CuI (1.2 equiv), PivOH (0.3 equiv), K_2CO_3 (2.3 equiv), DMA, under Ar, 130 °C, 14 h; (ii) $PdCl_2(PPh_3)_2$ (5 mol %), CuI (1.2 equiv), PivOH (0.3 equiv), K_2CO_3 (1.3 equiv), DMA, under Ar, 130 °C, 14 h.

Table 3. Synthesis of *N*-Substituted 5(4)-Bromo-4(5)-nitroimidazoles 10 and 11

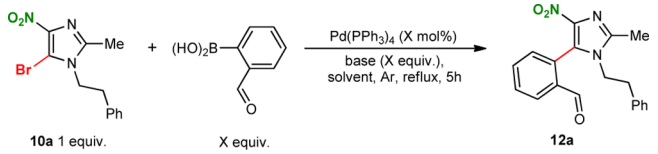


10, 11	R^2	10 (%)	11 (%)
a	$(CH_2)_2Ph$	57	31
b	$(CH_2)_2OPh$	58	38
c	$(CH_2)_3Ph$	55	40

alkylated in order to prepare the desired starting *N*-substituted imidazoles **10** and **11**. It should be mentioned that, unlike alkylation of simple 4-nitroimidazoles (Table 1), the alkylation reaction of 5(4)-bromo-4(5)-nitroimidazoles leads to a mixture of 5-bromo-4-nitroimidazole **10** and 4-bromo-5-nitroimidazole **11**, in approximately a 2:1 ratio. Three pairs of *N*-substituted nitroimidazoles were synthesized via this procedure (Table 3).

In the hope of identifying a practical and versatile catalytic procedure, we thoroughly examined the reaction parameters including metal catalyst, base, and loading of reactants, solvent, and temperature, and the selected results are listed in Table 4. According to the new pathway for the test reaction, we used imidazole **10a** and 2-formylphenylboronic acid as an aryl source (Table 4). As a catalyst for this transformation, $Pd(PPh_3)_4$ was chosen, since the literature data show that it is the most successful Pd source for the Suzuki−Miyaura cross-coupling reaction.[7] During optimization of the reaction conditions, a number of solvents were tested such as dioxane, toluene, etc.

Table 4. Optimization of Reaction Conditions for the Synthesis of Compound 12a



entry	catalyst (mol %)	$ArB(OH)_2$ (equiv)	base	solvent	% yield[a]
1	$Pd(PPh_3)_4$ (10)	1.3	K_2CO_3 (2 equiv)	dioxane	trace
2	$Pd(PPh_3)_4$ (10)	1.3	K_2CO_3 (2 equiv)	toluene	trace
3	$Pd(PPh_3)_4$ (10)	1.3	K_2CO_3 (2 equiv)	dioxane/H_2O (4:1)	20
4	$Pd(PPh_3)_4$ (10)	1.3	K_2CO_3 (2 equiv)	toluene/H_2O (4:1)	27
5	$Pd(PPh_3)_4$ (10)	1.3	K_3PO_4 (2 equiv)	toluene/H_2O (4:1)	15
6	$Pd(PPh_3)_4$ (10)	1.3	K_2CO_3 (2 equiv)	toluene/MeOH (5:1)	36
7	**$Pd(PPh_3)_4$ (10)**	**1.3**	**2 M aq K_2CO_3 (1 mL)**[b]	**toluene/MeOH (5:1)**	**62**
8	$Pd(PPh_3)_4$ (10)	1.0	2 M aq K_2CO_3 (1 mL)[b]	toluene/MeOH (5:1)	50
9	$Pd(PPh_3)_4$ (10)	2.0	2 M aq K_2CO_3 (1 mL)[b]	toluene/MeOH (5:1)	61
10	$Pd(PPh_3)_4$ (5)	1.3	2 M aq K_2CO_3 (1 mL)[b]	toluene/MeOH (5:1)	56

[a]Isolated yields. [b]For 1 mmol of starting imidazole.

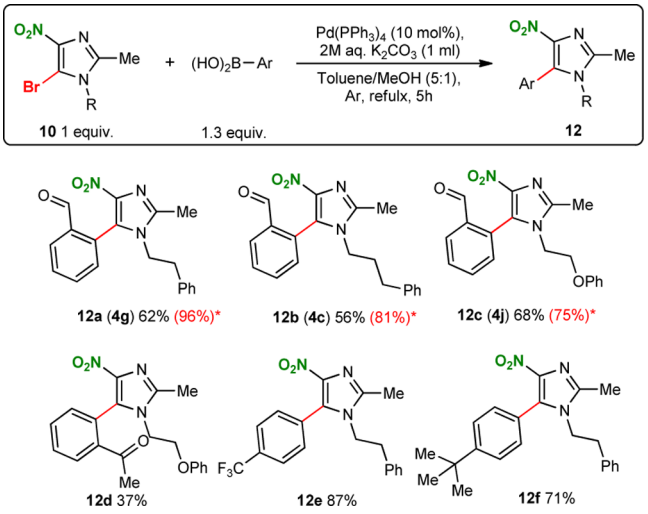
DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

Unfortunately, all our initial attempts to perform the desired coupling appeared to be unsuccessful (Table 4, entries 1 and 2). Hence, we tried to use different combination of solvents. Gratifyingly, we found that when the reaction was performed in standard solvents (mentioned above) using a drop of water the desired product forms in 20% and 27% yields in dioxane/H_2O and toluene/H_2O systems, respectively (Table 4, entries 3 and 4).

Meanwhile, the change of K_2CO_3 to K_3PO_4 decreased the yield of product (Table 4, entry 5); therefore, during further optimization only K_2CO_3 was used as a base. In addition, once MeOH was used instead of water, curiously the yield of the reaction increased up to 36% (Table 4, entry 6). Furthermore, using an aqueous solution of K_2CO_3 as a base we could obtain the desired product in 62% yield (Table 4, entry 7). During the next steps of optimization, we tried to increase the yields by changing quantities of boronic acid. Nevertheless, we could not obtain any positive results; 1.3 equiv of boronic acid showed the best efficiency (Table 4, entries 8 and 9). Finally, it should be mentioned that performing the reaction at slightly higher temperature (under reflux) in inert atmosphere provided better yields of arylation products.

Naturally, after development of an efficient Pd-catalyzed Suzuki–Miyaura cross-coupling reaction of 5-bromo-4-nitroimidazoles **10**, under the newly developed conditions we tried to prepare arylation products similar to those that were prepared by C–H arylation (Scheme 5). The comparison of

Scheme 5. Scope of the Suzuki–Miyaura Cross-Coupling Reaction[a]

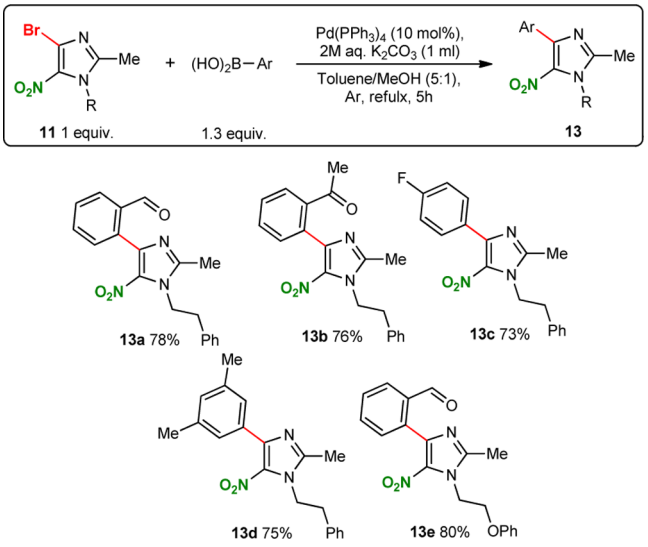


[a]Key: *In the parentheses in red are mentioned the yields of C–H arylation (Scheme 2).

these two procedures seems to be a useful task since Suzuki–Miyaura cross-coupling reaction requires more synthetic effort and expensive starting materials. In this context, we could demonstrate that the yields of the Suzuki–Miyaura cross-coupling reaction of 5-bromo-4-nitroimidazoles **10** were slightly lower in comparison to the yields obtained for similar compounds in the direct C–H activation reaction (Scheme 2). This may be the result of steric factors and/or poor solubility of the reaction components.

Although the C(4)–H bond of nitroimidazoles exhibits very low reactivity in the Pd- and Ni-catalyzed C–H arylation described above, precluding direct arylation of this position, nevertheless we could overcome this problem applying the Suzuki–Miyaura cross-coupling reaction of 4-bromo-5-nitroimidazoles **11**. Using this procedure, we successfully prepared a number of 4-arylated-5-nitroimidazoles **13** with good yields (Scheme 6).

Scheme 6. Scope of the Suzuki–Miyaura Cross-Coupling Reaction



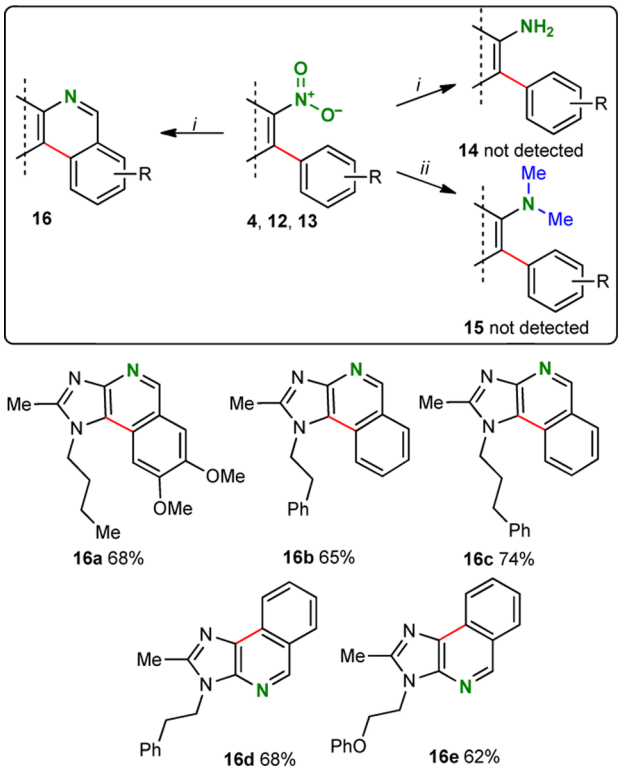
Eventually, to fully demonstrate the synthetic potential of this methodology, we briefly explored the chemical versatility of the directing group. The simple reduction of the nitro group was tested first (Scheme 7). Not surprisingly, we obtained an inseparable mixture of products, and along with this intensive polymerization was observed, most probably because of the instability of formed aminoimidazoles **14**.[21] Moreover, we obtained similar results when the reduction was performed in the presence of an excess of formalin; that is, instead of *N,N*-dimethylamines **15** we obtained a mixture of products. Fortunately, we could demonstrate that the reduction of arylated nitroimidazoles containing an *ortho* carbonyl group (**4t**, **12a**,**b**, **13a**,**e**) leads to the formation of 1*H*-imidazo[4,5-*c*]isoquinoline system **16** as a single product with good yields (Scheme 7). In this case, probably the reduction product amine undergoes a subsequent interaction with a carbonyl group leading to the aromatic isoquinoline system.

The structure of the synthesized arylated nitroimidazoles was mainly established by 1D and 2D NMR methods. The structures of compounds **3g**, **4d**,**t**, **5b**, **7a**,**c**, **10a**, and **12a** (**4g**) were independently confirmed by X-ray single-crystal analyses (Figures 1–8, Supporting Information).[22]

To gain more insight into the reaction pattern, a competitive experiment was conducted between imidazole **3c** and electronically different aryl bromides, namely with 1-bromo-3-methoxybenzene and 1-bromo-3-nitrobenzene (Scheme 8). The goal was to identify the comparable reactivity of different aryl bromides bearing either an electron-donating or an electron-withdrawing group. The results revealed that the reaction favored electron-deficient aryl bromides. Setting up the competitive arylation with two different aryl bromides (Scheme 8, A), we could isolate only one product **4u** in 82% yield corresponding to C–H arylation with 1-bromo-3-nitrobenzene (Scheme 8). This experiment clearly shows that aryl bromides

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103–2119

Scheme 7. Reduction of the Nitro Group[a]

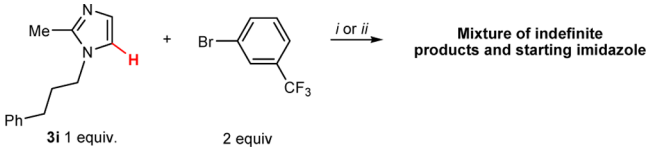


[a]Key: (i) MeOH, H_2, Pd/C (10 mol %), 20 °C, 5 h; (ii) MeOH, H_2, Pd/C (10 mol %), CH_2O in H_2O (37%, 6 equiv), 20 °C, 5 h.

with electron-withdrawing groups are much more reactive in C−H arylation reactions than the respective aryl bromides with an electron-donating group. The competitive experiment between two various imidazoles **3c** and **3g** along with 1-bromo-3-nitrobenzene was also performed (Scheme 8, B). In this case the goal was to identify the comparable reactivity between two different *N*-substituted imidazoles, in order to understand the impact of the steric influences of the substituent in the position 1 of the imidazole ring. During the course of study we found that there was almost no distinction between two imidazoles. In this case, a mixture of two products with almost similar quantities was observed (Scheme 8, see also the Supporting Information).

