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

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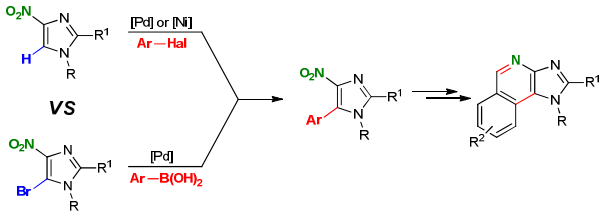


Abstract: Pd- or Ni-catalyzed C-H arylation of 4-nitroimidazole derivatives directed by a manipulable nitro group was developed. The reaction tolerates a wide range of substituted aryl halides and 4-nitroimidazoles. The experiments indicated that the nitro group has influence on regioselectivity of the reaction. In addition we could show that the efficiency of Suzuki-Miyaura cross-coupling reaction of nitroimidazoles is slightly lower in comparison to the direct C-H arylation. The exploration of chemical potential of 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] besides 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 bounds 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 pre-functionalized starting materials along with needs of "Green Chemistry" indicated its scope and efficiency limitations. However, during the last 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]

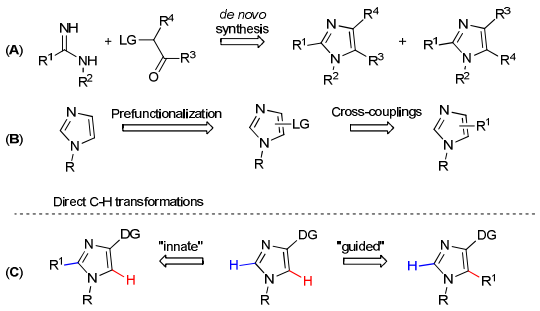
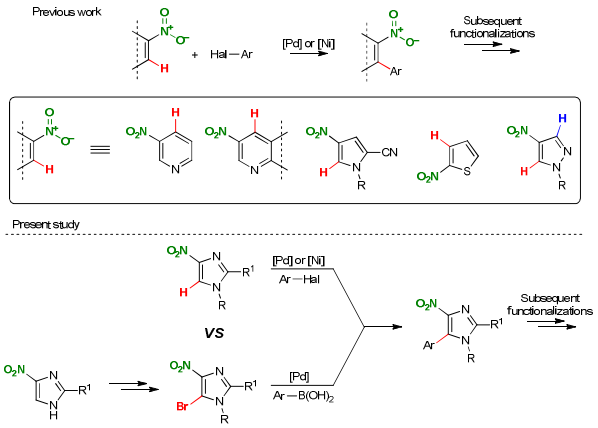


Figure 1. Common approaches for synthesis of functionalized imidazoles.

This approach eliminates the need for the organometallic starting materials required in traditional cross-coupling methods,[7] in addition, commonly these methods reduce reaction by-products, 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] However, in most of the cases these efficient moieties cannot be removed easily, or they are not apt to undergo further functionalizations. Due to this fact, substantial effort has been directed toward the discovery of multi-functional 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 plan the multi-task 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]



Scheme 1. The synthetic potential of TM-catalyzed nitro group directed C-H arylation of heteroarenes.

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

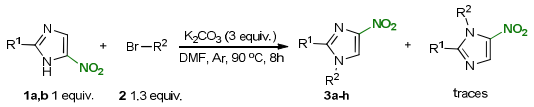
of 3-nitropyridine.[16b] In spite of this, the authors did not demonstrate the vast chemical potential of nitro group. In contrast to this, recently we communicated the selective and guided functionalization of 4-nitropyrazoles, fused 3-nitropyridines, 2-nitrothiophene and 4-nitro-1*H*-pyrroles by Pd- and Ni-catalyzed C-H arylation, that was followed by demonstration of multi-purpose character of nitro group as directing group (Scheme 1).[17] In our present study we would like to continue the amplification of this chemistry on the example of several *N*-substituted 4-nitroimidazoles (Scheme 1).

Results and discussion

Inspired by the tremendous chemical potential of nitro group[15] and our recent successful results on C-H arylation of different nitro-substituted heteroarenes,[17] we started 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.

Based on 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); 3) in this context interrelation between "guided" and "innate" C-H arylation reactions should be investigated (Figure 1). Subsequently the following criterias 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 multi-functionalized target compounds.

Table 1. Synthesis of starting *N*-substituted 4-nitroimidazoles **3a-h.**

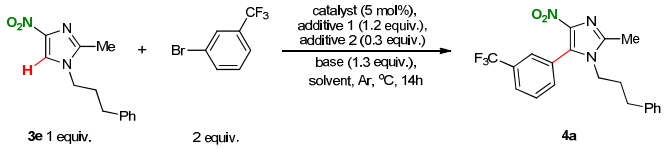


3	R^1	R^2	yield (%)
a	Me	Ethyl	82
b	Me	*n*-Butyl	88
c	Me	$(CH_2)_2Ph$	93
d	H	$(CH_2)_2Ph$	80
e	Me	$(CH_2)_3Ph$	78
f	Me	$(CH_2)_2OPh$	89
g	Me	CH_2-4-Tol	83
h	Me	2-BrC_6H_4	83

With the set of *N*-substituted 4-nitroimidazoles **3a-h** in hand we have focused as next on setting up optimal reaction conditions. For 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**. Basing on our previous results we considered the Pd catalysts with CuI as additive to be the starting point in this study.[17,18] To our delight, pilot experiments have indicated that indeed Pd/CuI system is rather

efficient in order to activate C(5)-H bond of 4-nitroimidazole **3e** (Table 2, entry 1-5), namely the best catalyst for the model compound **3e** turn up $PdCl_2(PPh_3)_2$, 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 (entry 1, 2, 4). Notably the copper salt such as CuI in stoichiometric amounts provides desired product in almost quantitative yield (entry 4). Though, absence or sub-stoichiometric amounts of CuI does not stop the reaction, namely we could isolate the product with reduced yield (entry 5).

