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The application of Stille cross-coupling reactions with multiple nitrogen containing heterocycles

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ABSTRACT

Substituted imidazoles and purine bioisosteres have been widely studied in the literature. We endeavored to combine these heterocyclic core structures into precursors, especially 7-azaindoles, of previously unknown pharmacologically relevant lead structures. A highly flexible synthetic procedure was developed, derived from investigations of the influence of the substrates, solvents, ligand systems, and side reactions.

1. Introduction

In recent years, purines and their bioisosteres have attracted special interest in medicinal chemistry[1–4] as inhibitors of kinase activity or of phosphodiesterase 4 (PDE-4). Therefore, these heterocycles may be potentially useful for the treatment of rheumatoid arthritis, COPD (chronic obstructive pulmonary disease), asthma, and rhinitis. The rigid donor–acceptor systems of these compounds constitute core subunits in many bioactive molecules and natural products. In addition, imidazoles have been also widely studied as potent p38 MAP kinase inhibitors.[5] Many synthetic efforts have been accomplished to introduce specific functionalizations to these heterocycles. As part of our drug research discovery program, we sought a robust method to functionalize the aforementioned heterocycles, faced with the difficulty of C–C bond formations between these core structures. In this study, we focussed on imidazole structures as basic framework, derived from known p38α MAP kinase inhibitors SB203580 and SKF86002 (Fig. 1). These inhibitors have already been optimized by substituting the pyridinyl moiety at the C-2 position by several alkyl- and arylamines **1** (Fig. 1). We envisioned an exchange of the flexible amine moiety with seven-membered heterocycles, which contain the essential hydrogen bond donor–acceptor system. Heterocycles like purines, pyrrolopyrimidines, and 7-azaindoles fulfill the specifications of such a system. Therefore, we were in need to a robust and flexible synthesis, suitable to introduce various substituents at the C-5 position of the imidazole core.

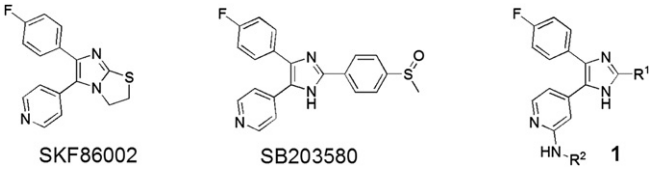
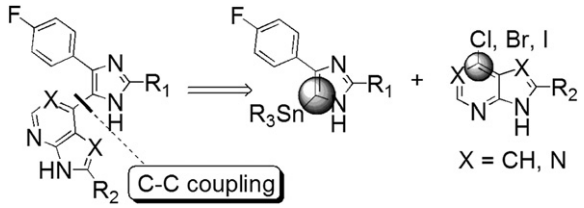


Fig. 1. p38 MAP kinase inhibitors.

We considered palladium-catalyzed cross-coupling reactions to introduce C-5 substituents to the central imidazole core as the most promising synthetic strategy to fulfill this objective (Scheme 1).



Scheme 1. Retrosynthetic analysis of the target structures, based on the C–C cross-coupling reaction.

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2. Results and discussion

2.1. Stannylation of imidazoles

Two possibilities appeared to be feasible for the cross-coupling reaction, using either the halogenated imidazoles[6] or the halogenated heterocycles and the corresponding transmetallation partners. We used the electron rich imidazoles as the transmetallating agents and the electron poor heterocycles for the oxidative addition (Scheme 1). Due to their electronic characters, C–C coupling should be enforced. The halogenation of the desired heterocycles (Fig. 2) can be achieved in good yields by literature known procedures.[2,7–9]

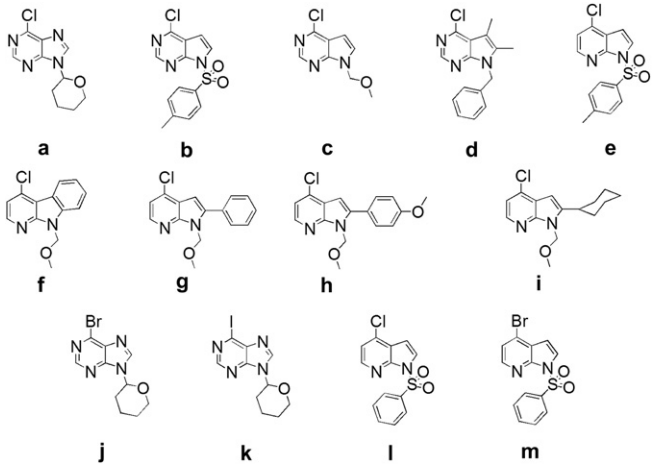


Fig. 2. Halogenated substrates for the cross-coupling reaction.

The described methods of generating transmetallation coupling centers on imidazoles led us to select the Stille-coupling reaction as the most effective method.[10]

We attempted to synthesize stannylated imidazoles of the corresponding imidazoles **2**–**9** with a fixed substitution pattern in 2- and 4-position (Fig. 3).

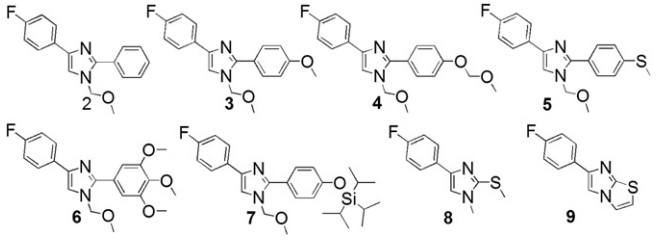
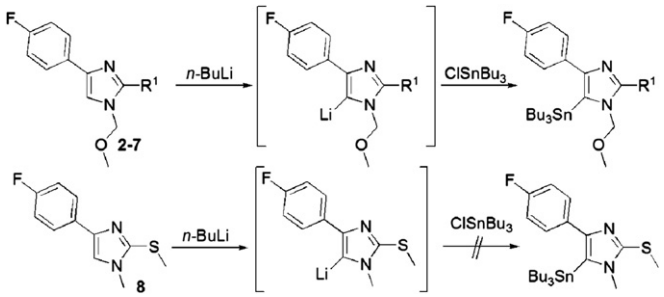


Fig. 3. Imidazoles for stannylation.

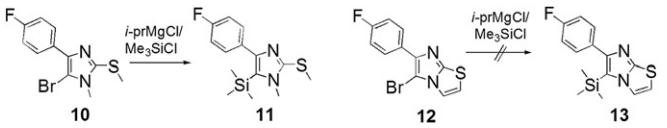
The C-5 stannylated derivatives of imidazoles **2**–**9** (Fig. 3) were expected to be useful as broad synthetic platform for the variation of the C-5 position of the central imidazole core. The synthesis of the imidazole derivatives **2**–**9** (Fig. 3) was accomplished by literature known procedures.[6,11–14] Stannylation of the diarylimidazoles **2**–**7** via C-5 lithiation yielded positive results (Scheme 2) and the stannylated imidazoles were used for the subsequent cross-coupling reaction without further purification, due to an observed protodestannylation. In the course of the imidazole stannylations, we could observe a strong dependency on the C-2 substitution of the imidazole core. This was supposed to be the reason for the failed stannylation of thioimidazole **8** (Scheme 2).

We assumed that the electron donating character of sulfur with its +M-effect, affording high electron density at the C-5 position of the imidazole, prevents the C–Sn bond formation. To evaluate this assumption, we synthesized the corresponding thiazole **9** where



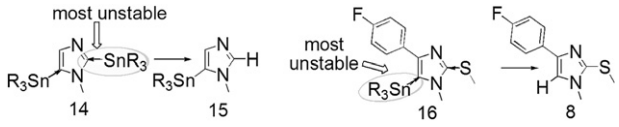
Scheme 2. Stannylation of the imidazole derivatives **2**–**8**.

the electron donating effect is assisted by the +M-effect of the bridged vinyl moiety. Then we tried to generate the more stable C–Si bonding in the C-5 position (Scheme 3) of the two thioimidazole derivatives **8** and **9** from the brominated derivatives **10** and **12**. The S–Me silylimidazole **11** could be synthesized while the synthesis of the corresponding silylimidazothiazole **13** failed (metalation of the thiazole **12** was proven by deuteration, see Supplementary data). This outcome supports our hypothesis, that the strengthened electron donating effect of sulfur is increased by the enforced +M-stabilization, resulting in a complete destabilization of the C–Si bonding.



Scheme 3. Silylation of thioimidazoles.

The same mechanism can be applied to the weaker C–Sn bonding (Scheme 4), which is now in a more unfavorable energetic range than the C–Si bonding. The electronic character of the S–Me bond of compound **8** is now sufficient to destabilize the C–Sn bonding. Similarly, this mechanism can also be observed by the stannylation of the *N*-Me imidazole (Scheme 4).[10] A destannylation occurs in the 5- and 2-positions (**14**) and the most unstable bonding, the C-2–Sn bond, is hydrolyzed to compound **15**. In the case of the thioimidazole **16**, the C–S bonding is the more stable bonding, so that cleavage of the more labile 5-stannyl moiety is favored.

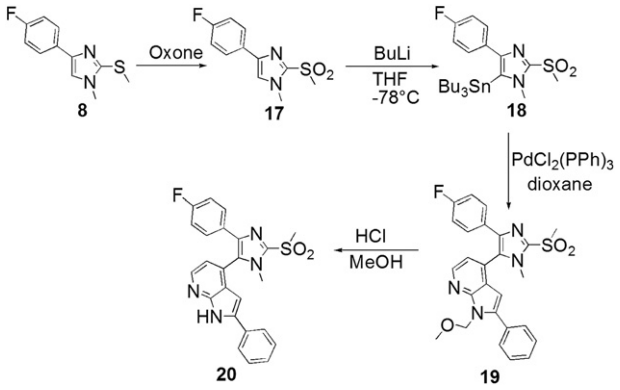


Scheme 4. Electronic effect of C-2 substitution.