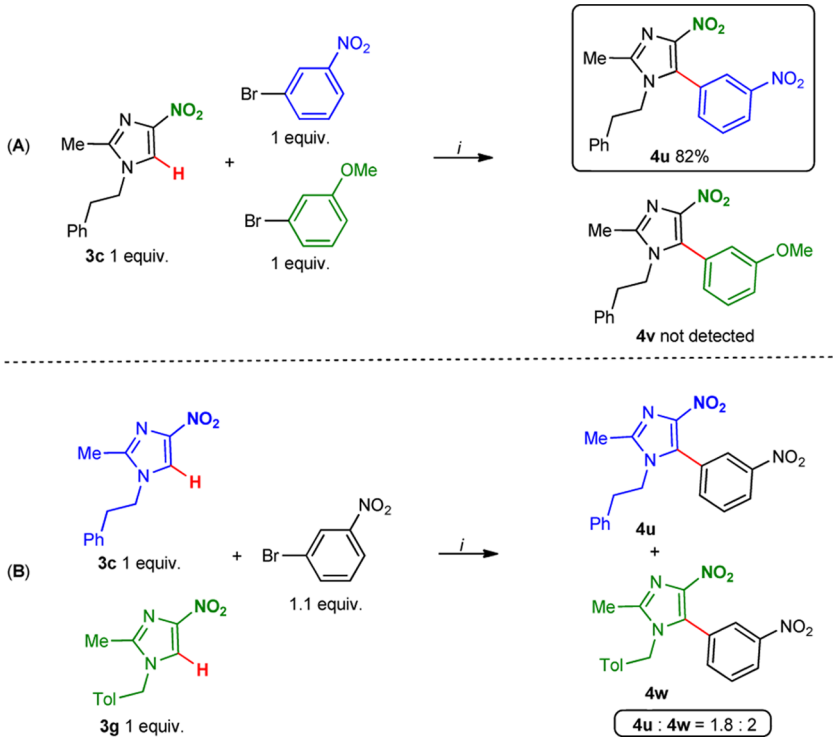
In order to obtain more insights into reaction mechanism and the directing ability of the nitro group, we designed the imidazole **3i**, which then was subjected to our standard Pd-catalyzed reaction conditions (Scheme 9). Nevertheless, all attempts to perform the C−H arylation under standard conditions, developed for nitroimidazoles, were unsuccessful; we obtained an inseparable mixture of products along with starting imidazole **3i**. These findings clearly show the crucial effect of nitro group on the outcome of the reaction.

Scheme 9. Exploration of Directing Ability of Nitro Group[a]



[a]Key: (i) $PdCl_2(PPh_3)_2$ (5 mol %), CuI (1.2 equiv), PivOH (0.3 equiv), K_2CO_3 (1.3 equiv), DMA, under Ar, 130 °C, 14 h; (ii) $PdCl_2(PPh_3)_2$ (5 mol %), PivOH (0.3 equiv), K_2CO_3 (1.3 equiv), DMA, under Ar, 130 °C, 14 h.

Scheme 8. Competitive Experiments between Imidazoles and Aryl Bromides[a]

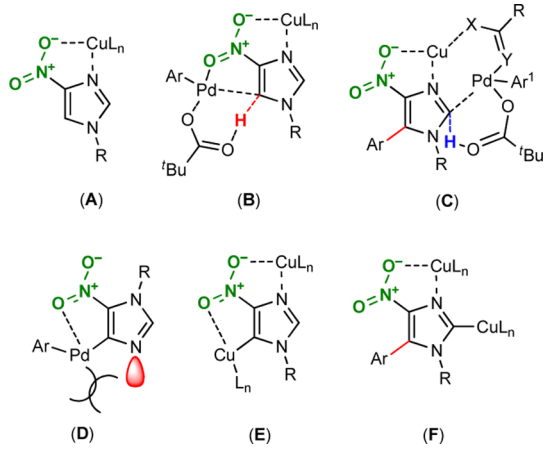


[a]Key: (i) $PdCl_2(PPh_3)_2$ (5 mol %), CuI (1.2 equiv), PivOH (0.3 equiv), K_2CO_3 (1.3 equiv), DMA, under Ar, 130 °C, 14 h.

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

Finally, the regioselectivity might be explained by the assumption that the catalyst (Pd or Ni) coordinated by the nitro group initiates C(5)-arylation of an imidazole ring via concerted metalation−deprotonation (CMD), as illustrated in Scheme 10 (B).[20] In this context, it should be mentioned that

Scheme 10. Proposed Mechanistic Explanation of the Regioselectivity



the salt of copper via double chelation by the nitro group and nitrogen of imidazole ring can immobilize the nitro group in the plane of imidazole ring, thus supporting the C−H bond cleavage by Pd or Ni (Scheme 10, A, B). In this connection, recently Huang et al. showed that the lone pair on the nitrogen atom in benzothiazole, *N*-methylbenzoimidazole, and related systems can bind to the copper center thereby initiating Pd-catalyzed C−H bond cleavage.[23] For C(2)-arylation of the imidazole ring, we assume that a cooperative action of Pd and Cu catalysts chelated by a bidentate ligand (solvent) may enable the direct C−H activation (Scheme 10, C).[24] Concerning the low reactivity of the C(4)−H bond of imidazoles, several authors following the analogy with unreactive α-position of pyridines described this phenomenon by the electronic repulsion between the electron lone pair on the *N*-3 and the C−Pd bond (Scheme 10, D).[25,16b,17a] Eventually, we did not exclude the formation of appropriate cuprates of imidazole that is followed by transmetalation to Pd or Ni (Scheme 10, E and F) since recent DFT calculations made by Fu et al. indicate that the C−H activity of different Ar−H species and both the dissociation of the Ar−H bond and the formation of the Ar−Cu bond make important contributions to the concerted C−H activation.[26]

CONCLUSIONS

In conclusion, we have studied in detail the transition-metal-catalyzed C−H arylation of nitroimidazoles by two different d-metals, namely Pd and Ni, using CuI as additive. The use of Pd proved to give better yields than Ni. Furthermore, we succeeded in activating the C−H bond using stoichiometric amounts of coupling partners. The scope of the reaction with respect to the aryl halogenide coupling partner as well as for nitroimidazoles was examined. The competitive experiments showed that aryl bromides with an electron-withdrawing group are much more reactive than the respective aryl bromides with an electron-donating group. In addition, we observed no differences in reactivity of different nitroimidazoles. Interestingly, during the course of optimization of the reaction conditions we observed a Pd-catalyzed intramolecular dehydrogenative 2-fold C−H cross-coupling reaction initiated by oxidant (Ag_2CO_3). Next, we performed a regioselective C−H arylation of 2,5-unsubstituted 4-nitroimidazole "guided" by the nitro group. Furthermore, a stepwise synthesis of 2,5-diaryl-4-nitroimidazole with two different aryl groups was accomplished. For arylation of position 4 of the imidazole ring, an efficient Pd-catalyzed Suzuki−Miyaura cross-coupling reaction of 5(4)-bromo-4(5)-nitroimidazoles was developed. Interestingly, we could demonstrate that the yields of the Suzuki−Miyaura cross-coupling reaction of 5-bromo-4-nitroimidazoles were slightly lower in comparison to the yields obtained for similar compounds in a direct C−H activation reaction. Within the course of study, the multipurpose character of nitro group was demonstrated. A mechanistic explanation of results was proposed. The developed method shows a number of advantages, including high experimental simplicity, catalyst efficiency, functional group compatibility, and low cost of the catalytic system and reactants. Further exploration of this chemistry is in progress in our laboratory.

EXPERIMENTAL SECTION

General Information. The dry solvents were purchased. Other solvents were purified by distillation. For ^{1}H, ^{19}F, and ^{13}C NMR spectra, the deuterated solvents indicated were used. NMR peaks were assigned by standard means of 2D NMR methods, such as H−H COSY, HMBC, and HMQC; selected spectra are included in the Supporting Information. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, isobutane), or electrospray ionization (ESI, mass analyzer type was ESI-TOF/MS). For preparative-scale chromatography, silica gel 60 (0.063−0.200 mm, 70−230 mesh) was used. The solvents for column chromatography were distilled before use.

General Procedure for the Synthesis of *N*-Substituted Imidazoles by Alkylation. Synthesis of Compounds 3a−i, 10a−c, and 11a−c. The corresponding imidazole (1 equiv) and K_2CO_3 (3 equiv) successively were weighed in air and placed in a Schlenk flask equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon. The dry DMF (8 mL for 1 g of imidazole) and corresponding alkyl bromide (1.3 equiv) were added via syringe, and the reaction was heated to 90 °C for 8 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The crude mass was washed with water, which was extracted with chloroform. Finally, the organic phase was dried (Na_2SO_4), filtered, and evaporated to dryness, or (if necessary) the residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired alkylated product.

General Procedure for Direct C−H Arylation of *N*-Substituted 4-Nitroimidazoles. Synthesis of Compounds 4a−t and 8a. The corresponding *N*-substituted 4-nitroimidazole **3b**,**c**,**e**−**g** or **7c** (1 equiv), CuI (1.2 equiv), K_2CO_3 (1.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and $PdCl_2(PPh_3)_2$ (or $NiCl_2(PPh_3)_2$) (0.05 equiv) successively were weighed in air and placed in a Schlenk flask equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.3 g of *N*-substituted 4-nitroimidazole) and aryl bromide (2 equiv) were added via syringe (in the case of solid aryl bromide, first it was dissolved in dry DMA under inert atmosphere), and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired arylated product.

Competitive Experiment between Imidazole 3c and Electronically Different Aryl Bromides. Synthesis of Compound 4u. The corresponding *N*-substituted 4-nitroimidazole **3c** (1 equiv), CuI (1.2 equiv), K_2CO_3 (1.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

$PdCl_2(PPh_3)_2$ (0.05 equiv) successively were weighed in air and placed in a Schlenk flask, equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.3 g of *N*-substituted 4-nitroimidazole) and aryl bromides (from each 1 equiv) were added via syringe (in case of solid aryl bromide, first it was dissolved in dry DMA under inert atmosphere), and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures.

Competitive Experiment between Two Various Imidazoles. Synthesis of Compounds 4u and 4w. The corresponding *N*-substituted 4-nitroimidazoles **3c** and **3g** (from each 1 equiv), CuI (1.2 equiv), K_2CO_3 (1.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and $PdCl_2(PPh_3)_2$ (0.05 equiv) successively were weighed in air and placed in a Schlenk flask, equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.6 g of *N*-substituted 4-nitroimidazoles) and aryl bromide (1.1 equiv) were added via syringe (in the case of solid aryl bromide, first it was dissolved in dry DMA under inert atmosphere), and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The mixture of compounds **4u** and **4w** was purified by column chromatography typically using heptane/ethyl acetate mixtures.

General Procedure for Pd-Catalyzed Intramolecular Dehydrogenative 2-Fold C−H Cross-Coupling Reaction. Synthesis of Compounds 5a−c. The corresponding *N*-substituted 4-nitroimidazole **3c,e,f** (1 equiv), Ag_2CO_3 (1.2 equiv), K_2CO_3 (1.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and $PdCl_2(PPh_3)_2$ (0.05 equiv) successively were weighed in air and placed in a Schlenk flask, equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.3 g of *N*-substituted 4-nitroimidazole) was added via a syringe, and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired product.

General Procedure for Direct C−H Arylation of 2,5-Unsubstituted 4-Nitroimidazole. Synthesis of Compounds 6a−c. The corresponding *N*-substituted 4-nitroimidazole **3d** (1 equiv), CuI (1.2 equiv), K_2CO_3 (2.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and $PdCl_2(PPh_3)_2$ (0.05 equiv) successively were weighed in air and placed in a Schlenk flask, equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.3 g of *N*-substituted 4-nitroimidazole) and aryl bromide (2.5 equiv) were added via syringe (in the case of solid aryl bromide, first it was dissolved in dry DMA under inert atmosphere), and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired arylated product.

General Procedure for Regioselective C(5)−H Arylation of 2,5-Unsubstituted 4-Nitroimidazole. Synthesis of Compounds 7a−c. The corresponding *N*-substituted 4-nitroimidazole **3d** (1 equiv), CuI (1.2 equiv), K_2CO_3 (1.3 equiv), $(CH_3)_3CCO_2H$ (0.3 equiv), and $PdCl_2(PPh_3)_2$ (0.05 equiv) successively were weighed in air and placed in a Schlenk flask, equipped with a magnetic stir bar, which then was capped with a rubber septum. The reaction vessel was evacuated and backfilled with argon (three times). The dry DMA (8 mL for 0.3 g of *N*-substituted 4-nitroimidazole) and aryl bromide (1.1 equiv) were added via syringe (in case of solid aryl bromide, first it was dissolved in dry DMA under inert atmosphere), and the reaction was heated to 130 °C for 14 h. Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired arylated product.

General Procedure for Pd-Catalyzed Suzuki−Miyaura Cross-Coupling Reaction of 5(4)-Bromo-4(5)-nitroimidazoles. Synthesis of Compounds 12a−f and 13a−e. The corresponding 5(4)-bromo-4(5)-nitroimidazole **10** or **11** (1 equiv), arylboronic acid (1.3 equiv), and $Pd(PPh_3)_4$ (0.10 equiv) successively were weighed in air and placed in a Schlenk flask (under the flow of Ar), equipped with a magnetic stir bar, which then was set with reflux and capped with a rubber septum. The toluene/MeOH (5:1) system (8 mL for 0.3 g of 5(4)-bromo-4(5)-nitroimidazole) and 2 M aqueous K_2CO_3 (1 mL for 1 mmol of starting nitroimidazole) were added via syringe (under the flow of Ar), and the reaction mixture was refluxed for 5 h in inert atmosphere (Ar balloon). Upon completion, the reaction was cooled to room temperature and concentrated under vacuum. The residue was purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired arylated product.

General Procedure for Reduction of Arylated Nitroimidazoles Containing a Carbonyl Group. Synthesis of Compounds 16a−e. To a Schlenk flask equipped with a magnetic stir bar and filled with corresponding arylated nitroimidazole **4t**, **12a,b**, **13a,e** (1 equiv) was added 10% Pd/C (0.1 equiv). The flask was fitted with a rubber septum and then held under vacuum for 3 min; it was then filled with MeOH (25 mL for 0.3 g of arylated nitroimidazole) and hydrogen. Holding under vacuum was repeated one more time, and after sequential filling with hydrogen, the reaction mixture was stirred for 5 h under H_2 atmosphere. After the reaction was stopped, the mixture was filtered through a Celite pad. The filtrate was evaporated to dryness and purified by column chromatography typically using heptane/ethyl acetate mixtures to provide the desired product.

*1-Ethyl-2-methyl-4-nitro-1H-imidazole (**3a**).* White solid (1.271 g, 82%). Mp: 64−65 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.46 (t, 3H, ^3J = 7.0 Hz, CH_2CH_3), 2.42 (s, 3H, Me), 3.96 (t, 2H, ^3J = 7.0 Hz, CH_2CH_3), 7.69 (s, 1H, CH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.0, 15.5 (Me), 42.0 (CH_2), 118.9 (CH), 144.4 (C). MS (GC, 70 eV): m/z = 155 (M^+, 61), 83 (20), 56 (41), 43 (100). HRMS (EI): calcd for $C_6H_9N_3O_2$ (M^+) 155.06893, found 155.06894. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3108 (w), 1532 (s), 1495 (m), 1453 (w), 1423 (m), 1399 (s), 1332 (s), 1292 (s), 1259 (s), 1190 (w), 1149 (m), 1082 (m), 1034 (w), 991 (m), 964 (m), 835 (s), 803 (m), 757 (s), 681 (s), 639 (w).