Table 2. Optimization of reaction conditions for the synthesis of compound **4a.**



3e 1 equiv. 2 equiv. **4a**

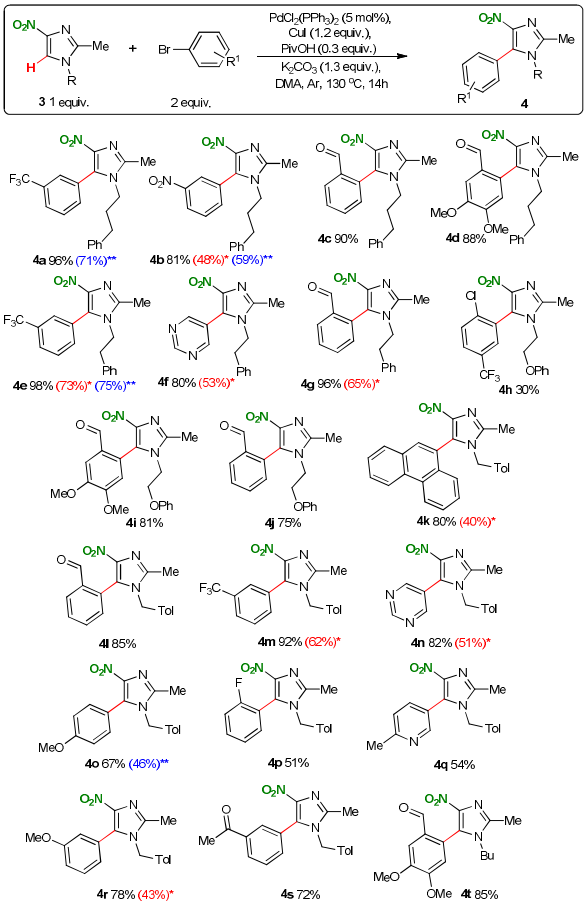
entry	catalyst	ligand	additive 1	additive 2	base	solvent	°C	%[a]
1	$Pd(OAc)_2$	Cy_3PxHBF_4	CuI	PivOH	K_2CO_3	DMA	130	78
2	$Pd(OAc)_2$	-	CuI	PivOH	K_2CO_3	DMA	130	76
3	-	-	CuI	PivOH	K_2CO_3	DMA	130	-
4	**$PdCl_2(PPh_3)_2$**	**-**	**CuI**	**PivOH**	**K_2CO_3**	**DMA**	**130**	**96**
5	$PdCl_2(PPh_3)_2$	-	-	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.

Interestingly the use of Lewis acids like CuCl or Ag_2CO_3 still provides the formation of desired product, however with reduced yields (entry 6, 7). The best base for the reaction was found to be K_2CO_3/PivOH system; any change in the system decreased the yields (entry 8-11). Employment of different solvents and temperatures has shown that the reaction runs effectively in DMF, DMA and NMP without any notable differences in yields (entry 4, 12-15). Finally, the usage of the other catalysts turned to be 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 that 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**), OMe (**4d**,**i**,**o**,**r**,**t**), and 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 equally actual in a wide range of substituted 4-nitroimidazoles with no changes in the reaction conditions. The usage of aryl iodides resulted in formation of a great amount of bipheniles *via* homocoupling induced by CuI: this demanded the large excess of the aryl halide, and the overall yields were visibly lower than with aryl bromides (**4a**,**b**,**e**,**o**). Together

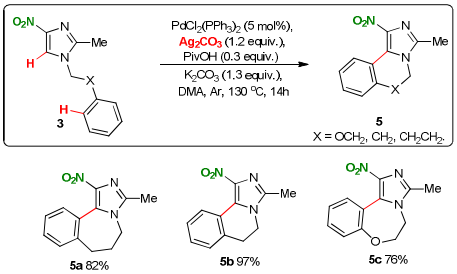
with this, aryl chlorides, in general, were not active enough in these reaction conditions (**4h**). Subsequently, the scope of the Ni-catalyzed C-H arylation reaction of corresponding 4-nitroimidazoles was examined. We have found that the reaction has general character allowing an efficient introduction of an aryl group into the imidazole ring in moderate yields (**4b**,**e**,**f**,**g**,**k**,**m**,**n**,**r**).



Scheme 2. Scope of the reaction with respect to aryl bromides and *N*-substituted 4-nitroimidazoles.* In the brackets on red are mentioned the yields of C-H arylation catalyzed by Ni.** In the brackets on blue are mentioned the yields of C-H arylation with appropriate aryl iodides.

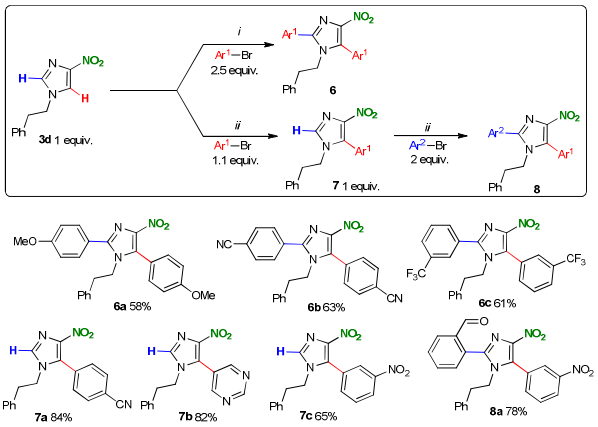
Surprisingly, during the course of reaction conditions optimisation we observed another interesting process. Namely when CuI was replaced by Ag_2CO_3 along with C-H arylation by aryl bromide (63 %), a Pd-catalyzed intramolecular dehydrogenative twofold C-H cross-coupling occurred (Table 2, entry 7, Scheme 3).[18a,19] Initially we observed traces of cyclisation product **5a** (8 %) together with C-H arylation product **4a** (63 %), nevertheless reducing amount of aryl bromide dramatically increased the yield of intramolecular dehydrogenative twofold 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 twofold C-H cross-coupling of 4-nitroimidazoles leading to different fused systems **5a-c** from 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 also 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 used catalytic system.[6a] Empirical studies indicated that the C-5 position of imidazoles exhibits higher reactivity, than that at the C-2 position, towards 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 consistent also with theoretically calculated CMD barriers for *N*-methylimidazole.[20]



Scheme 3. Synthesis of fused systems **5a-c**.

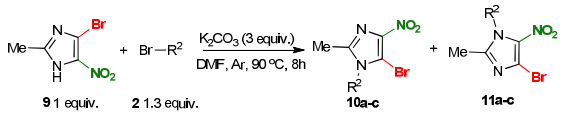
However, in our case the situation is different due to the nitro group that can direct the reaction. Thus, when we performed the reaction of 4-nitroimidazole **3d** with 2.5 equivalents of aryl bromide in standard reaction conditions, corresponding 2,5-disubstituted products **6** were observed (Scheme 4). Nevertheless, when the amount of aryl bromide was decreased to 1.1 equivalents, 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, entry 4, 5). This means that in 4-nitroimidazole **3d** the "guiding" effect of 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 compound **7c** using standard reaction conditions corresponding 2,5-disubstituted imidazole **8a** was successfully isolated in 78 % yield (Scheme 4).



Scheme 4. The regioselective C-H arylation of 4-nitroimidazoles; *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.