In conclusion, electron rich substituents at C-2 position of the imidazole prevent stannylation in C-5-position. Therefore, we changed the electron donating character of sulfur by its oxidation to the corresponding sulfone **17** (Scheme 5). The sulfone could be stannylated by the above mentioned procedure. The subsequent Stille-coupling provided compound **19**, further deprotection lead to compound **20**.

2.2. Reactivity of the stannylimidazoles with different purine biosisosters

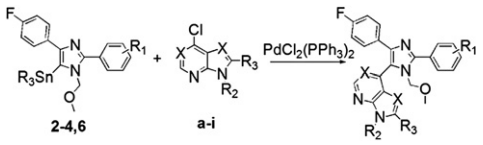
The rare literature known Stille couplings of imidazoles and halogenated heterocycles are confined to electron poor heterocycles and therefore activated species like pyridine,[15] pyrimidine[16] or



Scheme 5. Stannylation and C–C cross coupling of the sulfone **17**.

purine.[17] The reactivity of these heterocycles is sufficient enough for cross-coupling reactions without the problems we found in case of electron rich and therefore deactivated heterocycles. In analogy to the procedures of Liverton,[16] we performed cross-coupling experiments with several combinations of halogenated purines and bioisosteric structures (Fig. 2), using $PdCl_2(PPh_3)_2$ as pre-catalyst in THF (Table 1, entries 1–4). The yields corresponded to our expectations. The electron poor heterocycles, purines and pyrrolopyrimidines, excelled in providing high yields and high reaction rates due to their electron poor character (Table 1, entries 1–3).

Table 1
Accomplished cross-coupling reactions with the different heterocycles



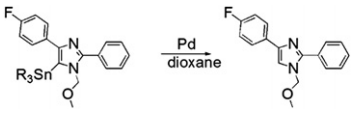
Entry[a]	Stannylated imidazole	Heterocycle[b]	Solvent	Isolated yield (%)
1	**2**	**a**	THF	62
2	**2**	**c**	THF	63
3	**2**	**b**	THF	55
4	**2**	**e**	THF	10
5	**2**	**d**	Dioxane	52
6	**2**	**a**	Dioxane	80
7	**2**	**e**	Dioxane	27
8	**2**	**f**	Dioxane	40
9	**2**	**g**	Dioxane	21
10	**2**	**h**	Dioxane	39
11	**2**	**i**	Dioxane	31
12	**3**	**g**	Dioxane	31
13	**4**	**g**	Dioxane	35
14	**6**	**g**	Dioxane	48

[a] Solvent (4 ml), stirring frequency 5r/s, 2 equiv of the stannylated imidazole **2**, reflux temperature.
[b] ~0.09 mmol.

The yields and reaction rates with 7-azaindole were strongly decreased (Table 1, entry 4) by virtue of the increased electron density, which led to decreased reactivity in the oxidative addition and the transmetallation. Therefore, we tried to develop a high yielding synthetic procedure focusing on this problem. A first modification of the reaction conditions was to change the solvent from THF to dioxane with the intention of higher reaction temperatures and thus higher reaction rates (Table 1, entries 5–14). The improved, but moderate yields led us decide to further investigate these coupling reactions.

To exclude the observed catalyst decomposition as reason for the lowered yields with the $PdCl_2(PPh_3)_2$ system, we tried to stabilize the catalyst by increasing the palladium/ligand ratio from 1/2 up to 1/4 (Table 2, entries 1–6).

Table 2
Cross-coupling with different Pd/ligand ratios



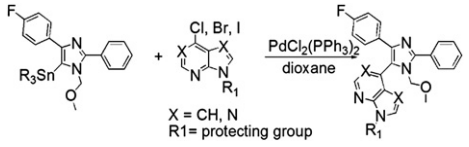
Entry	Conditions Catalyst loading	Ratio Pd/ligand (PPh_3)	t (min)	Yield[b] TOF
1	79 °C[a] 13.2 mol %	1/2	227	12% 0.21 h^{-1}
2	79 °C[a] 13.2 mol %	1/2	Overnight	26%
3	79 °C[a] 15.3 mol %	1/3	227	9% 0.14 h^{-1}
4	79 °C[a] 15.3 mol %	1/3	Overnight	29%
5	79 °C[a] 13.4 mol %	1/4	227	5% 0.09 h^{-1}
6	79 °C[a] 13.4 mol %	1/4	Overnight	8%

[a] Dioxane (3 ml), stirring frequency 5r/s, 2 equiv of the stannylated imidazole **2** (0.068 mmol).
[b] Quantified by HPLC.

The turn-over frequencies (TOFs) decreased with increasing Pd-ligand ratio (Table 2, entries 1, 3, and 5). The overall yield was shown to be equal to the 1/2 and 1/3 ratio (Table 2, entries 2 and 4), whereas the 1/4 ratio was shown to be ineffective (Table 2, entries 5 and 6). The observed catalyst decomposition was inhibited by raising the Pd/ligand ratio to 1/3. The decomposition could only be observed after heating overnight, in contrast to the 1/2 ratio with an observable decomposition after heating for 4 h.

To optimize the synthetic procedure to a high yielding procedure, it was necessary to determine the rate determining steps of the catalytic pathway. We performed several coupling experiments with activated purine and deactivated azaindole halogen derivatives with $Pd(PPh_3)Cl_2$ as the pre-catalyst (Table 3), using the stannylated imidazole **2** for the transmetallation.

Table 3
Cross-coupling of purine and azaindole derivatives with $PdCl_2(PPh_2)_3$

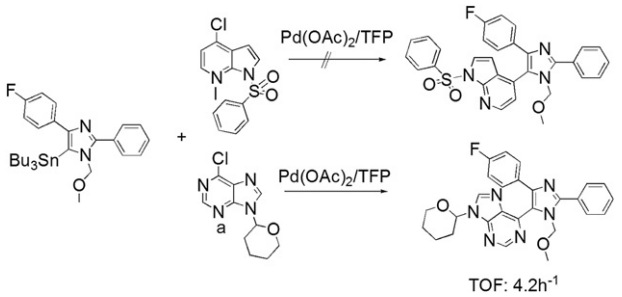


Entry[a]	Catalyst loading	Heterocycle[c]	t (min)	Yield[d] (TOF)
1[a]	20 mol %	**l**	20/40	16/22 (1.1 h^{-1}/0.7 h^{-1})
2[a]	23 mol %	**m**	20	35 (4.4 h^{-1})
3[a]	21 mol %	**a**	20/40	23/33 (3.3 h^{-1}/2.4 h^{-1})
4[a]	25 mol %	**j**	20/40	15/19 (1.8 h^{-1}/1.1 h^{-1})
5[a]	21 mol %	**k**	20/40	9/11 (1.2 h^{-1}/0.8 h^{-1})
6[b]	30 mol %	**a**	20	12 1.2 h^{-1}

[a] Dioxane (1 ml), stirring frequency 5r/s, 2 equiv of the stannylated imidazole **2**, 101 °C.
[b] Dioxane (1 ml), stirring frequency 5r/s, 2 equiv of the stannylated imidazole **2**, 72 °C.
[c] ~0.09 mmol.
[d] Quantified by HPLC.

As expected, the reactivity profile inverted with the substrate. The turn-over frequencies of the halogenated purines increased in the following order Cl>Br>I (Table 3, entries 3–5). This ranking corresponds to the transmetallation being the rate determining step and to an associative mechanism.[18] Two possible explanations for the inverted reactivities of the corresponding halogenated azaindoles (Table 3, entries 1 and 2) are feasible. The oxidative addition may be rate determining and therefore the chlorinated species is disfavored. On the other hand, a dissociative mechanism should present the same reactivity profile as the azaindole due to

a facilitated ligand dissociation in the case of the less electronegative halogenides. To clarify the observed reactivities, we performed the cross-coupling reactions with tri-2-furylphosphine (TFP) (Scheme 6). The lower σ-donor activity should favor the transmetallation reaction and decrease the rate of oxidative addition.[19,20] If the transmetallation is the rate determining step, an enhanced reaction rate should be observed in contrast to the PPh_3 ligand system. In the case of the chlorinated purine **a** (Fig. 2), a 3.5fold increase of the reaction rate was monitored at 72 °C (Scheme 6/Table 3, entry 6), whereas the chlorinated azaindole **l** showed no activity, even at higher temperatures. This result is consistent with our assumption that the transmetallation is the rate determining step in the cross-coupling reaction of purines, whereas the cross-coupling reaction of azaindoles seems to be determined by the oxidative addition, hindered by the lower nucleophilicity of the Pd–TFP-species.

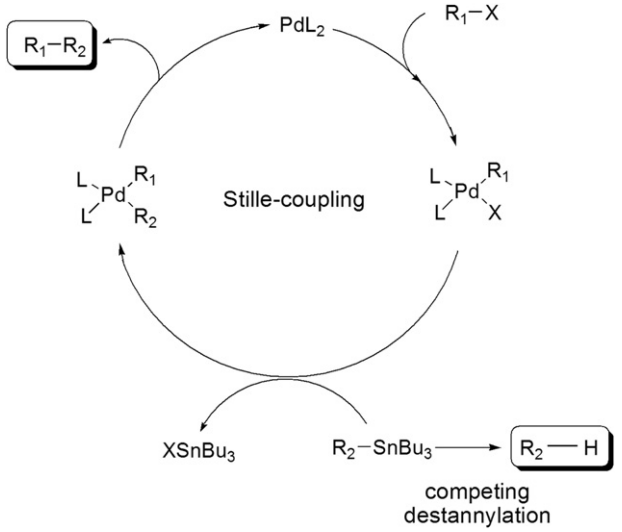


Scheme 6. Coupling reaction of the chlorinated azaindole and purine with TFP as ligand system (catalyst loading 11 mol %, dioxane, 72 °C).