*1-Butyl-2-methyl-4-nitro-1H-imidazole (**3b**).* White solid (1.610 g, 88%). Mp: 55−57 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, 3H, ^3J = 6.7 Hz, $CH_2CH_2CH_2CH_3$), 1.18−1.31 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.56−1.70 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.29 (s, 3H, Me), 3.81 (t, 2H, ^3J = 7.3 Hz, $CH_2CH_2CH_2CH_3$), 7.59 (s, 1H, CH). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 12.7, 13.1 (Me), 19.3, 31.9, 46.6 (CH_2), 119.5 (CH), 144.4, 145.9 (C). MS (GC, 70 eV): m/z = 183 (M^+, 58), 168 (21), 141 (64), 43 (100). HRMS (EI): calcd for $C_8H_{13}N_3O_2$ (M^+) 183.10023, found 183.100133. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3119 (w), 2960 (m), 2874 (w), 1531 (s), 1496 (m), 1466 (s), 1379 (m), 1330 (s), 1290 (s), 1261 (s), 1186 (m), 1135 (m), 1095 (m), 994 (m), 827 (s), 757 (s), 682 (m), 663 (m).

*2-Methyl-4-nitro-1-phenethyl-1H-imidazole (**3c**).* White solid (2.150 g, 93%). Mp: 111−113 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.08 (s, 3H, Me), 3.07 (t, 2H, ^3J = 6.8 Hz, CH_2), 4.24 (t, 2H, ^3J = 6.8 Hz, CH_2), 7.00−7.03 (m, 2H, CH_{Ar}), 7.16−7.17 (m, 1H, CH_{Ar}), 7.23−7.30 (m, 3H, CH_{Ar}), 7.48 (s, 1H, imidazole). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 11.8 (Me), 37.2, 49.8 (CH_2), 119.1, 127.5, 128.4 (CH_{Ar}), 128.6, 128.9 (C), 129.0, 135.9, 136.0 (CH_{Ar}), 147.9 (C). MS (GC, 70 eV): m/z = 231 (M^+, 40), 105 (25), 91 (100). HRMS (EI): calcd for $C_{12}H_{13}N_3O_2$ (M^+) 231.10023, found 231.100263. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3115 (w), 1516 (m), 1481 (s), 1438 (m), 1404 (m), 1377 (s), 1333 (s), 1286 (s), 1159 (w), 1124 (m), 1048 (w), 1015 (w), 982 (m), 863 (m), 822 (s), 751 (s), 698 (s), 654 (s), 621 (w), 564 (m).

*4-Nitro-1-phenethyl-1H-imidazole (**3d**).* White solid (1.736 g, 80%). Mp: 81−83 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.07 (t, 2H, ^3J = 6.9 Hz, CH_2), 4.24 (t, 2H, ^3J = 6.9 Hz, CH_2), 7.00−7.03 (m, 2H, CH_{Ar}), 7.17 (d, 1H, ^4J = 1.4 Hz, imidazole), 7.21−7.27 (m, 3H, CH_{Ar}), 7.58 (d, 1H, ^4J = 1.4 Hz, imidazole). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 37.2, 49.8 (CH_2), 119.1, 127.5, 128.4 (CH), 128.6, 128.9 (C), 129.1,

DOI: 10.1021/jo5025927
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135.9 (CH), 136.0, 147.9 (C). MS (GC, 70 eV): m/z = 217 (M^+, 40), 105 (25), 91 (100). HRMS (EI): calcd for $C_{11}H_{11}N_3O_2$ (M^+) 217.22394, found 217.22396. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3115 (w), 1516 (m), 1481 (s), 1438 (m), 1404 (m), 1377 (m), 1333 (s), 1286 (s), 1159 (w), 1124 (m), 1079 (w), 1048 (w), 982 (m), 932 (w), 863 (m), 822 (s), 751 (s), 698 (s), 672 (m), 654 (s), 564 (m).

2-Methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazole (**3e**). White solid (1.911 g, 78%). Mp: 82−84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.17−2.29 (m, 2H, CH_2), 2.42 (s, 3H, Me), 2.77 (t, 2H, ^3J = 7.4 Hz, CH_2), 3.97 (t, 2H, ^3J = 7.4 Hz, CH_2), 7.22−7.24 (m, 2H, CH_{Ar}), 7.31−7.43 (m, 3H, CH_{Ar}), 7.74 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.0 (Me), 31.3, 32.3, 46.3 (CH_2), 119.4, 126.7, 128.2, 128.8 (CH_{Ar}), 139.4, 144.7, 146.5 (C). MS (GC, 70 eV): m/z = 245 (M^+, 34), 141 (100), 117 (25), 91 (76), 43 (68). HRMS (EI): calcd for $C_{13}H_{15}N_3O_2$ (M^+) 245.11588, found 245.11586. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3104 (w), 3023 (w), 1531 (s), 1494 (s), 1464 (m), 1454 (m), 1419 (m), 1401 (m), 1358 (s), 1326 (s), 1289 (s), 1233 (w), 4498 (w), 1143 (m), 1039 (w), 991 (m), 910 (w), 833 (s), 747 (s), 698 (s), 681 (m), 641 (w), 618 (w), 591 (w), 572 (m).

2-Methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazole (**3f**). White solid (2.198g, 89%). Mp: 100−101 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (s, 3H, Me), 4.24−4.30 (m, 4H, 2 × CH_2), 6.80−6.83 (m, 2H, CH_{Ar}), 6.93−6.98 (m, 1H, CH_{Ar}), 7.22−7.27 (m, 2H, CH_{Ar}), 7.81 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.1 (Me), 46.5, 66.1 (CH_2), 114.3, 120.2, 121.8, 129.6 (CH), 145.2, 146.4, 157.4 (C). MS (GC, 70 eV): m/z = 247 (M^+, 100), 120 (60), 107 (72), 77 (73). HRMS (EI): calcd for $C_{12}H_{13}N_3O_3$ (M^+) 247.09514, found 247.09556. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3118 (w), 1588 (w), 1531 (m), 1495 (m), 1469 (m), 1385 (m), 1329 (s), 1290 (s), 1237 (s), 1161 (m), 1079 (m), 1050 (m), 993 (m), 907 (m), 827 (m), 787 (m), 753 (s), 690 (s), 678 (m), 617 (w), 599 (m), 568 (w).

1-(4-Methylbenzyl)-2-methyl-4-nitro-1H-imidazole (**3g**). White solid (1.917 g, 83%). Mp: 104−105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3H, Me), 2.38 (s, 3H, Me), 5.03 (s, 2H, CH_2), 7.02 (d, 2H, ^3J = 8.1 Hz, CH_{Ar}), 7.18 (d, 2H, ^3J = 8.1 Hz, CH_{Ar}), 7.60 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.3, 21.1 (Me), 50.8 (CH_2), 120.0, 127.3, 130.1 (CH), 130.7, 139.0, 145.0, 146.4 (C). MS (GC, 70 eV): m/z = 231 (M^+, 11), 105 (100). HRMS (EI): calcd for $C_{12}H_{13}N_3O_2$ (M^+) 231.10023, found 231.10038. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3099 (w), 1533 (s), 1493 (m), 1462 (m), 145 (w), 1396 (s), 1350 (m), 1329 (s), 1314 (m), 1286 (s), 1226 (m), 1141 (m), 1036n (w), 993 (m), 833 (m), 756 (s), 681 (s), 662 (m), 616 (w), 574 (m).

1-(2-Brombenzyl)-2-methyl-4-nitro-1H-imidazole (**3h**). Brown solid (2.449 g, 83%). Mp: 91−92 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.43 (s, 3H, Me), 5.15 (s, 2H, CH_2), 6.95 (dd, 1H, ^3J = 7.6 Hz, ^4J = 1.7 Hz, CH_{Ar}), 7.24−7.34 (m, 2H, CH_{Ar}), 7.56 (s, 1H, CH_{Ar}), 7.64 (dd, 1H, ^3J = 7.8 Hz, ^4J = 1.3 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.3 (Me), 51.0 (CH_2), 119.8 (CH), 123.3 (C), 128.5, 129.2, 130.8 (CH), 133.1 (C), 133.7 (CH), 145.2, 146.5 (C). MS (GC, 70 eV): m/z = 296 (M^+, 9), 296 (1), 295 (10), 171 (100), 169 (97), 90 (34), 89 (32). HRMS (EI): calcd for $C_{11}H_{10}N_3O_2Br$ (M^+) 296.12000, found 296.12012. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3127 (w), 1588 (w), 1532 (s), 1493 (s), 1438 (m), 1413 (m), 1380 (m), 1358 (m), 1324 (m), 1291 (s), 1268 (s), 1142 (m), 1127 (m), 1030 (m), 992 (m), 943 (w), 829 (m), 783 (m), 752 (s), 659 (m).

2-Methyl-1-(3-phenylpropyl)-1H-imidazole (**3i**). White viscous oil (1.345 g, 41%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.02−2.12 (m, 2H, CH_2), 2.32 (s, 3H, Me), 2.64 (t, 2H, ^3J = 7.4 Hz, CH_2), 3.82 (t, 2H, ^3J = 7.2 Hz, CH_2), 6.81−6.82 (m, 1H, imidazole), 6.91−6.92 (m, 1H, imidazole), 7.13−7.32 (m, 5H, CH_{Ar}). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 13.0 (Me), 32.0, 32.6, 45.3 (CH_2), 119.0, 126.4, 127.0, 128.3, 128.6 (CH_{Ar}), 140.4, 144.4, (C). MS (GC, 70 eV): m/z = 200 (M^+, 50), 117 (17), 117 (25), 96 (76), 91 (45). HRMS (ESI): calcd for $C_{13}H_{16}N_2$ (M + H) 201.13862, found 201.13866. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3034 (w), 2928 (w), 1589 (w), 1531 (m), 1492 (m), 1423 (m), 1349 (w), 1277 (w), 1232 (w), 1153 (w), 1095 (w), 1045 (w), 926 (w), 857 (w), 768 (s), 738 (s), 704 (s), 669 (s), 619 (w), 577 (m).

5-(4-(Trifluoromethyl)phenyl)-2-methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazole (**4a**). Green solid (0.373 g, 96%^{Pd}), (0.276 g, 71%$^{Ar-I}$). Mp: 118−120 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.77−1.87 (m, 2H, CH_2), 2.31 (s, 3H, Me), 2.71−2.77 (m, 2H, CH_2), 3.99−4.05 (m, 2H, CH_2), 65.8−6.88 (m, 2H, CH_{Ar}), 7.19−7.22 (m, 3H, CH_{Ar}), 7.62−7.77 (m, 3H, CH_{Ar}), 7.88−7.91 (m, 1H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO-d_6): δ = −62.7 (CF_3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.4 (Me), 31.3, 32.4, 44.2 (CH_2), 123.5 (q, ^1J = 274.3 Hz, CF_3), 126.7 (CH), 126.8 (q, ^3J = 8 Hz, C), 127.9 (CH), 128.4 (C), 128.7, 129.5 (CH), 130.2 (C), 131.3 (q, ^2J = 32.8 Hz, CCF_3), 133.5 (CH), 139.1, 143.5, 143.9 (C). MS (GC, 70 eV): m/z = 389 (M^+, 100), 285 (12), 211 (20), 198 (39), 178 (11), 117 (11), 91 (55). HRMS (EI): calcd for $C_{20}H_{18}N_3O_2F_3$ (M^+) 389.13456, found 389.13444. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2956 (w), 1602 (w), 1573 (w), 1533 (w), 1504 (s), 1437 (m), 1402 (m), 1331 (s), 1291 (s), 1245 (m), 1222 (w), 1190 (m), 1163 (m), 1120 (s), 1081 (s), 1020 (w), 930 (w), 872 (m), 804 (m), 778 (w), 750 (m), 732 (m), 698 (s), 674 (m), 565 (m).

2-Methyl-4-nitro-5-(3-nitrophenyl)-1-(3-phenylpropyl)-1H-imidazole (**4b**). Green solid (0.296 g, 81%^{Pd}), (0.157 g, 48%^{Ni}), (0.216 g, 59%$^{Ar-I}$). Mp: 164−166 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.69−1.79 (m, 2H, CH_2), 2.41−2.46 (m, 5H, Me, CH_2), 3.72−3.78 (m, 2H, CH_2), 6.94−6.97 (m, 2H, CH_{Ar}), 7.06−7.17 (m, 3H, CH_{Ar}), 7.74−7.80 (m, 1H, CH_{Ar}), 7.92−7.95 (m, 1H, CH_{Ar}), 8.33−8.37 (m, 2H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.0 (Me), 30.3, 31.5, 43.7 (CH_2), 124.5, 124.9, 125.8, 127.9, 128.1 (CH), 129.4, 130.1 (C), 130.2, 137.0 (CH), 140.1, 142.7, 144.3, 147.6 (C). MS (GC, 70 eV): m/z = 366 (M^+, 47), 175 (25), 117 (18), 91 (100). HRMS (EI): calcd for $C_{19}H_{18}N_4O_4$ (M^+) 366.37062, found 366.37064. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3060 (w), 1526 (s), 1504 (m), 1441 (w), 1402 (w), 1349 (s), 1290 (s), 1242 (m), 1099 (m), 1018 (w), 932 (w), 890 (w), 861 (w), 814 (m), 755 (s), 733 (m), 694 (s), 668 (m), 578 (w).

