DOI: 10.1002/adsc.201600173

Advanced Synthesis & Catalysis

Very Important Publication

Palladium-Catalyzed One-Pot Synthesis of 5-(1-Arylvinyl)-1*H*-benzimidazoles: Overcoming the Limitation of Acetamide Partners

Timothée Naret,[a] Pascal Retailleau,[b] Jérôme Bignon,[b] Jean-Daniel Brion,[a] Mouad Alami,[a,*] and Abdallah Hamze[a,*]

[a] Univ. Paris-Sud, CNRS, BioCIS-UMR 8076, Laboratoire de Chimie Thérapeutique, Equipe Labellisée Ligue Contre Le Cancer, LabEx LERMIT, Faculté de Pharmacie, 5 rue J.-B. Clément, 92296 Châtenay-Malabry, France
Fax: (+33)-1-46835828; Phone: (+33)-1-46835498; e-mail: mouad.alami@u-psud.fr or abdallah.hamze@u-psud.fr

[b] Laboratoire des Institut de Chimie des Substances Naturelles, UPR 2301, CNRS, Avenue de la Terrasse, 91198 Gif-sur-Yvette, France

Received: February 10, 2016; Revised: March 25, 2016; Published online: May 25, 2016

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201600173.

Abstract: A new one-pot palladium-catalyzed process between *N*-tosylhydrazones, *N*-(dihalophenyl)-imidates, and amines was designed. This reaction involves Barluenga cross-coupling and *N*-arylation followed by cyclization to produce functionalized benzimidazoles. During this transformation, one C–C bond and two C–N bonds were created by a single palladium-catalyzed reaction. Depending on the starting materials, a library of 5-(1-arylvinyl)-1*H*-benzimidazoles was synthesized. Among several arylvinylbenzimidazole derivatives evaluated, one compound exhibits excellent antiproliferative activity in the nanomolar concentration range against human colon carcinoma cell lines (HCT-116) and human lung adenocarcinoma epithelial cell lines (A549).

Keywords: benzimidazoles; hydrazones; olefination; one-pot reaction; palladium

Introduction

In search of new biologically active molecules, the incorporation of heterocycles appears as a priority. Among the multitude of known heterocyclic compounds, benzimidazole is a privileged structure and essential building block used in medicinal chemistry. It belongs to the top five most commonly used heterocycles in medicinal chemistry. Benzimidazoles are found in 13 FDA approved pharmaceuticals,[1] among them, a proton-pump inhibitor (esomeprazole), an angiotensin II receptor antagonist (candesartan), and an oral anticoagulant from the class of the direct thrombin inhibitors (dabigatran).[2]

Cancer is one of the major health challenges of the 21st century.[3] Among the developed strategies used to counter this disease, the search of new molecules with a novel mechanism of action is very desirable. In this direction, Pettit and co-workers discovered a natural compound, the combretastatin A-4 (CA-4), which presents a powerful activity against cancer.[4] This product disrupts the polymerization of tubulin and opens the way to a new therapeutic class, vascular disrupting agents.[5] Despite the great potential of this drug it suffers from some drawbacks. In particular, CA-4 presents chemical instability, leading to the inactive *trans*-isomer.[6] In our efforts to discover non-isomerizable CA-4 analogues,[7] we recently synthesized a series of 1,1-diarylethylene derivatives among which *iso*CA-4,[8] has emerged as a lead compound. This last compound has the particular feature of possessing a 1,1-diarylethylene scaffold, which exhibits the same cytotoxic properties as the CA-4, but without the stability problem due to the isomerization of the natural compound CA-4. In the aim of obtaining a novel type of potent cytotoxic agents, and increase the chemical diversity of our active compounds library in order to go further toward clinical development, we planned to associate the benzimidazole nucleus with a 1,1-disubstituted ethylene link.

Today, there is a growing interest in developing efficient chemical processes. In this context, a one-pot reaction in which three or more bonds are formed in a single vessel to obtain a final product is very desirable. This involves, among other advantages, important energy, time, and materials savings. As an attractive synthetic route, metal-catalyzed reactions by using *N*-tosylhydrazone reagents constitute a powerful method

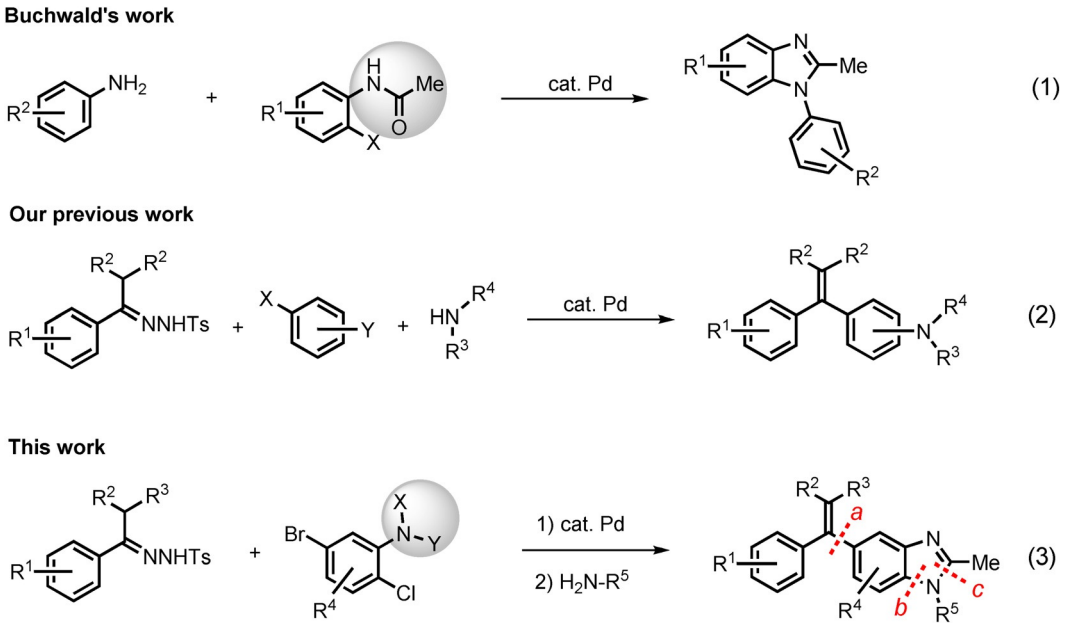
for C–C and C–N bond formation.[9] The synthetic method developed by Barluenga and co-workers[10] provides access to polysubstituted olefins,[11] allenes,[12] and substituted amines.[13] This method can be used for ring closing[14] and formation of other C–heteroatom bonds.[15] Despite these achievements, continuous effort is required, especially for the generation of versatile, and potential synthetic procedures to achieve complex molecules and libraries. In this way, the development of new methods to synthesize complex molecules containing benzimidazoles with remarkable biological activity using *N*-tosylhydrazones chemistry becomes a priority.

Recently, Buchwald and co-workers developed an interesting method employing $Pd_2(dba)_3$ and XPhos which permits the efficient synthesis of *N*-arylbenzimidazoles from starting *ortho*-haloanilides [Scheme 1, Eq. (1)].[16] On the other hand, a few catalytic systems based on a Pd carbene migratory insertion process with other coupling reactions have been reported for the construction of cyclic architectures.[17] Very recently, we developed a catalytic three-component one-pot reaction of hydrazones, dihaloarenes, and amines [Eq. (2)].[18] We hypothesized that *ortho*-haloanilides could be an appropriate substrate in which a combination of C–C [Eq. (3), ***a***], C–N [Eq. (3), ***b***], and N–C [Eq. (3), ***c***] bond forming reactions may be applied for the synthesis of elaborated arylvinylbenzimidazole derivatives. At first glance, this transformation seems to be a simple combination of conditions used in Eqs. (1) and (2). However, in this work, we will see that the elaboration of one-pot conditions still represents a big challenge. Here we report the process which led to the discovery and validation of our synthetic tool [Eq. (3)].

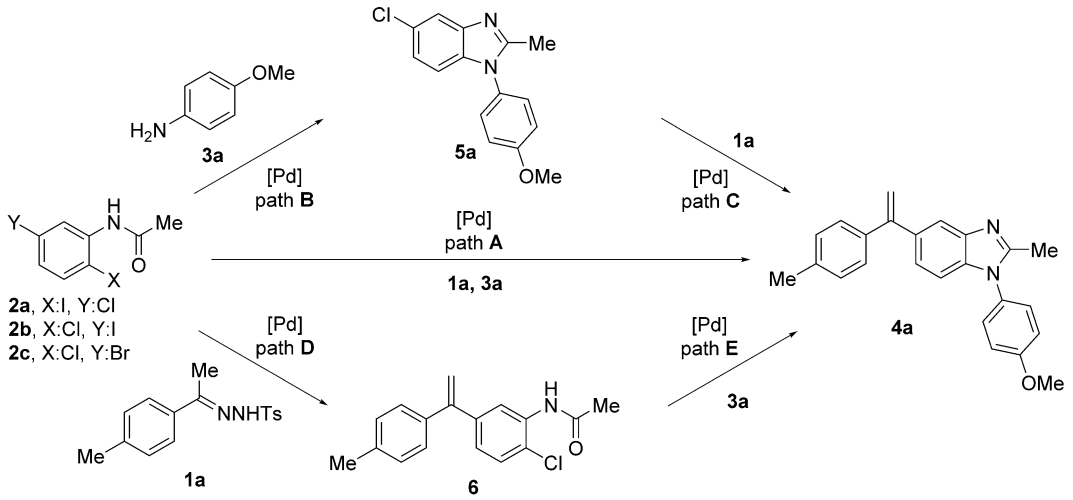
Results and Discussion

First, we investigated the one-pot synthesis of 5-(1-arylvinyl)-1*H*-benzoimidazole (Scheme 2, path A), by using a model reaction, from *N*-tosylhydrazone **1a** (1.2 equiv.), *N*-(2-chloro-5-iodophenyl)-acetamide **2a** (1.0 equiv.) and *p*-anisidine **3a** (1.2 equiv.). In the beginning of this work, we used conditions close to those of the protocol described by Buchwald and in our previous work [Eq. (2)]: $Pd_2(dba)_3{\cdot}CHCl_3$, XPhos, LiO-*t*-Bu in dioxane. Under these conditions, no trace of compound **4a** was observed, instead, we observed mainly the formation of the Bamford–Stevens by-product due to the degradation of *N*-tosylhydrazone.[19] To get some insight of what is going on, we decided to run the two steps of this one-pot reaction separately. Firstly, the formation of benzimidazole **5a** from *ortho*-haloanilide **2b** and *p*-anisidine **3a** was studied (Scheme 2, path B). A screening of the reaction conditions was realized (Table 1S, in the Supporting Information). As a result, the precatalyst G3-Pd-XPhos was more efficient than $Pd_2(dba)_3{\cdot}CHCl_3$, K_3PO_4 gave the best yield of **5a**, in comparison with LiO-*t*-Bu and NaO-*t*-Bu as a base. Among many tested solvents, *t*-BuOH was found as an appropriate choice as a solvent for this coupling, and **5a** was obtained in 70% yield.

Next, we turned our effort to the second coupling between benzimidazole derivative **5a** and hydrazone **1a** (Scheme 2, path C). We started our essay by using the optimal conditions for the first coupling: G3-Pd-XPhos, XPhos, and K_3PO_4 in *t*-BuOH. Unfortunately, after 12 h, a poor 22% yield of **4a** was obtained (Table 2S, in the Supporting Information). In view of this result, several conditions were tested, and the



Scheme 1. Catalytic approaches for building Csp^2–Csp^2 and Csp^2–N bonds.



Scheme 2. Different strategies used for the formation of arylvinyl-benzimidazole derivatives **4**.

best yield was obtained with $Pd_2(dba)_3{\cdot}CHCl_3$, XPhos, LiO-*t*-Bu in dioxane. As a conclusion, if *t*-BuOH constitutes the optimal solvent for the first coupling, it is not suitable for the second coupling. This result is not surprising since Barluenga and co-workers have demonstrated that the basic metal-free C–O bond forming reaction proceeds through decomposition of hydrazones in the presence of alcohols, and results in the insertion reaction of the carbene into the OH bond.[20]

In the framework of this separate study, we decided to inverse the order of coupling partners to find a better solvent, suitable for both coupling reactions (Scheme 2, path D). The coupling between hydrazone **1a** and *ortho*-haloanilides **2a** or **2c** can be performed effectively under several conditions: many sources of bases can be used including K_3PO_4, LiO-*t*-Bu, and NaO-*t*-Bu in dioxane or fluorobenzene as the solvent. The cross-coupling product was synthesized with an excellent yield >90% (Table 3S, in the Supporting Information). The best conditions found for this step were tested for the coupling between compound **6** and *p*-anisidine **3a** (Scheme 2, path E). Unfortunately, none of these new conditions afforded the desired product efficiently and, in the best case, the desired product **4a** was obtained with a low 19% yield (Table 4S, in the Supporting Information).

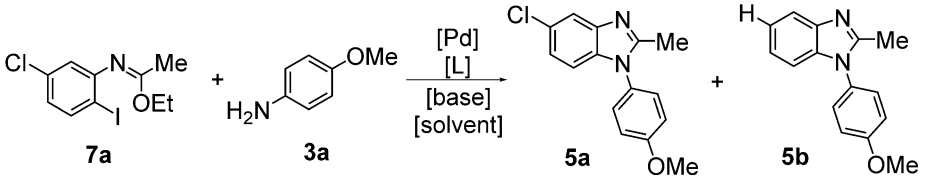
Following these attempts, it seems that the *ortho*-haloanilide partner is not suitable for the one-pot synthesis of arylvinylbenzimidazoles **4**. Screening experiments revealed that *t*-BuOH and K_3PO_4 constitute the optimal combination of solvent and base for the synthesis of *N*-arylbenzimidazoles from *ortho*-haloanilides. On the other hand, *t*-BuOH was found to be inefficient as a solvent for the coupling between hydrazone and aryl halide derivative, consequently, this makes impractical the realization of the one-pot reaction. This incompatibility of solvents pushes us to change drastically our strategy for the development of this one-pot reaction and to find other suitable electrophilic partners for the coupling with hydrazone.