The cross-coupling procedure for the purine substrates could be optimized with the TFP-ligand system by facilitation of the transmetallation reaction. In case of the azaindole substrates, this strategy is unfeasible, because of their supposed inversion of the rate determining steps.

2.3. Destannylation process

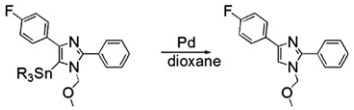
The limiting factor in this reaction is the stability of the individual stannylated imidazoles, expressed in the monitored decomposition of the stannyl derivatives as competitive reaction of the cross-couplings (Scheme 7). Especially, the cross-coupling reaction with the low reactive azaindoles is dominated by this side reaction. A further detrimental effect is the strong catalyst decomposition, indicated by Pd-black.



Scheme 7. Stille-coupling and competitive destannylation.

The observed destannylation is already described in literature.[21,22] In order to surpress the destannylation, we made additional series of experiments. To investigate a possible thermal decomposition of the stannyl substrate, we first heated the stannylated compound **2** (Table 4, entry 6) in dioxane for 1 h at reflux temperature. The decomposition of 1% is not corresponding to the observed decomposition within the cross-coupling reaction. Traces of water are a common assumed culprit for the destannylation via a mechanism of protodestannylation. Therefore, we examined the destannylation of the stannylated compound **2** under drastic water concentrations (compared to traces of water) of 0.1 ml per ml under reflux conditions and argon atmosphere. An enhanced decomposition took place, but the decomposition rate of 11% per hour (Table 4, entry 5) was also not in the range of the observed decomposition in the coupling reaction. Examination of the destannylation in combination with the catalyst resulted in strongly increased decomposition rates. The marked increase in the decomposition of the stannylated species by the catalyst indicates, that the destannylation step is involved in a catalytic mechanism. A further increase of catalyst decomposition was observed by the addition of water (0.1 ml per ml), indicating a direct dependency of the destannylation rates on the water concentration. Traces of water can be expected in the pre-catalyst and in the stannyl compound. We assumed, that traces of water are mainly originated from the stannyl substrate. This is in accordance with the synthesis of the stannylimidazoles, by using an excess of butyllithium and tributylstannyl chloride with subsequent quenching by water. Tributylstannyl hydroxide is formed as byproduct, which can further react to the distannylether under release of water by heating.[23] Thus, a water induced catalytic destannylation can take place. To elucidate a possible influence of the various ligands, we quantified the destannylation of the stannylated species **2** with different ligand systems of the catalyst by quantitative NMR (Table 4, entries 1–5).

Table 4
Effect of the catalyst on destannylation of the stannylated imidazole **2**



Entry[a]	Catalyst	*t* (h)	Additive	Decomposition[b]
1	$PdCl_2(PPh_3)_2$ 11 mol %	0.37	—	38.9% 1.8%/min (TOF 9.6)
2	$PdCl_2(PPh_3)_2$ 11 mol %	0.13	H_2O	22.7% 2.8%/min (TOF 16.5)
3	$Pd(OAc)_2$/X-Phos 13 mol %	0.37	—	33.2% 1.5%/min (TOF 6.82)
4	$Pd(OAc)_2$/X-Phos 16 mol %	0.13	H_2O	40.8% 5.1%/min (TOF 18.7)
5	$Pd(OAc)_2$/TFP 28 mol %	1.25	—	8.2% 0.1%/min (TOF 0.27)
6	—	1.03	—	1.3% 0.02%/min
7	—	0.55	H_2O	11.1% 0.3%/min

[a] Dioxane (2 ml), stirring frequency 5 r/s, 0.09 mmol of stannylated imidazole **2**, 72 °C.
[b] Quantified by NMR.

The destannylation rates were in the range between 0.02%/min (no catalyst, Table 4, entry 6) and 1.8%/min ($PdCl_2(PPh_3)_2$/11 mol %, Table 4, entry 1). The decomposition rates were further increased by adding water to the reaction mixture (Table 4, entries 2 and 4).

As shown, the destannylation process is strongly dependent on the water concentration. On this account, the monitored TOFs of the cross-coupling and the destannylation reactions should be evaluated with care, since the concentration of water can vary with the lot of the stannylated compounds. In comparison to PPh_3, nearly the same destannylation rates can be observed with X-Phos (2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl) as ligand system, whereas the low σ-donor TFP (trifurylphosphine) is significantly reducing the destannylation process. A high electron density on the Pd-center seems to be crucial for the destannylation process, exemplified by the PPh_3 (Table 4, entry 1) as well as the X-Phos system (Table 4, entry 3) with comparable reaction rates. In conclusion, the destannylation process is involved in a catalyst dependent reaction path. Regarding the overall cross-coupling procedure, there is a competing effect of the destannylation and the cross-coupling reaction on the catalyst. Therefore, the dominating reaction is determined by the reaction rates of the two individual reaction pathways.

2.4. Optimization of the cross-coupling reaction

Combining these gained results, we optimized the cross-coupling of the deactivated 7-azaindoles. At first, we focussed on a technical modification of the synthetic procedure by stepwise addition of the stannylimidazoles. As shown above, the oxidative addition was supposed to be the rate determining step in the case of azaindole with PPh_3 as ligand system. Consequently, the rate of the reaction should be independent of the concentration of the stannylated species. The rate of the destannylation proved to be dependent on the water concentrations, resulting from the stannylated compounds. By stepwise addition of the stannylimidazoles, the water concentration is reduced to a minimum without affecting the rates of the cross-coupling reactions. This strategy allowed us a threefold increase of the yields from 21% (Table 1, entry 9) to 67% (Table 5, entry 1), with $PdCl_2(PPh_3)_2$ as pre-catalyst. Similar results were obtained in further experiments with related stannylimidazoles (Table 5, entries 2–4).

Table 5
Improved cross-coupling procedure by stepwise addition of the stannyl compound

Entry	Stannylated imidazole	Heterocycle	Solvent	Isolated yield (%)
1	**2**	**g**	Dioxane	67
2	**3**	**g**	Dioxane	65
3	**5**	**g**	Dioxane	60
4	**7**	**g**	Dioxane	71

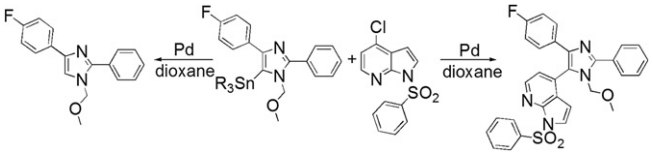
The effects of the ligand sphere on the destannylation process led us decide to use X-Phos in the following coupling experiments. In general, the rate constant of the coupling reaction should significantly exceed the rate constant of the competing destannylation. The inhibitory effect of 7-azaindoles in the coupling reaction is due to their obstructed oxidative addition. Thus, the cross-coupling reactions should be enhanced by using ligands with higher reactivity toward the oxidative addition and without affecting the rate of the destannylation. In our investigations of the destannylation, X-Phos and PPh_3 showed nearly the same reactivities (Table 4, entries 1 and 3). On the other hand, a markedly differing reactivity toward the oxidative addition was expected. Based on the bulkiness of X-Phos, an increase of the reactivity toward oxidative addition with X-Phos can be expected.[24–26] The rate constants of the electronic contrary chlorinated purine and azaindole derivatives with X-Phos as ligand system were determined by quantitative HPLC (Table 6), using the stannylated imidazole **2** as representative substrate for the transmetallation.

Table 6
Cross-coupling with $Pd(OAc)_2$/X-Phos (1/3) as pre-catalyst

Entry	Conditions Catalyst loading	Heterocycle[c]	*t* (min)	Yield[d] TOF
1	101 °C[a] 5 mol %	**l**	20	34% 16.6 h^{-1}
2	101 °C[b] 7 mol %	**l**	5	70% 121 h^{-1}
3	101 °C[a] 10 mol %	**m**	20	18% 1.2 h^{-1}
4	72 °C[a] 6 mol %	**a**	20	34% 17.1 h^{-1}
5	72 °C[a] 4 mol %	**j**	20	13% 9.7 h^{-1}
6	72 °C[a] 5 mol %	**k**	20	5% 2.6 h^{-1}

[a] Dioxane (1 ml), stirring frequency 5 r/s.
[b] Microwave 300 W, 101 °C, 1 ml dioxane.
[c] ~0.09 mmol, 2 equiv stannylimidazole.
[d] Quantified by HPLC.

The effect of X-Phos on the electron poor purine derivative was positively influenced by the accelerating effect of X-Phos on the transmetallation,[27] resulting in a fourfold increased reaction rate compared to TFP (Table 6, entry 4, Scheme 6). In the case of chlorazaindole **l** with X-Phos, the TOF is about 15-fold higher than in the case of the PPh_3 ligand system under the same conditions (Table 3, entry 1 and Table 6, entry 1). Another benefit of this ligand system is the stability in the course of the reaction. The TOFs with X-Phos were nearly constant and the catalyst decomposition was also strongly decreased, which allows a reliable product formation in contrast to $PdCl_2(PPh_3)_2$. To directly compare the effects of the PPh_3 and X-Phos ligand systems on the competing reaction of the cross-coupling, we measured the product formation and the destannylation via quantitative NMR and HPLC (Scheme 8/Fig. 4) by reacting the stannylated imidazole **2** and the chlorinated azaindole **l**.



Scheme 8. Quantification of cross-coupling with **l** versus destannylation of the stannylated imidazole **2**.