Inspired by the successful results on regioselective C-H arylation of positions 2 and 5 of 4-nitroimidazoles, next we envisioned that the C-H arylation of position 4 in 5-nitroimidazole can be an excellent extension of scope of the reaction. For this end, we designed and tested a number of reaction conditions, nevertheless the reactions failed, in spite of partial conversion of reactants only an inseparable mixture of compounds was observed. Further we tried to overcome this problem by finding another suitable procedure towards 4-arylaed 5-nitroimidazoles. For this purpose the Suzuki-Miyaura cross-coupling reaction of 5(4)-bromo-4(5)-nitroimidazoles **10**, **11** was tested (Table 3). To this end 5(4)-bromo-4(5)-nitro-1*H*-imidazole **9** was alkylated in order to prepare desired starting *N*-substituted imidazoles **10**, **11**. It should be mentioned that unlike alkylation of simple 4-nitroimidazoles (Table 1), the alkylation reaction of 5(4)-bromo-4(5)-nitroimidazoles leaded to a mixture of 5-bromo-4-nitroimidazole **10** and 4-bromo-5-nitroimidazole **11**, approximately in 2:1 ratio. Tree pairs of *N*-substituted nitroimidazoles were synthesised applying this procedure (Table 3).

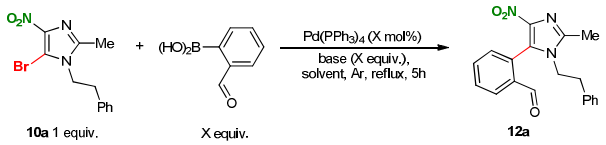
Table 3. Synthesis of *N*-substituted 5(4)-bromo-4(5)-nitroimidazoles **10, 11.**



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

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, 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 shows that it is the most successful Pd source for Suzuki-Miyaura cross-coupling reaction.[7] During optimization of the reaction conditions a number of solvents were tested such as dioxane, toluene etc. Unfortunately all our initial attempts to perform the desired coupling appeared unsuccessful (Table 4, entry 1, 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, entry 3, 4).

Table 4. Optimization of reaction conditions for the synthesis of compound **12a.**



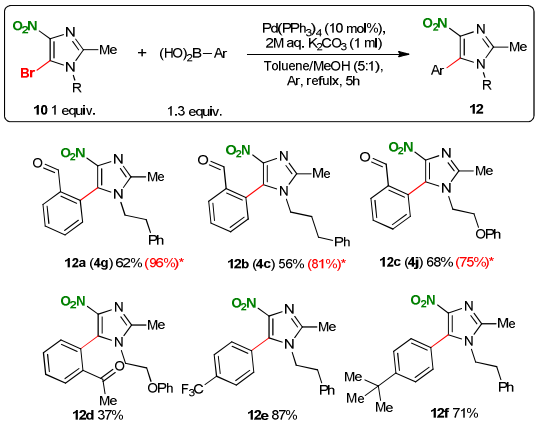
entry	catalyst	$ArB(OH)_2$	base	solvent	%[a]
1	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_2CO_3 (2 equiv.)	Dioxane	trace

2	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_2CO_3 (2 equiv.)	Toluene	trace
3	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_2CO_3 (2 equiv.)	Dioxane/H_2O (4:1)	20
4	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_2CO_3 (2 equiv.)	Toluene/H_2O (4:1)	27
5	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_3PO_4 (2 equiv.)	Toluene/H_2O (4:1)	15
6	$Pd(PPh_3)_4$ 10 mol%	1.3 equiv.	K_2CO_3 (2 equiv.)	Toluene/MeOH (5:1)	36
7	**$Pd(PPh_3)_4$ 10 mol%**	**1.3 equiv.**	**2M aq. K_2CO_3 (1 ml)[b]**	**Toluene/MeOH (5:1)**	**62**
8	$Pd(PPh_3)_4$ 10 mol%	1.0 equiv.	2M aq. K_2CO_3 (1 ml)[b]	Toluene/MeOH (5:1)	50
9	$Pd(PPh_3)_4$ 10 mol%	2.0 equiv.	2M aq. K_2CO_3 (1 ml)[b]	Toluene/MeOH (5:1)	61
10	$Pd(PPh_3)_4$ 5 mol%	1.3 equiv.	2M aq. K_2CO_3 (1 ml)[b]	Toluene/MeOH (5:1)	56

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

Meanwhile, the change of K_2CO_3 to K_3PO_4 decreased the yield of product (Table 4, entry 5), therefore during further optimisation 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, *via* 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 optimisation we tried to increase the yields by changing quantities of boronic acid. Nevertheless we could not get any positive result, 1.3 equivalent of boronic acid showed the best efficiency (Table 4, entry 8, 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**, further under the newly developed conditions we tried to prepare similar arylation products to those that were prepared by C-H arylation (Scheme 5). The comparison of these two procedures seems to be an actual 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 Suzuki-Miyaura cross-coupling reaction of 5-bromo-4-nitroimidazoles **10** were slightly lower in comparison to the yields obtained for similar compounds in direct C-H activation reaction (Scheme 2). This may be the result of steric factors and/or poor solubility of the reaction components.

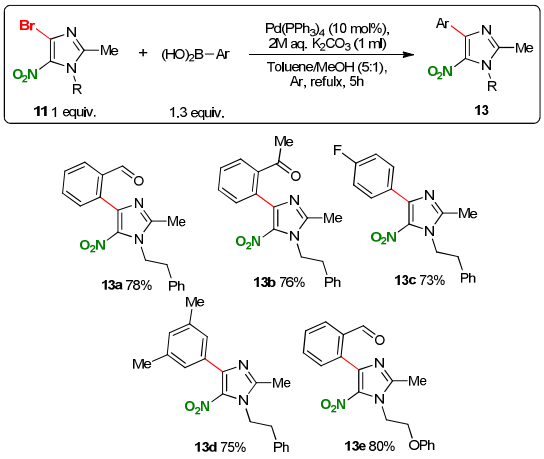


Scheme 5. Scope of the Suzuki-Miyaura cross-coupling reaction. *In the brackets on red are mentioned the yields of C-H arylation (Scheme 2).

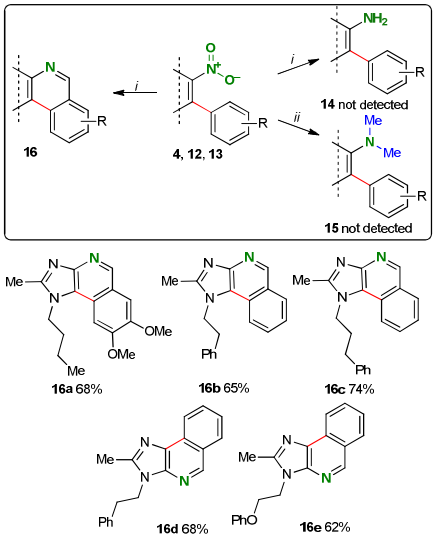
Although the C(4)-H bond of nitroimidazoles exhibits very low reactivity in the Pd- and Ni-catalyzed C-H arylation described above, precluding direct arylation of this position, nevertheless we could overcome this problem applying the

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).