2-(2-Methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazol-5-yl)-benzaldehyde (**4c**). Yellow solid (0.314 g, 90%^{Pd}). Mp: 126−128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71−1.82 (m, 2H, CH_2), 2.40 (s, 3H, Me), 2.44 (t, 2H, ^3J = 7.3 Hz, CH_2), 3.47−3.71 (m, 2H, CH_2), 6.88−6.92 (m, 2H, CH_{Ar}), 7.11−7.18 (m, 2H, CH_{Ar}), 7.27−7.31 (m, 1H, CH_{Ar}), 7.37−7.55 (m, 1H, CH_{Ar}), 7.66−7.74 (m, 2H, CH_{Ar}), 7.94−8.00 (m, 1H, CH_{Ar}), 9.85 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.4 (Me), 30.9, 32.3, 44.2 (CH_2), 126.4, 127.9 (CH), 128.3 (C), 128.6, 130.7 (CH), 131.7 (C), 131.9, 132.1, 134.0, 135.1 (CH), 139.2, 143.6 (C), 190.4 (CH). MS (GC, 70 eV): m/z = 349 (M^+, 1), 303 (100), 91 (44). HRMS (ESI): calcd for $C_{20}H_{20}N_3O_3$ (M + H) 350.14992, found 350.15086. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1683 (s), 1599 (w), 1564 (w), 1542 (m), 1490 (s), 1453 (m), 1398 (m), 1353 (m), 1337 (s), 1294 (s), 1269 (m), 1254 (m), 1225 (m), 1197 (m), 1120 (w), 1032 (w), 1005 (w), 978 (w), 850 (m), 823 (m), 764 (m), 738 (s), 698 (s), 671 (s), 614 (m), 540 (m).

4,5-Dimethoxy-2-(2-methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazol-5-yl)benzaldehyde (**4d**). Yellow solid (0.360 g, 88%^{Pd}). Mp: 165−167 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.77−1.82 (m, 2H, CH_2), 2.41−2.51 (m, 5H, Me, CH_2), 3.56−3.72 (m, 2H, CH_2), 3.87 (s, 3H, OMe), 4.02 (s, 3H, OMe), 6.67 (s, 1H, CH_{Ar}), 6.89−6.92 (m, 3H, CH_{Ar}), 7.17−7.19 (m, 2H, CH_{Ar}), 7.46 (br s, 1H, CH_{Ar}), 9.63 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.6 (Me), 30.3, 31.5, 43.8 (CH_2), 55.7, 56.2 (OMe), 111.5, 113.8 (CH), 123.3, 125.8 (C), 127.9, 128.1, 128.8 (CH), 129.6 (C), 131.4, 131.5 (CH), 132.0, 140.2, 143.4, 144.3, 149.7, 153.2 (C), 190.0 (CHO). MS (GC, 70 eV): m/z = 409 (M^+, 1), 363 (100), 91 (25). HRMS (ESI): calcd for $C_{22}H_{24}N_3O_5$ (M + H) 410.17105, found 410.17082. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2938 (w), 1681 (m), 1591 (m), 1514 (s), 1494 (m), 1441 (m), 1397 (m), 1352 (m), 1329 (m), 1268 (s), 1227 (m), 1145 (s), 1100 (m), 1021 (m), 866 (w), 824 (w), 749 (m), 699 (s), 641 (w), 586 (m), 540 (w).

5-(3-(Trifluoromethyl)phenyl)-2-methyl-4-nitro-1-phenethyl-1H-imidazole (**4e**). Green solid (0.368 g, 98%^{Pd}), (0.274 g, 73%^{Ni}), (0.281 g, 75%$^{Ar-I}$). Mp: 164−166 °C. ^{1}H NMR (300 MHz, DMSO): δ = 2.31 (s, 3H, Me), 2.71−2.77 (m, 2H, CH_2), 3.99−4.05 (m, 2H, CH_2), 6.58−6.88 (m, 2H, CH_{Ar}), 7.19−7.22 (m, 3H, CH_{Ar}), 7.62−7.77 (m, 3H, CH_{Ar}), 7.88−7.91 (m, 1H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO): δ = −61.03. ^{13}C NMR (62.9 MHz, DMSO): δ = 12.9 (Me), 34.8, 46.0 (CH_2), 123.8 (q, ^1J = 271 Hz, CF_3), 126.3, 126.8, 127.0, 128.5, 128.5 (CH), 129.3 (q, ^2J = 31 Hz, CCF_3), 129.7 (CH), 131.0 (C), 134.0

DOI: 10.1021/jo5025927
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(CH), 137.0, 142.6, 144.4 (C). MS (GC, 70 eV): m/z = 375 (M^+, 94), 105 (100), 91 (80). HRMS (EI): calcd for $C_{19}H_{16}N_3O_2F_3$ (M^+) 375.11891, found 375.11871. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1565 (w), 1533 (w), 1498 (m), 1440 (w), 1388 (w), 1354 (m), 1329 (s), 1308 (s), 1288 (s), 1254 (m), 1224 (w), 1201 (w), 1167 (m), 1117 (s), 1073 (s), 1020 (w), 935 (m), 900 (w), 856 (m), 806 (s), 755 (m), 698 (s), 672 (m), 649 (w).

5-(2-Methyl-4-nitro-1-phenethyl-1H-imidazol-5-yl)pyrimidine (**4f**). Yellow solid (0.247 g, 80%^{Pd}), (0.163 g, 53%^{Ni}). Mp: 183−185 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (s, 3H, Me), 2.86 (t, 2H, ^3J = 6.4 Hz, CH_2), 4.10 (t, 2H, ^3J = 6.4 Hz, CH_2), 6.76−6.78 (m, 2H, CH_{Ar}), 7.22−7.32 (m, 3H, CH_{Ar}), 8.37 (s, 2H, CH_{Ar}), 9.29 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.5 (Me), 35.9, 46.3 (CH_2), 122.7, 125.5 (C), 127.8, 128.5, 129.2 (CH), 131.9, 135.3, 144.2, 145.2 (C), 157.4, 158.9 (CH). MS (GC, 70 eV): m/z = 309 (M^+, 98), 105 (90), 91 (100), 77 (33). HRMS (EI): calcd for $C_{16}H_{15}N_5O_2$ (M^+) 309.12203, found 309.12208. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2920 (w), 1609 (w), 1549 (w), 1505 (s), 1453 (w), 1408 (s), 1342 (s), 1298 (m), 1253 (m), 1187 (m), 1119 (w), 997 (m), 919 (m), 865 (m), 754 (m), 724 (s), 705 (s), 665 (m), 625 (s), 564 (m).

2-(2-Methyl-4-nitro-1-phenethyl-1H-imidazol-5-yl)benzaldehyde (**4g**). Yellow solid (0.322 g, 96%^{Pd}), (0.218 g, 65%^{Ni}). Mp: 162−164 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, Me), 2.70 (t, 2H, ^3J = 7.1 Hz, CH_2), 3.72−3.81 (m, 1H, CH_2), 3.96−4.06 (m, 2H, CH_2), 6.78−6.81 (m, 2H, CH_{Ar}), 7.11−7.13 (m, 1H, CH_{Ar}), 7.17−7.22 (m, 2H, CH_{Ar}), 7.42−7.53 (m, 2H, CH_{Ar}), 7.62−7.73 (m, 1H, CH_{Ar}), 8.00−8.03 (m, 1H, CH_{Ar}), 9.81 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.4 (Me), 36.0, 46.5 (CH_2), 127.4 (CH), 128.4 (C), 128.6, 129.0, 130.6, 131.7, 132.1 (CH), 133.9, 135.1, 136.1 (C), 190.4 (CH). MS (GC, 70 eV): m/z = 335 (M^+, 1), 289 (100), 105 (39), 91 (15), 77 (14). HRMS (ESI): calcd for $C_{19}H_{18}N_3O_3$ (M + H) 336.13427, found 336.1346. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1695 (m), 1599 (w), 1531 (m), 1496 (s), 1437 (m), 1384 (m), 1319 (s), 1293 (s), 1270 (m), 1236 (s), 1201 (m), 1120 (w), 1092 (w), 1003 (w), 931 (w), 850 (m), 824 (m), 757 (s), 702 (s), 673 (m), 569 (m).

5-(2-Chloro-5-(trifluoromethyl)phenyl)-2-methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazole (**4h**). Green solid (0.318 g, 30%^{Pd}). Mp: 180−181 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.63 (s, 3H, Me), 3.93−4.19 (m, 4H, CH_2), 6.69−6.72 (m, 2H, CH_{Ar}), 6.94−6.98 (m, 1H, CH_{Ar}), 7.21−7.26 (m, 2H, CH_{Ar}), 7.67−7.76 (m, 3H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO-d_6): δ = −62.5 (CF_3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.9 (Me), 44.7, 65.6 (CH_2), 114.1, 121.9 (CH), 123.4 (q, ^1J = 273 Hz, CF_3), 127.5, 128.1 (C), 128.5 (q, ^3J = 4 Hz, CH), 129.3 (q, ^3J = 4 Hz, CH), 129.7 (CH), 130.2 (C), 130.8 (CH), 138.9, 144.1, 145.5, 157.4 (C). MS (GC, 70 eV): m/z = 425 (M^+, 16), 390 (59), 360 (100), 77 (39). HRMS (ESI): calcd for $C_{19}H_{16}N_3O_3F_3Cl$ (M + H) 426.08249, found 426.08249. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1738 (w), 1673 (w), 1588 (w), 1532 (w), 1504 (s), 1406 (m), 1329 (s), 1285 (m), 1239 (s), 1168 (s), 1121 (s), 1078 (s), 1017 (m), 918 (m), 859 (m), 814 (m), 791 (m), 753 (s), 689 (m), 605 (w), 535 (m).

4,5-Dimethoxy-2-(2-methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazol-5-yl)benzaldehyde (**4i**). Yellow solid (0.333 g, 81%^{Pd}). Mp: 141−143 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.56 (s, 3H, Me), 3.85 (s, 3H, OMe), 3.93 (s, 3H, OMe), 3.96−4.26 (m, 4H, 2 × CH_2), 6.73 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 6.91 (t, 1H, ^3J = 7.1 Hz, CH_{Ar}), 7.19−7.25 (m, 3H, CH_{Ar}), 7.56 (s, 1H, CH_{Ar}), 9.67 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.0 (Me), 43.6 (CH_2), 55.2, 55.8 (OMe), 65.2 (CH_2), 110.7, 113.7, 120.5 (CH), 123.0, 127.9, 128.1, 128.3, 128.9 (C), 129.4 (CH), 143.2, 144.6, 149.3, 152.7, 157.1 (C), 189.4 (CHO). MS (GC, 70 eV): m/z = 411 (M^+, 1), 365 (100), 77 (18). HRMS (ESI): calcd for $C_{21}H_{22}N_3O_6$ (M + H) 412.15031, found 412.15044. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2933 (w), 1737 (w), 1678 (m), 1586 (m), 1537 (m), 1495 (s), 1445 (m), 1398 (m), 1353 (m), 1329 (m), 1283 (s), 1222 (s), 1155 (s), 1119 (m), 1036 (m), 1016 (m), 882 (s), 856 (m), 815 (m), 743 (s), 691 (m), 585 (m).

2-(2-Methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazol-5-yl)-benzaldehyde (**4j**). Yellow solid (0.263 g, 75%^{Pd}). Mp: 148−150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3H, Me), 3.96−4.24 (m, 4H, 2 × CH_2), 6.70−6.74 (m, 2H, CH_{Ar}), 6.88−6.93 (m, 1H, CH_{Ar}), 7.19−7.25 (m, 2H, CH_{Ar}), 7.59−7.64 (m, 1H, CH_{Ar}), 7.77−7.89 (m, 2H, CH_{Ar}), 8.10 (dd, 1H, ^3J = 7.3 Hz, ^4J = 1.2 Hz, CH_{Ar}), 9.86 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.4 (Me), 44.1, 65.6 (CH_2), 114.2, 121.0, 128.7, 129.4 (CH), 130.6 (C), 130.7, 131.4, 131.5, 132.0, 134.2 (CH), 135.0, 143.3, 145.2, 157.5 (C), 194.8 (CHO). MS (GC, 70 eV): m/z = 351 (M^+, 1), 305 (21), 44 (100). HRMS (EI): calcd for $C_{19}H_{17}N_3O_4$ (M^+) 351.35598, found 351.35599. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2927 (w), 1690 (m), 1600 (m), 1565 (w), 1538 (w), 1496 (s), 1396 (m), 1353 (m), 1330 (s), 1293 (m), 1269 (m), 1230 (s), 1179 (m), 1119 (w), 1085 (m), 1051 (m), 962 (w), 908 (w), 886 (w), 849 (m), 828 (m), 757 (s), 721 (m), 692 (s), 670 (m), 631 (w), 592 (w), 539 (m).

1-(4-Methylbenzyl)-2-methyl-4-nitro-5-(phenanthren-10-yl)-1H-imidazole (**4k**). Dark brown viscous oil (0.258 g, 80%^{Pd}), (0.162 g, 40%^{Ni}). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3H, Me), 2.39 (s, 3H, Me), 4.62 (d, 1H, ^3J = 15.0 Hz, CH_2), 4.84 (d, 1H, ^3J = 15.0 Hz, CH_2), 6.55 (d, 2H, ^3J = 7.9 Hz, CH_{Ar}), 6.86 (d, 2H, ^3J = 7.9 Hz, CH_{Ar}), 7.36−7.67 (m, 7H, CH_{Ar}), 8.60 (t, 2H, ^3J = 9.8 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.7, 18.4, 20.9 (Me), 48.1 (CH_2), 126.3, 127.0, 129.5 (CH), 130.7, 131.7 (C), 134.2 (CH), 137.1, 137.9, 143.4, 144.1, 144.7 (C) 149.9 (CH). MS (GC, 70 eV): m/z = 407 (M^+, 53), 105 (100). HRMS (EI): calcd for $C_{26}H_{21}N_3O_2$ (M^+) 407.16283, found 407.16301. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1537 (m), 1504 (s), 1446 (m), 1385 (m), 1336(s), 1293 (s), 1222 (m), 1124 (w), 1018 (m), 933 (w), 859 (s), 796 (s), 766 (m), 756 (m), 719 (m), 665 (m), 624 (m), 594 (w).

3-(1-(4-Methylbenzyl)-2-methyl-4-nitro-1H-imidazol-5-yl)-benzaldehyde (**4l**). Yellow solid (0.285 g, 85%^{Pd}). Mp: 139−141 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.21 (s, 3H, Me), 2.39 (s, 3H, Me), 4−88−5.03 (m, 2H, CH_2), 6.74 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.03 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.48−7.51 (m, 1H, CH_{Ar}), 7.72−7.77 (m, 2H, CH_{Ar}), 7.95−7.99 (m, 1H, CH_{Ar}), 9.73 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.4, 20.5 (Me), 47.6 (CH_2), 126.4, 127.5 (CH), 128.4 (C), 129.1, 129.5, 130.5 (CH), 130.6 (C), 130.9, 131.5 (CH), 132.0 (C), 134.0, 134.7 (CH), 137.0, 143.4, 144.8 (C), 191.4 (CHO). MS (GC, 70 eV): m/z = 335 (M^+, 1), 105 (100). HRMS (ESI): calcd for $C_{19}H_{18}N_3O_3$ (M + H) 336.13427, found 336.1342. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2841 (w), 2751 (w), 1699 (m), 1601 (w), 1568 (w) 1533 (m), 1494 (s), 1435 (m), 1397 (m), 1377 (s), 1328 (s), 1288 (s), 1249 (s), 1199 (m), 1121 (m), 1036 (w), 1003 (w), 859 (m), 813 (s), 785 (s), 765 (s), 723 (m), 670 (m), 610 (m), 541 (s).