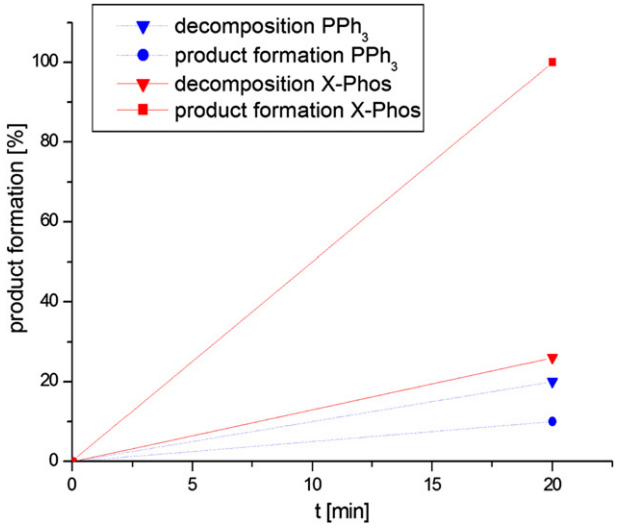


Fig. 4. Destannylation and product formation in the cross-coupling experiment with Cl-azaindole **l**.

The cross-coupling was performed with a stannyl overload of 2 equiv. The product to destannylation ratio of the cross-coupling with $PdCl_2(PPh_3)_2$ was 0.5 (Fig. 4), so the catalyst activity toward the coupling reaction was reduced to about 30%. A theoretical overload of 3 equiv of the stannylimidazole would be necessary to achieve a full product conversion. The observed poor stability of the catalyst is an additional factor to exclude a full product conversion. The product to destannylation ratio of 3.8 in the case of X-Phos was completely inverted (Fig. 4) with a catalyst activity of 80%. A theoretical overload of 1.2 equiv of the stannylimidazole would be sufficient for quantitative conversion. The stability of the catalyst with its constant turn-over frequencies (Table 3) guarantees a full product conversion, which was observed in the ongoing performed experiments.

In the case of the X-Phos ligand, a selective, nearly unidirectional acceleration of the cross-coupling path was shown. The cross-coupling reaction dominates the overall reaction. In contrast, the destannylation is the dominant factor in the cross-coupling reaction with PPh_3, reflected by the poor yields in the coupling experiments with the azaindoles (Table 1, entries 4 and 7–13). To further accelerate the cross-coupling reaction, we also used microwave irradiation and examined, in case of the chlorinated azaindole **l**, a strongly increased turn-over frequency (Table 6, entry 2). The TOF was raised up from 1.1 h^{-1} (Table 3, entry 1), 16.6 h^{-1} (Table 6, entry 1) to 120.9 h^{-1} (101 °C/microwave irradiation) (Table 6, entry 2). We transferred these gained results to the substituted azaindoles **f**, **g**, **i** and to the purine **a**. The cross-coupling experiments were performed under microwave irradiation for 10–15 min with a catalyst loading of 8 mol % (Table 7). The yields were comparable with the yields, which were obtained within 1 h under reflux conditions. The up to nearly quantitative yields were in accordance to our results of this optimization study.

Table 7
Cross-coupling procedure under microwave irradiation

Entry	Stannylated imidazole[a]	Heterocycle	Solvent[b]	Isolated yield (%)
1	**2**	**a**	Dioxane	79
2	**2**	**g**	Dioxane	94
3	**5**	**g**	Dioxane	92
4	**2**	**i**	Dioxane	50

[a] 2 equiv.
[b] 1 ml.

3. Conclusion

The performed optimization study of cross-coupling experiments with different activated and deactivated halogen derivatives of purine and its bioisosteres showed a substrate- and catalyst-dependent reactivity profile with respect to the cross-coupling reaction. A ligand-based substrate specific optimization for the cross-coupling of the electron poor halogen derivatives by using TFP as the ligand system was accomplished. We achieved an overall optimization for activated and deactivated halogenated heterocycles with up to nearly quantitative yields (Table 7) by using X-Phos as the ligand system, raising the turn-over frequencies from 1.1 h^{-1} to 120.9 h^{-1}. The competitive destannylation was demonstrated as a catalyst dependent reaction path as well as a ligand and substrate induced selectivity could be shown. The destannylation reaction could be significantly surpressed by a nearly unidirectional acceleration of the coupling reaction. The destannylation reaction could also be lowered by a technical modification, which can be generally applied to cross-coupling reactions with the problem of sensitive transmetallating substrates and deactivated halogenides.

4. Experimental section

4.1. General experimental methods

All commercially available reagents and solvents were used without further purification. NMR data were obtained on a Bruker Spectrospin AC 200 instrument at ambient temperature. High-resolution spectral mass data were obtained on a Thermo Finnigan TSQ70 instrument. Melting points were measured on a Buechi Melting Point B-545 instrument. IR-spectra were obtained by a Perkin–Elmer Spectrum One (ATR) instrument. LC–mass spectrometry (MS) spectra were recorded by a Finnigan TSQ Quantum triple quadrupole mass spectrometer (Finnigan MAT). GC–Mass spectrometry was done by Hewlett Packard HP 6890 Series GC-System (Hewlett Packard HP 5973 Mass Selective Detector). Method used for GC–MS: starting 120 °C, hold 2 min; heating rate 10–200 °C, hold 1 min; heating rate 10–300 °C, hold 5 min.

4.2. General procedure of stannylation of the imidazoles

The *N*-protected diarylimidazole was dissolved in THF and cooled to −78 °C. Then *n*-BuLi was added. The reaction mixture was stirred for 60 min at −78 °C, then $ClSnBu_3$ was added and the reaction mixture was stirred for 30 min at rt. The solvent was removed under reduced pressure and the obtained oily product was used for following coupling reactions without further purification.

4.3. General procedures of the cross-coupling procedures

4.3.1. General procedure of Stille-coupling (methods A and B). The halogenated *N*-protected heterocycle, $PdCl_2(PPh_3)_2$ (0.3 mol %) and the stannylimidazole (2 equiv) was dissolved in 3–6 ml THF (procedure A) or dioxane (procedure B). The reaction mixture was stirred at reflux temperature under argon atmosphere for up to 4 h. After quenching with KF (40% in water) and extracting with EtOAc, the crude product was purified by flash-chromatography.

4.3.2. General procedure of Stille-coupling (method C). The halogenated *N*-protected heterocycle, $PdCl_2(PPh_3)_2$ (0.3 mol %) was dissolved in 3–6 ml dioxane the stannylimidazole (2 equiv) was added stepwise (consumption of the stannyl derivative was monitored by TLC) to the reaction mixture at reflux temperature under argon atmosphere, after complete consumption of the added stannylimidazole. After quenching with KF (40% in water) and extracting with EtOAc, the crude product was purified by flash-chromatography.

4.3.3. General procedure of Stille-coupling (method D). A premilled mixture (0.1 mol % Pd) of $Pd(OAc)_2$ and X-Phos (1/3) was stirred in dioxane for 30 min, the yellow solution turned to a dark purple solution. The halogenated *N*-protected heterocycle and the stannylimidazole (2 equiv) was added to the reaction mixture and heated under microwave irradiation (300 W, 100 °C, 10–15 min) under nitrogen atmosphere. After quenching with KF (40% in water) and extracting with EtOAc, the crude product was purified by flash-chromatography.

4.3.4. General procedure of Stille-coupling (method E). A premilled mixture of $Pd(OAc)_2$ and X-Phos (1/3) was stirred in dioxane for 30 min, the yellow solution turned to a dark purple solution. The halogenated *N*-protected heterocycle and the stannylimidazole (2 equiv) was added to the reaction mixture and heated under nitrogen atmosphere until complete consumption of the starting materials (monitored by TLC).

4.3.5. General procedure of Stille-coupling (method F). A premilled mixture of $Pd(OAc)_2$ and TFP (1/3) was stirred in dioxane for

30 min, the yellow solution turned to a dark purple solution. The halogenated *N*-protected heterocycle and the stannylimidazole (2 equiv) was added to the reaction mixture and heated under nitrogen atmosphere.

*4.3.5.1. 4-(4-Fluorophenyl)-1-methyl-2-(methylthio)-5-(trimethylsilyl)-1H-imidazole (**11**).* 5-Bromo-4-(4-fluorophenyl)-1-methyl-2-(methylthio)-1*H*-imidazole 200 mg (0.7 mmol) was dissolved in 5 ml dry THF, after addition of 78 mg (0.7 mmol) isopropylmagnesium chloride (2 M in THF), the reaction mixture was stirred for 45 min. Then 70 mg (0.7 mmol) trimethylsilylchloride was added and the reaction mixture was stirred for 1 h. The reaction was quenched with water and extracted with ethylacetate. The organic layer was separated and solvent was removed under reduced pressure. The crude product was subjected to flash-chromatography (eluent ethylacetate/*n*-hexane 1/2) to yield 115 mg (59%) of the pure product. TLC (ethylacetate/*n*-hexane 1/2): R_f=0.81; IR (ATR) [cm^{-1}]: 2949, 1534, 1476, 1303, 1251, 1218, 1156, 1122, 1090, 837, 817, 765, 693; ^{1}H NMR (200 MHz, methanol-d_4) δ ppm 0.07 (s, 9H) 2.47 (s, 3H) 3.68 (s, 3H) 7.04 (m, 2H) 7.28 (m, 2H); ^{13}C NMR (50.33 MHz, methanol-d_4) δ ppm 0.48, 16.8, 34.9, 115.5 (2C, d, *J*=22.1 Hz), 130.2, 133.1 (d, *J*=8.6 Hz), 134.1 (d, *J*=3.5 Hz), 147.6, 152.0, 164.1 (d, *J*=245.6 Hz); MS (GC–MS) t_R, *m*/*z*: 8.410 min (GC–MS) t_R, *m*/*z*: 294, mp: 104 °C.

*4.3.5.2. 4-(4-Fluorophenyl)-2-[4-(methylthio)phenyl]-1H-imidazole (educt of **5**).* Yield 59.5% (1.95 g, 6.9 mmol); IR (ATR) [cm^{-1}]: 3234, 2923, 1606, 1537, 1536, 1490, 1428, 1217, 1130, 1108, 948, 844, 838, 824, 813, 777, 727, 697, 657; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 2.51 (s, 3H) 7.13 (m, 2H) 7.33 (d, *J*=8.59 Hz, 2H) 7.58 (s, 1H) 7.91 (m, 2H) 7.99 (d, *J*=8.59 Hz, 2H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm 14.3, 115.0 (d, *J*=21.6 Hz), 125.4, 126.1, 126.3 (d, *J*=7.9 Hz), 127.5, 146.2, 161.5 (d, *J*=242.9 Hz); MS (GC–MS) t_R, *m*/*z*: 21.7 min, 284; mp: 179 °C.