Recently, the group of Willis and co-workers developed a Pd-catalyzed synthesis of benzimidazoles from the corresponding imidates.[21] We envisaged that imidates **7** could be used to synthesize arylvinylbenzimidazole derivatives in a one-pot fashion. Accordingly, we studied first the benzimidazole synthesis from the model imidate **7a** (Table 1). The reaction of imidate **7a** in the presence of $Pd(OAc)_2$ and DavePhos with NaO-*t*-Bu as base and toluene afforded a low yield of benzimidazole **5a** (entry 1). Increasing the reaction temperature from 120 to 130 °C slightly increases the yield of product **5a** (entry 2) but we observed the formation of by-product **5b** resulting from dehalogenation of benzimidazole **5a**. The use of $Pd_2(dba)_3{\cdot}CHCl_3$ instead of $Pd(OAc)_2$ leads to a total conversion of imidate **7a** (entry 4). DavePhos was found to be more efficient as ligand than XPhos for this coupling (entries 4 and 5). Subsequently, a range of bases, such as K_3PO_4, Cs_2CO_3, and LiO-*t*-Bu was examined.

Among the studied bases, LiO-*t*-Bu produced the highest yield of **5a** and reduced significantly the amount of by-product **5b** (Table 1, entries 5–8). Decreasing the amount of the amine **3a** gave the product **5a** in a high yield (entries 9 and 10).

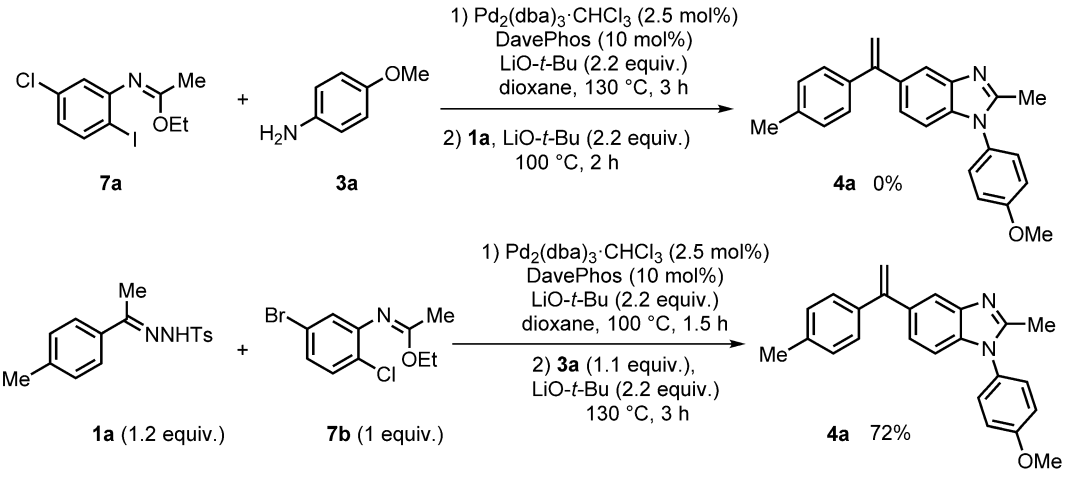
After optimization of the reaction conditions for the benzimidazole formation (**5a**), next, we tried to study the one-pot experiment, as mentioned in Scheme 3, after the coupling between imidate **7a** and *p*-anisidine **3a** for 3 h, hydrazone **1a**, and LiO-*t*-Bu were added and the reaction was continued for 2 additional hours. Again, to our great regret, the second coupling was unsuccessful, since no traces of arylvinylbenzimidazole **4** were isolated. One possible explanation of this result can be due to the formation of

Table 1. Optimization of the reaction conditions for Pd-catalyzed amination of imidates.[a]



Entry	[Pd]	[L]	Base	Solvent	Yield **5a**/**5b**
1	$Pd(OAc)_2$	DavePhos	NaO-*t*-Bu	toluene	11/0[b]
2	$Pd(OAc)_2$	DavePhos	NaO-*t*-Bu	toluene	31/10
3	$Pd(OAc)_2$	DavePhos	NaO-*t*-Bu	dioxane	9/42
4	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	NaO-*t*-Bu	dioxane	32/65
5	$Pd_2(dba)_3{\cdot}CHCl_3$	XPhos	NaO-*t*-Bu	dioxane	19/26
6	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	K_3PO_4	dioxane	60/18
7	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	Cs_2CO_3	dioxane	63/22
8	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	LiO-*t*-Bu	dioxane	68/15
9	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	LiO-*t*-Bu	dioxane	71/10[c]
10	$Pd_2(dba)_3{\cdot}CHCl_3$	DavePhos	LiO-*t*-Bu	dioxane	85/8[d]

[a] *Reaction onditions:* imidate **7a** (0.5 mmol), *p*-anisidine **3a** (0.75 mmol), [Pd] source (5 mol%), ligand (10 mol%), base (1.1 mmol), solvent (2.0 mL), sealed tube, 130 °C, 3 h.
[b] Reaction was performed at 120 °C.
[c] **3a** (1.3 equiv).
[d] **3a** (1.1 equiv.).



Scheme 3. One-pot reaction optimization.

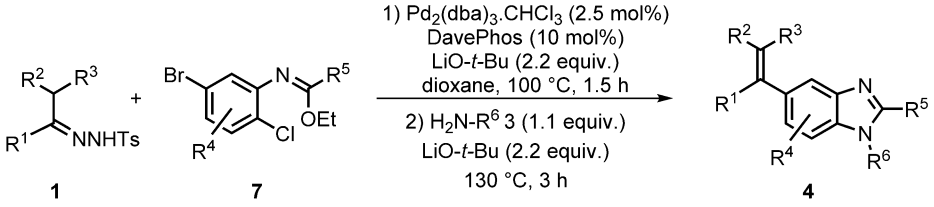
t-BuOH after the first coupling between imidate **7a** and aniline **3a**, which competes directly with the electrophile **5a** during the coupling with the hydrazone **1a**.[20]

At this stage, we still have a last possibility, which consists in carrying out the coupling first between the hydrazone **1a** and imidate **7b**, followed by formation of the benzimidazole in the second step (Scheme 3, *bottom part*). Finally, we are pleased that this last path constitutes the best way to obtain the arylvinylbenzimidazole **5a** in a one-pot fashion and in a good overall yield of 72%. This represents an average of ~90% yield for each step.

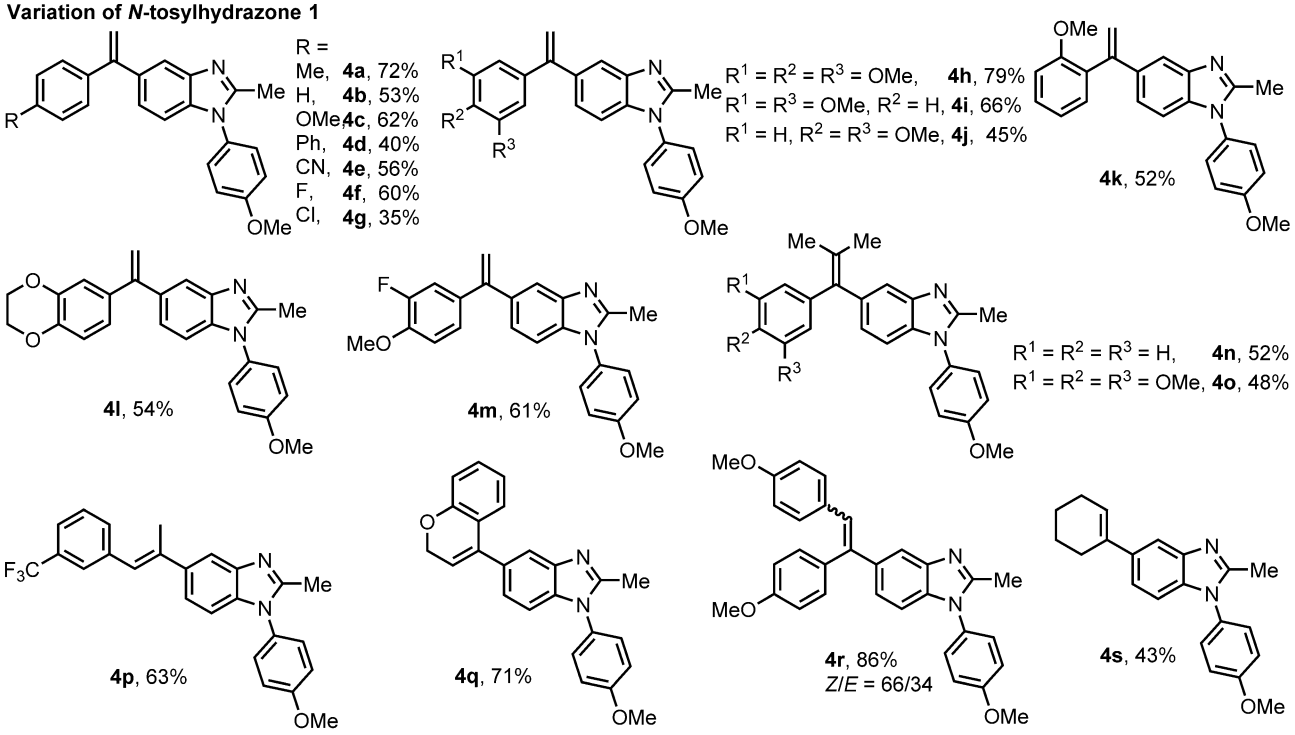
Scale up of this coupling was also realized with optimized conditions with 1 g (3.3 mmol) of hydrazone **1a** and a 65% yield was isolated (634 mg, 1.80 mmol).

Using the established optimized conditions, we subsequently examined the scope of the one-pot reaction. First, various *N*-tosylhydrazones were employed with imidate **7b** and amine **3a**. As presented in Table 2, the reaction could be carried out with an array of *N*-tosylhydrazones derived from acetophenones, phenylpro-

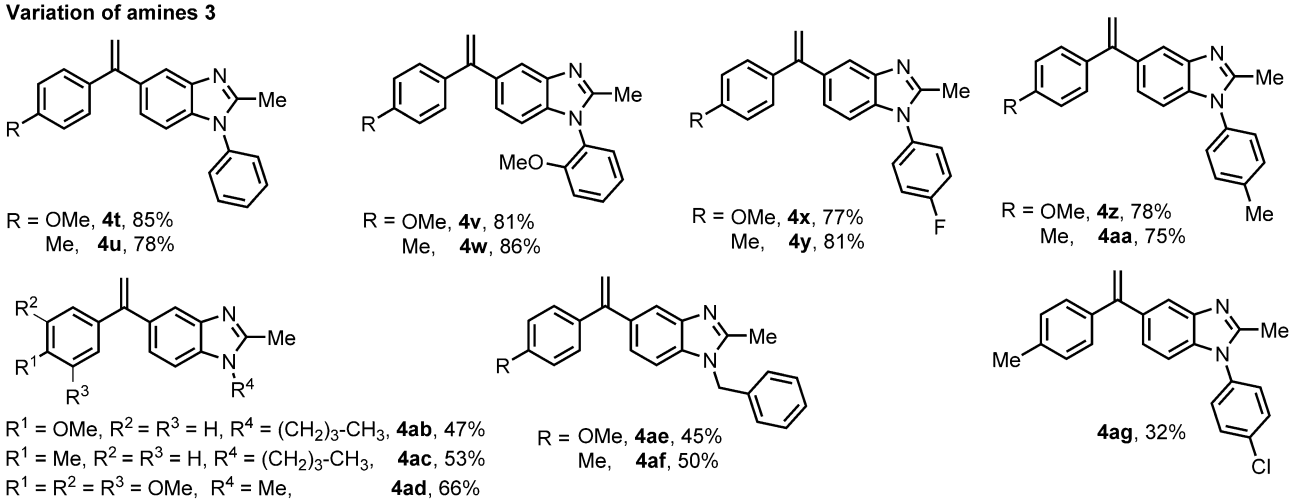
Table 2. Palladium-catalyzed one-pot synthesis of arylvinylbenzimidazoles from imidates **7**.[a]



Variation of *N*-tosylhydrazone 1



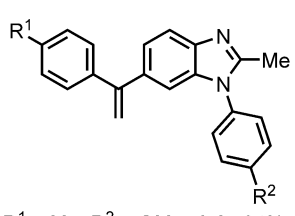
Variation of amines 3



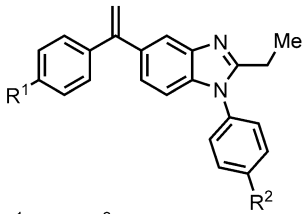
panones, chromanones, diphenylethanones and cyclohexanones (**4a–s**). The reaction in general afforded the corresponding products in moderate to good yields. The reaction was globally unaffected by electronic effects of the substituents of hydrazones, since both hydrazones containing electron-withdrawing and electron-donating groups were coupled efficiently (**4a**, **4e–g**, and **4p**). The reactions with *para*-, *meta*-, and *ortho*-substituted hydrazones all proceeded efficiently (**4a–g**, **4k**, and **4p**). In the cases where trisubstituted

Table 2 (continued)

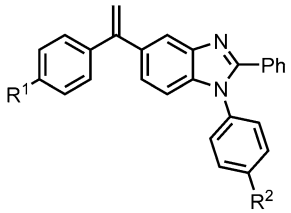
Variation of imidate 7



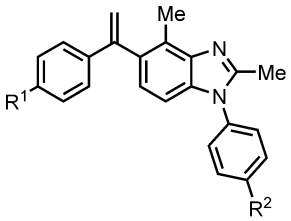
R^1 = Me, R^2 = OMe, **4ah**, 84%
R^1 = CN, R^2 = F, **4ai**, 74%



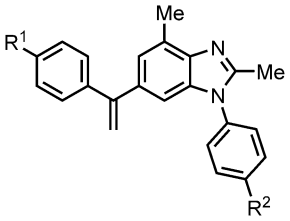
R^1 = Me, R^2 = OMe, **4aj**, 79%
R^1 = CN, R^2 = F, **4ak**, 81%