Eventually, to fully demonstrate the synthetic potential of this methodology, we briefly explored the chemical versatility of directing group. The simple reduction of nitro group was tested first (Scheme 7). Not surprisingly, we got an inseparable mixture of products, along with this intensive polymerization was observed, most probably because of instability of formed aminoimidazoles **14**.[21] Moreover, we got 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 carbonyl group leading to the aromatic isoquinoline system.



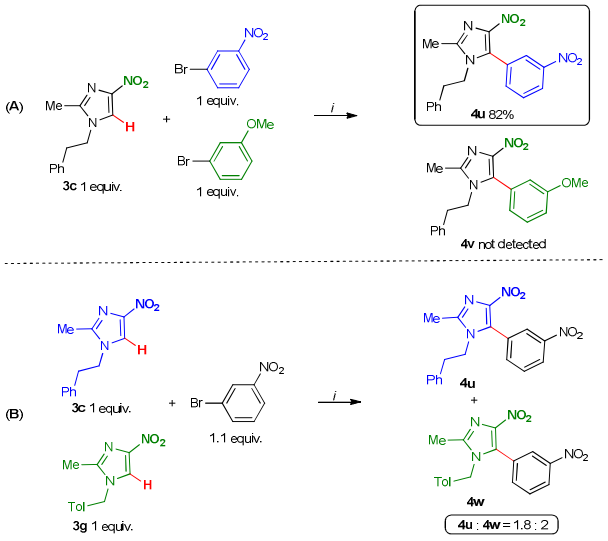
Scheme 6. Scope of the Suzuki-Miyaura cross-coupling reaction.



Scheme 7. Reduction of the nitro group; *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.

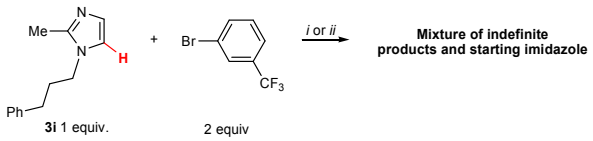
The structure of the synthesized arylated nitroimidazoles was mainly established by 1D and 2D NMR methods. The structures of compounds **3g**, **4d**,**t**, **5b**, **7a**,**c**, **10a** and **12a** (**4g**) were independently confirmed by X-ray single crystal analyses (Figures 1-8, supplementary information).[22]

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 favoured by 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 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 supplementary information).



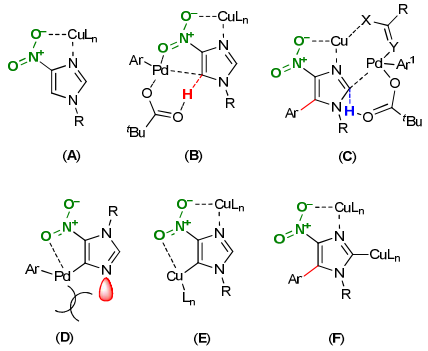
Scheme 8. The competitive experiments between imidazoles and aryl bromides; *i*: $PdCl_2(PPh_3)_2$ (5 mol%), CuI (1.2 equiv.), PivOH (0.3 equiv.), K_2CO_3 (1.3 equiv.), DMA, under Ar, 130 °C, 14 h.

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 in standard conditions, developed for nitroimidazoles, were unsuccessful; we got 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; *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.

Finally, the regioselectivity might be explained, by an assumption that the catalyst (Pd or Ni) coordinated by the nitro group initiates C(5)-arylation of imidazole ring *via* concerted metalation-deprotonation (CMD), as illustrated in Scheme 10 (**B**).[20] In this context it should be mentioned that the salt of copper *via* double chelation by 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 centre thereby initiating Pd-catalyzed C-H bond cleavage.[23] For C(2)-arylation of 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 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 do not exclude the formation of appropriate cuprates of imidazole that is followed by transmetallation to Pd or Ni (Scheme 10, **E** and **F**), since recently 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]



Scheme 10. Proposed mechanistic explanation of the regioselectivity.

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 to activate 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 optimisation of the reaction conditions we observed a Pd-catalyzed intramolecular dehydrogenative twofold 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 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 Suzuki-Miyaura cross-coupling reaction of 5-bromo-4-nitroimidazoles were slightly lower in comparison to the yields obtained for similar compounds in direct C-H activation reaction. Within the course of study the multi-purpose 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, 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 enclosed in SI. 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: Corresponding imidazole (1 equiv.) and K_2CO_3 (3 equiv.) successively were weighed to 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 back filled with argon. The dry DMF (8 ml for 1 g of imidazole) and corresponding alkyl bromide (1.3 equiv.) were added *via* a 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, 8a: Corresponding *N*-substituted 4-nitroimidazole **3b**,**c**,**e-g 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 to 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 back filled 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* a 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.

The competitive experiment between imidazole 3c and electronically different aryl bromides. Synthesis of compound 4u: 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 $PdCl_2(PPh_3)_2$ (0.05 equiv.) successively were weighed to 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 back filled 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* a 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.

The competitive experiment between two various imidazoles. Synthesis of compounds 4u, 4w: Corresponding *N*-substituted 4-nitroimidazoles **3c 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 to 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 back filled 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* a 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 mixture of compounds **4u** and **4w** was purified by column chromatography typically using heptane/ethyl acetate mixtures.