*4.3.5.3. 4-(4-Fluorophenyl)-1-(methoxymethyl)-2-[4-(methylthio)phenyl]-1H-imidazole (**5**).* Yield 60% (1.04 g, 3.2 mmol); IR (ATR) [cm^{-1}]: 1561, 1493, 1424, 1362, 1214, 1181, 1152, 1113, 1096, 916, 843, 812, 763, 729, 661; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 2.50 (s, 3H) 3.39 (s, 3H) 5.20 (s, 2H) 7.06 (m, 2H) 7.32 (m, 3H) 7.77 (m, 4H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 15.3, 56.3, 76.1115.3 (2C, d, *J*=21.5 Hz), 116.6, 126.0, 126.0, 126.6 (d, *J*=8.0 Hz), 129.2, 129.8 (d, *J*=3.1 Hz), 140.3, 148.5, 162.0 (d, *J*=245.6 Hz); MS (GC–MS) t_R, *m*/*z*: 21.5, 328; mp: 80 °C.

*4.3.5.4. 4-(4-Fluorophenyl)-2-[4-(methoxymethoxy)phenyl]-1-(methoxymethyl)-1H-imidazole (**4**).* Yield 92% (0.247 g; 0.7 mmol); ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 3.43 (s, 3H) 3.46 (s, 3H) 5.26 (s, 2H) 5.36 (s, 2H) 7.13 (m, 4H) 7.73 (s, 1H) 7.77 (d, *J*=8.97 Hz, 2H) 7.91 (m, 2H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm: 55.2, 55.4, 77.1, 94.0, 114.9 (2C, d, *J*=21.7 Hz), 116.0, 117.7, 124.1, 126.3 (d, *J*=7.8 Hz), 129.8, 145, 157.8, 161.4; mp. oily substance at rt.

*4.3.5.5. 4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazole (**2**).* Yield 83% (0.850 g, 3 mmol); IR (ATR) [cm^{-1}]: 2939, 1563, 1495, 1364, 1213, 1174, 1154, 1101, 1072, 918, 843, 837, 772, 754, 721, 700, 686; ^{1}H NMR (200 MHz, methanol-d_4) δ ppm 3.22 (s, 3H) 5.09 (s, 2H) 6.96 (m, 2H) 7.35 (m, 3H) 7.51 (m, 1H) 7.64 (m, 4H); ^{13}C NMR (50.33 MHz, methanol-d_4) δ ppm 56.3, 78.0, 115.9 (d, *J*=21.6 Hz), 118.6, 127.5 (d, *J*=21.6 Hz), 129.3, 129.8, 130.2, 130.4, 130.9 (d, *J*=3.0 Hz), 140.67, 149.9, 162.5 (d, *J*=244.6 Hz) MS (GC–MS) t_R, *m*/*z*:17.7 min,238; mp107 °C.

*4.3.5.6. 4-(4-Fluorophenyl)-1-(methoxymethyl)-2-(4-methoxyphenyl)-1H-imidazole (**3**).* Yield 84% (0.732 g, 2.3 mmol); IR (ATR) [cm^{-1}]: 2934, 1610, 1540, 1498, 1481, 1458, 1428, 1391, 1299, 1251, 1221, 1174, 1157, 1079, 1024, 976, 970, 843, 814, 764, 745, 667; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 3.38 (s, 3H) 3.84 (s, 3H) 5.20 (s, 2H) 7.03 (m, 4H) 7.31 (s, 1H) 7.77 (m, 4H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.3, 56.3, 77.3, 114.1, 115.8 (d, *J*=21.6 Hz), 116.2, 122.4, 126.6 (d=8.0 Hz), 130.1 (d, *J*=3.0 Hz), 130.4, 140.2, 148.9, 160.36, 162.0 (d, *J*=245.1 Hz); MS (GC–MS) t_R; *m*/*z*: 19.9Min,312; mp. 71 °C.

*4.3.5.7. 4-(4-Fluorophenyl)-2-(4-methoxyphenyl)-1H-imidazole (educt of **3**).* Yield 56% (0.814 g, 3 mmol); IR (ATR) [cm^{-1}]: 3003, 1614, 1570, 1502, 1435, 1254, 1216, 1175, 1134, 1027, 836, 814, 781, 740, 678, 634, 553, 530, 519; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 3.75 (s, 3H) 6.81 (d, *J*=8.34 Hz, 2H) 6.99 (m, 2H) 7.64 (m, 2H) 7.74 (d, *J*=8.46 Hz, 2H) 9.58 (s, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.2, 114.1, 115.4 (2C, d, *J*=21.6 Hz), 122.6, 126.6 (d, *J*=7.9 Hz), 127.0, 129.1 (d, *J*=3.3 Hz), 138.6, 147.4, 160.1, 161.9 (d, *J*=245.8 Hz); MS (GC–MS) t_R, *m*/*z*:19.7, 268; mp: 145 °C.

*4.3.5.8. 4-(4-Fluorophenyl)-2-(3,4,5-trimethoxyphenyl)-1H-imidazole (educt of **6**).* Yield 72% (4.2 g, 15 mmol); IR (ATR) [cm^{-1}]: 2938, 1588, 1499, 1464, 1432, 1230, 1123, 999, 836, 813, 768, 729, 665; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 3.67 (s, 3H) 3.79 (s, 6H) 6.99 (m, 2H) 7.16 (s, 2H) 7.30 (s, 1H) 7.64 (m, 2H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.2, 59.7, 102.7, 114.9 (d, *J*=22.1 Hz), 125.5, 126.4 (d, *J*=8.1 Hz), 129.1 (d, *J*=3.0 Hz), 138.3, 147.2, 153.4, 161.9 (d, *J*=244.6 Hz), MS (GC–MS) t_R, *m*/*z*: 22.3 min, 328; mp: 118 °C.

*4.3.5.9. 4-(4-Fluorophenyl)-1-(methoxymethyl)-2-(3,4,5-trimethoxyphenyl)-1H-imidazole (**6**).* Yield 74% (2.3 g, 6.2 mmol); IR (ATR) [cm^{-1}]: 2932, 1590, 1562, 1500, 1473, 1464, 1381, 1323, 1240, 1135, 1075, 1000, 967, 956, 733; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 3.38 (s, 3H) 3.90 (s, 3H) 3.92 (s, 6H) 7.15 (m, 5H) 7.55 (m, 2H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.1, 56.1, 60.8, 75.0, 105.9, 115.9 (d, *J*=21.5 Hz), 125.1, 125.6 (d, *J*=3.2 Hz), 126.7, 130.4 (d, *J*=8.1 Hz), 134.6, 139.0, 150.0, 153.3, 162.73 (d, *J*=248.6 Hz); MS (GC–MS) t_R, *m*/*z*: 22.3 min, 328; mp: 117 °C.

*4.3.5.10. 4-(4-Fluorophenyl)-2-{4-[(triisopropylsilyl)oxy]phenyl}-1H-imidazole (educt of **7**).* Yield 46% (2.72 g, 6.62 mmol); IR (ATR) [cm^{-1}]: 2943, 2867, 1609, 1499, 1481, 1439, 1265, 1234, 1123, 912, 883, 839, 771, 740, 687, 671; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 1.06 (s, 9H) 1.09 (s, 9H) 1.24 (m, 3H) 6.87 (d, *J*=8.72 Hz, 2H) 7.01 (m, 2H) 7.20 (m, 1H) 7.65 (m, 2H) 7.74 (d, *J*=8.72 Hz, 2H) 8.66 (m, 1H); ^{13}C NMR (50.33 MHz, CHLOROFORM-D) δ ppm 12.5, 115.5 (d, *J*=21.6 Hz), 120.3, 122.8, 126.5 (d, *J*=7.9 Hz), 126.8, 129.1 (d, *J*=3.1 Hz), 147.3, 156.9, 161.9 (d, *J*=245.8 Hz); MS (LC–MS) t_R, *m*/*z*: 7.38 min, 411 [M+H$^+$]; mp: 137 °C.

*4.3.5.11. 4-(4-Fluorophenyl)-1-(methoxymethyl)-2-{4-[(triisopropylsilyl)oxy]phenyl}-1H-imidazole (**7**).* Yield 54% (0.800 g, 1.76 mmol); IR (ATR) [cm^{-1}]: 2944, 2867, 1609, 1532, 1498, 1476, 1461, 1426, 1362, 1281, 1264, 1211, 1172, 1099, 909, 881, 842, 773, 748, 732, 683; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 1.12 (s, 9H) 1.15 (s, 9H) 1.33 (m, 3H) 3.42 (s, 3H) 5.33 (s, 2H) 7.03 (d, *J*=8.72 Hz, 2H) 7.12 (m, 2H) 7.73 (s, 1H) 7.79 (d, *J*=8.72 Hz, 2H) 7.91 (m, 2H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm; 12.4, 17.3, 55.4, 77.1, 114.9 (d, *J*=21.5 Hz), 117.6, 119.7, 123.7, 126.3 (d, *J*=8.0 Hz), 130.0, 131.1 (d, *J*=3.1 Hz), 139.3, 148.0, 156.6, 161.6 (d, *J*=243 Hz); MS (LC–MS) t_R, *m*/*z*: 12.84 min, 455 [M+H$^+$]; mp: 79 °C.