1-(4-Methylbenzyl)-5-(3-(trifluoromethyl)phenyl)-2-methyl-4-nitro-1H-imidazole (**4m**). Green solid (0.368 g, 92%^{Pd}), (0.191 g, 62%^{Ni}). Mp: 152−154 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.31 (s, 3H, Me), 2.43 (s, 3H, Me), 4.90 (s, 2H, CH_2), 6.71 (d, 2H, ^3J = 6.0 Hz, CH_{Ar}), 7.45 (d, 2H, ^3J = 6.0 Hz, CH_{Ar}), 7.45−7.56 (m, 3H, CH_{Ar}), 7.68−7.71 (m, 1H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO-d_6): δ = −62.9 (CF_3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.7, 21.0 (Me), 48.2 (CH_2), 123.4 (q, ^1J = 273.2 Hz, CF_3), 125.7 (CH), 126.7 (q, ^3J = 4.1 Hz, CH), 127.1 (q, ^3J = 4.1 Hz, CH), 128.2 (C), 129.3 (CH), 129.9 (C), 130.7 (CH), 131.1 (q, ^2J = 32.6 Hz, CCF_3), 131.3 (C), 133.5 (CH), 138.4, 143.5, 144.7 (C). MS (GC, 70 eV): m/z = 375 (M^+, 10), 105 (100). HRMS (EI): calcd for $C_{19}H_{16}N_3O_2F_3$ (M^+) 375.11891, found 375.11887. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1538 (m), 1499 (m), 1429 (w), 1399 (m), 1328 (s), 1288 (s), 1252 (m), 1184 (m), 1164 (s), 1111 (s), 1076 (s), 1024 (m), 926 (m), 857 (m), 812 (m), 796 (s), 766 (m), 726 (m), 700 (m), 663 (m), 644 (w), 599 (w).

5-(1-(4-Methylbenzyl)-2-methyl-4-nitro-1H-imidazol-5-yl)-pyrimidine (**4n**). Yellow solid (0.253 g, 82%^{Pd}), (0.157 g, 51%^{Ni}). Mp: 183−185 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.25 (s, 3H, Me), 2.39 (s, 3H, Me), 5.14 (s, 2H, CH_2), 6.82 (d, 2H, ^3J = 8.1 Hz, CH_{Ar}), 7.10 (d, 2H, ^3J = 8.1 Hz, CH_{Ar}), 8.84 (s, 2H, CH_{Ar}), 9.25 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.2, 20.6 (Me), 47.5 (CH_2), 123.0 (C), 126.1 (CH), 126.8 (C), 128.6, 129.4, 131.4, 131.5 (CH), 132.0, 137.1, 143.8, 145.5 (C), 157.7, 158.7 (CH). MS (GC, 70 eV): m/z = 309 (M^+, 10), 105 (100). HRMS (EI): calcd for $C_{16}H_{15}N_5O_2$ (M^+) 309.12203, found 309.12176. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2965 (w), 1551 (w), 1529 (w), 1501 (s), 1432 (m), 1401 (m), 1339 (s), 1299 (m), 1271 (m), 1189 (m), 1120 (m), 1002 (m), 917 (w),

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

858 (m), 789 (m), 756 (w), 723 (s), 694 (m), 665 (m), 628 (m), 537 (m).

*1-(4-Methylbenzyl)-5-(4-methoxyphenyl)-2-methyl-4-nitro-1H-imidazole (**4o**).* Yellow viscous oil (0.226 g, 67%^{Pd}), (0.155 g, 46%$^{Ar-I}$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.29 (s, 3H, Me), 2.33 (s, 3H, Me), 3.79 (s, 3H, OMe), 4.91 (s, 2H, CH_2), 6.75 (d, 2H, ^3J = 7.6 Hz, CH_{Ar}), 6.90 (d, 2H, ^3J = 8.5 Hz, CH_{Ar}), 7.09 (d, 2H, ^3J = 7.6 Hz, CH_{Ar}), 7.19 (d, 2H, ^3J = 8.5 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8, 21.0 (Me), 47.8 (CH_2), 55.3 (OMe), 114.2 (CH), 115.4, 119.0 (C), 125.8, 128.7, 129.8, 130.1, 131.6 (CH), 133.1, 138.1, 143.2, 144.1, 160.8 (C). MS (GC, 70 eV): m/z = 337 (M^+, 32), 105 (100). HRMS (EI): calcd for $C_{19}H_{19}N_3O_3$ (M^+) 337.14209, found 337.14203. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2926 (w), 1666 (w), 1613 (w), 1506 (s), 1441 (w), 1335 (s), 1288 (s), 1247 (s), 1176 (s), 1110 (w), 1032 (m), 856 (s), 797 (m), 717 (m), 669 (w), 620 (w), 596 (m), 529 (m).

*1-(4-Methylbenzyl)-5-(2-fluorophenyl)-2-methyl-4-nitro-1H-imidazole (**4p**).* Green solid (0.166 g, 51%^{Pd}). Mp: 115−117 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.26 (s, 3H, Me), 2.34 (s, 3H, Me), 4.82−4.99 (m, 2H, CH_2), 6.72 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.05 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.09−7.22 (m, 3H, CH_{Ar}), 7.39−7.46 (m, 1H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO-d_6): δ = −111.23 (CF). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.4, 20.8 (Me), 48.0 (CH_2), 115.2 (d, ^3J = 15.4 Hz, C), 115.9 (d, ^2J = 22.2 Hz, CH), 124.3 (d, J = 4.1 Hz, C), 125.8 (CH), 126.5 (C), 129.5, 131.1, 131.5, 132.1, 132.3 (CH), 137.9, 143.9, 144.9 (C), 159.3 (d, ^1J = 249.7 Hz, CF). MS (GC, 70 eV): m/z = 325 (M^+, 21), 105 (100). HRMS (ESI): calcd for $C_{18}H_{17}N_3O_2F$ (M + H) 326.12993, found 326.13006. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1532 (m), 1495 (s), 1444 (m), 1397 (m), 1378 (m), 1328 (s), 1288 (m), 1269 (m), 1251 (m), 1221 (m), 1116 (w), 1095 (w), 1007 (w), 863 (w), 840 (m), 808 (s), 765 (s), 716 (m), 665 (m), 607 (m).

*2-Methyl-5-(2-methyl-1-(4-methylbenzyl)-4-nitro-1H-imidazol-5-yl)pyridine (**4q**).* Yellow viscous oil (0.220 g, 54%^{Pd}). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3H, Me), 2.36 (s, 6H, Me), 5.16 (s, 2H, CH_2), 6.76 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.02 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.45 (d, 1H, ^3J = 8.0 Hz, CH_{Ar}), 7.53−7.56 (m, 1H, CH_{Ar}), 8.51 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.7, 18.4, 20.6 (Me), 48.0 (CH_2), 126.3, 127.1, 129.5 (CH), 130.8, 131.8, 134.2 (C), 137.1 (CH), 137.9, 143.5, 144.1, 144.8 (C), 150.0 (CH). MS (GC, 70 eV): m/z = 322 (M^+, 10), 305 (100), 263 (34), 146 (26), 119 (23), 105 (52). HRMS (EI): calcd for $C_{18}H_{18}N_4O_2$ (M^+) 322.14243, found 322.14228. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1733 (w), 1668 (w), 1564 (w), 1497 (s), 1441 (m), 1384 (m), 1336 (s), 1282 (m), 1226 (w), 1136 (m), 1039 (w), 901 (m), 864 (w), 839 (w), 810 (w), 749 (s), 725 (s), 616 (m).

*1-(4-Methylbenzyl)-5-(3-methoxyphenyl)-2-methyl-4-nitro-1H-imidazole (**4r**).* Yellow solid (0.263 g, 78%^{Pd}), (0.145 g, 43%^{Ni}). Mp: 146−148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.31 (s, 3H, Me), 2.35 (s, 3H, Me), 3.67 (s, 3H, OMe), 4.91 (s, 2H, CH_2), 6.75−6.77 (m, 3H, CH_{Ar}), 6.84−6.87 (m, 1H, CH_{Ar}), 6.95−6.99 (m, 1H, CH_{Ar}), 7.09−7.12 (m, 2H, CH_{Ar}), 7.29−7.34 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8, 21.0 (Me), 47.9 (CH_2), 55.2 (OMe), 115.4, 115.9, 122.2, 125.8 (CH), 128.3 (C), 129.7, 129.8 (CH), 131.8, 132.8, 138.1, 144.2, 159.5 (C). MS (GC, 70 eV): m/z = 337 (M^+, 24), 105 (100). HRMS (EI): calcd for $C_{19}H_{19}N_3O_3$ (M^+) 337.14209, found 337.14198. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2919 (w), 1589 (m), 1568 (m), 1536 (m), 1503 (s), 1451 (m), 1398 (s), 1344 (s), 1292 (s), 1223 (s), 1180 (m), 1125 (m), 1039 (m), 1016 (m), 897 (m), 873 (m), 829 (m), 786 (s), 765 (m), 706 (m), 689 (m), 665 (m), 555 (w).

*1-(3-(2-Methyl-1-(4-methylbenzyl)-4-nitro-1H-imidazol-5-yl)-phenyl)ethanone (**4s**).* Yellow solid (0.251 g, 72%^{Pd}). Mp: 173−174 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.23 (s, 3H, Me), 2.34 (s, 3H, Me), 2.49 (s, 3H, Me), 5.03 (s, 2H, CH_2), 6.80 (d, 2H, ^3J = 7.5 Hz, CH_{Ar}), 7.09 (d, 2H, ^3J = 7.5 Hz, CH_{Ar}), 7.58−7.70 (m, 2H, CH_{Ar}), 7.91 (br s, 1H, CH_{Ar}), 8.01−8.05 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.2, 20.5, 26.6 (Me), 47.3 (CH_2), 126.0 (CH), 128.0 (C), 129.0, 129.1, 129.3, 130.0 (CH), 132.2, 132.4 (C), 134.8 (CH), 136.8, 136.9, 142.7, 144.4 (C), 197.2 (COMe). MS (GC, 70 eV): m/z = 349 (M^+, 8), 105 (100). HRMS (EI): calcd for $C_{20}H_{19}N_3O_3$ (M^+) 349.14209, found 349.14266. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2921 (w), 1683 (s), 1564 (w), 1535 (w), 1501 (s), 1424 (w), 1396 (m), 1335 (s), 1274 (s), 1231 (s), 1122 (w), 1020 (w), 958 (w), 904 (w), 796 (m), 766 (m), 693 (m), 588 (m).

*2-(1-Butyl-2-methyl-4-nitro-1H-imidazol-5-yl)-4,5-dimethoxybenzaldehyde (**4t**).* Brown solid (0.295 g, 85%^{Pd}). Mp: 212−214 °C. ^{1}H NMR (300 MHz, DMSO): δ = 0.67 (t, 3H, ^3J = 7.3 Hz, $CH_2CH_2CH_2CH_3$), 1.04−1.17 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.33−1.42 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.46 (s, 3H, Me), 3.61−3.82 (m, 2H, $CH_2CH_2CH_2CH_3$), 3.85 (s, 3H, OMe), 3.92 (s, 3H, OMe), 7.19 (m, 1H, CH_{Ar}), 7.58 (s, 1H, CH_{Ar}), 9.70 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.1, 13.2 (Me), 18.9, 31.1, 44.2 (CH_2), 55.7, 56.3 (OMe), 111.6, 114.5 (CH), 123.5, 128.2, 129.6, 132.0, 143.4, 149.8, 153.2 (C), 189.9 (CHO). MS (GC, 70 eV): m/z = 347 (M^+, 1), 303 (100), 91 (44). HRMS (ESI): calcd for $C_{17}H_{21}N_3O_5$ (M + H) 348.1554, found 348.1560. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 1666 (m), 1582 (m), 1498 (s), 1447 (w), 14023 (m), 1351 (m), 1291 (m), 1276 (s), 1222 (s), 1132 (s), 1132 (s), 1077 (m), 1019 (m), 978 (w), 889 (m), 859 (w), 814 (m), 749 (m), 720 (m), 698 (m), 585 (m), 539 (m).

*5-(3-(Nitrophenyl)-2-methyl-4-nitro-1-phenethyl-1H-imidazole (**4u**).* Green solid (0.290 g, 82%^{Pd}). Mp: 132−133 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.31 (s, 3H, Me), 2.74 (d, 2H, ^3J = 7.0 Hz, CH_2), 4.07 (d, 2H, ^3J = 7.0 Hz, CH_2), 6.84−6.88 (m, 2H, CH_{Ar}), 7.15−7.17 (m, 3H, CH_{Ar}), 7.75−7.77 (m, 2H, CH_{Ar}), 8.04−8.05 (m, 1H, CH_{Ar}), 8.33−8.36 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 12.9 (Me), 34.9, 46.0 (CH_2), 124.3, 125.3, 126.7, 128.4, 128.6, 128.8 (CH), 129.1 (C), 130.1, 131.5 (CH), 132.0 (C), 136.7 (CH), 137.0, 142.6, 144.6, 147.7 (C). MS (GC, 70 eV): m/z = 352 (M^+, 100), 105 (85), 91 (80). HRMS (EI): calcd for $C_{18}H_{16}N_4O_4$ (M^+) 352.34404, found 352.34406. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3056 (w), 1520 (s), 1494 (m), 1402 (w), 1342 (s), 1291 (s), 1247 (m), 1162 (w), 1120 (w), 1086 (w), 1019 (w), 929 (w), 884 (w), 856 (s), 837 (w), 810 (w), 767 (w), 745 (s), 735 (s), 693 (s), 667 (m), 566 (w), 540 (m).