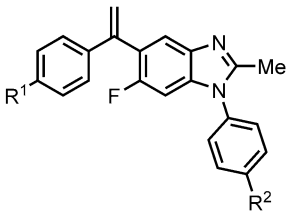
R^1 = Me, R^2 = OMe, **4al**, 65%
R^1 = CN, R^2 = F, **4am**, 71%



R^1 = Me, R^2 = OMe, **4an**, 70%
R^1 = CN, R^2 = F, **4ao**, 82%



R^1 = Me, R^2 = OMe, **4ap**, 80%
R^1 = CN, R^2 = F, **4aq**, 77%



R^1 = Me, R^2 = OMe, 4ar, 66%
R^1 = CN, R^2 = F, *4as*, 86%

[a] Yields are for the isolated products.

olefins were formed, the coupling only afforded the product with *E* selectivity (compound **4p**). However, when the steric hindrance was similar for the *E* and *Z* isomers, a mixture of the two isomers was obtained (compound **4r**, *Z*/*E* = 66/34). Interestingly, the coupling reaction is also effective even with more challenging sterically hindered hydrazones. Accordingly, the expected olefins **4n** and **4o** were obtained in moderate yields of 52% and 48%. It is noteworthy that the chloro substituent on the phenyl ring of the hydrazone was tolerated and compound **4g** was obtained in 35% yield, this will enable the realization further metal-catalyzed functionalization processes. Next we examined the efficiency of this one-pot reaction with respect to the nature of the amine. Reactions with *para*- and *ortho*-substituted anilines proceeded efficiently to form the expected products (**4v**–**4aa**) in good yields. This demonstrates that steric factors have little influence on the rate of C–N bond formation. The electronic nature of the substituents on the anilines did not have a significant effect on the reaction. Electron-donating or electron-withdrawing substrates all reacted to give the corresponding products in good yields (**4x**–**4aa**). Then, in the hope of further pushing the limits of the scope of the reaction, we examined the formation of arylvinylbenzimidazoles with aliphatic and benzylic amines. Accordingly, under our standard conditions, we found that the coupling proved to be efficient, giving rise to the desired products **4ab**–**af**, with good isolated yields. It should be noted that, in the case of alkylamines derivatives, we realized a comparative study of the reactivity between *N*-arylacetamide or *N*-arylimidate on one side, and *n*-butylamine on the other side. Thus, we performed the reaction between *N*-arylacetamide **2a** and *n*-butylamine under the reaction conditions described in Buchwald's work,[16] in this case, no trace of benzimidazole **5** was detected in the crude ^{1}H NMR. In contrast, the desired benzimidazole **5** was obtained with a moderate yield of 60% by using, *N*-arylimidate **7a** and *n*-butylamine under our coupling conditions, this proves that the imidate is a more suitable partner for the formation of benzimidazole since it tolerates both aromatic and aliphatic amines. To study the selectivity issue, we realized a coupling using our optimized conditions between *N*-tosylhrazone **1a**, imidate **7b** and 4-chloroaniline. In this case, the desired product **4ag** was isolated with 32% yield.

To broaden the substrate scope, we further investigated the potential of this one-pot reaction with respect to imidates **7**. Fortunately, as depicted in Table 2, the entire coupling proceeded cleanly and selectively in good to excellent yields.

Depending on the used imidate, the molecular diversity can be obtained easily: (i) modification of the connection position between aryl and benzimidazole ring (compounds **4ah**–**ai**), (ii) changing the methyl group (R^5) by an ethyl, or phenyl group (compounds **4aj**–**am**) and (iii) modification of the nature of the substituent (R^4) on the aromatic ring (**4an**–**as**). Finally, for the trisubstituted olefin **4p**, the *E* configuration was unambiguously confirmed by X-ray diffraction. The structure of **4a** is also presented (Figure 1, for other X-ray structures of compounds **4t**, **4ak**, **4al** and **4ao**, see the Supporting Information).[22]

To evaluate the ability of the novel arylvinylbenzimidazoles to inhibit the cellular proliferation of tumor cells, synthesized compounds (**4**) were screened

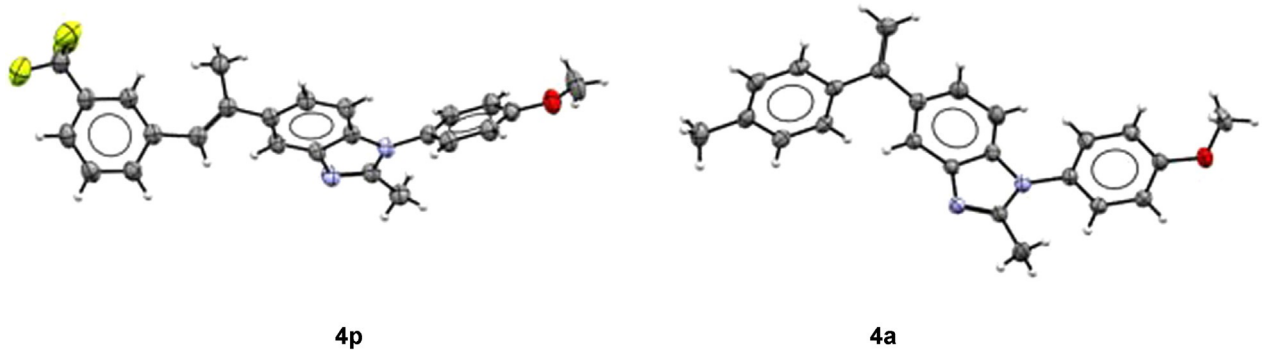


Figure 1. X-ray structures of **4p** and **4a**.

using the CellTiter-96 assay.[23] All arylvinylbenzimidazole **4** were tested at 1 μM concentration, in triplicate (Table 5, in the Supporting Information) against human colon carcinoma cell line (HCT116). Results were expressed as a percentage of cell cytotoxicity, comparing with 0.1% DMSO control. Among the tested compounds, the best results were obtained with compounds **4aj**, **4an**, and **4aq** which have percentages of cell cytotoxicity of 50%, 48%, and 98%, respectively. Following these encouraging results, a determination of IC_{50} was performed on these three molecules on HCT-116 and human lung adenocarcinoma epithelial (A549) cells. The cytotoxic activity was initially evaluated using *iso*CA-4 ($IC_{50}=2$ nM),[8b] and phenstatin ($IC_{50}=33$ nM)[24] as reference compounds. Compounds **4aj** and **4an** gave a moderate activity and inhibited the growth of HCT-116 cell line with an IC_{50} value of 2 μM and 3 μM, respectively.

The best result was obtained with compound **4aq** which retained potent growth inhibitory activity at nanomolar concentrations against both HCT-116 and A549 cancer cells, with an IC_{50} value of 30 and 35 nM, respectively. Interestingly, compound **4aq** presents an original template for further study because it is still active without the trimethoxyphenyl ring of our original lead, *iso*CA-4.

Conclusions

In conclusion, we have developed the palladium-catalyzed synthesis of a library of 5-(1-arylvinyl)-1*H*-benzimidazole derivatives. This one-pot reaction associates Barluenga cross-coupling and *N*-arylation, followed by cyclization to create one C–C bond and two C–N bonds with the same catalytic species. Through this work, we demonstrated that imidates constitute an ideal partner for the cross-coupling with hydrazones in comparison with acetamides. Our method, based on simple starting materials, tolerates various functional groups. From this new series of arylvinylbenzimidazoles, we have identified compound **4aq** which showed a remarkable nanomolar level of cytotoxicity against two human cancer cell lines. We believe that our method can be used to obtain other functionalized benzimidazoles, and will contribute to the discovery of new biologically active compounds.

Experimental Section

General Procedure for the Synthesis of 1-Aryl-5-(1-arylvinyl)-1*H*-benzimidazoles 4 from *N*-(Dihalophenyl)-imidates 7, *N*-Tosylhydrazones 1 and N-Nucleophiles 3

A 6-mL microwave tube containing a stir bar was charged with *N*-(dihalophenyl)-imidate (0.5 mmol, 1.0 equiv.), *N*-tosylhydrazone (0.6 mmol, 1.2 equiv.), $Pd_2dba_3{\cdot}CHCl_3$ (13 mg, 2.5 mol%), DavePhos (20 mg, 10 mol%) and lithium *tert*-butoxide (88 mg, 1.1 mmol, 2.2 equiv.). The tube was capped and purged with argon three times, then distilled dioxane was added *via* syringe. After sealing the tube, it was put into a pre-heated oil bath at 100 °C and stirred for 1.5 h. Then, the tube was removed from the oil bath, degassed, and N-nucleophile (0.55 mmol, 1.1 equiv.) and lithium *tert*-butoxide (88 mg, 1.1 mmol, 2.2 equiv.) were added in one time. The tube was sealed again and put in a pre-heated oil bath at 130 °C. After stirring for 3 h, the reaction mixture was allowed to cool to room temperature. EtOAc was added to the mixture, which was filtered through Celite®. The solvents were evaporated under reduce pressure and the crude residue was purified by flash chromatography on silica gel.

1-(4-Methoxyphenyl)-2-methyl-5-(1-(*p*-tolyl)vinyl)-1*H*-benzo[*d*]imidazole (4a): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4a** as a yellow solid: yield: 128 mg (0.36 mmol, 72%); mp 106–108 °C; TLC: $R_f=0.25$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu=1611$, 1573, 1477, 1393, 1329, 1296, 1250, 1169, 1108, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta=7.76$ (s, 1H, H^{Ar}), 7.30 (dd, $J=8.6$, 2.1 Hz, 4H, H^{Ar}), 7.19–7.02 (m, 6H, H^{Ar}), 5.45 (d, $J=2.3$ Hz, 2H, $=CH_2$), 3.92 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=159.9$ (C), 152.6 (C), 150.5 (C), 142.7 (C), 139.2 (C), 137.5 (C), 136.7 (C), 136.6 (C), 128.9 (2CH), 128.4 (2CH), 128.3 (2CH), 123.4 (CH), 119.0 (CH), 115.2 (2CH), 113.1 (CH_2), 109.4 (CH), 55.7 (CH_3), 21.3 (CH_3), 14.5

(CH_3); HR-MS (ESI): m/z = 355.1814, calculated for $C_{24}H_{23}N_2O$ $(M+H)^+$: 355.1810.

1-(4-Methoxyphenyl)-2-methyl-5-(1-phenylvinyl)-1*H*-benzo[*d*]imidazole (4b): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4b** as a white solid: yield: 90 mg (0.26 mmol, 53%); mp 89–91 °C; TLC: R_f = 0.36 (cyclohexane/acetone, 7/3, SiO_2). IR (film): ν = 1612, 1514, 1444, 1393, 1329, 1297, 1251, 1190, 1108, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.86 (s, 1H, H^{Ar}), 7.55–7.36 (m, 7H, H^{Ar}), 7.29 (d, J = 9.3 Hz, 1H, H^{Ar}), 7.20 (d, J = 8.7 Hz, 2H, H^{Ar}), 7.15 (d, J = 8.4 Hz, 1H, H^{Ar}), 5.60 (d, J = 6.1 Hz, 2H, =CH_2), 4.03 (s, 3H, CH_3), 2.61 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.7 (C), 150.6 (C), 142.68 (C), 142.1 (C), 136.7 (C), 136.4 (C), 128.7 (C), 128.5 (2CH), 128.4 (2CH), 128.2 (2CH), 127.7 (CH), 123.4 (CH), 119.0 (CH), 115.2 (2CH), 113.8 (CH_2), 109.4 (CH), 55.7 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 341.1667, calculated for $C_{23}H_{21}N_2O$ $(M+H)^+$: 341.1654.

1-(4-Methoxyphenyl)-5-[1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4c): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4c** as a white solid; yield: 115 mg (0.31 mmol, 62%); mp 99–101 °C; TLC: R_f = 0.31 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2961, 2836, 1607, 1512, 1462, 1393, 1298, 1248, 1171, 1109, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.87 (s, 1H, H^{Ar}), 7.43 (t, J = 8.8 Hz, 4H, H^{Ar}), 7.30 (d, J = 8.4 Hz, 1H, H^{Ar}), 7.20 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.15 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.99 (d, J = 8.7 Hz, 2H, H^{Ar}), 5.52 (d, J = 5.9 Hz, 2H, =CH_2), 4.03 (s, 3H, CH_3), 3.95 (s, 3H, CH_3), 2.62 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 159.4 (C), 152.63 (C), 150.1 (C), 142.6 (C), 136.7 (C), 134.6 (C), 132.7 (CH), 129.6 (2CH), 128.7 (C), 128.4 (2CH), 123.5 (CH), 118.9 (CH), 115.2 (2CH), 113.6 (2CH), 112.4 (CH_2), 109.4 (CH), 55.7 (CH_3), 55.4 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 371.1771, calculated for $C_{24}H_{23}N_2O_2$ $(M+H)^+$: 371.1760.

5-{1-([1,1′-Biphenyl]-4-yl)vinyl}-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4d): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4d** as a white solid; yield: 83 mg (0.20 mmol, 40%); mp 181–183 °C; TLC: R_f = 0.32 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1611, 1513, 1486, 1428, 1394, 1330, 1298, 1251, 1169, 1108, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1H, H^{Ar}), 7.53 (d, J = 7.5 Hz, 2H, H^{Ar}), 7.47 (d, J = 8.1 Hz, 2H, H^{Ar}), 7.40–7.32 (m, 4H, H^{Ar}), 7.26 (d, J = 7.5 Hz, 1H, H^{Ar}), 7.20 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.12 (dd, J = 8.3, 1.3 Hz, 1H, H^{Ar}), 7.00 (s, 1H, H^{Ar}), 6.96 (d, J = 9.1 Hz, 2H, H^{Ar}), 5.43 (d, J = 8.3 Hz, 2H, =CH_2), 3.81 (s, 3H, CH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.71 (C), 150.2 (2C), 142.7 (C), 141.1 (C), 141.0 (C), 140.6 (C), 136.73 (C), 136.3 (C), 128.9 (2CH), 128.8 (2CH), 128.4 (2CH), 127.4 (CH), 127.2 (2CH), 126.9 (2CH), 123.4 (CH), 119.0 (CH), 115.2 (2CH), 113.8 (CH_2), 109.5 (CH), 55.7 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 417.1970, calculated for $C_{29}H_{25}N_2O$ $(M+H)^+$: 417.1967.