General procedure for Pd-catalyzed intramolecular dehydrogenative twofold C-H cross-coupling reaction. Synthesis of compounds 5a-c: 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 to 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 back filled 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: 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 to 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 back filled 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* a 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 regioselective C(5)-H arylation of 2,5-unsubstituted 4-nitroimidazole. Synthesis of compounds 7a-c: 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 to 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 back filled 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* a 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: Corresponding 5(4)-bromo-4(5)-nitroimidazole **10**, **11** (1 equiv.), arylboronic acid (1.3 equiv.), and $Pd(PPh_3)_4$ (0.10 equiv.) successively were weighed to 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 2M aqueous K_2CO_3 (1 ml for 1 mmol of starting nitroimidazole) were added *via* a 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, after that it was 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, 70eV): *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, 70eV): *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, 70eV): *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, 135.9 (CH), 136.0, 147.9 (C).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 2xCH_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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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%$^{Ar\text{-}I}$), 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, *C*CF_3), 133.5 (CH), 139.1, 143.5, 143.9 (C).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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%$^{Ar\text{-}I}$), mp 164-166 ^{o}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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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 (CH).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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%$^{Ar\text{-}I}$), mp 164-166 ^{o}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, ^{1}J = 271 Hz, CF_3), 126.3, 126.8, 127.0, 128.5, 128.5 (CH), 129.3 (q, ^{2}J = 31 Hz, CCF_3), 129.7 (CH), 131.0 (C), 134.0 (CH), 137.0, 142.6, 144.4 (C).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.45 (s, 3H, Me), 2.86 (t, 2H, ^{3}J = 6.4 Hz, CH_2), 4.10 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.26 (s, 3H, Me), 2.70 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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, ^{1}J = 273 Hz, CF_3), 127.5, 128.1 (C), 128.5 (q, ^{3}J = 4 Hz, CH), 129.3 (q, ^{3}J = 4 Hz, CH), 129.7 (CH), 130.2 (C), 130.8 (CH), 138.9, 144.1, 145.5, 157.4 (C).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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, 2xCH_2), 6.73 (d, 2H, ^{3}J = 8.0 Hz, CH_{Ar}), 6.91 (t, 1H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.57 (s, 3H, Me), 3.96-4.24 (m, 4H, 2xCH_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, ^{3}J = 7.3 Hz, ^{4}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 15.0 Hz, CH_2), 4.84 (d, 1H, ^{3}J = 15.0 Hz, CH_2), 6.55 (d, 2H, ^{3}J = 7.9 Hz, CH_{Ar}), 6.86 (d, 2H, ^{3}J = 7.9 Hz, CH_{Ar}), 7.36-7.67 (m, 7H, CH_{Ar}), 8.60 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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, ^{3}J = 8.0 Hz, CH_{Ar}), 7.03 (d, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}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, ^{3}J = 6.0 Hz, CH_{Ar}), 7.45 (d, 2H, ^{3}J = 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, ^{1}J = 273.2 Hz, CF_3), 125.7 (CH), 126.7 (q, ^{3}J = 4.1 Hz, CH), 127.1 (q, ^{3}J = 4.1 Hz, CH), 128.2 (C), 129.3 (CH), 129.9 (C), 130.7 (CH), 131.1 (q, ^{2}J = 32.6 Hz, CCF_3), 131.3 (C), 133.5 (CH), 138.4, 143.5, 144.7 (C).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 8.1 Hz, CH_{Ar}), 7.10 (d, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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), 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%$^{Ar\text{-}I}$). ^{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, ^{3}J = 7.6 Hz, CH_{Ar}), 6.90 (d, 2H, ^{3}J = 8.5 Hz, CH_{Ar}), 7.09 (d, 2H, ^{3}J = 7.6 Hz, CH_{Ar}), 7.19 (d, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 8.0 Hz, CH_{Ar}), 7.05 (d, 2H, ^{3}J = 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, ^{3}J = 15.4 Hz, C), 115.9 (d, ^{2}J = 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, ^{1}J = 249.7 Hz, CF).

MS (GC, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 8.0 Hz, CH_{Ar}), 7.02 (d, 2H, ^{3}J = 8.0 Hz, CH_{Ar}), 7.45 (d, 1H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^oC. ^1H 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, 70eV): *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}): $\widetilde{\nu}$ = 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}). ^1H 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, 70eV): *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}): $\widetilde{\nu}$ = 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^oC. ^1H 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, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 5.9 Hz, CH_2), 4.49 (t, 2H, ^{3}J = 5.9 Hz, CH_2), 7.20 (dd, 1H, ^{3}J = 8.0 Hz, ^{4}J = 1.1 Hz, CH_{Ar}), 7.31 (dt, 1H, ^{3}J = 7.6 Hz, ^{4}J = 1.3 Hz, CH_{Ar}), 7.47 (dt, 1H, ^{3}J = 7.6 Hz, ^{4}J = 1.9 Hz, CH_{Ar}), 7.84 (dd, 1H, ^{3}J = 7.8 Hz, ^{4}J = 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, 70eV): *m/z* (%) = 245 (M^+, 100).

HRMS (EI): Calcd for $C_{12}H_{11}N_3O_3$ (M^+) 245.08004. Found 245.08010.

IR (ATR, cm^{-1}): $\widetilde{\nu}$ = 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, ^{3}J = 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, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 6.8 Hz, CH_2), 4.15 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, ^{3}J = 6.7 Hz, CH_2), 4.20 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, DMSO): δ = 2.84 (t, 2H, ^{3}J = 6.6 Hz, CH_2), 3.98 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3H, Me), 3.02 (t, 2H, ^{3}J = 7.0 Hz, CH_2), 4.18 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.63 (s, 3H, Me), 4.28 (t, 2H, ^{3}J = 5.0 Hz, CH_2), 4.44 (t, 2H, ^{3}J = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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).

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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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, 70eV): *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, *C*HCCF_3), 127.5, 128.8, 129.1, 130.0 (CH), 131.3 (q, ^2J = 33.2 Hz, *C*CF_3), 134.9, 136.5, 141.9, 148.7 (C).

MS (GC, 70eV): *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, 70eV): *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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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).

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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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}): $\widetilde{\nu}$ = 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, 70eV): *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).

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Supporting Information Available

