JOC The Journal of Organic Chemistry

ARTICLE

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Direct, Metal-Free Amination of Heterocyclic Amides/Ureas with NH-Heterocycles and N-Substituted Anilines in $POCl_3$

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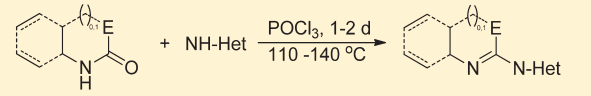
Supporting Information

ABSTRACT: A $POCl_3$-mediated, direct amination reaction of heterocyclic amides/ureas with NH-heterocycles or N-substituted anilines is described. Compared to the existing methods, this operationally simple protocol provides unique reactivity and functional group compatibility because of the metal-free, acidic reaction conditions. The yields are generally excellent.



E = C, N, S. NH-Het = azoles, anilines. up to 98% yield, 34 examples

INTRODUCTION

2-Aminosubstituted heterocycles with generic structure **1** are ubiquitous in biologically active compounds[1] including the blockbuster drugs Tarceva, Avandia, Gleevec, Crestor, and Lunesta (Figure 1).

Typical syntheses of **1** start from heterocyclic amides **2**, which often come from condensation reactions of appropriate precursors (Scheme 1, ***a***). Activation of the tautomerizable hydroxyl group in **2** to halides is usually required for the subsequent S_NAr (nucleophilic aromatic substitution) reaction to occur with nitrogen nucleophiles to afford **1**.[2] Highly dependent on the nature of the coupling partner, the S_NAr reactions are particularly difficult for weak nucleophiles such as NH-heterocycles and anilines. In these cases, harsh conditions are usually necessary, and diminished yields are often obtained.[3] One of the solutions to this problem is the employment of highly reactive phosphonium derivatives of heterocyclic amide **2** for the S_NAr reaction.[4] The reaction conditions are generally mild even for weak nucleophiles such as NH-heterocycles and anilines. The downsides of this very useful method are cost of the expensive phosphonium reagents such as BOP ((Benzotriazol-1-yloxy)tris-(dimethylamino)phosphonium hexafluorophosphate) or PyBroP (Bromotripyrrolidinophosphonium hexafluorophosphate), poor atom economy, and potentially carcinogenic byproducts. Another successful approach involves metal (either Pd[5] or Cu[6])-catalyzed Buchwald−Hartwig cross-coupling amination reaction of heteroaryl halides or triflates, which has significantly improved the reactivity and versatility of this process. However, the use of metal catalysts and expensive ligands renders the metal-catalyzed processes less cost-effective. Very recently, direct, oxidative amination of heteroarene through metal-catalyzed C−H activation has also been achieved, but the reaction scopes are fairly narrow so far.[7] Acids generated in the amination processes (HX, TfOH, etc.) are generally believed to impede the desired nucleophilic displacement, presumably by protonation of the amine nucleophiles.[8] Therefore, stoichiometric amounts of bases are almost always employed in the above amination processes, either to scavenge the acids or to promote the displacement processes through deprotonation of the nucleophilic species. That is probably the reason that S_NAr amination reactions of heteroaryl halides under acidic conditions are much rarer in the literature and harsh reaction conditions are usually required.[9] Despite this conventional wisdom, we reasoned that in certain cases involving weak nitrogen nucleophiles, acids might as well facilitate the displacement process of intermediate **3** through coordination of the adjacent nitrogen atom (Scheme 1, ***b***). Furthermore, by choosing an appropriate acid-compatible C−O bond activator, isolation of intermediate **3** might not be necessary and direct amination of heterocyclic amides **2** might be feasible (Scheme 1, ***c***).[10] We report that inexpensive $POCl_3$ is such an activator, promoting direct amination of a variety of