4-{1-[1-(4-Methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazol-5-yl]vinyl}benzonitrile (4e): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4e** as a yellow solid; yield: 102 mg (0.28 mmol, 56%); mp:116–117 °C; TLC: R_f = 0.28 (cyclohexane/acetone, 7/3, SiO_2). IR (film): ν = 2227, 1606, 1514, 1430, 1393, 1329, 1398, 1251, 1170, 1108, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, J = 9.9 Hz, 2H, H^{Ar}), 7.61 (s, 1H, H^{Ar}), 7.49 (d, J = 8.2 Hz, 2H, H^{Ar}), 7.30 (d, J = 9.4 Hz, 2H, H^{Ar}), 7.18–7.01 (m, 4H, H^{Ar}), 5.59 (d, J = 19.7 Hz, 2H, =CH_2), 3.92 (s, 3H, CH_3), 2.50 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0 (C), 153.1 (C), 149.3 (C), 147.3 (C), 142.8 (C), 137.0 (C), 135.0 (C), 132.1 (2CH), 129.1 (2CH), 128.5 (C), 128.4 (2CH), 123.1 (CH), 119.1 (C), 118.9 (CH), 116.4 (CH_2), 115.3 (2CH), 111.3 (C), 109.8 (CH), 55.8 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 366.1614, calculated for $C_{24}H_{20}N_3O$ $(M+H)^+$: 366.1606.

5-[1-(4-Fluorophenyl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4f): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4f** as a white solöid; yield: 108 mg (0.30 mmol, 60%); mp 131–132 °C; TLC: R_f = 0.31 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1602, 1511, 1477, 1429, 1393, 1328, 1295, 1250, 1190, 1158, 1108, 1030 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.61 (d, J = 1.2 Hz, 1H, H^{Ar}), 7.29–7.15 (m, 4H, H^{Ar}), 7.05 (dd, J = 8.4, 1.6 Hz, 1H, H^{Ar}), 7.02–6.85 (m, 5H, H^{Ar}), 5.34 (d, J = 14.3 Hz, 2H, =CH_2), 3.80 (s, 3H, CH_3), 2.39 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.5 (d, J = 245.0 Hz, C), 159.9 (C), 152.8 (C), 149.6 (C), 142.7 (C), 138.2 (C), 136.7 (C), 136.1 (C), 130.0 (d, J = 7.9 Hz, 2CH), 128.6 (C), 128.3 (2CH), 123.2 (CH), 118.8 (CH), 115.2 (2CH), 115.0 (d, J = 21.8 Hz, 2CH), 113.6 (CH_2), 109.5 (CH), 55.7 (CH_3), 14.4 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −113.1 (s); HR-MS (ESI): m/z = 359.1565, calculated for $C_{23}H_{20}N_2OF$ $(M+H)^+$: 359.1560.

5-[1-(4-Chlorophenyl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4g): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4g** as a yellow oil; yield: 65 mg (0.175 mmol, 35%); TLC: R_f = 0.64 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2960, 1612, 1558, 1514, 1490, 1430, 1394, 1328, 1296, 1251, 1168, 1090, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.72 (s, 1H), 7.33–7.27 (m, 6H), 7.14 (dd, J = 8.4, 1.3 Hz, 1H), 7.10 (d, J = 8.9 Hz, 2H), 7.04 (d, J = 8.5 Hz, 1H), 5.48 (d, J = 9.5 Hz, 2H), 3.93 (s, 3H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0 (C), 149.5 (C), 140.6 (C), 136.1 (C), 133.6 (C), 130.1 (C), 129.7 (2CH), 128.6 (C), 128.4 (4CH), 123.4 (CH), 118.8 (CH), 115.3 (2CH), 114.3 (CH_2), 109.7 (CH), 55.8 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 375.1265, calculated for $C_{23}H_{20}ClN_2O$ $(M+H)^+$: 375.1264.

1-(4-Methoxyphenyl)-2-methyl-5-[1-(3,4,5-trimethoxyphenyl)vinyl]-1*H*-benzo[*d*]imidazole (4h): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 5/5) afforded **4h** as a yellow solid; yield: 170 mg (0.395 mmol, 79%); mp 143–145 °C; TLC: R_f = 0.16 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 3000, 2936, 2836, 1613, 1513, 1463, 1393, 1344, 1296, 1236, 1188, 1125, 1036 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.89 (s, 1H, H^{Ar}), 7.43 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.33 (d, J = 8.4 Hz, 1H, H^{Ar}), 7.22 (d, J = 8.9 Hz, 2H, H^{Ar}), 7.16 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.74 (s, 2H, H^{Ar}), 5.57 (d, J = 12.2 Hz, 2H, =CH_2), 4.04 (s, 3H, CH_3), 4.01 (s, 3H, CH_3), 3.94 (s, 6H, 2 CH_3), 2.63 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.9 (C), 152.9 (C), 150.6 (C), 142.5 (C), 137.9 (C), 137.6 (C), 137.0 (C), 136.3 (C), 128.6 (C), 128.4 (2CH), 124.9 (CH), 123.5 (CH), 118.4 (CH), 115.3 (2CH), 113.6 (CH_2), 109.7 (CH), 105.8 (2CH), 61.0 (CH_3), 56.2 (2CH_3), 55.7 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 431.1960, calculated for $C_{26}H_{27}N_2O_4$ $(M+H)^+$: 431.1971.

5-[1-(3,5-Dimethoxyphenyl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4i): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 5/5) afforded **4i** as a yellow solid; yield: 131 mg (0.33 mmol, 66%); mp 134–136 °C; TLC: R_f = 0.2 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 3001, 2933, 2836, 1589, 1513, 1455, 1424, 1395, 1350, 1297, 1250, 1205, 1155, 1108, 1064 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1H, H^{Ar}), 7.20 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.08 (dd, J = 8.4, 0.7 Hz, 1H, H^{Ar}), 6.99 (d, J = 8.8 Hz, 2H, H^{Ar}), 6.93 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.45 (d, J = 2.2 Hz, 2H, H^{Ar}), 6.35 (t, J = 2.1 Hz, 1H, H^{Ar}), 5.38 (d, J = 4.9 Hz, 2H, =CH_2), 3.82 (s, 3H, CH_3), 3.67 (s, 6H, 2CH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.6 (2 C), 159.9 (C), 152.6 (C), 150.6 (C), 144.3 (C), 142.6 (C), 136.7 (C), 136.1 (C), 128.7 (C), 128.4 (2CH), 123.4 (CH), 118.9 (CH), 115.2 (2CH), 113.9 (CH_2), 109.4 (CH), 106.8 (2CH), 100.0 (CH), 55.7 (CH_3), 55.5 (2CH_3), 14.45 (CH_3); HR-MS (ESI): m/z = 401.1856, calculated for $C_{25}H_{25}N_2O_3$ $(M+H)^+$: 401.1865.

5-[1-(3,4-Dimethoxyphenyl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4j): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 5/5) afforded **4j** as a white solid; yield: 90 mg (0.225 mmol, 45%); mp 118–119 °C; TLC: R_f = 0.13 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2963, 1613, 1513, 1463, 1399, 1321, 1299, 1253, 1173, 1142, 1111, 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.68 (s, 1H, H^{Ar}), 7.23 (s, 1H, H^{Ar}), 7.20 (d, J = 3.8 Hz, 2H, H^{Ar}), 7.09 (dd, J = 8.2, 1.1 Hz, 1H, H^{Ar}), 7.00 (d, J = 8.8 Hz, 2H, H^{Ar}), 6.94 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.85 (s, 1H, H^{Ar}), 6.75 (d, J = 7.9 Hz, 1H, H^{Ar}), 5.33 (s, 2H, =CH_2), 3.83 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 2.41 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.7 (C), 150.4 (C), 148.9 (C), 148.7 (C), 142.7 (C), 136.7 (C), 136.5 (C), 135.1 (C), 128.8 (C), 128.4 (2CH), 123.5 (CH), 121.1 (CH), 119.0 (CH), 115.2 (2CH), 112.6 (CH_2), 111.7 (CH), 110.9 (CH), 109.4 (CH), 56.1 (CH_3), 56.0 (CH_3), 55.8 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 401.1876, calculated for $C_{25}H_{25}N_2O_3$ $(M+H)^+$: 401.1865.

1-(4-Methoxyphenyl)-5-[1-(2-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4k): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4k** as a yellow soldi; yield: 97 mg (0.26 mmol, 52%); mp 110–112 °C; TLC: R_f = 0.28 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2960, 1669, 1515, 1470, 1374, 1295, 1258, 1235, 1082 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.72 (s, 1H, H^{Ar}), 7.26–7.14 (m, 7H, H^{Ar}), 7.10 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.99 (d, J = 8.9 Hz, 2H, H^{Ar}), 6.95 (d, J = 8.5 Hz, 1H, H^{Ar}), 6.44 (s, 1H, H^{Ar}), 3.83 (s, 3H, CH_3), 3.69 (s, 3H, CH_3), 2.41 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.2 (C), 145.9 (CH_2), 142.2 (C), 141.0 (C), 135.7 (C), 132.2 (C), 128.8 (C), 128.4 (2CH), 128.3 (2CH), 128.1 (2CH), 126.4 (CH), 125.0 (CH), 121.2 (C), 120.6 (CH), 115.2 (2CH), 109.5 (CH), 60.6 (CH_3), 55.7 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 371.1763, calculated for $C_{24}H_{23}N_2O_2$ $(M+H)^+$: 371.1760.

5-[1-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4l): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 5/5) afforded **4l** as a white solid; yield: 107 mg (0.27 mmol, 54%); mp 141–143 °C; TLC: R_f = 0.18 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2933, 2842, 1611, 1578, 1514, 1460, 1426, 1395, 1322, 1284, 1250, 1169, 1124, 1066 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (s, 1H, H^{Ar}), 7.20 (d, J = 8.9 Hz, 2H, H^{Ar}), 7.08 (dd, J = 8.4, 1.4 Hz, 1H, H^{Ar}), 6.99 (d, J = 8.9 Hz, 2H, H^{Ar}), 6.93 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.82 (d, J = 1.9 Hz, 1H, H^{Ar}), 6.78 (dd, J = 8.3, 2.0 Hz, 1H, H^{Ar}), 6.72 (d, J = 8.3 Hz, 1H, H^{Ar}), 5.30 (d, J = 8.4 Hz, 2H, =CH_2), 4.17 (s, 4H, 2 CH_2), 3.82 (s, 3H, CH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.60 (C), 149.9 (C), 143.41 (C), 143.2 (C), 142.6 (C), 136.7 (C), 136.5 (C), 135.7 (C), 128.8 (C), 128.4 (2CH), 123.5 (CH), 121.7 (CH), 119.0 (CH), 117.3 (CH), 116.9 (CH), 115.2 (2 CH), 112.7 (CH_2), 109.4 (CH), 64.6 (CH_2), 64.5 (CH_2), 55.7 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 399.1705, calculated for $C_{25}H_{23}N_2O_3$ $(M+H)^+$: 399.1709.

5-[1-(3-Fluoro-4-methoxyphenyl)vinyl]-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4m): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 6/4) afforded **4m** as a white solid; yield: 118 mg (0.305 mmol, 61%); mp 114–115 °C; TLC: R_f = 0.19 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1613, 1576, 1514, 1429, 1394, 1321, 1300, 1251, 1181, 1138, 1101, 1021 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1H, H^{Ar}), 7.21 (d, J = 8.9 Hz, 2H, H^{Ar}), 7.07 (d, J = 8.3 Hz, 1H, H^{Ar}), 7.00 (m, 4H, H^{Ar}), 6.95 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.82 (t, J = 8.7 Hz, 1H, H^{Ar}), 5.33 (d, J = 2.2 Hz, 2H, =CH_2), 3.82 (s, 6H, 2 CH_3), 2.41 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.8 (C), 152.1 (d, J = 243.0 Hz, C), 149.2 (C), 147.3 (d, J = 10.8 Hz, C), 142.4 (C), 136.7 (C), 136.1 (C), 135.3 (d, J = 6.1 Hz, C), 128.6 (s, C), 128.4 (s, 2CH), 124.2 (d, J = 2.8 Hz, CH), 123.4 (CH), 118.9 (CH), 116.1 (d, J = 18.8 Hz, CH), 115.2 (2CH), 113.4 (CH_2), 113.0 (CH), 109.6 (CH), 56.4 (CH_3), 55.7 (CH_3), 14.4 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −133.99 (s); HR-MS (ESI): m/z = 389.1668, calculated for $C_{24}H_{22}N_2O_2F$ $(M+H)^+$: 389.1665.

1-(4-Methoxyphenyl)-2-methyl-5-(2-methyl-1-phenylprop-1-en-1-yl)-1*H*-benzo[*d*]imidazole (4n): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4n** as a yellow solid; yyield: 96 mg (0.26 mmol, 52%); mp 98–100 °C; TLC: R_f = 0.38 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2964, 2844, 1613, 1512, 1475, 1142, 1393, 1323, 1295, 1248, 1169, 1107, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.57 (s, 1H, H^{Ar}), 7.28–7.24 (m, 4H, H^{Ar}), 7.21–7.12 (m, 3H, H^{Ar}), 7.06 (d, J = 8.8 Hz, 2H, H^{Ar}), 6.97 (d, J = 8.3 Hz, 1H, H^{Ar}), 6.92 (d, J = 8.3 Hz, 1H, H^{Ar}), 3.89 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 1.85 (s, 6H, 2 CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8 (C), 152.2 (C), 143.9 (C), 142.4 (C), 138.0 (C), 137.5 (C), 135.4 (C), 130.8 (C), 130.0 (2CH), 129.0 (C), 128.4 (2CH), 127.9 (2CH), 126.0 (CH), 124.8 (CH), 120.2 (CH), 115.1 (2CH), 109.4 (CH), 55.7 (CH_3), 22.7 (sCH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 369.1981, calculated for $C_{25}H_{25}N_2O$ $(M+H)^+$: 369.1967.