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 and references

1. For some recent examples, see: (a) I. F. Sevrioukova, T. L. Poulos, *J. Med. Chem.* **2013**, *56*, 3733-3741; (b) P. Chong, P. Sebahar, M. Youngman, D. Garrido, H. Zhang, E. L. Stewart, R. T. Nolte, L. Wang, R. G. Ferris, M. Edelstein, K. Weaver, A. Mathis, A. Peat, *J. Med. Chem.* **2012**, *55*, 10601-10609; (c) D. Dimova, P. Iyer, M. Vogt, F. Totzke, M. H. G. Kubbutat, C. Schachtele, S. Laufer, J. Bajorath, *J. Med. Chem.* **2012**, *55*, 11067-11071; (d) Y. Song, Z. Shao, T. S. Dexheimer, E. S. Scher, Y. Pommier, M. Cushman, *J. Med. Chem.* **2010**, *53*, 1979-1989; (e) B. Vacher, P. Funes, P. Chopin, D. Cussac, P. Heusler, A. Tourette, M. Marien, *J. Med. Chem.* **2010**, *53*, 6986-6995; (f) K. Bonezzi, G. Taraboletti, P. Borsotti, F. Bellina, R. Rossi, R. Giavazzi, *J. Med. Chem.* **2009**, *52*, 7906-7910.
2. For a review, see: Z. Jin, *Nat. Prod. Rep.* **2005**, *22*, 196-229.
3. For some recent reviews and books on N-heterocyclic carbene based ligands, see: (a) *N-Heterocyclic Carbenes: From Laboratory Curiosities to Efficient Synthetic Tools*, S. Diez-Gonzalez (Ed.), RSC Catalysis Series No. 6, Royal Society of Chemistry, **2011**, ISBN: 978-1-84973-042-6; (b) H. D. Velazquez, F. Verpoort, *Chem. Soc. Rev.* **2012**, *41*, 7032-7060; (c) F. Wang, L.-j. Liu, W. Wang, S. Li, M. Shi, *Coord. Chem. Rev.* **2012**, *256*, 804-853; (d) A. Monge-Marcet, R. Pleixats, X. Cattoen, M. W. C. Man, *Catal. Sci. Technol.* **2011**, *1*, 1544-1563; (e) G. C. Fortman, S. P. Nolan, *Chem. Soc. Rev.* **2011**, *40*, 5151-5169; (f) M. Asay, C. Jones, M. Driess, *Chem. Rev.* **2011**, *111*, 354-396; (g) O. Schuster, L. Yang, H. G. Raubenheimer, M. Albrecht, *Chem. Rev.* **2009**, *109*, 3445-3478; (h) M. Poyatos, J. A. Mata, E. Peris, *Chem. Rev.* **2009**, *109*, 3677-3707; (i) R. Corberan, E. Mas-Marza, E. Peris, *Eur. J. Inorg. Chem.* **2009**, 1700-1716; (j) S. Diez-Gonzalez, N. Marion, S. P. Nolan, *Chem. Rev.* **2009**, *109*, 3612-3676; (k) J. M. Praetorius, C. M. Crudden, *Dalton Trans.* **2008**, 4079-4094; (l) N. Marion, S. P. Nolan, *Chem. Soc. Rev.* **2008**, *37*, 1776-1782; (m) S. T. Liddle, I. S. Edworthy, P. L. Arnold, *Chem. Soc. Rev.* **2007**, *36*, 1732-1744.

4. For some reviews on organocatalysis based on N-heterocyclic carbenes, see: (a) X. Bugaut, F. Glorius, *Chem. Soc. Rev.* **2012**, *41*, 3511-3522; (b) P. H.-Y. Cheong, C. Y. Legault, J. M. Um, N. Celebi-Ölcum, K. N. Houk, *Chem. Rev.* **2011**, *111*, 5042-5137.
5. Some selected reviews on ionic liquids, see: (a) T. D. Ho, C. Zhang, L. W. Hantao, J. L. Anderson, *Anal. Chem.* **2014**, *86*, 262-285; (b) Y. Y. Dai, J. van Spronsen, G.-J. Witkamp, R. Verpoorte, Y. H. J. Choi, *Nat. Prod.* **2013**, *76*, 2162-2173; (c) X. Sun, H. Luo, S. Dai, *Chem. Rev.* **2012**, *112*, 2100-2128; (d) J. P. Hallett, T. Welton, *Chem. Rev.* **2011**, *111*, 3508-3576; (e) M. A. P. Martins, C. P. Frizzo, D. N. Moreira, N. Zanatta, H. G. Bonacorso, *Chem. Rev.* **2008**, *108*, 2015-2050.
6. For some selected reviews on synthesis of functionalized imidazoles, see: (a) F. Bellina, R. Rossi, *Adv. Synth. Catal.* **2010**, *352*, 1223-1276; (b) F. Bellina, S. Cauteruccio, R. Rossi, *Tetrahedron* **2007**, *63*, 4571-4624; (c) S. Kamijo, Y. Yamamoto, *Chem. Asian J.* **2007**, *2*, 568-578; (d) H. Du, Y. He, S. Rasapalli, C. J. Lovely, *Synlett* **2006**, 965-1002.
7. For selected reviews on cross-coupling reactions, see: (a) R. A. D. Arancon, C. S. K. Lin, C. Vargas, R. Luque, *Org. Biomol. Chem.* **2014**, *12*, 10-35; (b) J. Bariwal, E. Van der Eycken, *Chem. Soc. Rev.* **2013**, *42*, 9283-9303; (c) H. Li, C. C. C. J. Seechurn, T. J. Colacot, *ACS Catal.* **2012**, *2*, 1147-1164; (d) W. Shi, C. Liu, A. Lei, *Chem. Soc. Rev.* **2011**, *40*, 2761-2776; (e) I. P. Beletskaya, V. P. Ananikov, *Chem. Rev.* **2011**, *111*, 1596-1636; (f) J. Magano, J. R. Dunetz, *Chem. Rev.* **2011**, *111*, 2177-2250; (g) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg, V. Percec, *Chem. Rev.* **2011**, *111*, 1346-1416; (h) D. Mc Cartney, P. J. Guiry, *Chem. Soc. Rev.* **2011**, *40*, 5122-5150; (i) V. F. Slagt, A. H. M. de Vries, J. G. de Vries, R. M. Kellogg, *Org. Process Res. Dev.* **2010**, *14*, 30-47; (j) L. Xue, Z. Lin, *Chem. Soc. Rev.* **2010**, *39*, 1692-1705; (k) M. Schnürch, R. Flasik, A. F. Khan, M. Spina, M. D. Mihovilovic, P. Stanetty, *Eur. J. Org. Chem.* **2006**, 3283-3307.
8. For comprehensive books on C-H activation, see: (a) *Catalyzed Carbon-Heteroatom Bond Formation*, A. K. Yudin (Ed.), WILEY-VCH, **2011**, ISBN: 978-3-527-32428-6; (b) *C-H Activation*, J.-Q. Yu and Z. Shi (Ed.), Springer Heidelberg Dordrecht London New York, **2010**; (c) *Modern Arylation Methods*, L. Ackermann (Ed.), WILEY-VCH, **2009**, ISBN: 978-3-527-31937-4; (d) *Handbook of C–H Transformations*, G. Dyker (Ed.), Vol. *1-2*, WILEY-VCH, **2005**, ISBN: 3-527-31074-6; (e) *Activation of Unreactive Bonds and Organic Synthesis*, S. Murai (Ed.), Topics in Organometallic Chemistry, Vol. *3*, Springer-Verlag Berlin Heidelberg **1999**.
9. For some selected reviews on practical application of C-H activation reactions, see: (a) H. Schçnherr, T. Cernak, *Angew. Chem. Int. Ed.* **2013**, *52*, 12256-12267; (b) L. G. Mercier, M. Leclerc, *Acc. Chem. Res.* **2013**, *46*, 1597-1605; (c) K. Okamoto, J. Zhang, J. B. Housekeeper, S. R. Marder, C. K. Luscombe, *Macromolecules* **2013**, *46*, 8059-8078; (d) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009; (e) D. Y.-K. Chen, S. W. Youn, *Chem. Eur. J.* **2012**, *18*, 9452-9474; (f) W. R. Gutekunst, P. S. Baran, *Chem. Soc. Rev.* **2011**, *40*, 1976-1991; (g) M. Pitie, G. Pratvie, *Chem. Rev.* **2010**, *110*, 1018-1059; (h) R. Giri, B.-F. Shi, K. M. Engle, N. Maugel, J.-Q. Yu, *Chem. Soc. Rev.* **2009**, *38*, 3242-3272.
10. For selected reviews on heteroatom directed C-H activation, see: (a) B. Butschke, H. Schwarz, *Chem. Sci.* **2012**, *3*, 308-326; (b) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879-5918; (c) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788-802; (d) T. Brückl, R. D. Baxter, Y. Ishihara, P. S. Baran, *Acc. Chem. Res.* **2012**, *45*, 826-839; (e) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2012**, *45*, 814-825; (f) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215-1292; (g) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212-11222; (h) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147-1169; (i) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624-655; (j) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074-1086; (k) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174-238.
11. For reviews on usage of removable and/or manipulable directing groups on C-H activation, see: (a) C. Wang, Y. Huang, *Synlett* **2013**, *24*, 145-149; (b) G. Rousseau, B. Breit, *Angew. Chem. Int. Ed.* **2011**, *50*, 2450-2494.