*4.3.5.12. 2-Cyclohexyl-1H-pyrrolo[2,3-b]pyridine (educt of **i**).* IR (ATR) [cm^{-1}]: 3126, 3071, 2920, 2849, 1609, 1587, 1538, 1423, 1276, 892, 820, 797, 767, 760, 725, 661; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 1.64 (m, 8H) 2.21 (m, 2H) 2.90 (m, 1H, *ipso*-ChH) 6.20 (s, 1H) 7.05 (m, 1H) 7.86 (dd, *J*=7.71, 1.39 Hz, 1H) 8.24 (dd, *J*=4.93, 1.52 Hz, 1H) 12.43 (s, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 26.1,

26.3, 32.6, 37.8, 94.9, 115.2, 121.7, 127.7, 140.2, 147.0, 149.0; MS (GC–MS) t_R, *m/z*: 13.2 min, 200; mp: 171 °C; yield: 47%.

*4.3.5.13. 4-Chloro-2-cyclohexyl-1H-pyrrolo[2,3-b]pyridine (educt of **i**).* Yield 45% (0.789 g, 3.4 mmol) IR (ATR) [cm^{-1}]: 3126, 2927, 1607, 1577, 1534, 1447, 1408, 1297, 1184, 1155, 961, 871, 849, 799, 789, 761, 669; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 1.44 (m, 5H) 1.84 (m, 3H) 2.15 (m, 2H) 2.84 (m, 1H) 6.30 (s, 1H) 7.08 (d, *J*=5.31 Hz, 1H) 8.09 (d, *J*=5.18 Hz, 1H) 11.74 (s, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 27.0, 26.1, 37.6, 94.0, 115.6, 120.8, 134.9, 140.6, 147.4, 149.1; MS (GC–MS) t_R, *m/z*:15.2 min, 234; mp: 191 °C; yield: 61%.

*4.3.5.14. 4-Chloro-2-cyclohexyl-1-(methoxymethyl)-1H-pyrrolo [2,3-b]pyridine (**i**).* Yield 36% (0.300 g, 1.08 mmol); IR (ATR) [cm^{-1}]: 2928, 2853, 1591, 1561, 1536, 1475, 1272, 1255, 1163, 1112, 1069, 912, 808, 785, 757, 725; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 1.71 (m, 10H) 2.85 (m, 1H) 3.27 (s, 3H) 5.67 (s, 2H) 6.36 (s, 1H) 7.05 (d, *J*=5.31 Hz, 1H) 8.10 (d, *J*=5.18 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 25.9, 26.4, 33.4, 35.6, 56.1, 72.1, 95.2, 116.4, 119.9; 134.7, 141.8, 147.7; MS (GC–MS) t_R, *m/z*: 15.0 min, 278; mp: colorless oil at rt; yield: 42%.

*4.3.5.15. 4-Chloro-9-(methoxymethyl)-9H-pyrido[2,3-b]indole (**f**).* Yield 62.8%; IR (ATR) [cm^{-1}]: 2934, 2828, 1588, 1557, 1464, 1454, 1412, 1367, 1292, 1221, 1119, 1070, 1056, 903, 810, 784, 749, 737, 675; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 3.29 (s, 3H) 5.92 (s, 2H) 7.34 (d, *J*=5.43 Hz, 1H) 7.41 (td, *J*=8.08, 1.01 Hz, 1H) 7.63 (td, *J*=7.20, 1.14 Hz, 1H) 7.76 (d, *J*=8.34 Hz, 1H) 8.44 (m, 2H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 56.4, 72.6, 110.1, 114.0, 116.9, 119.9, 121.2, 123.2, 127.5, 138.1, 139.2, 145.8, 152.4; MS (GC–MS) t_R, *m/z*: 13.8 min, 246; mp: 94 °C.

*4.3.5.16. 2-(4-Methoxyphenyl)-1H-pyrrolo[2,3-b]pyridin (educt of **h**).* Yield 80.4% (6.97 g, 31.1 mmol); IR (ATR) [cm^{-1}]: 3147, 2837, 1613, 1490, 1441, 1277, 1245, 1182, 1114, 1029, 013, 827, 799, 761, 725; ^{1}H NMR (200 MHz, DMSO-d_6) δ ppm 3.78 (s, 3H) 6.74 (m, 1H) 7.01 (m, 3H) 7.86 (m, 3H) 8.17 (dd, *J*=4.67, 1.52 Hz, 1H) 12.05 (s, 1H); ^{13}C NMR (50.33 MHz, DMSO-d_6) δ ppm 55.5, 96.0, 114.7, 116.2, 121.5, 124.6, 127.1, 127.6, 138.8, 140.5, 150.0, 159.6, MS (GC–MS) t_R, *m/z*: 17.1, 224; mp: 211 °C.

*4.3.5.17. 4-Chloro-1-(methoxymethyl)-2-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (**h**).* Yield 33%; IR (ATR) [cm^{-1}]: 2939, 2833, 1616, 1591, 1499, 1474, 1376, 1300, 1289, 1250, 1180, 1156, 1072, 1032, 996, 906, 826, 794, 770, 758, 697; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 3.41 (s, 3H) 3.87 (s, 3H) 5.61 (s, 2H) 6.64 (s, 1H) 7.08 (d, *J*=8.84 Hz, 2H) 7.22 (d, *J*=5.18 Hz, 1H) 7.75 (d, *J*=8.97 Hz, 2H) 8.23 (d, *J*=5.18 Hz, 1H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm 56.4, 57.6, 74.3, 99.2, 115.7, 118.3, 121.0, 125.1, 129.4, 129.4, 130.7, 132.1, 134.7, 135.6, 144.6, 152.0, 162.0, 206.70; MS (GC–MS) t_R, *m/z*: 18.0 min, 302; mp: 98 °C.

*4.3.5.18. 4-Chloro-2-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (educt of **h**).* Yield 48% (0.650 g, 2.5 mmol); IR (ATR) [cm^{-1}]: 2839, 1766, 1614, 1575, 1500, 1349, 1291, 1281, 1247, 1177, 1024, 859, 832, 782, 748, 623, 567, 527; ^{1}H NMR (200 MHz, DMSO-d_6) δ ppm 3.80 (s, 3H) 6.85 (s, 1H) 7.03 (d, *J*=8.84 Hz, 2H) 7.16 (d, *J*=5.18 Hz, 1H) 7.93 (d, *J*=8.97 Hz, 2H) 8.11 (d, *J*=5.18 Hz, 1H) 12.39 (s, 1H); ^{13}C NMR (50.33 MHz, DMSO-d_6) δ ppm 55.3, 93.6, 114.4, 115.7, 120.1, 123.4, 127.1, 132.9, 139.5, 142.7, 150.1, 159.6; MS (GC–MS) t_R, *m/z*: 18.7 min, 260; mp:251 °C.

*4.3.5.19. 4-(4-(4-Fluorophenyl)-1-(methoxymethyl)-2-{4-[(triisopropylsilyl)oxy]phenyl}-1H-imidazol-5-yl)-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**7g**).* According to general procedure C (Table 5) TLC (ethylacetate/*n*-hexane 1/4): R_f=0.22; IR (ATR) [cm^{-1}]: 2944, 2893, 1608, 1510, 1480, 1379, 1252, 1220, 1168, 1079, 921, 883, 840, 805, 758, 744, 682, 662; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 1.12 (s, 9H) 1.16 (m, 9H) 1.34 (s, 3H) 3.09 (s, 3H) 3.42 (m, 3H) 5.18 (m, 2H) 5.69 (m, 2H) 6.33 (s, 1H) 6.93 (m, 2H) 7.08 (d, *J*=8.84 Hz, 2H) 7.46 (m, 6H) 7.65 (m, 2H) 7.87 (d, *J*=8.84 Hz, 1H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm 12.42, 17.3, 57.8, 55.8, 72.5, 75.0, 100.4, 114.5 (d, *J*=21.5 Hz), 118.7, 119.8, 120.0, 123.7, 125.9, 128.5 (d, *J*=8.3 Hz), 128.9, 130.3, 131.2 (d, *J*=3.1 Hz), 131.5, 137.7, 142.7, 143.2, 149.3, 150.4, 156.9, 161.6 (d, *J*=243.9 Hz); HRMS (ESI): calcd for $C_{41}H_{47}FN_4O_3Si$ $[M+H]^+$ 691.34742, found 691.34763 (error 0.09 ppm); mp: 105 °C.

*4.3.5.20. 4-{4-(4-Fluorophenyl)-1-(methoxymethyl)-2-[4-(methylthio)phenyl]-1H-imidazol-5-yl}-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**5g**).* According to general procedures C and D (Tables 5 and 7) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.58; IR (ATR) [cm^{-1}]: 2928, 1599, 1507, 1478, 1370, 1247, 1219, 1156, 1080, 964, 908, 839, 776, 756, 742, 698; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 2.53 (s, 3H) 3.13 (s, 3H) 3.50 (s, 3H) 5.02 (m, 2H) 5.64 (m, 2H) 6.22 (s, 1H) 6.87 (m, 2H) 7.45 (m, 10H) 7.85 (d, *J*=8.72 Hz, 2H) 8.47 (d, *J*=4.93 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm: 15.2, 55.5, 56.5, 100.5, 114.97 (d, *J*=21.4 Hz), 118.7, 120.3, 126.0, 126.1, 128.6, 128.7, 128.8, 129.1, 129.3, 129.9, 131.3, 138.3, 140.6, 143.1 (d, *J*=8.1 Hz), 149.5, 150.2, 161.9 (d, *J*=246.2 Hz); HRMS (ESI): calcd for $C_{33}H_{29}FN_4O_2S$ $[M+H]^+$ 565.2068, found 565.2066 (error 0.39 ppm); mp: 159 °C.