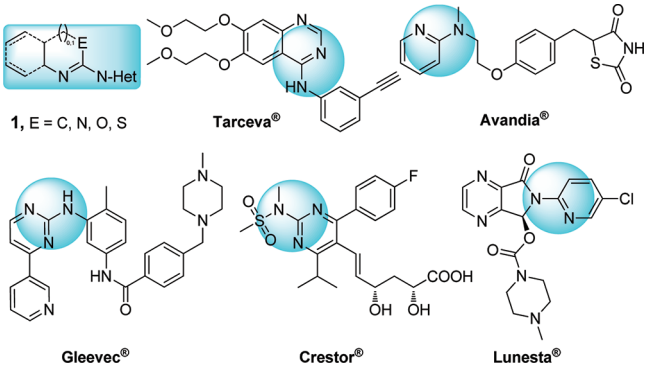
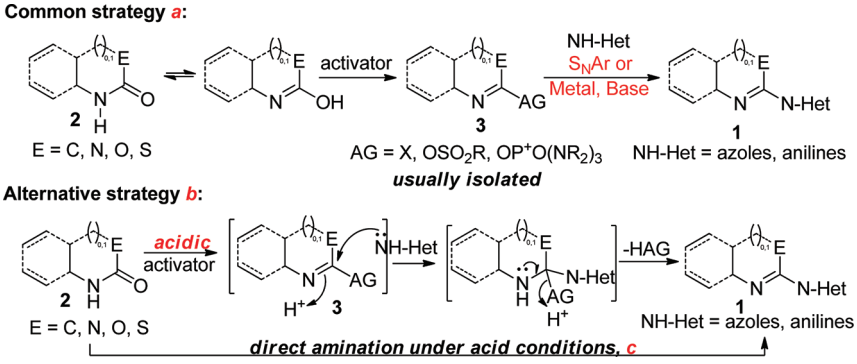


Figure 1. Blockbuster drugs containing the 2-aminoheterocycle motif represented generically as **1**.

Received: July 11, 2011
Published: September 07, 2011

Scheme 1. Common and Alternative Strategies for Synthesis of 1



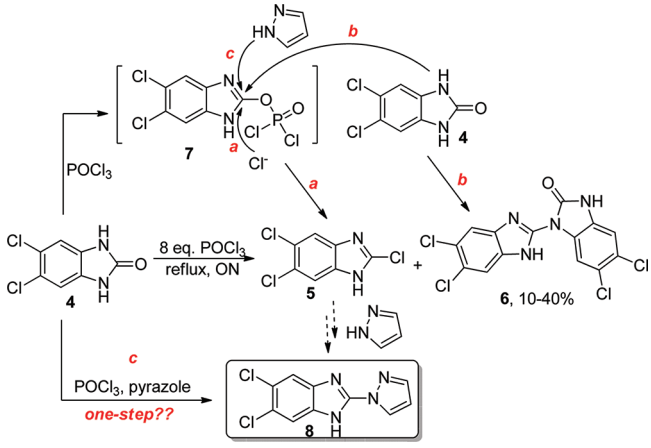
heterocyclic amides with NH-heterocycles or N-substituted anilines. This operationally simple reaction requires no metal catalyst and is usually high yielding. It offers clear advantages over existing amination methods in terms of simplicity and efficiency. It also provides complementary reactivity and functional group compatibility because of the acidic reaction conditions. We expect wide applicability of this method in organic synthesis.