12. For examples of C-H activation directed by oxidizing directing groups, see: (a) S.-C. Chuang, P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2013**, *15*, 5750-5753; (b) C. Wang, Y. Huang, *Org. Lett.* **2013**, *15*, 5294-5297; (c) B. Liu, C. Song, C. Sun, S. Zhou, J. Zhu, *J. Am. Chem. Soc.* **2013**, *135*, 16625-16631; (d) L. Zheng, J. Ju, Y. Bin, R. Hua, *J. Org. Chem.* **2012**, *77*, 5794-5800; (e) B. Li, J. Ma, N. Wang, H. Feng, S. Xu, B. Wang, *Org. Lett.* **2012**, *14*, 736-739; (f) R. K. Chinnagolla, S. Pimparkar, M. Jeganmohan, *Org. Lett.* **2012**, *14*, 3032-3035; (g) F. W. Patureau, F. Glorius, *Angew. Chem. Int. Ed.* **2011**, *50*, 1977-1979; (h) T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 11846-11848; (i) L. Ackermann, S. Fenner, *Org. Lett.* **2011**, *13*, 6548-6551; (j) B. Li, H. Feng, S. Xu, B. Wang, *Chem. Eur. J.* **2011**, *17*, 12573-12577; (k) Y. Tan, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 3676-3677; (l) N. Guimond, C. Gouliaras, K. Fagnou, *J. Am. Chem. Soc*. **2010**, *132*, 6908-6909; (m) K. Parthasarathy, C.-H. Cheng, *J. Org. Chem.* **2009**, *74*, 9359-9364; (n) K. Parthasarathy, M. Jeganmohan, C.-H. Cheng, *Org. Lett.* **2008**, *10*, 325-328.

13. For selected examples of C-H activation directed by removable directing groups, see: (a) A. Garcia-Rubia, M. A. Fernandez-Ibaez, R. G. Arrays, J. C. Carretero, *Chem. Eur. J.* **2011**, *17*, 3567-3570; (b) W. Ma, L. Ackermann, *Chem. Eur. J.* **2013**, *19*, 13925-13928; (c) X. Cong, J. You, G. Gao, J. Lan, *Chem. Commun.* **2013**, *49*, 662-664; (d) J. Yao, M. Yu, Y. Zhang, *Adv. Synth. Catal.* **2012**, *354*, 3205-3210; (e) C. Huang, N. Chernyak, A. S. Dudnik, V. Gevorgyan, *Adv. Synth. Catal.* **2011**, *353*, 1285-1305; (f) N. Chernyak, A. S. Dudnik, C. Huang, V. Gevorgyan, *J. Am. Chem. Soc.* **2010**, *132*, 8270-8272; (g) A. S. Dudnik, N. Chernyak, C. Huang, V. Gevorgyan, *Angew. Chem. Int. Ed.* **2010**, *49*, 8729-8732; (h) T. Truong, O. Daugulis, *Angew. Chem. Int. Ed.* **2012**, *51*, 11677-11679; (i) C. Wang, H. Chen, Z. Wang, J. Chen, Y. Huang, *Angew. Chem. Int. Ed.* **2012**, *51*, 7242-7245; (j) C. Huang, B. Chattopadhyay, V. Gevorgyan, *J. Am. Chem. Soc.* **2011**, *133*, 12406-12409; (k) J. Cornella, M. Righi, I. Larrosa, *Angew. Chem. Int. Ed.* **2011**, *50*, 9429-9432.

14. For examples of cyclometalation directed by nitro group, see: (a) M. Puri, S. Gatard, D. A. Smith, O. V. Ozerov, *Organometallics* **2011**, *30*, 2472-2482; (b) X. Zhang, M. Kanzelberger, T. J. Emge, A. S. Goldman, *J. Am. Chem. Soc.* **2004**, *126*, 13192-13193.

15. For comprehensive books on chemistry of nitro group, see: (a) *The Nitro Group In Organic Synthesis*, N. Ono (Ed.), WILEY-VCH, **2001**, ISBN: 0-471-31611-3; (b) *Nitroazoles: Synthesis, Structure and Applications*, L. Larina and V. Lopyrev, Springer Science, **2009**, ISBN: 978-0-387-98069-0.

16. (a) L. Caron, L.-C. Campeau, K. Fagnou, *Org. Lett.* **2008**, *10*, 4533-4536; (b) P. Guo, J. M. Joo, S. Rakshit, D. Sames, *J. Am. Chem. Soc.* **2011**, *133*, 16338-16341.

17. (a) V. O. Iaroshenko, A. Gevorgyan, O. Davydova, A. Villinger, P. Langer, *J. Org. Chem.* **2014**, *79*, 2906-2915; (b) V. O. Iaroshenko, A. Gevorgyan, S. Mkrtchyan, T. Grigoryan, E. Movsisyan, A. Villinger, P. Langer, *ChemCatChem* **2015**, *7*, 316-324.

18. (a) V. O. Iaroshenko, D. Ostrovskyi, M. Milyutina, A. Maalik, A. Villinger, A. Tolmachev, D. M. Volochnyuk, P. Langer, *Adv. Synth. Catal.* **2012**, 2495-2503; (b) V. O. Iaroshenko, I. Ali, S. Mkrtchyan, V. Semeniuchenko, D. Ostrovskyi, P. Langer, *Synlett* **2012***, 23,* 2603-2608.