1-(4-Methoxyphenyl)-2-methyl-5-[2-methyl-1-(3,4,5-trimethoxyphenyl)prop-1-en-1-yl]-1*H*-benzo[*d*]imidazole (4o): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 5/5) afforded **4o** as a yellow solid; yield: 110 mg (0.24 mmol, 48%); mp 151–153 °C; TLC: R_f = 0.15 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2924, 1595, 1494, 1464, 1321, 1299, 1260, 1213, 1153, 1107, 1023 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.57 (s, 1H, H^{Ar}), 7.28 (d, J = 8.7 Hz, 2H, H^{Ar}), 7.06 (d, J = 8.7 Hz, 2H, H^{Ar}), 6.99 (d, J = 8.3 Hz, 1H, H^{Ar}), 6.95 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.40 (s, 2H, H^{Ar}), 3.90 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 3.79 (s, 6H, 2 CH_3), 2.48 (s, 3H, CH_3), 1.85 (s, 3H, CH_3), 1.83 (s, 3H,

CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.8 (2C), 152.2 (C), 141.8 (C), 139.6 (C), 137.8 (C), 137.5 (C), 136.3 (C), 135.3 (C), 130.9 (C), 128.6 (C), 128.4 (2CH), 124.8 (CH), 119.7 (CH), 115.2 (2CH), 109.5 (CH), 107.0 (2 CH), 61.0 (CH_3), 56.2 (2CH_3), 55.7 (CH_3), 22.8 (CH_3), 22.6 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 459.2290, calculated for $C_{28}H_{31}N_2O_4$ $(M+H)^+$: 459.2284.

(*E*)-1-(4-Methoxyphenyl)-2-methyl-5-{1-[3-(trifluoromethyl)phenyl]prop-1-en-2-yl}-1*H*-benzo[*d*]imidazole (4p): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4p** as a white solid; yield: 133 mg (0.315 mmol, 63%); mp 122–124 °C; TLC: R_f = 0.25 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1613, 1587, 1513, 1479, 1443, 1395, 1331, 1295, 1248, 1206, 1180, 1161, 1120, 1094, 1031 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.79 (s, 1H, H^{Ar}), 7.54 (s, 1H, H^{Ar}), 7.46 (d, J = 3.8 Hz, 1H, H^{Ar}), 7.40 (d, J = 4.7 Hz, 2H, H^{Ar}), 7.31 (dd, J = 8.5, 1.5 Hz, 1H, H^{Ar}), 7.20 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.01–6.98 (m, 3H, H^{Ar}), 6.77 (s, 1H, H^{Ar}), 3.82 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.26 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 152.79 (C), 142.8 (C), 139.9 (C), 139.4 (C), 138.4 (C), 136.5 (C), 132.5 (CH), 130.6 (q, J = 31.8 Hz, CF_3), 128.7 (CH), 128.3 (2CH), 126.2 (C), 125.9 (d, J = 3.5 Hz, CH), 125.7 (CH), 123.0 (d, J = 3.5 Hz, CH), 122.6 (C), 121.1 (CH), 116.6 (CH), 115.2 (2CH), 109.7 (CH), 55.7 (CH_3), 18.2 (CH_3), 14.5 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −60.73 (s); HR-MS (ESI): m/z = 423.1681, calculated for $C_{25}H_{22}N_2OF_3$ $(M+H)^+$: 423.1684.

5-(2*H*-Chromen-4-yl)-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4q): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4q** as a white solid; yield: 131 mg (0.355 mmol, 71%); mp 178–180 °C; TLC: R_f = 0.38 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1720, 1603, 1512, 1477, 1446, 1394, 1318, 1297, 1246, 1222, 1186, 1107, 1065 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (s, 1H, H^{Ar}), 7.19 (d, J = 8.9 Hz, 2H, H^{Ar}), 7.09–7.02 (m, 2H, H^{Ar}), 7.02–6.93 (m, 4H, H^{Ar}), 6.79 (d, J = 8.0 Hz, 1H, H^{Ar}), 6.71 (t, J = 7.5 Hz, 1H, H^{Ar}), 5.72 (t, J = 3.9 Hz, 1H, H^{Ar}), 4.76 (d, J = 3.9 Hz, 2H, H^{Ar}), 3.79 (s, 3H, CH_3), 2.39 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9 (C), 154.8 (C), 152.7 (C), 142.7 (C), 137.5 (C), 136.6 (C), 132.7 (C), 129.2 (CH), 128.6 (C), 128.3 (2CH), 126.1 (CH), 124.2 (C), 123.5 (CH), 121.2 (CH), 119.8 (CH), 119.0 (CH), 116.2 (CH), 115.2 (2CH), 109.7 (CH), 65.4 (CH_2), 55.7 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 369.1599, calculated for $C_{24}H_{21}N_2O_2$ $(M+H)^+$: 369.1603.

(*Z*/*E*)-1-(4-Methoxyphenyl)-5-[2-(3-methoxyphenyl)-1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4r). Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4r** as a mixture of two diastereoisomers (*Z*:*E*, 66:34); white solid; yield: 204 mg (0.43 mmol, 86%); mp 198–200 °C; TLC: R_f = 0.29/0.25 (cyclohexane/acetone, 7/3, SiO_2); IR (film, mixture): ν = 1605, 1511, 1462, 1394, 1320, 1299, 1246, 1175, 1108, 1033 cm^{-1}; ^1H NMR [major compound (*Z* isomer); 400 MHz, $CDCl_3$]: δ = 7.60 (s, 1H, H^{Ar}), 7.33 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.27 (d, J = 8.0 Hz, 2H, H^{Ar}), 7.09–7.07 (m, 2H, H^{Ar}), 7.05–7.04 (m, 1H, H^{Ar}), 7.02–6.98 (m, 3H, H^{Ar}), 6.88 (s, 1H, CH), 6.82 (d, J = 8.8 Hz, 2H, H^{Ar}), 6.63 (d, J = 8.8 Hz, 2H, H^{Ar}), 3.89 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.71 (s, 3H, CH_3), 2.50 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8 (C), 158.99 (C), 158.1 (C), 152.3 (C), 142.7 (C), 140.6 (C), 136.9 (C), 136.2 (C), 135.0 (C), 130.7 (2CH), 128.7 (2CH), 128.3 (2CH, 2C), 125.9 (CH), 125.3 (CH), 120.8 (CH), 115.1 (2CH), 113.5 (2CH), 113.5 (2CH), 109.3 (CH), 55.6 (CH_3), 55.3 (CH_3), 55.1 (CH_3), 14.4 (CH_3); ^1H NMR [minor compound (*E* isomer); 400 MHz, $CDCl_3$]: δ = 7.71 (s, 1H, H^{Ar}), 7.33 (d, J = 8.8 Hz, 2H, H^{Ar}), 7.17 (d, J = 8.6 Hz, 3H, H^{Ar}), 7.09–7.07 (m, 2H, H^{Ar}), 7.05–7.04 (m, 3H, H^{Ar}), 6.89–6.86 (m, 3H, CH, 2 H^{Ar}), 6.70 (d, J = 8.8 Hz, 2H, H^{Ar}), 3.83 (s, 3H, CH_3), 3.83 (s, 3H, CH_3), 3.75 (s, 3H, CH_3), 2.48 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8 (C), 158.8 (C), 158.1 (C), 152.5 (C), 143.0 (C), 141.0 (C), 139.1 (C), 136.4 (C), 133.4 (C), 131.7 (2CH), 130.7 (2CH), 130.6 (C), 128.2 (2CH, C), 126.6 (CH), 122.7 (CH), 118.2 (CH), 115.1 (2CH), 114.1 (2CH), 113.5 (2CH), 110.1 (CH), 55.6 (CH_3), 55.3 (CH_3), 55.2 (CH_3), 14.4 (CH_3); HR-MS (ESI, mixture): m/z = 477.2174, calculated for $C_{31}H_{29}N_2O_3$ $(M+H)^+$: 477.2178.

5-(Cyclohex-1-en-1-yl)-1-(4-methoxyphenyl)-2-methyl-1*H*-benzo[*d*]imidazole (4s): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 6/4) afforded **4s** as a white solid; yield: 68 mg (0.215 mmol, 43%); mp 112–114 °C; TLC: R_f = 0.24 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2930, 2834, 1513, 1478, 1430, 1395, 1321, 1298, 1211, 1171, 1108, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.64 (s, 1H, H^{Ar}), 7.21 (s, 1H, H^{Ar}), 7.19 (d, J = 2.5 Hz, 2H, H^{Ar}), 6.99 (d, J = 8.8 Hz, 2H, H^{Ar}), 6.93 (d, J = 8.5 Hz, 1H, H^{Ar}), 6.09–5.93 (m, 1H, =CH-), 3.83 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 2.15 (m, 2H, CH_2), 1.79–1.70 (m, 2H, CH_2), 1.68–1.57 (m, 4H, 2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8 (C), 152.2 (C), 142.7 (C), 137.9 (C), 137.1 (C), 135.8 (C), 128.8 (C), 128.3 (2 CH), 124.1 (CH), 120.3 (CH), 115.3 (CH), 115.1 (2CH), 109.4 (CH), 55.7 (CH_3), 28.1 (CH_2), 26.1 (CH_2), 23.3 (CH_2), 22.4 (CH_2), 14.4 (CH_3); HR-MS (ESI): m/z = 319.1801, calculated for $C_{21}H_{23}N_2O$ $(M+H)^+$: 319.1810.

5-[1-(4-Methoxyphenyl)vinyl]-2-methyl-1-phenyl-1*H*-benzo[*d*]imidazole (4t): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4t** as a yellow solid; yield: 145 mg (0.425 mmol, 85%); mp 110–112 °C; TLC: R_f = 0.34 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2836, 1598, 1499, 1458, 1399, 1330, 1304, 1283, 1246, 1176, 1111, 1074, 1032 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.66 (s, 1H, H^{Ar}), 7.45 (m, 3H, H^{Ar}), 7.28 (d, J = 7.4 Hz, 2H, H^{Ar}), 7.22 (d, J = 8.7 Hz, 2H, H^{Ar}), 7.08 (dd, J = 8.4, 1.4 Hz, 1H, H^{Ar}), 6.96 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.76 (d, J = 8.7 Hz, 2H, H^{Ar}), 5.30 (d, J = 5.7 Hz, 2H, =CH_2), 3.72 (s, 3H, CH_3), 2.42 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4 (C), 152.2 (C), 150.0 (C), 142.5 (C), 136.8 (C), 136.3 (C), 136.2 (C), 134.6 (C), 130.0 (2CH), 129.5 (2CH), 128.9 (CH), 127.1 (2CH), 123.5 (CH), 119.0 (CH), 113.6 (2CH), 112.4 (CH_2), 109.4 (CH), 55.4 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 341.1649, calculated for $C_{23}H_{21}N_2O$ $(M+H)^+$: 341.1654.

2-Methyl-1-phenyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4u): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4u** as a yellow solid; yield: 127 mg (0.39 mmol, 78%); mp 131–133 °C; TLC: R_f = 0.48 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1598, 1524, 1500, 1476, 1388, 1369, 1329, 1305, 1234, 1188, 1074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = (ppm) 7.66 (s, 1H, H^{Ar}), 7.43 (m, 3H, H^{Ar}), 7.26 (d, J = 7.6 Hz, 2H, H^{Ar}), 7.17 (d, J = 8.0 Hz, 2H, H^{Ar}), 7.06 (d, J = 9.0 Hz, 1H, H^{Ar}), 7.02 (d, J = 8.0 Hz, 2H, H^{Ar}), 6.94 (d, J = 8.4 Hz, 1H, H^{Ar}), 5.33 (d, J =

2.4 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.25 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.1 (C), 150.3 (C), 142.7 (C), 139.1 (C), 137.4 (C), 136.6 (C), 136.2 (C), 136.1 (C), 130.0 (2CH), 128.8 (3CH), 128.2 (2CH), 127.0 (2CH), 123.5 (CH), 118.9 (CH), 113.1 (CH_2), 109.4 (CH), 21.2 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 325.1709, calculated for $C_{23}H_{21}N_2(M+H)^+$: 325.1705.

1-(2-Methoxyphenyl)-5-[1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4v): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4v** as a yellow solid; yield: 150 mg (0.405 mmol, 81%); mp 83–85 °C; TLC: R_f = 0.33 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2836, 1648, 1601, 1508, 1464, 1429, 1391, 1330, 1281, 1247, 1178, 1117, 1027 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.64 (s, 1H, H^{Ar}), 7.38 (td, J = 8.0, 1.3 Hz, 1H), 7.20 (m, 3H, H^{Ar}), 7.02 (m, 3H, H^{Ar}), 6.82 (d, J = 8.3 Hz, 1H, H^{Ar}), 6.74 (d, J = 8.7 Hz, 2H, H^{Ar}), 5.27 (d, J = 3.2 Hz, 2H, =CH_2), 3.69 (s, 3H, CH_3), 3.63 (s, 3H, CH_3), 2.31 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (s), 155.2 (s), 153.3 (s), 150.0 (s), 142.6 (s), 136.3 (s), 134.6 (s), 130.7 (s), 129.5 (s), 129.1 (s), 124.3 (s), 123.2 (s), 121.1 (s), 118.7 (s), 113.5 (s), 112.5 (s), 112.2 (s), 109.3 (s), 55.6 (s), 55.3 (s), 14.0 (s); HR-MS (ESI): m/z = 371.1754, calculated for $C_{24}H_{23}N_2O_2$ $(M+H)^+$: 371.1760.