*3-Methyl-1-nitro-6,7-dihydro-5H-benzo[c]imidazo[1,5-a]azepine (**5a**).* Yellow viscous oil (0.199 g, 82%^{Pd}). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.23 (t, 2H, ^3J = 6.8 Hz, CH_2), 2.48 (s, 3H, Me), 2.64 (t, 2H, ^3J = 6.6 Hz, CH_2), 3.76 (br s, 2H, CH_2), 7.27−7.31 (m, 1H, CH_{Ar}), 7.38−7.42 (m, 2H, CH_{Ar}), 7.74−7.78 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.1 (Me), 29.9, 30.8, 42.5 (CH_2), 126.9 (CH), 127.3 (C), 129.0, 130.5, 131.5 (CH), 132.2, 138.3, 142.3 (C). MS (GC, 70 eV): m/z = 243 (M^+, 100), 212 (11), 156 (22), 144 (45), 128 (31), 116 (66). HRMS (EI): calcd for $C_{13}H_{13}N_3O_2$ (M^+) 243.10023, found 243.10027. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2922 (w), 2854 (w), 1577 (w), 1562 (w), 1529 (m), 1494 (s), 1454 (m), 1399 (m), 1380 (m), 1329 (s), 1316 (s), 1279 (s), 1238 (m), 1120 (w), 1025 (w), 1004 (m), 956 (w), 855 (s), 822 (m), 772 (m), 757 (s), 722 (m), 690 (m), 665 (m).

*3-Methyl-1-nitro-5,6-dihydroimidazo[5,1-a]isoquinoline (**5b**).* Yellow solid (0.222 g, 97%^{Pd}). Mp: 151−152 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.40 (s, 3H, Me), 3.09 (t, 2H, ^3J = 6.6 Hz, CH_2), 4.08 (t, 2H, ^3J = 6.8 Hz, CH_2), 7.36−7.44 (m, 2H, CH_{Ar}), 8.25−8.29 (m, 2H, CH_{Ar}). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 12.6 (Me), 28.4, 40.8 (CH_2), 124.2 (C), 127.0, 127.4, 128.2, 129.9 (CH), 134.8, 142.9 (C). MS (GC, 70 eV): m/z = 229 (M^+, 85), 159 (15), 140 (34), 130 (100), 115 (41), 103 (29). HRMS (EI): calcd for $C_{12}H_{11}N_3O_2$ (M^+) 229.08458, found 229.08425. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2957 (w), 1741 (w), 1610 (w), 1531 (m), 1480 (m), 1403 (m), 1375 (m), 1344 (m), 1309 (w), 1269 (s), 1066 (m), 1131 (m), 1043 (m), 1002 (m), 937 (m), 845 (s), 780 (s), 761 (s), 700 (m), 683 (m), 650 (m).

*3-Methyl-1-nitro-5,6-dihydrobenzo[f]imidazo[1,5-d][1,4]-oxazepine (**5c**).* Yellow viscous oil (0.186 g, 76%^{Pd}). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.51 (s, 3H, Me), 4.01 (t, 2H, ^3J = 5.9 Hz, CH_2), 4.49 (t, 2H, ^3J = 5.9 Hz, CH_2), 7.20 (dd, 1H, ^3J = 8.0 Hz, ^4J = 1.1 Hz, CH_{Ar}), 7.31 (dt, 1H, ^3J = 7.6 Hz, ^4J = 1.3 Hz, CH_{Ar}), 7.47 (dt, 1H, ^3J = 7.6 Hz, ^4J = 1.9 Hz, CH_{Ar}), 7.84 (dd, 1H, ^3J = 7.8 Hz, ^4J = 1.7 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.0 (Me), 42.7, 73.8 (CH_2), 121.8 (CH), 122.6 (C), 125.0 (CH), 130.1 (C), 132.1, 132.2 (CH), 142.0, 153.3 (C). MS (GC, 70 eV): m/z = 245 (M^+, 100).

DOI: 10.1021/jo5025927
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HRMS (EI): calcd for $C_{12}H_{11}N_3O_3$ (M^+) 245.08004, found 245.08010. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2881 (w), 1743 (w), 1531 (m), 1504 (m), 1450 (m), 1402 (m), 1380 (m), 1329 (s), 1275 (s), 1231 (m), 1145 (w), 1109 (w), 1043 (m), 884 (w), 837 (m), 799 (m), 753 (m), 663 (w).

2,5-Bis(4-methoxyphenyl)-4-nitro-1-phenethyl-1H-imidazole (**6a**). Yellow solid (0.249 g, 58%^{Pd}). Mp: 153−155 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.47−2.51 (m, 2H, CH_2), 3.04 (s, 3H, OMe), 3.85 (s, 3H, OMe), 4.16 (t, 2H, ^3J = 7.2 Hz, CH_2), 6.64−6.67 (m, 2H, CH_{Ar}), 7.07−7.17 (m, 7H, CH_{Ar}), 7.32−7.34 (m, 2H, CH_{Ar}), 7.55 (d, 2H, ^3J = 9.0 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 34.5, 46.7 (CH_2), 55.2, 55.3 (OMe), 114.0, 114.2 (CH), 119.3, 121.4 (C), 126.7, 128.3, 128.5, 130.4, 131.7 (CH), 133.6, 136.7, 143.2, 145.4, 160.2, 160.3 (C). MS (GC, 70 eV): m/z = 429 (M^+, 100), 135 (27), 105 (60). HRMS (EI): calcd for $C_{25}H_{23}N_3O_4$ (M^+) 429.46782, found 429.46784. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1613 (m), 1575 (w), 1505 (m), 1489 (m), 1454 (m), 1379 (m), 1341 (m), 1289 (m), 1245 (s), 1171 (s), 1110 (m), 1020 (m), 861 (m), 833 (s), 797 (m), 739 (s), 697 (s), 645 (m), 535 (m).

4,4′-(4-Nitro-1-phenethyl-1H-imidazole-2,5-diyl)dibenzonitrile (**6b**). Brown solid (0.264 g, 63%^{Pd}). Mp: 224−226 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.46 (t, 2H, ^3J = 6.8 Hz, CH_2), 4.15 (t, 2H, ^3J = 6.8 Hz, CH_2), 6.47−6.50 (m, 2H, CH_{Ar}), 7.05−7.19 (m, 3H, CH_{Ar}), 7.25−7.29 (m, 2H, CH_{Ar}), 7.55−7.58 (m, 2H, CH_{Ar}), 7.69−7.74 (m, 4H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.9, 47.5 (CH_2), 114.1, 114.3, 117.8 (C), 127.7, 128.3, 129.1, 129.6, 131.1 (CH), 131.4 (C), 131.6 (CH), 132.6 (C), 132.6 (CH), 132.9, 135.1, 144.5, 144.9 (C). MS (GC, 70 eV): m/z = 419 (M^+, 86), 389 (22), 128 (22), 105 (100), 91 (62). HRMS (ESI): calcd for $C_{25}H_{18}N_5O_2$ (M + H) 420.1455, found 420.14487. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2233 (m), 1514 (s), 1480 (m), 1453 (w), 1393 (m), 1346 (s), 1308 (m), 1260 (m), 1181 (w), 1078 (w), 1007 (w), 918 (w), 858 (m), 845 (s), 754 (m), 746 (m), 699 (s), 659 (m), 557 (s), 549 (s).

2,5-Bis(3-(trifluoromethyl)phenyl)-4-nitro-1-phenethyl-1H-imidazole (**6c**). Yellow solid (0.308 g, 61%^{Pd}). Mp: 184−185 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (t, 2H, ^3J = 6.7 Hz, CH_2), 4.20 (t, 2H, ^3J = 6.7 Hz, CH_2), 6.54−6.57 (m, 2H, CH_{Ar}), 7.10−7.20 (m, 3H, CH_{Ar}), 7.46−7.53 (m, 2H, CH_{Ar}), 7.62−7.82 (m, 6H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO): δ = −62.7 (CF_3). ^{13}C NMR: due to bed solubility it was not possible to measure. MS (GC, 70 eV): m/z = 505 (M^+, 51), 173 (14), 145 (13), 105 (100), 91 (24). HRMS (EI): calcd for $C_{25}H_{17}N_3O_2F_6$ (M^+) 505.12195, found 505.12226. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1568 (w), 1505 (s), 1456 (w), 1381 (w), 1325 (s), 1311 (s), 1240 (m), 1167 (s), 1120 (s), 1072 (s), 923 (m), 900 (m), 851 (m), 811 (m), 795 (s), 751 (m), 728 (w), 715 (m), 695 (s), 671 (m), 648 (m).

4-(4-Nitro-1-phenethyl-1H-imidazol-5-yl)benzonitrile (**7a**). Yellow solid (0.267 g, 84%^{Pd}). Mp: 131−133 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.90 (t, 2H, ^3J = 6.8 Hz, CH_2), 4.07 (t, 2H, ^3J = 6.8 Hz, CH_2), 6.82−6.85 (m, 2H, CH_{Ar}), 7.18−7.29 (m, 3H, CH_{Ar}), 7.43−7.67 (m, 3H, CH_{Ar}), 7.72−7.74 (m, 2H, CH_{Ar}). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 37.0, 47.6 (CH_2), 113.8 (CH), 118.0 (C), 127.5 (CH), 128.2 (C), 128.4, 128.5 (CH), 128.7 (C), 128.8, 129.1, 129.7 (CH), 130.3, 130.7 (C), 131.0, 132.4, 132.6 (CH), 133.0 (C). MS (GC, 70 eV): m/z = 318 (M^+, 83), 105 (56), 91 (100). HRMS (EI): calcd for $C_{18}H_{14}N_4O_2$ (M^+) 318.11113, found 318.111300. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2233 (m), 1574 (w), 1514 (s), 1496 (s), 1437 (m), 1405 (w), 1337 (s), 1275 (m), 1226 (m), 1190 (m), 1112 (m), 1028 (w), 1000 (m), 933 (w), 845 (s), 748 (s), 720 (m), 697 (s), 655 (s), 566 (m), 541 (s).

5-(4-Nitro-1-phenethyl-1H-imidazol-5-yl)pyrimidine (**7b**). Yellow solid (0.242 g, 82%^{Pd}). Mp: 137−139 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.90 (t, 2H, ^3J = 6.6 Hz, CH_2), 4.20 (t, 2H, ^3J = 6.6 Hz, CH_2), 6.94−6.97 (m, 2H, CH_{Ar}), 7.21−7.23 (m, 2H, CH_{Ar}), 7.57−7.63 (m, 1H, CH_{Ar}), 8.07 (s, 1H, CH_{Ar}), 8.74 (s, 2H, CH_{Ar}), 9.31 (s, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.8, 47.0 (CH_2), 122.3, 126.2 (C), 126.8, 128.6, 128.8, 131.4, 131.5 (CH), 136.9 (C), 137.5 (CH), 144.5 (C) 157.7, 158.8 (CH). MS (GC, 70 eV): m/z = 295 (M^+, 38), 278 (12), 105 (40), 91 (100), 77 (27). HRMS (EI): calcd for $C_{15}H_{13}N_5O_2$ (M^+) 295.10638, found 295.10607. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3127 (w), 1714 (w), 1599 (w), 1552 (m), 1495 (s), 1454 (m), 1408 (m), 1371 (s), 1333 (s), 1266 (s), 1223 (m), 1189 (m), 1156 (m), 1119 (m), 1080 (w), 996 (m), 913 (w), 864 (w), 831 (s), 760 (s), 725 (s), 702 (s), 652 (m), 628 (s), 588 (w), 566 (m), 539 (s).

4-Nitro-5-(3-nitrophenyl)-1-phenethyl-1H-imidazole (**7c**). Yellow solid (0.220 g, 65%^{Pd}). Mp: 128−130 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 2.85 (t, 2H, ^3J = 6.7 Hz, CH_2), 4.13 (t, 2H, ^3J = 6.7 Hz, CH_2), 6.89−6.92 (m, 2H, CH_{Ar}), 7.17−7.19 (m, 3H, CH_{Ar}), 7.74−7.81 (m, 2H, CH_{Ar}), 8.03 (br s, 1H, CH_{Ar}), 8.09 (br s, 1H, CH_{Ar}), 8.35−8.37 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.7, 46.9 (CH_2), 124.5, 125.2, 126.7, 128.4 (CH), 128.4 (C), 128.5, 128.8 (CH), 130.0 (C), 130.1, 131.5 (CH), 132.0 (C), 136.7, 136.8 (CH), 137.0, 147.7 (C). MS (GC, 70 eV): m/z = 338 (M^+, 70), 105 (46), 91 (100). HRMS (EI): calcd for $C_{17}H_{14}N_4O_4$ (M^+) 338.10096, found 338.10087. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3126 (w), 1526 (s), 1496 (s), 1436 (m), 1383 (w), 1345 (s), 1296 (s), 1249 (w), 1212 (m), 1158 (m), 1103 (m), 1028 (w), 1004 (m), 902 (m), 829 (s), 763 (m), 731 (s), 692 (s), 647 (s), 538 (s).

2-(4-Nitro-5-(3-nitrophenyl)-1-phenethyl-1H-imidazol-2-yl)benzaldehyde (**8a**). Yellow solid (0.345 g, 78%^{Pd}). Mp: 152−154 °C. ^{1}H NMR (300 MHz, DMSO): δ = 2.84 (t, 2H, ^3J = 6.6 Hz, CH_2), 3.98 (t, 2H, ^3J = 6.6 Hz, CH_2), 6.52−6.55 (m, 2H, CH_{Ar}), 7.04−7.15 (m, 3H, CH_{Ar}), 7.33−7.36 (m, 1H, CH_{Ar}), 7.61−7.74 (m, 4H, CH_{Ar}), 7.96−7.99 (m, 1H, CH_{Ar}), 8.12−8.13 (m, 1H, CH_{Ar}), 8.30−8.34 (m, 1H, CH_{Ar}), 9.90 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 35.8, 47.1 (CH_2), 123.9, 124.8, 125.4, 127.5, 127.6, 138.4 (CH), 128.7 (C), 129.0, 130.0 (CH), 130.2 (C) 131.2 (CH), 132.0 (C), 134.0, 134.9, 135.1 (CH), 135.6 (C), 136.4 (CH), 144.2, 144.6, 148.2 (C), 190.9 (CHO). MS (GC, 70 eV): m/z = 442 (M^+, 70), 310 (77), 264 (22), 105 (100). HRMS (ESI): calcd for $C_{24}H_{18}N_4O_5$ (M + H) 443.1350, found 443.13495. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 3084 (w), 2858 (w), 1693 (m), 1600 (w), 1525 (s), 1470 (m), 1453 (m), 1389 (m), 1346 (s), 1246 (m), 1196 (m), 1137 (w), 1078 (w), 906 (w), 876 (w), 829 (m), 776 (m), 739 (s), 698 (s), 573 (w).