RESULTS AND DISCUSSION

In connection with one of our drug discovery programs, we were interested in preparing 2-pyrrazolobenzimidazole **8** (Scheme 2).[11] The BOP- or PyBrop-mediated direct amination of compound **4** with pyrazole under basic conditions failed to provide the desired compound.[4] We then turned our attention to the classic sequence through the chloride intermediate **5**. It turned out that preparation of compound **5** through a variety of chlorination methods was rather difficult, especially on multigram scales.[12] Careful examination of the chlorination reaction of compound **4** in $POCl_3$ revealed that the major byproduct was pseudodimeric **6**. Yields of compound **6** ranged from 10% to as high as 40%, depending on the reaction scales. We postulated that there were two competing pathways ***a*** and ***b*** for the $POCl_3$-mediated reaction. On the same activated intermediate **7**,[13] either Cl^- or another molecule of starting material **4** could serve as the nucleophile, affording compounds **5** and **6**, respectively. With this insight, we reasoned that an in situ nitrogen nucleophile (pyrazole) that was more nucleophilic than both starting material **4** and Cl^- should react preferentially with **7** through pathway ***c***. Therefore, a direct, one-step amination method from compound **4** to produce compound **8** under acidic conditions might be feasible.

To test the above hypothesis, an equimolar mixture of benzimidazol-2-one and pyrazole was heated at reflux in $POCl_3$ (1.1 mol/L) for 16 h (Table 1, entry 1). Much to our pleasure, the desired direct amination reaction went cleanly, and a simple $POCl_3$ quench with ice−water followed by pH adjustment to ∼10 afforded compound **9** in 90% isolated yield. Compound **9** was collected as a white solid via filtration in >95% purity. Interestingly, other chlorination reagents such as $SOCl_2$ and oxalyl chloride did not work for this reaction. Encouraged by this result, we investigated a variety of nitrogen nucleophiles other than pyrazole (Table 1). It appears that the $POCl_3$-mediated, direct amination reaction succeeds only in cases where the following criteria are met: (1) The nitrogen nucleophile can not react directly with $POCl_3$ under the refluxing reaction conditions.

Scheme 2. Synthesis of 8 via 5 or through a Proposed Direct, One-Step Amination

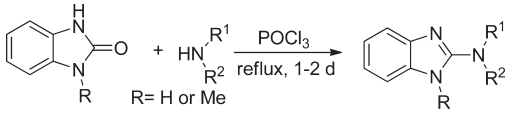


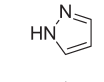
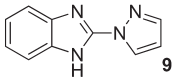
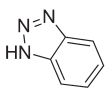
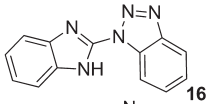
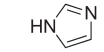
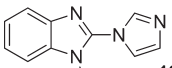
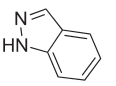
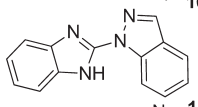
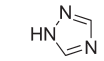
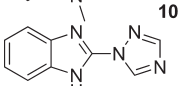
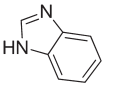
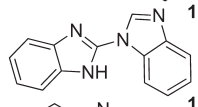
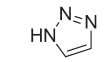
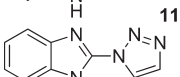
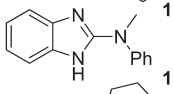
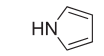
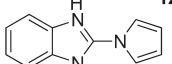
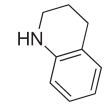
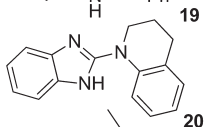
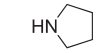
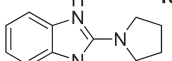
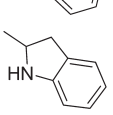
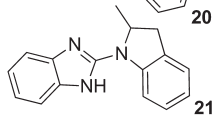
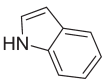
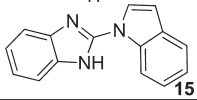
Strong nucleophiles such as dialkyl amines (morpholine and pyrrolidine, entry 6), alcohols (IPA and *n*-BuOH), phenol, or thiophenol were not suitable for this reaction. (2) The nucleophile has to be more nucleophilic than benzimidazol-2-one itself to avoid the formation of compound **6**-type pseudodimer. Weak nucleophiles such as amides (PhCONHPh, pyrrolidin-2-one, indolin-2-one)[14] or sulfonamides ($PhNHSO_2Ph$) were not suitable for this reaction either. (3) The nucleophile must be acid-stable. For this reason, 1,2,3-triazole (entry 4), pyrrole (entry 5), indole (entry 7), and succinimide were also incompetent partners. In contrast, nucleophiles that met these criteria such as azoles (entries 1−3) and benzo-azoles (entries 8−10) afforded excellent yields of the amination products. In addition, secondary anilines proved to be good partners for this reaction as well (entries 11−13). Higher temperature (140 °C for 2 days) in a sealed tube was usually required to drive the reactions to completion, probably due to the lower nucleophilicity of secondary anilines. It is worth noting that primary anilines did participate in the reaction, however, affording a mixture of mono and double amination products. An appropriate protecting group might address this issue.