1-(2-Methoxyphenyl)-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4w): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4w** as a brown solid; yield: 152 mg (0.43 mmol, 86%); mp 92–94 °C; TLC: R_f = 0.40 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2922, 1599, 1527, 1506, 1427, 1389, 1329, 1298, 1263, 1246, 1182, 1117, 1048, 1024 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (s, 1H, H^{Ar}), 7.61–7.42 (m, 1H, H^{Ar}), 7.39–7.25 (m, 3H, H^{Ar}), 7.18–7.12 (m, 5H, H^{Ar}), 6.95 (d, J = 8.3 Hz, 1H, H^{Ar}), 5.46 (s, 2H, =CH_2), 3.77 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.2 (C), 153.3 (C), 150.5 (C), 142.8 (C), 139.2 (C), 137.3 (C), 136.4 (C), 136.2 (C), 130.7 (CH), 129.1 (CH), 128.8 (2CH), 128.3 (2 CH), 124.4 (C), 123.2 (CH), 121.2 (CH), 118.7 (CH), 112.9 (CH_2), 112.5 (CH), 109.3 (CH), 55.7 (CH_3), 21.2 (CH_3), 14.0 (CH_3); HR-MS (ESI): m/z = 355.1819, calculated for $C_{24}H_{23}N_2O$ $(M+H)^+$: 355.1810.

1-(4-Fluorophenyl)-5-[1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4x): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4x** as a brown solid; yield: 138 mg (0.385 mmol, 77%); mp 97–99 °C; TLC: R_f = 0.35 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1605, 1511, 1430, 1393, 1329, 1248, 1225, 1177, 1155, 1033 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (s, 1H, H^{Ar}), 7.43–7.25 (m, 6H, H^{Ar}), 7.20 (dd, J = 8.4, 1.4 Hz, 1H, H^{Ar}), 7.03 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.87 (d, J = 8.8 Hz, 2H, H^{Ar}), 5.41 (dd, J = 8.8, 1.0 Hz, 2H, =CH_2), 3.83 (s, 3H, CH_3), 2.51 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.7 (d, J = 251.7 Hz, C), 159.4 (C), 152.2 (C), 149.9 (C), 142.7 (C), 137.0 (C), 136.4 (C), 134.3 (C), 132.2 (d, J = 1.5 Hz, C), 129.5 (s, 2CH), 129.0 (d, J = 8.7 Hz, 2CH), 123.7 (CH), 119.1 (CH), 117.1 (d, J = 22.9 Hz, 2 CH), 113.6 (2CH), 112.6 (CH_2), 109.2 (CH), 55.4 (CH_3), 14.5 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −109.79 (s); HR-MS (ESI): m/z = 359.1563, calculated for $C_{23}H_{20}FN_2O$ $(M+H)^+$: 359.1560.

1-(4-Fluorophenyl)-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4y): Flash chromatography on silica gel (cyclohexane/ácetone, 10/0 to 7/3) afforded **4y** as a white solid; yield: 139 mg (0.405 mmol, 81%); mp 114–116 °C; TLC: R_f = 0.0.49 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1606, 1510, 1477, 1427, 1392, 1328, 1312, 1225, 1187, 1155, 1095 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (s, 1H, H^{Ar}), 7.38 (dd, J = 8.7, 4.9 Hz, 2H, H^{Ar}), 7.31 (d, J = 4.0 Hz, 2H, H^{Ar}), 7.28 (d, J = 3.4 Hz, 2H, H^{Ar}), 7.20 (dd, J = 8.4, 1.4 Hz, 1H, H^{Ar}), 7.15 (d, J = 7.9 Hz, 2H, H^{Ar}), 7.03 (d, J = 8.4 Hz, 1H, H^{Ar}), 5.46 (d, J = 4.6 Hz, 2H, =CH_2), 2.51 (s, 3H, CH_3), 2.38 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.5 (d, J = 248.3 Hz, C), 152.2 (C), 150.3 (C), 142.6 (C), 139.1 (C), 137.5 (C), 136.8 (C), 136.3 (C), 132.1 (d, J = 2.9 Hz, C), 129.0 (d, J = 9.0 Hz, 2CH), 128.8 (2CH), 128.3 (2CH), 123.7 (CH), 119.0 (CH), 117.1 (d, J = 22.9 Hz, 2CH), 113.2 (CH_2), 109.16 (CH), 21.2 (CH_3), 14.4 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −109.78 (s); HR-MS (ESI): m/z = 343.1613, calculated for $C_{23}H_{20}N_2F$ $(M+H)^+$: 343.1611.

5-[1-(4-Methoxyphenyl)vinyl]-2-methyl-1-(*p*-tolyl)-1*H*-benzo[*d*]imidazole (4z): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4z** as a brown solid; yield: 138 mg (0.39 mmol, 78%); mp 125–127 °C; TLC: R_f = 0.47 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1606, 1511, 1477, 1428, 1391, 1329, 1302, 1284, 1246, 1176, 1110, 1032 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1H, H^{Ar}), 7.20 (t, J = 8.9 Hz, 4H, H^{Ar}), 7.09 (d, J = 8.2 Hz, 2H, H^{Ar}), 7.03 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.91 (d, J = 8.4 Hz, 1H, H^{Ar}), 6.71 (d, J = 8.7 Hz, 2H, H^{Ar}), 5.25 (d, J = 4.7 Hz, 2H, =CH_2), 3.65 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3 (C), 152.2 (C), 149.9 (C), 142.6 (C), 138.9 (C), 136.5 (C), 136.3 (C), 134.5 (C), 133.3 (C), 130.5 (2CH), 129.4 (2CH), 126.7 (2CH), 123.3 (CH), 118.8 (CH), 113.4 (2CH), 112.2 (C), 109.3 (CH), 55.2 (CH_3), 21.2 (CH_3), 14.3 (CH_3); HR-MS (ESI): m/z = 355.1810, calculated for $C_{24}H_{23}N_2O$ $(M+H)^+$: 355.1810.

2-Methyl-1-(*p*-tolyl)-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4aa): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4aa** as a white solid; yield: 127 mg (0.375 mmol, 75%); mp 143–145 °C; TLC: R_f = 0.52 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1608, 1513, 1477, 1429, 1391, 1328, 1300, 1235, 1213, 1190, 1111, 1039 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78 (s, 1H, H^{Ar}), 7.39 (d, J = 8.3 Hz, 2H, H^{Ar}), 7.29 (t, J = 8.8 Hz, 4H, H^{Ar}), 7.17 (m, 3H), 7.06 (d, J = 8.4 Hz, 1H, H^{Ar}), 5.46 (d, J = 2.1 Hz, 2H, =CH_2), 2.52 (s, 3H, CH_3), 2.50 (s, 3H), 2.39 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.3 (C), 150.4 (C), 142.6 (C), 139.2 (C), 139.0 (C), 137.5 (C), 136.6 (C), 136.4 (C), 133.5 (C), 130.6 (2CH), 128.9 (2CH), 128.3 (2CH), 126.9 (2CH), 123.5 (CH), 118.9 (CH), 113.1 (CH_2), 109.4 (CH), 21.3 (CH_3), 21.3 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z = 339.1844, calculated for $C_{24}H_{23}N_2$ $(M+Na)^+$: 339.1861.

1-Butyl-5-[1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4ab): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ab** as a viscous oil; yield: 75 mg (0.235 mmol, 47%); TLC: R_f = 0.15 (cyclohexane/acetone, 6/4, SiO_2); IR (film): ν = 2938, 2831, 1605, 1510, 1463, 1429, 1399, 1361, 1333, 1283, 1246, 1177, 1103, 1031 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.68 (s, 1H, HAr), 7.30 (d, J = 8.5 Hz, 2H, HAr), 7.20 (s, 2H, HAr), 6.85 (d, J = 8.5 Hz, 2H, HAr), 5.37 (d, J = 3.5 Hz, 2H, =CH_2), 4.08 (t, J = 7.3 Hz, 2H, CH_2), 3.82 (s, 3H, CH_3), 2.59 (s, 3H,

CH_3), 1.79 (dt, J=15.1, 7.6 Hz, 2H, CH_2), 1.45–1.32 (m, 2H, CH_2), 0.97 (t, J=7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.4 (C), 152.1 (C), 150.1 (C), 142.8 (C), 136.1 (C), 135.0 (C), 134.7 (C), 129.6 (2 CH), 122.9 (CH), 119.0 (CH), 113.6 (2CH), 112.3 (CH_2), 108.6 (CH), 55.4 (CH_3), 43.9 (CH_2), 32.0 (CH_2), 20.3 (CH_2), 14.1 (CH_3), 13.9 (CH_3); HR-MS (ESI): m/z=321.1963, calculated for $C_{21}H_{25}N_2O$ $(M+H)^+$: 321.1967.

1-Butyl-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4ac): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ac** as acpolorless oil; yield: 81 mg (0.265 mmol, 53%); TLC: R_f=0.25 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν=2958, 2929, 1607, 1512, 1483, 1429, 1398, 1361, 1322, 1290, 1165, 1113, 1034 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.71 (s, 1H, H^{Ar}), 7.29 (d, J=7.7 Hz, 2H, H^{Ar}), 7.22 (s, 2H, H^{Ar}), 7.15 (d, J=7.5 Hz, 2H, H^{Ar}), 5.44 (s, 2H, =CH_2), 4.11 (t, J=7.3 Hz, 2H, CH_2), 2.62 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 1.92–1.68 (m, 2H, CH_2), 1.43 (tt, J=14.7, 7.5 Hz, 2H, CH_2), 0.99 (t, J=7.3 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.1 (C), 150.5 (C), 142.8 (C), 139.3 (C), 137.5 (C), 136.0 (C), 135.0 (C), 128.9 (2CH), 128.4 (2CH), 122.9 (CH), 119.0 (CH), 113.0 (CH_2), 108.6 (CH), 43.9 (CH_2), 32.0 (CH_2), 21.3 (CH_3), 20.3 (CH_2), 14.1 (CH_3), 13.9 (CH_3); HR-MS (ESI): m/z= 305.2012, calculated for $C_{21}H_{25}N_2$ $(M+H)^+$: 305.2018.

1,2-Dimethyl-5-[1-(3,4,5-trimethoxyphenyl)vinyl]-1*H*-benzo[*d*]imidazole (4ad): Flash chromatography on silica gel (cyclohexane/acetone, 5/5 to 0/10) afforded **4ad** as a colorless oil; yield: 111 mg (0.33 mmol, 66%); TLC: R_f=0.35 (acetone, SiO_2); IR (film): ν=2936, 1579, 1504, 1465, 1430, 1398, 1345, 1237, 1177, 1126 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.63 (s, 1H, H^{Ar}), 7.21–7.15 (m, 2H, H^{Ar}), 6.51 (s, 2H, H^{Ar}), 5.36 (d, J=12.5 Hz, 2H, =CH_2), 3.80 (s, 3H, CH_3), 3.72 (s, 6H, 2 CH_3), 3.67 (s, 3H, CH_3), 2.54 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=153.0 (3C), 152.6 (C), 150.7 (C), 142.5 (C), 138.0 (C), 137.9 (C), 135.8 (C), 123.0 (CH), 119.0 (CH), 113.3 (CH_2), 108.4 (CH), 105.9 (2CH), 61.0 (CH_3), 56.2 (2CH_3), 30.1 (CH_3), 14.0 (CH_3); HR-MS (ESI): m/z=339.1703, calculated for $C_{20}H_{23}N_2O_3$ $(M+H)^+$: 339.1708.

1-Benzyl-5-[1-(4-methoxyphenyl)vinyl]-2-methyl-1*H*-benzo[*d*]imidazole (4ae): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ae** as a yellow solid; yield: 80 mg (0.225 mmol, 45%); mp 127–129 °C; TLC: R_f=0.25 (cyclohexane/acetone, 6/4, SiO_2); IR (film): ν=1648, 1608, 1511, 1430, 1397, 1332, 1303, 1250, 1172, 1109, 1031 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.65 (s, 1H, H^{Ar}), 7.26–7.21 (m, 5H, H^{Ar}), 7.09 (d, J=2.5 Hz, 2H, H^{Ar}), 7.00 (d, J=7.5 Hz, 2H, H^{Ar}), 6.78 (d, J=8.6 Hz, 2H, H^{Ar}), 5.30 (d, J=3.7 Hz, 2H, CH_2), 5.24 (s, 2H, CH_2), 3.74 (s, 3H, CH_3), 2.50 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.4 (C), 152.5 (C), 150.0 (C), 142.4 (C), 136.6 (C), 135.8 (C), 135.2 (C), 134.6 (C), 129.6 (2CH), 129.2 (2CH), 128.1 (CH), 126.4 (2CH), 123.4 (CH), 119.0 (CH), 113.6 (2CH), 112.6 (CH_2), 108.9 (CH), 55.4 (CH_3), 47.4 (CH_2), 14.1 (CH_3); HR-MS (ESI): m/z=355.1815, calculated for $C_{24}H_{23}N_2O$ $(M+H)^+$: 355.1810.

1-Benzyl-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4af): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4af** as a yellow solid; yield: 84 mg (0.25 mmol, 50%); mp 133–135 °C; TLC: R_f=0.28 (cyclohexane/acetone, 7/3, SiO_2). IR (film): ν=1606, 1521, 1481, 1454, 1428, 1395, 1354, 1331, 1247, 1160, 1113, 1031 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.77 (d, J= 0.5 Hz, 1H, H^{Ar}), 7.34–7.29 (m, 5H, H^{Ar}), 7.20–7.13 (m, 4H, H^{Ar}), 7.12–7.05 (m, 2H, H^{Ar}), 5.46 (s, 2H, =CH_2), 5.31 (s, 2H, CH_2), 2.58 (s, 3H, CH_3), 2.39 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.5 (C), 150.4 (C), 142.8 (C), 139.2 (C), 137.4 (C), 136.2 (C), 135.9 (C), 135.3 (C), 129.1 (2CH), 128.9 (2CH), 128.3 (2CH), 128.0 (CH), 126.4 (2CH), 123.2 (CH), 119.1 (CH), 113.1 (CH_2), 108.8 (CH), 47.3 (CH_2), 21.2 (CH_3), 14.1 (CH_3); HR-MS (ESI): m/z=339.1839, calculated for $C_{24}H_{23}N_2$ $(M+H)^+$: 339.1861.