*4.3.5.21. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**2g**).* According to general procedures B, C, and D (Tables 1, 5, and 7) TLC (ethylacetate/*n*-hexane 2/1): R_f=0.58, TLC (ethylacetate/*n*-hexane 1/1): R_f=0.51, IR (ATR) [cm^{-1}]: 3061, 2929, 1590, 1511, 1475, 1379, 1357, 1325, 1250, 1222, 1189, 1076, 958, 843, 761, 698; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 3.10 (s, 3H, ImMOMCH$_3$) 3.43 (s, 3H) 5.22 (m, 2H) 5.70 (m, 2H) 6.34 (s, 1H) 6.95 (m, 2H) 7.49 (m, 9H) 7.67 (m, 2H) 7.95 (m, 2H) 8.49 (d, *J*=4.93 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.5, 56.5, 72.8, 75.0, 100.5, 115.0 (d, *J*=21.5 Hz), 118.7, 120.3, 126.0, 126.1, 128.6, 128.7, 128.8, 129.1, 129.4, 129.9, 131.3, 138.3, 143.0, 143.2, 149.8, 150.2, 161.9 (d, *J*=246.7 Hz); HRMS (ESI): calcd for $C_{32}H_{27}FN_4O_2$ $[M+H]^+$ 519.21908, found 519.219057 (error 0.04 ppm); mp: 137 °C.

*4.3.5.22. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-(4-methoxyphenyl)-1H-imidazol-5-yl]-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**3g**).* According to general procedures B and C (Tables 1 and 5) IR (ATR) [cm^{-1}]: 2939, 1590, 1512, 1482, 1378, 1251, 1173, 1070, 1031, 955, 843, 831, 762, 700; ^{1}H NMR (200 MHz, chloroform-*d*) δ ppm 3.13 (s, 3H) 3.50 (s, 3H) 3.87 (s, 3H) 5.02 (m, 2H) 5.63 (m, 2H) 6.21 (s, 1H) 6.89 (m, 2H) 7.04 (d, *J*=9.10 Hz, 2H) 7.50 (m, 7H) 7.90 (d, *J*=8.84 Hz, 2H) 8.48 (d, *J*=5.18 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.3, 55.8, 56.6, 72.8, 75.2, 100.2, 114.3, 115.2 (d, *J*=22.2 Hz), 115.5, 118.7, 120.2, 120.2, 128.7, 128.8, 129.1, 130.5, 131.1, 143.2, 150.1; HRMS (ESI): calcd for $C_{33}H_{29}FN_4O_3$ $[M+H]^+$ 549.2297, found 549.2300 (error 0.70 ppm).

*4.3.5.23. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-(3,4,5-trimethoxyphenyl)-1H-imidazol-5-yl]-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**6g**).* According to general procedure B (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.32; IR (ATR) [cm^{-1}]: 2937, 1587, 1510, 1486, 1422, 1374, 1321, 1238, 1133, 1076, 848, 837, 762, 701; ^{1}H NMR (200 MHz, acetone-d_6) δ ppm 3.19 (s, 3H) 3.43 (s, 3H) 3.80 (s, 3H) 3.91 (m, 6H) 5.20 (m, 2H) 5.70 (m, 2H) 6.30 (s, 1H) 6.95 (m, 2H) 7.29 (s, 2H) 7.48 (m, 6H) 7.66 (m, 2H) 8.49 (d, *J*=4.93 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 55.6, 56.2, 56.5, 72.8, 75.0, 100.4, 106.6, 115.1 (d, *J*=21.5 Hz), 118.6, 120.3, 126.2, 128.6, 128.8, 128.9, 129.1, 131.2, 131.2, 143.2, 149.5, 150.2,

153.3; HRMS (ESI): calcd for $C_{35}H_{33}FN_4O_5$ $[M+H]^+$ 609.2508, found 609.2506 (error 0.30 ppm); mp: 175 °C.

*4.3.5.24. 7-Benzyl-4-[4-(4-fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-5,6-dimethyl-7H-pyrrolo[2,3-d]pyrimidine (**2d**).* According to general procedure B (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.47; IR (ATR) [cm^{-1}]: 2956, 2920, 1555, 1505, 1466, 1448, 1376, 1349, 1216, 1156, 1094, 1042, 840, 809, 774, 698; ^1H NMR (200 MHz, chloroform-*d*) δ ppm 1.71 (s, 3H) 2.16 (s, 3H) 2.95 (s, 3H) 5.30 (m, 2H) 5.52 (m, 2H) 6.83 (m, 2H) 7.01 (m, 2H), 7.28 (m, 2H) 7.46 (m, 6H) 7.87 (m, 2H) 8.97 (s, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 8.09, 10.0, 45.1, 55.8, 75.1, 106.3, 114.9 (d, *J*=21.44 Hz), 119.1, 125.1, 126.3126.4 (d, *J*=7.6 Hz), 127.5, 128.4, 128.6, 128.7, 129.3, 129.4, 130.1, 130.2 (d, *J*=3.2 Hz), 135.8, 137.0, 139.8, 147.8, 149.8, 150.5, 151.9, 161.9 (d, *J*=246.0 Hz); HRMS (ESI): calcd for $C_{32}H_{28}FN_5O$ $[M+H]^+$ 518.2351, found 518.2354 (error 0.58 ppm); mp: 168 °C.

*4.3.5.25. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-1-(methoxymethyl)-2-(4-methoxyphenyl)-1H-pyrrolo[2,3-b]pyridine (**2h**).* According to general procedure B (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.48; IR (ATR) [cm^{-1}]: 2923, 2853, 1609, 1587, 1589, 1477, 1443, 1376, 1356, 1326, 1295, 1246, 1088, 1070, 1039,957, 839, 803, 810, 771, 700; ^1H NMR (200 MHz, DMSO-d_6) δ ppm 3.36 (s, 3H) 3.79 (s, 3H) 5.62 (m, 2H) 6.27 (m, 1H) 7.05 (m, 3H) 7.40 (m, 5H) 7.57 (m, 4H) 7.89 (m, 2H) 8.44 (d, *J*=4.80 Hz, 1H); ^{13}C NMR (50.33 MHz, DMSO-d_6) δ ppm 55.6, 55.6, 56.5, 72.8, 75.4, 99.6115.4 (d, *J*=21.4 Hz), 119.1, 120.0, 123.6, 126.6, 128.7 (d, *J*=8.3 Hz), 129.1, 129.6, 130.4, 130.5, 130.9, 131.0, 137.7, 142.7, 143.2, 149.3, 150.2, 160.1; HRMS (ESI): calcd for $C_{33}H_{29}FN_4O_3$ $[M+H]^+$ 549.2297, found 549.2230 (error 0.61 ppm); mp: 156 °C.

*4.3.5.26. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-7-(methoxymethyl)-7H-pyrrolo[2,3-d]pyrimidine (**2c**).* According to general procedure A (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.44; IR (ATR) [cm^{-1}]: 2929, 1569, 1502, 1469, 1448, 1403, 1338, 1284, 1219, 1181, 1163, 1095, 1079, 1061, 906, 842, 775, 755, 740, 708, 699; ^1H NMR (200 MHz, DMSO-d_6) δ ppm 2.82 (s, 3H) 3.21 (s, 3H) 5.58 (s, 4H) 5.95 (d, *J*=3.41 Hz, 1H) 7.05 (m, 2H) 7.38 (m, 2H) 7.55 (m, 4H) 7.62 (d, *J*=3.92 Hz, 1H) 7.86 (m, 2H) 9.04 (s, 1H); ^{13}C NMR (50.33 MHz, DMSO-d_6) δ ppm 55.7, 56.5, 74.7, 75.4, 100.8, 115.5 (d, *J*=21.4 Hz), 117.7, 125.2, 125.5, 126.5 (d, *J*=7.85 Hz), 128.5, 129.1, 129.4, 129.5, 129.7, 129.8, 130.2, 130.8 (d, *J*=3.2 Hz), 131.4, 140.5, 149.4, 150.4, 151.8, 152.0, 161.8 (d, *J*=244.5 Hz); HRMS (ESI): calcd for $C_{25}H_{22}FN_5O_2$ $[M+H]^+$ 444.1830, found 444.1832 (error 0.29 ppm); mp: 177 °C.

*4.3.5.27. 6-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-9-tetrahydro-2H-pyran-2-yl-9H-purine (**2a**).* According to general procedures A, B, and D (Tables 1 and 7) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.15; IR (ATR) [cm^{-1}]: 2925, 2854, 1580, 1507, 1439, 1439, 1325, 1210, 1159, 1084, 1043, 907, 839, 775, 744, 695; ^1H NMR (200 MHz, methanol-d_4) δ ppm 1.67 (m, 5H, THP) 2.10 (m, 3H, THP) 2.80 (s, 3H, $MOMCH_3$) 3.74 (m, 1H, THP) 4.06 (m, 1H, THP) 5.46 (s, 2H, $MOMCH_2$) 5.81 (m, 1H, THP) 6.87 (m, 2H, *meta*-4F-PhH) 7.33 (m, 2H, *ortho*-4FPhH) 7.51 (m, 3H, *meta*-, *para*-PhH) 7.75 (m, 2H, *ortho*-PhH) 8.51 (s, 1H, Pur.8-H) 8.97 (m, 1H, Pur.2-H); ^1H NMR (200 MHz, chloroform-*d*) ppm 1.88 (m, 6H) 2.94 (s, 3H) 3.80 (m, 1H) 4.18 (m, 1H) 5.57 (s, 2H) 5.81 (m, 1H) 6.86 (m, 2H) 7.48 (m, 5H) 7.81 (m, 2H) 8.13 (s, 1H) 9.07 (m, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 26.7, 24.7, 31.5, 55.7, 64.8, 75.8, 81.9, 114.8 (d, *J*=21.4 Hz), 122.9, 128.3, 128.6, 129.6, 129.6, 130.0, 130.4 (d, *J*=3.2 Hz), 132.1, 142.5, 143.2, 149.2, 151.3, 151.5, 151.8, 162.1 (d, *J*=246.1 Hz); HRMS (ESI): calcd for $C_{27}H_{25}FN_6O_2$ $[M+H]^+$ 485.2096, found 485.2095 (error 0.16 ppm); mp: 98 °C.