The reaction scope with respect to the heterocyclic amides was investigated next. It was found that *N*-1 substitutions on the benzimidazol-2-one were tolerated (Table 1, entry 2; Table 2, entry 1). 4,5-Diphenyl imidazol-2-one also worked well in the reaction (Table 2, entry 2). Replacement of NH of benzimidazol-2-one with

dx.doi.org/10.1021/jo201425q |J. Org. Chem. 2011, 76, 8262–8269

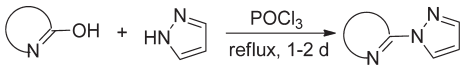
Table 1. Reaction Scope with Respect to Nitrogen Nucleophiles

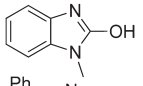
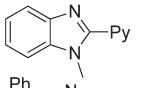
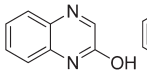
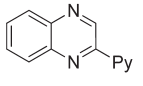
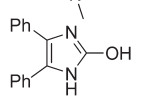
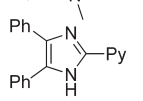
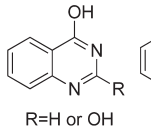
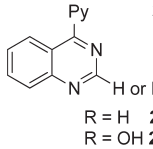
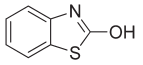
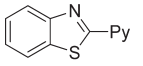
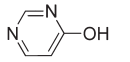
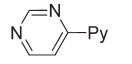


entry	substrate	product	yield	entry	substrate	product	yield
1		 **9**	90%	8		 **16**	89%
2		 **10**	75%	9		 **17**	91%
3		 **11**	88%	10		 **18**	82%
4		 **12**	0%	11		 **19**	93%[a]
5		 **13**	0%	12		 **20**	61%[a]
6		 **14**	0%	13		 **21**	56%[a]
7		 **15**	0%				

[a] 140 °C, sealed tube, 2 d.

Table 2. Reaction Scope with Respect to Heterocyclic Amides



entry	substrate	product	yield	entry	substrate	product	yield
1		 **22**	93%	8			98%
2		 **23**	98%	9	 R=H or OH	 R = H **29a** R = OH **29b**	**28** a. 83% b. 80%*
3		 **24**	98%	10		 **30**	91%
4		**25**	0%	11		**31**	94%
5		**26**	0%	12		**32**	74%
6		**9**	15%	13		**33**	96%
7		**27**	90%				

[*] R = OH, 2 equiv of pyrazole was used.

sulfur did not affect the reaction (entry 3). The total lack of the amination products for benzoxazol-2-one (entry 4) and indolin-2-one (entry 5) might suggest the importance of the aromaticity of the tautomerizable amides. Interestingly, benzoimidazol-2-thione

dx.doi.org/10.1021/jo201425q |J. Org. Chem. 2011, 76, 8262–8269

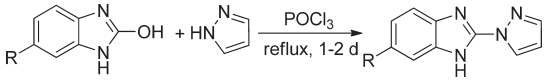
afforded the desired product **9** as well, although in low yield (entry 6).[15] A wide range of six-membered heterocyclic amides also afforded the desired amination products in excellent yields (entries 7−13).

The electronic properties of the substituents at the phenyl ring of benzimidazol-2-one had little effect on the reaction (Table 3). As long as the substituents could survive the acidic reaction conditions, excellent yields of the amination products were obtained (entries 1−5).