5-Bromo-2-methyl-4-nitro-1-phenethyl-1H-imidazole (**10a**). Brown solid (1.767 g, 57%). Mp: 127−129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3H, Me), 3.02 (t, 2H, ^3J = 7.0 Hz, CH_2), 4.18 (t, 2H, ^3J = 7.0 Hz, CH_2), 6.98−7.01 (m, 2H, CH_{Ar}), 7.25−7.27 (m, 3H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.5 (Me), 35.6, 48.0 (CH_2), 104.2 (C), 127.5, 128.7, 129.1 (CH_{Ar}), 136.0, 145.3 (C). MS (GC, 70 eV): m/z = 309 (M^+, 4), 230 (100), 213 (50), 105 (70), 91 (99), 77 (35). HRMS (EI): calcd for $C_{12}H_{12}N_3BrO_2$ (M^+) 309.01074, found 309.010864. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2927 (w), 1724 (w), 1632 (w), 1599 (w), 1537 (w), 1515 (s), 1476 (m), 1453 (m), 1381 (s), 1281 (s), 1239 (m), 1181 (w), 1153 (m), 1082 (w), 1040 (m), 1013 (m), 930 (w), 899 (w), 842 (m), 759 (m), 750 (s), 673 (m), 634 (m), 570 (m).

5-Bromo-2-methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazole (**10b**). Brown solid (1.891 g, 58%). Mp: 93−95 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3H, Me), 4.28 (t, 2H, ^3J = 5.0 Hz, CH_2), 4.44 (t, 2H, ^3J = 5.0 Hz, CH_2), 6.81−6.85 (m, 2H, CH_{Ar}), 6.95−7.02 (m, 1H, CH_{Ar}), 7.25−7.31 (m, 2H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.3 (Me), 45.8, 65.3 (CH_2), 104.4 (C), 114.0, 121.6, 129.5 (CH_{Ar}), 146.2, 157.3 (C). MS (GC, 70 eV): m/z = 325 (M^+, 1), 246 (100), 107 (15), 77 (31). HRMS (ESI): calcd for $C_{12}H_{12}N_3BrO_3$ (M + H) 326.01348, found 326.0141. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2931 (w), 1587 (w), 1526 (s), 1494 (s), 1466 (m), 1376 (m), 1336 (s), 1279 (m), 1244 (s), 1157 (w), 1080 (m), 1057 (m), 1038 (m), 916 (m), 882 (w), 842 (m), 788 (m), 753 (s), 687 (s), 603 (m).

5-Bromo-2-methyl-4-nitro-1-(3-phenylpropyl)-1H-imidazole (**10c**). Brown solid (1.782 g, 55%). Mp: 62−64 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01−2.12 (m, 2H, CH_2), 2.37 (s, 3H, Me), 2.72 (t, 2H, ^3J = 7.5 Hz, CH_2), 3.93−3.98 (m, 2H, CH_2), 7.16−7.34 (m, 5H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.9 (Me), 30.7, 32.5, 45.7 (CH_2), 104.5 (C), 126.6, 128.1, 128.7 (CH_{Ar}), 139.4, 144.6 (C). MS (GC, 70 eV): m/z = 323 (M^+, 1), 244 (24), 198 (100), 117 (18), 91 (64). HRMS (EI): calcd for $C_{13}H_{14}N_3BrO_2$ (M^+) 323.02639, found 323.02638. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1519 (s), 1479 (m), 1384 (s), 1334 (s), 1285 (s), 1254 (s), 1173 (w), 1148 (m), 1084 (w), 1028 (m), 907 (w), 867 (m), 834 (m), 752 (m), 718 (s), 693 (s), 670 (m), 631 (w).

DOI: 10.1021/jo5025927
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*4-Bromo-2-methyl-5-nitro-1-phenethyl-1H-imidazole (**11a**).* Brown solid (0.960 g, 31%). Mp: 125−127 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3H, Me), 3.03 (t, 2H, ^3J = 7.0 Hz, CH_2), 4.49 (t, 2H, ^3J = 7.0 Hz, CH_2), 7.02−7.05 (m, 2H, CH_{Ar}), 7.27−7.29 (m, 3H, CH_{Ar}). ^{13}C NMR (62.96 MHz, $CDCl_3$): δ = 13.6 (Me), 36.4, 49.2 (CH_2), 120.8 (C), 127.4, 128.7, 129.0 (CH), 136.4, 149.1 (C). MS (GC, 70 eV): m/z = 309 (M^+, 1), 263 (44), 184 (100), 104 (72), 91 (76), 77 (41). HRMS (EI): calcd for $C_{12}H_{12}N_3BrO_2$ (M^+) 309.01074, found 309.011022. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2931 (w), 1526 (s), 1497 (w), 1462 (m), 1415 (m), 1384 (m), 1357 (s), 1332 (s), 1275 (w), 1249(s), 1192 (m), 1175 (s), 1085 (w), 1032 (w), 1002 (m), 852 (w), 830 (s), 802 (w), 755 (s), 741 (m), 704 (s), 686 (m), 671 (m), 630 (w), 610 (w), 563 (m).

*4-Bromo-2-methyl-5-nitro-1-(2-phenoxyethyl)-1H-imidazole (**11b**).* Brown solid (1.239 g, 38%). Mp: 100−102 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.60 (s, 3H, Me), 4.29 (t, 2H, ^3J = 5.0 Hz, CH_2), 4.70 (t, 2H, ^3J = 5.0 Hz, CH_2), 6.76−6.80 (m, 2H, CH_{Ar}), 6.92−6.98 (m, 1H, CH_{Ar}), 7.22−7.28 (m, 2H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.6 (Me), 47.2, 66.3 (CH_2), 114.1 (CH), 121.2 (C), 121.7, 129.6 (CH), 150.4, 157.5 (C). MS (GC, 70 eV): m/z = 325 (M^+, 5), 263 (44), 281 (85), 232 (71), 200 (56), 107 (26), 77 (100). HRMS (EI): calcd for $C_{12}H_{12}N_3BrO_3$ (M + H) 326.01348, found 326.0141. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2930 (w), 1586 (w), 1516 (s), 1488 (m), 1454 (s), 1413 (s), 1355 (s), 1329 (s), 1235 (s), 1172 (s), 1083 (m), 1063 (m), 1022 (m), 912 (m), 890 (w), 829 (m), 758 (s), 693 (s), 632 (w), 591 (m).

*4-Bromo-2-methyl-5-nitro-1-(3-phenylpropyl)-1H-imidazole (**11c**).* Brown solid (1.296 g, 40%). Mp: 50−52 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.94−2.06 (m, 2H, CH_2), 2.24 (s, 3H, Me), 2.64 (t, 2H, ^3J = 7.5 Hz, CH_2), 4.18 (t, 2H, ^3J = 7.5 Hz, CH_2), 7.09−7.25 (m, 5H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.7 (Me), 31.0, 32.4, 46.8 (CH_2), 120.3 (C), 126.3, 128.0, 128.5 (CH), 139.5, 148.4 (C). MS (GC, 70 eV): m/z = 323 (M^+, 1), 277 (52), 198 (50), 175 (32), 117 (51), 91 (100). HRMS (ESI): Calcd for $C_{13}H_{15}N_3BrO_2$ (M + H) 324.03422. Found 324.03456. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1514 (s), 1495 (m), 1452 (s), 1409 (s), 1378 (m), 1343 (s), 1250 (s), 1230 (s), 1170 (s), 1032 (m), 910 (w), 885 (w), 830 (s), 765 (s), 745 (s), 721 (s), 695 (s), 643 (w), 585 (w).

*1-(2-(2-Methyl-4-nitro-1-(2-phenoxyethyl)-1H-imidazol-5-yl)-phenyl)ethanone (**12d**).* Yellow viscous oil (0.233 g, 37%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.11 (s, 3H, Me), 2.49 (s, 3H, Me), 2.70−2.76 (m, 2H, CH_2), 3.69−3.79 (m, 1H, CH_2), 3.94−4.12 (m, 1H, CH_2), 6.89−6.97 (m, 2H, CH_{Ar}), 7.04−7.07 (m, 1H, CH_{Ar}), 7.18−7.24 (m, 3H, CH_{Ar}), 7.51−7.62 (m, 2H, CH_{Ar}), 7.89−7.92 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.1, 27.8 (Me), 35.4, 46.7 (CH_2), 127.0 (C), 128.5, 128.6, 128.7, 129.3 (CH), 129.3 (C), 130.1, 131.4, 131.8 (CH), 132.6, 136.8, 138.9, 143.9, 199.3 (C). MS (GC, 70 eV): m/z = 365 (M^+, 1), 319 (100). HRMS (ESI): calcd for $C_{20}H_{20}N_3O_4$ (M + H) 366.14483, found 366.14499. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1699 (m), 1601 (w), 1531 (m), 1496 (s), 1442 (m), 1384 (m), 1319 (s), 1293 (s), 1275 (m), 1236 (s), 1205 (m), 1120 (w), 1092 (w), 1000 (w), 931 (w), 852 (s), 824 (m), 759 (m), 702 (s), 673 (m), 569 (m).

*2-Methyl-4-nitro-1-phenethyl-5-(4-(trifluoromethyl)phenyl)-1H-imidazole (**12e**).* Green solid (0.326 g, 87%). Mp: 155−156 °C. ^{1}H NMR (300 MHz, *DMSO-d*$_6$): δ = 2.17 (s, 3H, Me), 3.10 (t, 2H, ^3J = 7.1 Hz, CH_2), 4.52 (t, 2H, ^3J = 7.1 Hz, CH_2), 7.08−7.11 (m, 2H, CH_{Ar}), 7.27−7.31 (m, 3H, CH_{Ar}), 7.69 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}), 7.87 (d, 2H, ^3J = 8.0 Hz, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO-d_6): δ = −62.8 (CF_3). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ = 13.8 (Me), 36.5, 48.8 (CH_2), 124.8 (q, ^1J = 270.5 Hz, CF_3), 125.0 (q, ^4J = 3.7 Hz, $CHCCF_3$), 127.5, 128.8, 129.1, 130.0 (CH), 131.3 (q, ^2J = 33.2 Hz, CCF_3), 134.9, 136.5, 141.9, 148.7 (C). MS (GC, 70 eV): m/z = 375 (M^+, 10), 329 (100), 105 (58), 91 (49), 77 (26). HRMS (EI): calcd for $C_{19}H_{16}N_3O_2F_3$ (M^+) 375.11891, found 375.11984. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1714 (w), 1558 (w), 1506 (w), 1468 (m), 1359 (m), 1317 (s), 1186 (m), 1108 (s), 1067 (s), 1018 (m), 848 (s), 746 (s), 701 (s), 661 (w), 593 (m).

*5-(4-tert-Butylphenyl)-2-methyl-4-nitro-1-phenethyl-1H-imidazole (**12f**).* Yellow viscous oil (0.258 g, 71%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 9H, *t*-Bu), 2.55 (s, 3H, Me), 2.70 (t, 2H, ^3J = 7.2 Hz, CH_2), 3.97 (t, 2H, ^3J = 7.2 Hz, CH_2), 6.76−6.80 (m, 2H, CH_{Ar}), 7.19−7.21 (m, 5H, CH_{Ar}), 7.50 (d, 2H, ^3J = 8.5 Hz, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.3 (Me), 31.2 (*t*-Bu), 34.9 (*Ct*-Bu), 36.2, 46.4 (CH_2), 124.1 (C), 125.8, 127.3, 128.6, 129.0, 129.7 (CH), 132.5, 136.3, 143.7, 153.2 (C). MS (GC, 70 eV): m/z = 363 (M^+, 100), 348 (89), 244 (15), 115 (11), 105 (97), 91 (28), 77 (27). HRMS (ESI): calcd for $C_{22}H_{26}N_3O_2$ (M + H) 364.20195, found 364.2019. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2960 (w), 1575 (w), 1544 (w), 1504 (s), 1452 (m), 1398 (m), 1383 (s), 1331 (s), 1294 (s), 1248 (s), 1201 (w), 1100 (w), 1048 (w), 1029 (w), 1003 (m), 867 (s), 832 (m), 769 (m), 744 (s), 698 (s), 669 (m), 629 (w), 577 (m), 558 (m).

*2-(2-Methyl-5-nitro-1-phenethyl-1H-imidazol-4-yl)benzaldehyde (**13a**).* Brown viscous oil (0.262 g, 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.06 (s, 3H, Me), 3.07 (t, 2H, ^3J = 6.8 Hz, CH_2), 4.53 (t, 2H, ^3J = 6.8 Hz, CH_2), 7.06−7.09 (m, 1H, CH_{Ar}), 7.24−7.27 (m, 1H, CH_{Ar}), 7.41−7.44 (m, 2H, CH_{Ar}), 7.46−7.51 (m, 2H, CH_{Ar}), 7.54−7.56 (m, 1H, CH_{Ar}), 7.64−7.67 (m, 1H, CH_{Ar}) 7.95 (dd, 1H, ^3J = 7.5 Hz, ^4J = 1.47 Hz, CH_{Ar}), 9.91 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.6 (Me), 36.3, 48.5 (CH_2), 127.3 (CH), 128.3 (C), 128.5 (CH), 128.7 (C), 128.9 (CH), 129.1 (C), 129.4 (CH), 130.9 (C), 131.8, 132.0, 133.2 (CH), 134.4, 136.5 (C), 190.8 (CHO). MS (GC, 70 eV): m/z = 335 (M^+, 100). HRMS (ESI): calcd for $C_{19}H_{18}N_3O_3$ (M + H) 336.13427, found 336.13499. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1697 (m), 1600 (w), 1531 (m), 1496 (s), 1440 (m), 1384 (m), 1319 (s), 1293 (s), 1271 (m), 1236 (s), 1201 (m), 1120 (w), 1092 (w), 1005 (w), 931 (w), 850 (m), 825 (m), 757 (s), 700 (s), 673 (m), 569 (m).