*4.3.5.28. 2-Cyclohexyl-4-[4-(4-fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-1-(methoxymethyl)-1H-pyrrolo[2,3-b]pyridine (**2i**).* According to general procedures B and D (Tables 1 and 7) TLC (ethylacetate/*n*-hexane 1/2): 0.38, TLC (ethylacetate/*n*-hexane 1/1): R_f=0.65; IR (ATR) [cm^{-1}]: 2927, 2853, 1736, 1599, 1538, 1447, 1380, 1364, 1321, 1221, 1156, 1077, 911, 838, 772, 699; ^1H NMR (200 MHz, chloroform-*d*) δ ppm 1.26 (m, 6H) 1.73 (m, 4H) 2.74 (m, 1H) 3.10 (s, 3H) 3.31 (s, 3H) 4.97 (m, 2H) 5.67 (m, 2H) 5.83 (s, 1H) 6.81 (m, 2H) 7.23 (m, 1H) 7.45 (m, 5H) 7.90 (m, 2H) 8.32 (d, *J*=4.93 Hz, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 25.9, 26.3, 33.3, 35.5, 55.4, 56.1, 71.8, 74.9, 96.8, 114.8 (d, *J*=21.4 Hz), 117.9, 120.2, 126.5, 128.6, 128.7 (d, *J*=8.1 Hz), 129.0, 129.1, 129.2, 130.2, 130.3 (d, *J*=3.1 Hz), 138.4, 141.9, 148.7, 149.5, 149.7, 161.8 (d, *J*=245.7 Hz); HRMS (ESI): calcd for $C_{32}H_{33}FN_4O_2$ $[M+H]^+$ 525.2660, found 525.2658 (error 0.35 ppm); mp: 127 °C.

*4.3.5.29. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-7-[(4-methylphenyl)sulfonyl]-7H-pyrrolo[2,3-d]pyrimidine (**2b**).* According to general procedure A (Table 1) TLC (ethylacetate/*n*-hexane 1/2): R_f=0.33; TLC (ethylacetate/*n*-hexane 1/1): R_f=0.58; IR [cm^{-1}]: 2927, 1596, 1564, 1504, 1440, 1378, 1358, 1222, 1191, 1177, 1140, 1090, 1008, 972, 910, 841, 813, 776, 702, 682, 660; ^1H NMR (200 MHz, chloroform-*d*) δ ppm 2.43 (m, 3H) 2.96 (m, 3H) 5.58 (s, 2H) 5.91 (d, *J*=4.04 Hz, 1H) 6.85 (m, 2H) 7.35 (m, 4H) 7.49 (m, 4H) 7.81 (m, 2H) 8.09 (d, *J*=8.34 Hz, 2H) 9.12 (s, 1H); ^{13}C NMR (50.33 MHz, chloroform-*d*) δ ppm 21.6, 55.6, 75.3, 104.5, 115.3 (d, *J*=21.49 Hz), 119.1, 126.6, 128.2, 128.6, 129.4, 129.6, 129.7, 129.8, 134.6, 142.7, 145.9, 150.8, 151.7, 151.9, 153.0, 162.3 (d, *J*=247.4 Hz); HRMS (ESI): calcd for $C_{30}H_{24}FN_5O_3S$ $[M+H]^+$ 554.1657, found 554.1658 (error 0.27 ppm); mp: 86 °C.

*4.3.5.30. 4-[4-(4-Fluorophenyl)-2-[4-(methoxymethoxy)phenyl]-1-(methoxymethyl)-1H-imidazol-5-yl]-1-(methoxymethyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**4g**).* According to general procedure B (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.47; IR (ATR) [cm^{-1}]: 2900, 1589, 1512, 1481, 1376, 1326, 1231, 1192, 1150, 1079, 1005, 959, 922, 841, 812, 762, 700; ^1H NMR (200 MHz, methanol-*d*) δ ppm 3.11 (s, 3H) 3.38 (s, 3H) 3.48 (s, 3H) 5.10 (m, 2H) 5.27 (s, 2H) 5.61 (m, 2H) 6.16 (s, 1H) 6.94 (m, 2H) 7.22 (d, *J*=8.97 Hz, 2H) 7.41 (m, 6H) 7.53 (m, 2H) 7.81 (d, *J*=8.84 Hz, 2H) 8.43 (d, *J*=5.05 Hz, 1H); ^{13}C NMR (50.33 MHz, methanol-*d*) ppm δ 54.5, 54.8, 55.2, 72.3, 75.0, 93.9, 100.2, 114.6 (d, *J*=21.8 Hz), 116.0, 118.3, 120.2, 122.7, 126.1, 128.3, 128.4, 128.8, 129.1 (d, *J*=8.15 Hz), 129.9, 130.4, 131.2, 138.1, 142.5, 143.0, 149.9, 158.6; HRMS (ESI): calcd for $C_{34}H_{31}FN_4O_4$ $[M+H]^+$ 579.2402, found 579.2398 (error 0.76 ppm); mp: 137 °C.

*4.3.5.31. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-9-(methoxymethyl)-9H-pyrido[2,3-b]indole (**2f**).* According to general procedure B (Table 1) TLC (ethylacetate/*n*-hexane 1/1): R_f=0.52; IR (ATR) [cm^{-1}]: 2930, 1563, 1507, 1462, 1413, 1364, 1324, 1288, 1212, 1156, 1112, 1085, 998, 973, 914, 839, 774, 752, 739, 699; ^1H NMR (200 MHz, methanol-d_4) δ ppm 2.80 (s, 3H) 3.26 (s, 3H) 5.85 (s, 2H) 6.73 (m, 2H) 7.01 (m, 1H) 7.22 (d, *J*=7.96 Hz, 1H) 7.35 (m, 5H) 7.49 (m, 3H) 7.58 (d, *J*=8.21 Hz, 1H) 7.81 (m, 2H) 8.52 (d, *J*=5.18 Hz, 1H); ^{13}C NMR (50.33 MHz, methanol-d_4) δ ppm 55.7, 55.3, 72.0, 75.1, 110.0, 114.8 (d, *J*=21.6 Hz), 115.0, 118.6, 119.5, 120.8, 121.5, 125.4, 127.3, 128.2 (d, *J*=21.6 Hz), 128.5, 129.1, 129.1, 129.5 (d, *J*=4.4 Hz), 129.6, 132.3, 137.7, 139.6, 145.6, 146.6, 150.3, 152.0, 162.0 (d, *J*=245.8 Hz); HRMS (ESI): calcd for $C_{30}H_{25}FN_4O_2$ $[M+H]^+$ 493.2034, found 493.2036 (error 0.27 ppm); mp: 63 °C.

*4.3.5.32. 4-[4-(4-Fluorophenyl)-1-methyl-2-(methylsulfonyl)-1H-imidazol-5-yl]-2-phenyl-1H-pyrrolo[2,3-b]pyridine (**20**).* The coupling reaction was performed according to method B. The crude product was purified by flash-chromatography, the obtained product was further refluxed in $HCl_{concd.}$/MeOH for 3 h. After

evaporation of the solvent, the crude product was purified by flash-chromatography, to obtain 17 mg (18%) of the pure product. IR (ATR) [cm^{-1}]: 3031, 1609, 1517, 1306, 1253, 1222, 1159, 1128, 963, 844, 768, 749, 743, 685, 661; ^1H NMR (200 MHz, acetone-d_6) δ ppm 3.52 (s, 3H) 3.80 (s, 3H) 6.70 (s, 1H) 6.96 (m, 2H) 7.17 (d, J=4.67 Hz, 1H) 7.44 (m, 5H) 7.92 (m, 2H) 8.38 (d, J=5.31 Hz, 1H) 11.47; ^{13}C NMR (50.33 MHz, DMSO-d_6) δ ppm 33.4 (CH_3), 43.6 (CH_3), 96.5 (CH), 115.7 (d, J=21.4 Hz), 118.2 (C_q), 121.0 (CH), 126.0, 127.6, 128.6 (d, J=8.1 Hz), 128.8, 129.2, 129.8 (d, J=3.1 Hz), 130.2, 131.3, 137.2, 140.4, 143.5, 150.5, 161.7 (d, J=244.6 Hz); HRMS (ESI): calcd for $C_{24}H_{19}FN_4O_2S$ $[M+Na]^+$ 469.1105, found 469.1103 (error 0.47 ppm).

*4.3.5.33. 4-[4-(4-Fluorophenyl)-1-(methoxymethyl)-2-phenyl-1H-imidazol-5-yl]-1-[(4-methylphenyl)sulfonyl]-1H-pyrrolo[2,3-b] pyridine (**2e**).* According to general procedures A and B (Table 1) IR (ATR) [cm^{-1}]: 1596, 1506, 1362, 1176, 1155, 1089, 840, 775, 702, 680, 657; ^1H NMR (200 MHz, acetone-d_6) δ ppm 2.41 (s, 3H) 3.05 (s, 3H) 5.09 (m, 2H) 6.31 (d, J=4.04 Hz, 1H) 6.90 (m, 2H) 7.48 (m, 9H) 7.77 (d, J=4.04 Hz, 1H) 7.92 (m, 2H) 8.09 (d, J=8.72 Hz, 2H) 8.54 (d, J=4.93 Hz, 1H); ^{13}C NMR (50.33 MHz, acetone-d_6) δ ppm: 20.5, 54.6, 75.0, 104.8, 114.7 (d, J=21.6 Hz), 120.4, 122.4, 125.1, 127.1, 128.5, 128.5, 128.8, 129.1, 129.7, 130.6 (d, J=3.2 Hz), 131.9, 135.4, 144.9, 145.6, 149.7; HRMS (ESI): calcd for $C_{31}H_{25}FN_4O_3S$ $[M+H]^+$ 553.17042, found 553.170227 (error 0.35 ppm); mp: 82 °C.

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Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.09.053.

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