A variety of substituted pyrazole nucleophiles were next studied. Pyrazoles with either electron-donating (Table 4, entries 1, 4, and 6) or electron-withdrawing (entries 2, 3, and 5) substituents all afforded excellent yields of the desired amination products. The steric effects of the substituents on the regioselectivity of the reaction were also studied. The results indicated that the formation of sterically less hindered products was preferred. For instance, in the case of 3-substituted pyrazoles (entries 2, 3, 6−8), only regioisomers with 3-substituents away from the benzimidazole ring were observed. With a 3,5-disubstituted pyrazole (entry 9), sterically less hindered product **47** was the major product. It is notable that even highly sterically hindered 3,5-diisopropylpyrazole afforded the desired amination product **49**, albeit at higher temperature (entry 10).

With respect to the mechanism of the reaction, we observed two competing pathways, depending on the nucleophiles (Scheme 3). Activation of the heterocyclic amide with $POCl_3$ is presumed to take place first, affording active species **51**. From there, either pathway ***a*** or ***b*** is feasible. Control experiments on a representative reaction (Table 1, entry 1) showed that heating pure isolated 2-chlorobenzimidazole and pyrazole in $POCl_3$ provided compound **9**, albeit in lower yield. However, with pyrazole already present in the reaction solution, no detectable formation of 2-chlorobenzimidazole was observed during the reaction course based on HPLC and in situ NMR studies. The same observation held true with all the reactions that went to completion at reflux temperature (110 °C). In those cases, pathway ***a*** is likely the dominant one.[16] In comparison, in the cases of N-substituted anilines and sterrically hindered pyrazole as the nucleophiles (Table 1, entries 11−13 and Table 4, entry 10), where the reaction was more sluggish and higher temperature was required for the reaction to proceed, formation of chloride intermediate **52** was observed prior to the amination product. Apparently, in those cases, pathway ***b*** is the preferred one.

Table 3. Reaction Scope with Respect to Substituents on Benzimidazol-2-one



entry	R	product	yield
1	-COOMe	**34**	98%
2	-NO_2	**35**	95%
3	-CF_3	**36**	93%
4	-CN	**13**	92%
5	-OMe	**38**	98%

Scheme 3. Two Plausible Pathways

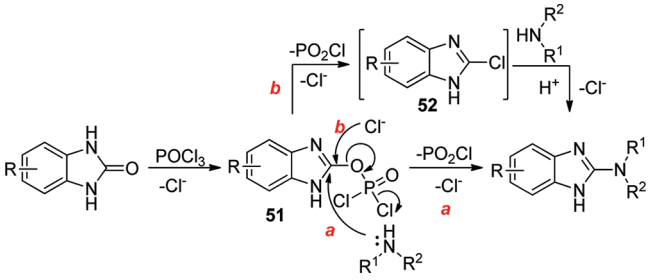
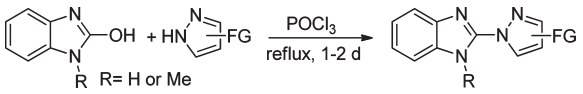
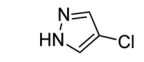
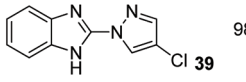
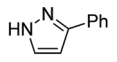
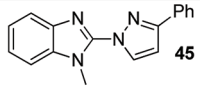
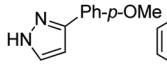
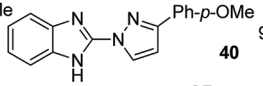
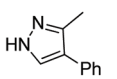
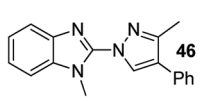
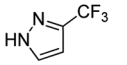
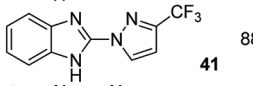
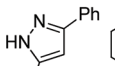
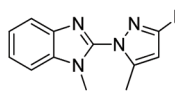
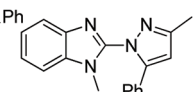
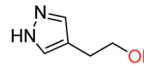
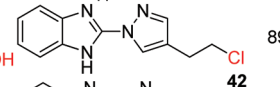
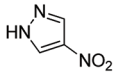
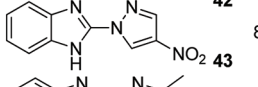
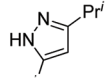
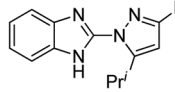
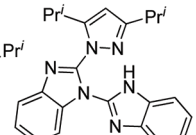
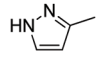
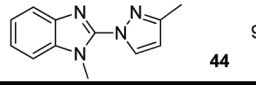