19. For selected reviews on dehydrogenative twofold C-H cross-coupling reactions, see: (a) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236-10254; (b) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; (c) X. Bugaut, F. Glorius, *Angew. Chem. Int. Ed.* **2011**, *50*, 7479-7481; (d) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215-1292; (e) J. A. Ashenhurst, *Chem. Soc. Rev.* **2010**, *39*, 540-548.

20. For an advanced review on theoretically calculated CMD activation barriers of C-H bond on a wide range of heterocycles, see: (a) S. I. Gorelsky, *Coord. Chem. Rev.* **2013**, *257*, 153-164; see also: (b) S. I. Gorelsky, *Organometallics* **2012**, *31*, 794-797.

21. Aminoimidazoles are rather unstable compounds, though they can be prepared *in situ* for further subsequent transformations. For some selected examples, see: (a) V. O. Iaroshenko, M. Vilches-Herrera, A. Gevorgyan, S. Mkrtchyan, K. Arakelyan, D. Ostrovskyi, M. S. A.

Abbasi, L. Supe, A. Hakobyan, A. Villinger, D. M. Volochnyuk, A. Tolmachev, *Tetrahedron* **2013**, *69*, 1217-1228; (b) D. Ostrovskyi, V. O. Iaroshenko, I. Ali, S. Mkrtchyan, A. Villinger, A. Tolmachev, P. Langer, *Synthesis* **2011**, *1*, 133-141; (c) V. O. Iaroshenko, D. Ostrovskyi, A. Petrosyan, S. Mkrtchyan, A. Villinger, P. Langer, *J. Org. Chem.* **2011**, *76*, 2899-2903; (d) V. O. Iaroshenko, A. Maalik, D. Ostrovskyi, A. Villinger, A. Spannenberg, P. Langer, *Tetrahedron* **2011**, *67*, 8321-8330; (e) V. O. Iaroshenko, V. Specowius, K. Vlach, M. Vilches-Herrera, D. Ostrovskyi, S. Mkrtchyan, A. Villinger, P. Langer, *Tetrahedron* **2011**, *67*, 5663-5677; (f) D. Ostrovskyi, V. O. Iaroshenko, A. Petrosyan, S. Dudkin, I. Ali, A. Villinger, A. Tolmachev, P. Langer, *Synlett* **2010**, *15*, 2299-2303; (g) V. O. Iaroshenko, *Synthesis* **2009**, *23*, 3967-3974.

22. X-Ray Crystallographic data (excluding structure factors) for the structure **3g**, **4d**,**t**, **5b**, **7a**,**c**, **10a** and **12a** (**4g**) reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. 1033372-1033379 can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk, or *via* www.ccdc.cam.ac.uk/data_request/cif.
23. J. Huang, J. Chan, Y. Chen, C. J. Borths, K. D. Baucom, R. D. Larsen, M. M. Faul, *J. Am. Chem. Soc.* **2010**, *132*, 3674-3675.
24. For some examples of polinuclear C-H activation, see: with Ru-Ru system (a) J. A. Cabeza, M. Damonte, P. Garcia-Alvarez, M. G. Hernandez-Cruz, A. R. Kennedy, *Organometallics* **2012**, *31*, 327-334; (b) T. Fukuyama, N. Chatani, J. Tatsumi, F. Kakiuchi, S. Murai, *J. Am. Chem. Soc.* **1998**, *120*, 11522-11523; (c) T. Takao, M. Moriya, M. Kajigaya, H. Suzuki, *Organometallics* **2010**, *29*, 4770-4773; (d) J. A. Cabeza, M. Damonte, P. Garcia-Alvarez, *Organometallics* **2011**, *30*, 2371-2376; (e) S. K. Patra, J. K. Bera, *Organometallics* **2006**, *25*, 6054-6060; (f) A. Sinha, M. Majumdar, M. Sarkar, T. Ghatak, J. K. Bera, *Organometallics* **2013**, *32*, 340-349; (g) T. Kawashima, T. Takao, H. Suzuki, *J. Am. Chem. Soc.* **2007**, *129*, 11006-11007; with Ru-Cu system (h) M.-L. Louillat, F. W. Patureau, *Org. Lett.* **2013**, *15*, 164-167; with Ru-Ln system (i) A. P. Sobaczynski, T. Bauer, R. Kempe, *Organometallics* **2013**, *32*, 1363-1369; with Rh-Rh system (j) J. Lloret, K. Bieger, F. Estevan, P. Lahuerta, P. Hirva, J. Perez-Prieto, M. Sanau, *Organometallics* **2006**, *25*, 5113-5121; (k) J. Kwak, M. Kim, S. Chang, *J. Am. Chem. Soc.* **2011**, *133*, 3780-3783; with Pd-Pd system (l) M. Sarkar, H. Doucet, J. K. Bera, *Chem. Commun.* **2013**, *49*, 9764-9766; (m) C. Reitsamer, W. Schuh, H. Kopacka, K. Wurst, E. P. Ellmerer, P. Peringer, *Organometallics* **2011**, *30*, 4220-4223; (n) D. C. Powers, T. Ritter, *Acc. Chem. Res.* **2012**, *45*, 840-850; with Os-Os system (o) M. A. Mottalib, N. Begum, S. M. T. Abedin, T. Akter, S. E. Kabir, M. A. Miah, *Organometallics* **2005**, *24*, 4747-4759; (p) S. E. Kabir, M. A. Miah, N. C. Sarker, G. M. G. Hussain, K. I. Hardcastle, E. Nordlander, E. Rosenberg, *Organometallics* **2005**, *24*, 3315-3320; with Ir-Ir system (q) Y. Yuan, M. V. Jimenez, E. Sola, F. J. Lahoz, L. A. Oro, *J. Am. Chem. Soc.* **2002**, *124*, 752-753; (r) K.-i. Fujita, H. Nakaguma, T. Hamada, R. Yamaguchi, *J. Am. Chem. Soc.* **2003**, *125*, 12368-12369; (s) W. Yang, S. Zhang, Y. Ding, L. Shi, Q. Song, *Chem. Commun.* **2011**, *47*, 5310-5312; with Au-Ag system (t) X.-L. Pei, Y. Yang, Z. Lei, Q.-M. Wang, *J. Am. Chem. Soc.* **2013**, *135*, 6435-6437.
25. (a) F. Shibahara, E. Yamaguchi, T. Murai, *J. Org. Chem.* **2011**, *76*, 2680-2693; (b) J. M. Joo, B. B. Toure, D. Sames, *J. Org. Chem.* **2010**, *75*, 4911-4920.
26. Q. Lu, H. Yu, Y. Fu, *Chem. Commun.* **2013**, *49*, 10847-10849.