1-(4-Chlorophenyl)-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4ag): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 6/4) afforded **4ag** as a yellow oil; yield: 57 mg (0.16 mmol, 32%); TLC: R_f=0.33 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν=2924, 1596, 1558, 1513, 1495, 1430, 1390, 1328, 1312, 1259, 1189, 1092, 1010 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.77 (d, J= 1.1 Hz, 1H), 7.59 (d, J=8.7 Hz, 2H), 7.35 (d, J=8.7 Hz, 2H), 7.29 (d, J=8.0 Hz, 2H), 7.20 (dd, J=8.4, 1.6 Hz, 1H), 7.15 (d, J=7.9 Hz, 2H), 7.05 (d, J=8.4 Hz, 1H), 5.46 (d, J= 5.6 Hz, 2H), 2.53 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=152.0 (C), 150.3 (C), 142.7 (C), 139.1 (C), 137.6 (C), 137.0 (C), 136.1 (C), 134.98 (C), 134.7 (C), 130.4 (2CH), 129.0 (2CH), 128.5 (2CH), 128.3 (2CH), 123.8 (CH), 119.1 (CH), 113.4 (CH_2), 109.2 (CH), 21.3 (CH_3), 14.6 (CH_3); HR-MS (ESI): m/z=359.1308, calculated for $C_{23}H_{20}ClN_2$ $(M+H)^+$: 359.1315.

1-(4-Methoxyphenyl)-2-methyl-6-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4ah): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ah** as a white solid; yield: 149 mg (0.42 mmol, 84%); mp 132–134 °C; TLC: R_f=0.26 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν=1607, 1581, 1512, 1443, 1395, 1334, 1298, 1250, 1168, 1108, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.79 (d, J=8.3 Hz, 1H, H^{Ar}), 7.40 (d, J=8.7 Hz, 2H, H^{Ar}), 7.34 (m, 3H, H^{Ar}), 7.24 (m, 3H, H^{Ar}), 7.18 (d, J=8.7 Hz, 2H, H^{Ar}), 5.49 (d, J=19.8 Hz, 2H, =CH_2), 4.01 (s, 3H, CH_3), 2.61 (s, 3H, CH_3), 2.48 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=159.8 (C), 152.7 (C), 150.8 (C), 142.4 (C), 139.0 (C), 137.5 (C), 137.0 (C), 136.8 (C), 128.9 (2CH), 128.6 (C), 128.4 (2CH), 128.2 (2CH), 123.6 (CH), 118.3 (CH), 115.2 (2CH), 113.4 (CH_2), 109.7 (CH), 55.7 (CH_3), 21.3 (CH_3), 14.5 (CH_3); HR-MS (ESI): m/z=355.1817, calculated for $C_{24}H_{23}N_2O$ $(M+H)^+$: 355.1810.

4-{1-[1-(4-Fluorophenyl)-2-methyl-1*H*-benzo[*d*]imidazol-6-yl]vinyl}benzonitrile (4ai): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 6/4) afforded **4ai** as a brown solid; yield: 131 mg (0.37 mmol, 74%); mp 138–140 °C; TLC: R_f=0.20 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν=2231, 1604, 1510, 1478, 1447, 1395, 1335, 1268, 1225, 1155, 1095 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.60 (d, J=8.3 Hz, 1H, H^{Ar}), 7.51 (d, J=8.2 Hz, 2H, H^{Ar}), 7.34 (d, J=8.2 Hz, 2H, H^{Ar}), 7.29 (d, J=4.9 Hz, 1H, H^{Ar}), 7.26 (d, J=4.8 Hz, 1H, H^{Ar}), 7.23–7.15 (m, 2H, H^{Ar}), 7.06 (dd, J=8.3, 1.5 Hz, 1H, H^{Ar}), 6.92 (s, 1H, H^{Ar}), 5.43 (d, J= 2.0 Hz, 2H, =CH_2), 2.42 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ=162.6 (d, J=249.9 Hz, C), 152.7 (C), 149.2 (C), 146.4 (C), 142.7 (C), 136.8 (C), 135.5 (C), 132.1 (2CH) 131.8 (d, J=3.0 Hz, C), 129.0 (d, J=8.8 Hz, 2CH), 128.9 (2CH), 123.4 (CH), 118.9 (C), 118.9 (CH), 117.2 (d, J=22.9 Hz, 2CH), 116.7 (CH_2), 111.4 (C), 109.4 (CH), 14.5 (CH_3);

^{19}F NMR (188 MHz, $CDCl_3$): $\delta = -109.45$ (s); HR-MS (ESI): $m/z = 354.1401$, calculated for $C_{23}H_{17}N_3F$ $(M+H)^+$: 354.1407.

2-Ethyl-1-(4-methoxyphenyl)-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4aj): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4aj** as a white solid; yield: 145 mg (0.395 mmol, 79%); mp 140–142 °C; TLC: $R_f = 0.73$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu = 2972$, 1612, 1518, 1464, 1421, 1377, 1340, 1289, 1236, 1199, 1152, 1101, 1073 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.69$ (s, 1H, H^{Ar}), 7.18 (s, 2H, H^{Ar}), 7.15 (d, $J = 2.0$ Hz, 2H, H^{Ar}), 7.06 (d, $J = 9.3$ Hz, 1H, H^{Ar}), 7.01 (d, $J = 7.9$ Hz, 2H, H^{Ar}), 6.95 (d, $J = 8.8$ Hz, 2H, H^{Ar}), 6.89 (d, $J = 8.4$ Hz, 1H, H^{Ar}), 5.32 (s, 2H, $=CH_2$), 3.78 (s, 3H, CH_3), 2.67 (q, $J = 7.5$ Hz, 2H, CH_2), 2.25 (s, 3H, CH_3), 1.25 (t, $J = 7.5$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.9$ (C), 157.3 (C), 150.5 (C), 142.5 (C), 139.2 (C), 137.4 (C), 136.7 (C), 136.4 (C), 128.8 (2CH), 128.6 (C), 128.5 (2 CH), 128.3 (2CH), 123.3 (CH), 119.1 (CH), 115.1 (2CH), 113.0 (CH_2), 109.3 (CH), 55.6 (CH_3), 21.3 (CH_2), 21.2 (CH_3), 12.1 (CH_3); HR-MS (ESI): $m/z = 369.1965$, calculated for $C_{25}H_{25}N_2O$ $(M+H)^+$: 369.1967.

4-{1-[2-Ethyl-1-(4-fluorophenyl)-1*H*-benzo[*d*]imidazol-5-yl]vinyl}benzonitrile (4ak): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ak** as a white solid; yield: 149 mg (0.405 mmol, 81%); mp 157–159 °C; TLC: $R_f = 0.78$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu = 2976$, 2228, 1604, 1511, 1450, 1418, 1377, 1338, 1266, 1239, 1219, 1154, 1122, 1096, 1074 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.72$ (s, 1H, H^{Ar}), 7.61 (d, $J = 8.1$ Hz, 2H, H^{Ar}), 7.48 (d, $J = 8.2$ Hz, 2H, H^{Ar}), 7.70–7.35 (m, 2H, H^{Ar}), 7.32–7.27 (m, 2H, H^{Ar}), 7.13 (d, $J = 9.3$ Hz, 1H, H^{Ar}), 7.03 (d, $J = 8.4$ Hz, 1H, H^{Ar}), 5.58 (d, $J = 21.1$ Hz, 2H, $=CH_2$), 2.79 (q, $J = 7.5$ Hz, 2H, CH_2), 1.37 (t, $J = 7.5$ Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 162.7$ (d, $J = 249.8$ Hz, C), 157.4 (C), 149.1 (C), 146.7 (C), 142.7 (C), 136.8 (C), 135.2 (C), 132.1 (2CH), 131.8 (d, $J = 2.8$ Hz, C), 129.2 (d, $J = 8.7$ Hz, 2CH), 129.0 (2CH), 123.3 (CH), 119.2 (CH), 119.0 (C), 117.2 (d, $J = 22.9$ Hz, 2CH), 116.3 (CH_2), 111.3 (C), 109.6 (CH), 21.3 (CH_2), 11.9 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): $\delta = -109.44$ (s); HR-MS (ESI): $m/z = 368.1563$, calculated for $C_{24}H_{19}N_3F$ $(M+H)^+$: 368.1563.

1-(4-Methoxyphenyl)-2-phenyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4al): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 8/2) afforded **4al** as a white solid; yield: 135 mg (0.325 mmol, 65%); mp 164–166 °C; TLC: $R_f = 0.55$ (cyclohexane/acetone, 95/5, SiO_2); IR (film): $\nu = 1609$, 1512, 1471, 1446, 1384, 1327, 1299, 1248, 1182, 1168, 1108, 1075, 1031 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.92$ (s, 1H, H^{Ar}), 7.63 (dd, $J = 7.7$, 1.6 Hz, 2H, H^{Ar}), 7.36–7.31 (m, 5H, H^{Ar}), 7.26 (d, $J = 9.2$ Hz, 3H, H^{Ar}), 7.18 (d, $J = 3.1$ Hz, 2H, H^{Ar}), 7.15 (d, $J = 3.7$ Hz, 1H, H^{Ar}), 7.03 (d, $J = 8.8$ Hz, 2H, H^{Ar}), 5.50 (s, 2H, $=CH_2$), 3.90 (s, 3H, CH_3), 2.40 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.6$ (C), 153.1 (C), 150.4 (C), 143.0 (C), 139.2 (C), 137.5 (C), 137.4 (C), 137.2 (C), 130.1 (C), 129.7 (C), 129.5 (3CH), 128.9 (2CH), 128.6 (2CH), 128.4 (2CH), 128.3 (2CH), 124.2 (CH), 119.7 (CH), 115.2 (2CH), 113.3 (CH_2), 110.0 (CH), 55.7 (CH_3), 21.3 (CH_3); HR-MS (ESI): $m/z = 417.1973$, calculated for $C_{29}H_{25}N_2O$ $(M+H)^+$: 417.1967.

4-{1-[1-(4-Fluorophenyl)-2-phenyl-1*H*-benzo[*d*]imidazol-5-yl]vinyl]benzonitrile (4am): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 8/2) afforded **4am** as a yellow solid; yield: 147 mg (0.355 mmol, 71%); mp 155–156 °C; TLC: $R_f = 0.51$ (cyclohexane/acetone, 95/5, SiO_2); IR (film): $\nu = 2227$, 1604, 1510, 1474, 1448, 1429, 1383, 1326, 1267, 1225, 1155, 1112, 1094, 1075 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.70$ (s, 1H, H^{Ar}), 7.50 (d, $J = 8.1$ Hz, 2H, H^{Ar}), 7.45 (d, $J = 6.8$ Hz, 2H, H^{Ar}), 7.38 (d, $J = 8.2$ Hz, 2H, H^{Ar}), 7.26–7.16 (m, 5H, H^{Ar}), 7.14–7.05 (m, 4H, H^{Ar}), 5.49 (d, $J = 22.8$ Hz, 2H, $=CH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 162.3$ (d, $J = 248.3$ Hz, C), 153.3 (C), 148.9 (C), 146.5 (C), 143.1 (C), 137.3 (C), 135.7 (C), 132.8 (d, $J = 2.9$ Hz, C), 132.1 (2CH), 129.8 (CH), 129.5 (C), 129.4 (2CH), 129.1 (d, $J = 8.7$ Hz, 2CH), 129.0 (2CH), 128.5 (2CH), 124.0 (CH), 119.7 (CH), 118.9 (C), 117.1 (d, $J = 22.9$ Hz, 2CH), 116.4 (CH_2), 111.3 (C), 110.1 (CH); ^{19}F NMR (188 MHz, $CDCl_3$): $\delta = -109.62$ (s); HR-MS (ESI): $m/z = 416.1562$, calculated for $C_{28}H_{19}N_3F$ $(M+H)^+$: 416.1563.

1-(4-Methoxyphenyl)-2,4-dimethyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4an): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4an** as a yellow solid; yield: 129 mg (0.35 mmol, 70%); mp 163–164 °C; TLC: $R_f = 0.57$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu = 1611$, 1512, 1442, 1386, 1318, 1297, 1250, 1227, 1183, 1169, 1107, 1034 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.19$ (d, $J = 8.8$ Hz, 2H, H^{Ar}), 7.11 (d, $J = 8.1$ Hz, 2H, H^{Ar}), 6.97 (m, 5H, H^{Ar}), 6.83 (d, $J = 8.2$ Hz, 1H, H^{Ar}), 5.71 (s, 1H, $=CH_2$), 5.07 (s, 1H, $=CH_2$), 3.79 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 2.22 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 159.8$ (C), 151.6 (C), 149.2 (C), 142.1 (C), 138.5 (C), 137.3 (C), 135.8 (C), 135.7 (C), 129.0 (2CH), 128.9 (C), 128.4 (2CH), 127.1 (C), 126.6 (2CH), 125.0 (CH), 115.1 (2CH), 114.3 (CH_2), 107.0 (CH), 55.7 (CH_3), 21.2 (CH_3), 14.4 (2CH_3); HR-MS (ESI): $m/z = 369.1973$, calculated for $C_{25}H_{25}N_2O$ $(M+H)^+$: 369.1967.

4-{1-[1-(4-Fluorophenyl)-2,4-dimethyl-1*H*-benzo[*d*]imidazol-5-yl]vinyl}benzonitrile (4ao): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 6/4) afforded **4ao** as a white solid; yield: 150 mg (0.41 mmol, 82%); mp 170–172 °C; TLC: $R_f = 0.44$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu = 2227$, 1605, 1511, 1424, 1386, 1328, 1220, 1155, 1095, 1042 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.46$ (d, $J = 8.2$ Hz, 2H, H^{Ar}), 7.29 (m, 4H, H^{Ar}), 7.20 (m, 2H, H^{Ar}), 6.95 (d, $J = 8.2$ Hz, 1H, H^{Ar}), 6.85 (d, $J = 8.2$ Hz, 1H, H^{Ar}), 5.85 (s, 1H, $=CH_2$), 5.31 (s, 1H, $=CH_2$), 2.43 (s, 3H, CH_3), 2.32 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 162.6$ (d, $J = 247.5$ Hz, C), 151.6 (C), 148.0 (C), 145.8 (C), 142.3 (C), 135.9 (C), 134.3 (C), 132.2 (2CH), 132.1 (d, $J = 3.0$ Hz, C), 129.0 (d, $J = 8.7$ Hz, 2CH), 127.2 (2CH), 125.0 (CH), 119.0 (2C), 118.4 (CH_2), 117.1 (d, $J = 22.9$ Hz, 2CH), 111.0 (C), 107.2 (CH), 14.4 (2CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): $\delta = -109.67$ (s); HR-MS (ESI): $m/z = 368.1559$, calculated for $C_{24}H_{19}N_3F$ $(M+H)^+$: 368.1563.