*1-(2-(2-Methyl-5-nitro-1-phenethyl-1H-imidazol-4-yl)phenyl)-ethanone (**13b**).* Red solid (0.265 g, 76%). Mp: 123−125 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.00 (s, 3H, Me), 2.56 (s, 3H, Me), 3.07 (t, 2H, ^3J = 6.6 Hz, CH_2), 4.50 (t, 2H, ^3J = 6.6 Hz, CH_2), 7.14−7.16 (m, 2H, CH_{Ar}), 7.25−7.34 (m, 3H, CH_{Ar}), 7.45−7.56 (m, 3H, CH_{Ar}), 7.77−7.80 (m, 1H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.4, 27.6 (Me), 36.3, 48.4 (CH_2), 126.9, 128.0, 128.7, 128.8, 128.9, 131.0, 131.1 (CH), 131.9, 133.3, 136.7, 138.7, 145.1, 149.0, 199.6 (C). MS (GC, 70 eV): m/z = 349 (M^+, 1), 303 (100), 199 (17), 105 (71). HRMS (ESI): calcd for $C_{20}H_{20}N_3O_3$ (M + H) 350.14992, found 350.15029. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1694 (s), 1549 (m), 1498 (m), 1462 (s), 1418 (s), 1353 (s), 1327 (s), 1308 (s), 1249 (s), 1186 (s), 998 (w), 836 (m), 779 (m), 754 (s), 701 (s), 633 (w), 593 (s).

*4-(4-Fluorophenyl)-2-methyl-5-nitro-1-phenethyl-1H-imidazole (**13c**).* Brown viscous oil (0.238 g, 73%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.15 (s, 3H, Me), 3.08 (t, 2H, ^3J = 7.4 Hz, CH_2), 4.52 (t, 2H, ^3J = 7.4 Hz, CH_2), 7.08−7.15 (m, 4H, CH_{Ar}), 7.26−7.31 (m, 3H, CH_{Ar}), 7.75−7.80 (m, 2H, CH_{Ar}). ^{19}F NMR (235 MHz, DMSO): δ = −110.8 (CF). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.6 (Me), 36.5, 48.7 (CH_2), 115.2 (d, ^3J = 20 Hz, CH), 127.4 (CH), 127.5 (C), 128.8, 129.0 (CH), 131.7 (d, ^3J = 8 Hz, CH), 136.6, 142.9, 148.5 (C), 163.4 (d, ^1J = 249.9 Hz, CF). MS (GC, 70 eV): m/z = 325 (M^+, 30), 279 (100), 238 (15), 133 (14), 105 (48), 91 (40) 77 (19). HRMS (ESI): calcd for $C_{18}H_{17}FN_3O_2$ (M + H) 326.12993, found 326.13008. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1499 (w), 1456 (w), 1409 (w), 1376 (w), 1351 (w), 1329 (m), 1312 (m), 1261 (w), 1219 (m), 1183 (m), 1156 (m), 1083 (m), 1016 (m), 841 (s), 795 (s), 759 (s), 708 (s), 643 (w), 593 (m).

*2-Methyl-4-(3,5-dimethylphenyl)-5-nitro-1-phenethyl-1H-imidazole (**13d**).* Brown viscous oil (0.252 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.09 (s, 3H, Me), 2.33 (s, 6H, 2xMe), 3.05 (t, 2H, ^3J = 7.0 Hz, CH_2), 4.46 (t, 2H, ^3J = 7.0 Hz, CH_2), 7.02−7.09 (m, 3H, CH_{Ar}), 7.22−7.32 (m, 5H, CH_{Ar}). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8 (Me), 21.3 (2xMe), 36.6, 48.6 (CH_2), 125.0, 127.1 (C), 127.3, 128.7, 128.8, 129.0 (CH), 131.3 (C), 131.4 133.8, 136.8 (CH), 137.6, 138.0, 144.4, 148.3 (C). MS (GC, 70 eV): m/z = 335 (M^+, 64), 305 (14), 289 (90), 233 (22), 160 (15), 132 (24), 115 (27), 105 (100), 91 (57), 77 (42). HRMS (ESI): calcd for $C_{20}H_{22}N_3O_2$ (M + H) 336.17065, found 336.17099. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2959 (w), 1602 (w), 1537 (w), 1501 (m), 1454 (m), 1417 (s), 1376 (w), 1354 (s), 1323 (s), 1245 (m), 1178 (s), 1085 (w), 1031 (w), 903 (w), 892 (w), 854 (m), 816 (m), 752 (s), 700 (s), 656 (w), 632 (m), 571 (w), 536 (w).

DOI: 10.1021/jo5025927
J. Org. Chem. 2015, 80, 2103−2119

*2-(2-Methyl-5-nitro-1-(2-phenoxyethyl)-1H-imidazol-4-yl)-benzaldehyde (**13e**).* Brown viscous oil (0.281 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.66 (s, 3H, Me), 4.38 (t, 2H, ^3J = 4.8 Hz, CH_2), 4.76 (t, 2H, ^3J = 4.8 Hz, CH_2), 6.82−6.86 (m, 2H, CH_{Ar}), 6.95−7.00 (m, 1H, CH_{Ar}), 7.25−7.30 (m, 2H, CH_{Ar}), 7.50−7.66 (m, 3H, CH_{Ar}), 7.98 (dd, 1H, ^3J = 7.4 Hz, ^4J = 1.1 Hz, CH_{Ar}), 9.92 (s, 1H, CHO). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.6 (Me), 46.7, 66.5 (CH_2), 114.2, 121.6, 128.8, 129.6, 131.0, 133.2, 134.5 (CH), 141.6, 150.2, 157.7 (C), 190.9 (CHO). MS (GC, 70 eV): m/z = 351 (M^+, 1), 305 (100), 183 (24), 77 (46). HRMS (ESI): calcd for $C_{19}H_{18}N_3O_4$ (M + H) 352.121914, found 352.121963. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1693 (m), 1598 (m), 1491 (s), 1459 (m), 1413 (s), 1354 (m), 1323 (s), 1296 (m), 1240 (s), 1186 (s), 1082 (m), 1062 (m), 912 (m), 823 (m), 770 (s), 751 (s), 696 (m), 677 (m), 637 (m), 610 (m).

*1-Butyl-7,8-dimethoxy-2-methyl-1H-imidazo[4,5-c]isoquinoline (**16a**).* Brown viscous oil (0.203 g, 68%). ^{1}H NMR (300 MHz, *DMSO-d_6*): δ = 0.71 (t, 3H, ^3J = 7.1 Hz, $CH_2CH_2CH_2CH_3$), 1.09−1.15 (m, 2H, $CH_2CH_2CH_2CH_3$), 1.42−1.44 (m, 2H, $CH_2CH_2CH_2CH_3$), 2.54 (s, 3H, Me), 3.66−3.84 (m, 2H, $CH_2CH_2CH_2CH_3$), 3.90 (s, 3H, OMe), 3.97 (s, 3H, OMe), 7.23 (s, 1H, CH_{Ar}), 7.62 (s, 1H, CH_{Ar}), 9.74 (s, 1H, isoquinoline). ^{13}C NMR (62.9 MHz, *DMSO-d_6*): δ = 13.1, 13.2 (Me), 18.9, 31.1, 44.2 (CH_2), 55.7, 56.3 (OMe), 111.5, 114.5 (CH), 123.5, 128.2, 129.6, 143.4, 144.3, 149.8, 153.2 (C), 189.9 (CH). MS (GC, 70 eV): m/z = 299 (M^+, 100). HRMS (EI): calcd for $C_{17}H_{21}N_3O_2$ (M^+) 299.36754, found 299.36755. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2933 (w), 1665 (m), 1582 (m), 1498 (s), 1448 (m), 1351 (s), 1291 (m), 1267 (s), 1059 (w), 1132 (s), 1077 (s), 1019 (s), 978 (w), 889 (m), 859 (m), 814 (m), 749 (m), 675 (w), 639 (w), 585 (m).

*2-Methyl-1-phenethyl-1H-imidazo[4,5-c]isoquinoline (**16b**).* Brown solid (0.186 g, 65%). Mp: 262−264 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (s, 3H, Me), 3.20 (br s, 2H, CH_2), 4.70 (br s, 2H, CH_2), 6.88−6.91 (m, 2H, CH_{Ar}), 7.22−7.25 (m, 3H, CH_{Ar}), 7.52 (t, 1H, ^3J = 7.3 Hz, CH_{Ar}), 7.66 (t, 1H, ^3J = 7.3 Hz, CH_{Ar}), 7.79 (d, 1H, ^3J = 8.3 Hz, CH_{Ar}), 8.11 (d, 1H, ^3J = 7.8 Hz, ^4J = 0.8 Hz, CH_{Ar}), 8.68 (s, 1H, isoquinoline). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.4 (Me), 36.0, 47.9 (CH_2), 120.9, 118.8 (CH), 119.4, 122.9, 126.2 (C), 126.3, 126.9, 127.5, 128.7, 128.8, 129.1, 132.1 (CH), 136.4, 143.1, 151.4 (C). MS (GC, 70 eV): m/z = 287 (M^+, 81), 196 (100), 128 (36). HRMS (EI): calcd for $C_{19}H_{17}N_3$ (M^+) 287.14170, found 287.14121. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2999 (w), 1526 (m), 1499 (m), 1454 (m), 1414 (m), 1362 (m), 1337 (m), 1304 (s), 1228 (m), 1190 (m), 1135 (m), 994 (m), 928 (w), 885 (m), 804 (w), 775 (s), 752 (s), 670 (s), 665 (m), 649 (m), 619 (s), 569 (m).

*2-Methyl-1-(3-phenylpropyl)-1H-imidazo[4,5-c]isoquinoline (**16c**).* Yellow solid (0.222 g, 74%). Mp: 126−128 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.07 (br s, 2H, CH_2), 2.51 (s, 3H, Me), 2.70 (t, 2H, ^3J = 6.6 Hz, CH_2), 4.28 (br s, 2H, CH_2), 7.10−7.15 (m, 2H, CH_{Ar}), 7.17−7.35 (m, 6H, CH_{Ar}), 7.57−7.59 (m, 1H, CH_{Ar}), 8.52 (s, 1H, isoquinoline). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8 (Me), 31.2, 32.8, 45.1 (CH_2), 118.6 (CH), 119.0 (C), 124.3, 124.4 (CH), 125.8 (C), 128.5, 128.7, 129.6, 130.3 (CH), 139.9 (C), 148.3 (CH), 150.3, 150.4 (C). MS (GC, 70 eV): m/z = 301 (M^+, 100), 196 (39), 182 (39), 169 (15), 128 (24), 91 (29). HRMS (EI): calcd for $C_{20}H_{19}N_3$ (M^+) 301.15735, found 301.15740. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 1578 (w), 1529 (m), 1503 (m), 1454 (m), 1415 (m), 1309 (s), 1284 (m), 1231 (m), 1189 (s), 1127 (m), 1044 (w), 991 (m), 903 (m), 829 (w), 776 (m), 754 (s), 702 (s), 669 (m), 654 (s), 577 (s).

*2-Methyl-3-phenethyl-3H-imidazo[4,5-c]isoquinoline (**16d**).* Red solid (0.195 g, 68%). Mp: 138−140 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.24 (s, 3H, Me), 3.20 (t, 2H, ^3J = 6.8 Hz, CH_2), 4.56 (t, 2H, ^3J = 6.8 Hz, CH_2), 6.97−7.00 (m, 2H, CH_{Ar}), 7.20−7.24 (m, 3H, CH_{Ar}), 7.51−7.57 (m, 1H, CH_{Ar}), 7.75−7.80 (m, 1H, CH_{Ar}), 8.07 (d, 1H, ^3J = 8.3 Hz, CH_{Ar}), 8.51 (dd, 1H, ^3J = 8.3 Hz, ^4J = 0.8 Hz, CH_{Ar}), 8.95 (s, 1H, isoquinoline). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 13.8 (Me), 36.2, 44.7 (CH_2), 120.9, 124.8 (CH), 126.3 (C), 126.9, 128.4, 128.7, 128.9 (CH), 129.4 (C), 130.4, 132.0, 132.2 (CH), 138.0, 142.4 (C), 146.5 (CH), 149.8 (C). MS (GC, 70 eV): m/z = 287 (M^+, 79), 196 (72), 183 (100), 128 (33), 116 (24), 77 (16). HRMS (ESI): calcd for $C_{19}H_{18}N_3$ (M + H) 288.14952, found 288.14934. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2971 (w), 1630 (m), 1572 (m), 1491 (w), 1453 (m), 1436 (m), 1360 (s), 1225 (m), 1118 (m), 1024 (m), 1003 (m), 895 (w), 796 (w), 751 (s), 694 (s), 665 (m), 580 (m).

*2-Methyl-3-(2-phenoxyethyl)-3H-imidazo[4,5-c]isoquinoline (**16e**).* Brown viscous oil (0.188 g, 62%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.83 (s, 3H, Me), 4.39 (t, 2H, ^3J = 5.2 Hz, CH_2), 4.74 (t, 2H, ^3J = 5.2 Hz, CH_2), 6.78−6.81 (m, 2H, CH_{Ar}), 6.87−6.92 (m, 1H, CH_{Ar}), 7.18−7.23 (m, 2H, CH_{Ar}), 7.49−7.54 (m, 1H, CH_{Ar}), 7.73−7.79 (m, 1H, CH_{Ar}), 8.03 (d, 1H, ^3J = 8.3 Hz, CH_{Ar}), 8.50 (dd, 1H, ^3J = 8.3 Hz, ^4J = 0.7 Hz, CH_{Ar}), 8.90 (s, 1H, isoquinoline). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 14.6 (Me), 42.5, 66.3 (CH_2), 114.2, 120.8, 121.2, 124.9 (CH), 126.3 (C), 128.3 (CH), 128.7 (C), 129.5, 130.5 (CH), 142.3 (C), 146.4 (CH), 150.5, 158.0 (C). MS (GC, 70 eV): m/z = 303 (M^+, 26), 183 (100). HRMS (ESI): calcd for $C_{19}H_{18}N_3O$ (M + H) 304.14444, found 304.14427. IR (ATR, cm^{-1}): $\tilde{\nu}$ = 2928 (w), 1724 (w), 1633 (w), 1597 (m), 1496 (m), 1458 (m), 1438 (m), 1403 (m), 1358 (s), 1291 (m), 1237 (s), 1176 (m), 1082 (m), 1059 (m), 996 (m), 890 (m), 748 (s), 690 (s), 668 (s), 577 (m).

■ ASSOCIATED CONTENT

Supporting Information

Characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support by the DAAD (scholarship for A.G. and S.M.) and by the State of Mecklenburg-Vorpommern is gratefully acknowledged. We are grateful to Enamine Ltd. Co. (Ukraine) for support. We are grateful to Dr. Dirk Michalik for NMR measurements.

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