Table 4. Reaction Scope with Respect to Substituents on Pyrazoles

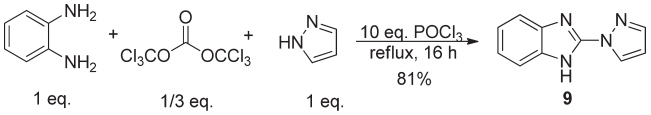


entry	substrate	product	yield	entry	substrate	product	yield
1		 **39**	98%	7		 **45**	91%
2		 **40**	96%	8		 **46**	95%
3		 **41**	88%	9[a]		 **47**, 60%  **48**, 6%	
4		 **42**	89%				
5		 **43**	84%	10[b]		 **49**, 55%  **50**, 18%	
6		 **44**	98%				

[a] 110 °C, 4 d.b [b] 140 °C, 1 d.

dx.doi.org/10.1021/jo201425q |*J. Org. Chem.* 2011, 76, 8262–8269

Scheme 4. Three-Component, One-Pot Synthesis of Compound 9



We also explored the feasibility of a one-pot synthesis of compound **9** directly from phenylene-1,2-diamine without the isolation of benzimidazol-2-one (Scheme 4). Acid-compatible triphosgene was slowly added to the suspension mixture of phenylene-1,2-diamine and pyrazole in $POCl_3$ at room temperature. The mixture was stirred at room temperature for 30 min and then at reflux for 16 h to afford compound **9** in 81% isolated yield after the same acid quench/pH adjustment isolation procedures. Apparently, the presence of pyrazole did not interfere with the formation of benzimidazol-2-one from phenylene-1,2-diamine and triphosgene. Subsequent direct amination reaction of benzimidazol-2-one with pyrazole delivered compound **9** in a one-pot fashion. This facile, one-pot protocol should be applicable to the synthesis of other 2-aminobenzimidazoles as well.

In summary, we have developed a simple, direct amination method for heterocyclic amides/ureas via C−O activation in $POCl_3$. This reaction works best with weak, acid-stable nitrogen nucleophiles such as azoles and N-substituted anilines. It has broad substrate scope with respect to heterocyclic amides/ureas, and the yields are usually excellent. Performed under metal-free, acidic conditions, this highly economical method offers complementary reactivity and functional group compatibility to the existing amination methods. A three-component, one-pot protocol to 2-pyrazolo-benzimidazole directly from phenylene-1,2-diamine, triphosgene, and pyrazole is also demonstrated. It is worth to note that the reaction is readily scalable to >100 g.

EXPERIMENTAL SECTION

General Experimental Methods. Proton and carbon NMR spectra were recorded at a 500 MHz or a 600 MHz NMR spectrometer. One-dimension NOE experiments were performed by the method of Stott et al. with a mixing time of 0.8 s.[17] Flash column chromatography was performed using Merck silica gel 60. The analytical HPLC conditions were Agilent ZORBAX Eclipse XDB-C8, 5 μm, 4.6 mm × 150 mm, flow rate 1 mL/min, gradient (acetonitrile/water with 0.05% trifluoroacetic acid) 1% acetonitrile/99% water to 99% acetonitrile/1% water ramp over 8 min, then hold at 99% acetonitrile/1% water. HRMS (ESI) was performed on a μTOF apparatus.