1-(4-Methoxyphenyl)-2,4-dimethyl-6-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4ap): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ap** as a white solid; yield: 147 mg (0.40 mmol, 80%); mp 180–182 °C; TLC: $R_f = 0.40$ (cyclohexane/acetone, 7/3, SiO_2); IR (film): $\nu = 1612$, 1590, 1513, 1442, 1416, 1337, 1300, 1251, 1222, 1183, 1169, 1109, 1035 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.27$ (dd, $J = 8.1$, 5.0 Hz, 4H, H^{Ar}), 7.14 (s, 1H, H^{Ar}), 7.12 (s, 1H, H^{Ar}), 7.06 (m, 3H, H^{Ar}), 6.97 (s, 1H, H^{Ar}), 5.37 (d, $J = 18.2$ Hz, 2H, $=CH_2$), 3.89 (s, 3H, CH_3), 2.70 (s,

3H, CH_3), 2.53 (s, 3H, CH_3), 2.37 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7 (C), 151.8 (C), 150.6 (C), 141.5 (C), 139.1 (C), 137.4 (C), 136.7 (C), 136.5 (C), 128.8 (2CH, C), 128.4 (2CH), 128.1 (2CH, C), 123.9 (CH), 115.1 (2CH), 113.2 (CH_2), 107.4 (CH), 55.6 (CH_3), 21.2 (CH_3), 16.8 (CH_3), 14.4 (CH_3); HR-MS (ESI): m/z = 369.1968, calculated for $C_{25}H_{25}N_2O$ $(M+H)^+$: 369.1967.

4-{1-[1-(4-Fluorophenyl)-2,4-dimethyl-1*H*-benzo[*d*]imidazol-6-yl]vinyl}benzonitrile (4aq): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4aq** as a brown solid; yield: 141 mg (0.385 mmol, 77%); mp 132–134 °C; TLC: R_f = 0.40 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2228, 1604, 1511, 1450, 1418, 1377, 1338, 1266, 1239, 1154, 1122, 1096, 1074 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, J = 8.2 Hz, 2H, H^{Ar}), 7.34 (d, J = 8.3 Hz, 2H, H^{Ar}), 7.28–7.23 (m, 2H, H^{Ar}), 7.20–7.14 (m, 2H, H^{Ar}), 6.87 (s, 1H, H^{Ar}), 6.75 (s, 1H, H^{Ar}), 5.41 (d, J = 3.9 Hz, 2H, $=CH_2$), 2.57 (s, 3H, CH_3), 2.43 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.6 (d, J = 248.3 Hz, C), 151.9 (C), 149.3 (C), 146.6 (C), 141.9 (C), 136.4 (C), 135.4 (C), 132.1 (2CH), 132.0 (d, J = 1.9 Hz, C), 129.0 (d, J = 8.8 Hz, 2CH), 128.9 (2CH, C), 123.8 (CH), 119.0 (2C), 117.2 (d, J = 22.9 Hz, 2CH), 116.5 (C), 111.3 (C), 107.2 (CH), 16.8 (CH_3), 14.5 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −109.56 (s); HR-MS (ESI): m/z = 368.1558, calculated for $C_{24}H_{19}N_3F$ $(M+H)^+$: 368.1563.

6-Fluoro-1-(4-methoxyphenyl)-2-methyl-5-[1-(*p*-tolyl)vinyl]-1*H*-benzo[*d*]imidazole (4ar): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4ar** as a white solid; yield: 123 mg (0.33 mmol, 66%); mp 204–206 °C; TLC: R_f = 0.45 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 1629, 1608, 1512, 1469, 1442, 1396, 1324, 1300, 1250, 1184, 1169, 1146, 1111, 1035 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, J = 6.6 Hz, 1H, H^{Ar}), 7.28 (t, J = 8.9 Hz, 4H, H^{Ar}), 7.11 (t, J = 8.2 Hz, 4H, H^{Ar}), 6.80 (d, J = 9.7 Hz, 1H, H^{Ar}), 5.57 (d, J = 103.2 Hz, 2H, $=CH_2$), 3.92 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 2.36 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.0 (C), 157.2 (d, J = 240.8 Hz, C), 152.9 (C), 144.9 (C), 138.6 (C), 138.1 (C), 137.5 (C), 136.6 (d, J = 12.8 Hz, C), 128.9 (2CH), 128.3 (C), 128.1 (2CH), 126.6 (2CH), 125.0 (d, J = 17.8 Hz, C), 120.9 (d, J = 4.7 Hz, CH), 115.71 (C), 115.2 (2CH), 97.0 (d, J = 29.0 Hz, CH), 55.6 (CH_3), 21.1 (CH_3), 14.3 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −116.28 (s); HR-MS (ESI): m/z = 373.1715, calculated for $C_{24}H_{22}N_2OF$ $(M+H)^+$: 373.1716.

4-{1-[6-Fluoro-1-(4-fluorophenyl)-2-methyl-1*H*-benzo[*d*]-imidazol-5-yl]vinyl}benzonitrile (4as): Flash chromatography on silica gel (cyclohexane/acetone, 10/0 to 7/3) afforded **4as** as a white solid; yield: 160 mg (0.43 mmol, 86%); mp 220–222 °C; TLC: R_f = 0.38 (cyclohexane/acetone, 7/3, SiO_2); IR (film): ν = 2227, 1630, 1603, 1512, 1472, 1445, 1397, 1325, 1226, 1149, 1111, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.67 (d, J = 6.6 Hz, 1H, H^{Ar}), 7.61 (d, J = 8.3 Hz, 2H, H^{Ar}), 7.45 (d, J = 8.3 Hz, 2H, H^{Ar}), 7.41–7.27 (m, 4H, H^{Ar}), 6.80 (d, J = 9.7 Hz, 1H, H^{Ar}), 5.73 (d, J = 69.3 Hz, 2H, $=CH_2$), 2.52 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.8 (d, J = 249.0 Hz, C), 157.1 (d, J = 249.0 Hz, C), 153.0 (C), 145.6 (C), 144.0 (C), 138.9 (C), 136.8 (d, J = 12.6 Hz, C), 132.3 (2CH), 131.6 (d, J = 2.3 Hz, C), 128.9 (d, J = 8.7 Hz, 2CH), 127.4 (2CH), 123.8 (d, J = 17.7 Hz, C), 121.1 (d, J = 4.3 Hz, CH), 119.6 (CH_2), 119.0 (C), 117.4 (d, J = 23.0 Hz, 2CH), 111.3 (C), 97.3 (d, J = 28.9 Hz, CH), 14.5 (CH_3); ^{19}F NMR (188 MHz, $CDCl_3$): δ = −108.94 (s), −115.52 (s); HR-MS (ESI): m/z = 372.1312, calculated for $C_{23}H_{16}N_3F_2$ $(M+H)^+$: 372.1312.

Acknowledgements

The authors gratefully acknowledge support of this project by CNRS, University Paris Sud and by "La LigueContre le Cancer" through an "Equipe Labellisée 2014" grant. BioCIS UMR 8076 laboratory is a member of the Laboratory of Excellence LERMIT supported by a grant from ANR (ANR-10-LABX-33).

References

[1] E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257–10274.
[2] For a recent discussion of bioactive thiazole compounds, see the following: a) G. Sachs, J. M. Shin, C. W. Howden, *Aliment. Pharmacol. Ther.* **2006**, *23*, 2–8; b) M. Gaba, S. Singh, C. Mohan, *Eur. J. Med. Chem.* **2014**, *76*, 494–505.
[3] L. A. Torre, F. Bray, R. L. Siegel, J. Ferlay, J. Lortet-Tieulent, A. Jemal, *CA Cancer J. Clin.* **2015**, *65*, 87–108.
[4] G. R. Pettit, S. B. Singh, E. Hamel, C. M. Lin, D. S. Alberts, D. Garcia-Kendal, *Experientia* **1989**, *45*, 209–211.
[5] J. C. Y. Lu, M. Xiao, W. Li, D. D. Miller, *Pharm. Res.* **2012**, *29*, 2943–2971.
[6] S. L. Young, D. J. Chaplin, *Expert Opin. Invest. Drugs* **2004**, *13*, 1171–1182.
[7] a) C. Mousset, A. Giraud, O. Provot, A. Hamze, J. Bignon, J.-M. Liu, S. Thoret, J. Dubois, J.-D. Brion, M. Alami, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3266–3271; b) S. Messaoudi, A. Hamze, O. Provot, B. Treguier, J. R. De Losada, J. Bignon, J. M. Liu, J. Wdzieczak-Bakala, S. Thoret, J. Dubois, J. D. Brion, M. Alami, *ChemMedChem* **2011**, *6*, 488–497.
[8] a) S. Messaoudi, B. Treguier, A. Hamze, O. Provot, J. F. Peyrat, J. R. De Losada, J. M. Liu, J. Bignon, J. Wdzieczak-Bakala, S. Thoret, J. Dubois, J. D. Brion, M. Alami, *J. Med. Chem.* **2009**, *52*, 4538–4542; b) A. Hamze, A. Giraud, S. Messaoudi, O. Provot, J.-F. Peyrat, J. Bignon, J.-M. Liu, J. Wdzieczak-Bakala, S. Thoret, J. Dubois, J.-D. Brion, M. Alami, *ChemMedChem* **2009**, *4*, 1912–1924.
[9] For reviews on *N*-Tosylhydrazones, see: a) J. Barluenga, C. Valdés, *Angew. Chem.* **2011**, *123*, 7626–7640; *Angew. Chem. Int. Ed.* **2011**, *50*, 7486–7500; b) Z. Shao, H. Zhang, *Chem. Soc. Rev.* **2012**, *41*, 560–572.
[10] J. Barluenga, P. Moriel, C. Valdés, F. Aznar, *Angew. Chem.* **2007**, *119*, 5683–5686; *Angew. Chem. Int. Ed.* **2007**, *46*, 5587–5590.
[11] J. Barluenga, L. Florentino, F. Aznar, C. Valdés, *Org. Lett.* **2011**, *13*, 510–513.
[12] F. Ye, C. Wang, X. Ma, M. L. Hossain, Y. Xia, Y. Zhang, J. Wang, *J. Org. Chem.* **2015**, *80*, 647–652.
[13] a) J. Aziz, J.-D. Brion, A. Hamze, M. Alami, *Adv. Synth. Catal.* **2013**, *355*, 2417–2429; b) J. Aziz, G.

Frison, M. Gomez, J. D. Brion, A. Hamze, M. Alami, *ACS Catal.* **2014**, *4*, 4498–4503.
[14] L. Zhou, Y. Shi, Q. Xiao, Y. Liu, F. Ye, Y. Zhang, J. Wang, *Org. Lett.* **2011**, *13*, 968–971.
[15] a) L. Wu, X. O. Zhang, Q.-Q. Chen, A.-K. Zhou, *Org. Biomol. Chem.* **2012**, *10*, 7859–7862; b) X.-W. Feng, J. Wang, J. Zhang, J. Yang, N. Wang, X.-Q. Yu, *Org. Lett.* **2010**, *12*, 4408–4411.
[16] N. Zheng, K. W. Anderson, X. Huang, H. N. Nguyen, S. L. Buchwald, *Angew. Chem.* **2007**, *119*, 7653–7656; *Angew. Chem. Int. Ed.* **2007**, *46*, 7509–7512.
[17] a) X.-X. Wu, P.-X. Zhou, L.-J. Wang, P.-F. Xu, Y.-M. Liang, *Chem. Commun.* **2014**, *50*, 3882–3884; b) P.-X. Zhou, J.-Y. Luo, L.-B. Zhao, Y.-Y. Ye, Y.-M. Liang, *Chem. Commun.* **2013**, *49*, 3254–3256; c) X. S. Shang, N. T. Li, H. X. Siyang, P. N. Liu, *J. Org. Chem.* **2015**, *80*, 4808–4815; d) Y. Xia, Y. Xia, Y. Zhang, J. Wang, *Org. Biomol. Chem.* **2014**, *12*, 9333–9336; e) R. Barroso, R. A. Valencia, M.-P. Cabal, C. Valdés, *Org. Lett.* **2014**, *16*, 2264–2267; f) E. S. Gutman, V. Arredondo, D. L. Van Vranken, *Org. Lett.* **2014**, *16*, 5498–5501; g) X. Liu, X. Ma, Y. Huang, Z. Gu, *Org. Lett.* **2013**, *15*, 4814–4817; h) Z. Liu, Y. Xia, S. Zhou, L. Wang, Y. Zhang, J. Wang, *Org. Lett.* **2013**, *15*, 5032–5035.
[18] M. Roche, A. Hamze, J.-D. Brion, M. Alami, *Org. Lett.* **2013**, *15*, 148–151.
[19] W. R. Bamford, T. S. Stevens, *J. Chem. Soc.* **1952**, 4735–4740.
[20] J. Barluenga, M. Tomás-Gamasa, F. Aznar, C. Valdés, *Angew. Chem.* **2010**, *122*, 5113–5116; *Angew. Chem. Int. Ed.* **2010**, *49*, 4993–4996.
[21] J. E. R. Sadig, R. Foster, F. Wakenhut, M. C. Willis, *J. Org. Chem.* **2012**, *77*, 9473–9486.
[22] CCDC 1444539 (**4a**), CCDC 1444540 (**4p**), CCDC 1444541 (**4t**), CCDC 1444542 (**4ak**), CCDC 1444543 (**4al**) and CCDC 1444544 (**4ao**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.
[23] S. P. Crouch, R. Kozlowski, K. J. Slater, J. Fletcher, *J. Immunol. Methods* **1993**, *160*, 81–88.
[24] G. R. Pettit, B. Toki, D. L. Herald, P. Verdier-Pinard, M. R. Boyd, E. Hamel, R. K. Pettit, *J. Med. Chem.* **1998**, *41*, 1688–1695.