Unless specified, all solvents and reagents were purchased from commercial sources and used without further purification.

General Procedure for the Amination Reaction

2-(1*H*-Pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 9. In a sealed tube[18] equipped with a magnetic stirring bar were suspended 1*H*-benzo[*d*]imidazol-2-ol (134 mg, 1.0 mmol, 1.0 equiv) and pyrazole (82 mg, 1.2 mmol, 1.2 equiv) in $POCl_3$ (0.92 mL, 10 mmol, 10 equiv). The reaction mixture was heated to reflux temperature (110 °C) for 16 h. The hot reaction solution was carefully poured into an ice−water solution with sufficient stirring. Saturated aqueous NaOH solution was added to adjust the pH to ∼10. After stirring at room temperature for 2 h, the precipitated white solid was collected via filtration, washed with water, and dried to afford the title compound (165 mg, 0.9 mmol, 90%). No further purification was performed. ^{1}H NMR (600 MHz, DMSO) δ 13.10 (s, 1H), 8.60 (dd, J = 2.6, 0.5 Hz, 1H), 7.95 (dd, J = 1.6, 0.5 Hz, 1H), 7.59 (br s, 1H), 7.46 (br s, 1H), 7.20 (dd, J = 5.8, 2.3 Hz, 2H), 6.67 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 145.8, 142.6, 141.5, 133.4, 128.8, 122.1, 121.8, 118.1, 111.3, 108.8. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_9N_4$ 185.0822; found 185.0826.

One-Pot Procedure. In a 100 mL round-bottom flask was suspended a mixture of benzene-1,2-diamine (5.0 g, 46 mmol, 1.0 equiv) and pyrazole (3.1 g, 46 mmol, 1.0 equiv) in $POCl_3$ (43 mL, 460 mmol, 10 equiv). Triphosgene (4.5 g, 15.3 mmol, 0.33 equiv) was added as solid slowly at room temperature (exothermic reaction). After stirring at room temperature for 30 min, the reaction mixture was heated to reflux temperature (110 °C) for 16 h. The hot reaction solution was carefully poured into an ice−water solution with sufficient stirring. Saturated aqueous NaOH solution was added to adjust the pH to ∼10. After stirring at room temperature for 2 h, the precipitated white solid was collected via filtration, washed with water, and dried to afford the title compound (6.9 g, 37 mmol, 81%).

5,5′,6,6′-Tetrachloro-1′*H*-[1,2′-bibenzo[*d*]imidazol]-2(3*H*)-one, Compound 6. 1*H*-Benzo[*d*]imidazol-2-ol (20 g, 1.0 mmol, 1.0 equiv) was heated in $POCl_3$ (150 mL) for 24 h. After cooling to rt, the reaction solution was carefully poured into ice−water with stirring. The precipitated solid was collected by filtration and dried. Compound **6** was isolated as the major byproduct after column chromatography. The yield varied from batch to batch, depending on quality of the reagents and the scale of the reaction. ^{1}H NMR (500 MHz, DMSO) δ 8.46 (s, 1H), 7.82 (s, 2H), 7.32 (s, 1H). ^{13}C NMR (126 MHz, DMSO) δ 152.5, 145.5, 129.7, 126.5, 125. 6, 124.0, 123.2, 114.5, 111.0.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_6Cl_4N_4O$ 386.9368; found 386.9378.

2-(1*H*-Imidazol-1-yl)-1-methyl-1*H*-benzo[*d*]imidazole, Compound 10. Following the general method described above, the title compound was isolated in 75% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.28 (t, J = 1.3 Hz, 1H), 7.82 (t, J = 1.3 Hz, 1H), 7.68 (ddd, J = 5.4, 4.6, 2.4 Hz, 2H), 7.36 (ddd, J = 8.3, 7.3, 1.1 Hz, 1H), 7.31 (ddd, J = 8.1, 7.3, 1.1 Hz, 1H), 7.25−7.21 (m, 1H), 3.78 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 143.7, 140.1, 137.8, 135.2, 129.5, 123.0, 122.6, 120.1, 119.0, 110.7, 30.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{11}N_4$ 199.0978; found 199.0972.

2-(1*H*-1,2,4-Triazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 11. Following the general method described above, the title compound was isolated in 88% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.46 (s, 1H), 8.45 (s, 1H), 7.59 (dd, J = 5.2, 3.2 Hz, 2H), 7.33−7.23 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 153.1, 143.5, 143.1, 122.6.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_9H_8N_5$ 186.0744; found 186.0778.

1-(1*H*-Benzo[*d*]imidazol-2-yl)-1*H*-benzo[*d*][1,2,3]triazole, Compound 16. Following the general method described above, the title compound was isolated in 89% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.78 (s, 1H), 8.59 (dt, J = 8.3, 0.9 Hz, 1H), 8.28 (dt, J = 8.3, 0.9 Hz, 1H), 7.84 (ddd, J = 8.1, 7.0, 0.9 Hz, 1H), 7.80−7.50 (br m, 2H), 7.64 (ddd, J = 8.1, 7.0, 0.9 Hz, 1H), 7.37−7.24 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 145.6, 143.9, 130.8, 130.0, 125.8, 122.8, 119.8, 113.4.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{13}H_{10}N_5$ 236.0931; found 236.0930 .

1-(1*H*-Benzo[*d*]imidazol-2-yl)-1*H*-indazole, Compound 17. Following the general method described above, the title compound was isolated in 91% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.61 (s, 1H), 9.24 (d, J = 1.0 Hz, 1H), 7.85 (dt, J = 8.5, 0.9 Hz, 1H), 7.77 (dd, J = 8.8, 0.9 Hz, 1H), 7.74−7.64 (m, 1H), 7.57−7.50 (m, 1H), 7.42 (ddd, J = 8.8, 6.5, 1.0 Hz, 1H), 7.32−7.24 (m, 2H), 7.19 (ddd, J = 8.5, 6.5, 0.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 149.6, 145.9, 141.6, 133.8, 128.2, 123.0, 122.9, 122.5, 122.2, 122.1, 121.5, 118.6, 117.3, 111.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_{11}N_4$ 235.0978; found 235.0966.

1′*H*-1,2′-Bibenzo[*d*]imidazole, Compound 18. Following the general method described above, the title compound was isolated in 82% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.01 (s, 1H), 8.48 (d, J = 8.1 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.65 (dd, J = 5.8, 3.2 Hz, 2H), 7.51 (t, J = 7.7 Hz, 1H), 7.43 (t, J = 7.6 Hz, 1H), 7.28 (dd, J = 6.0, 3.1 Hz, 2H).

dx.doi.org/10.1021/jo201425q |*J. Org. Chem.* 2011, 76, 8262–8269

^{13}C NMR (151 MHz, DMSO) δ 143.6, 142.8, 141.3, 131.4, 124.6, 123.7, 122.3, 119.7, 114.0.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_{11}N_4$ 235.0978; found 235.0975.

_N_-Methyl-_N_-phenyl-1_H_-benzo[_d_]imidazol-2-amine, Compound 19. Following the general method described above except that the reaction was heated at 140 °C for 3 days, the title compound was isolated in 93% yield. ^{1}H NMR (600 MHz, DMSO) δ 11.26 (s, 1H), 7.49−7.38 (m, 4H), 7.21 (dt, J = 8.7, 4.3 Hz, 3H), 6.95 (dd, J = 5.8, 3.2 Hz, 2H), 3.31 (br s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 154.0, 144.9, 129.4, 124.5, 123.5, 119.9, 38.9.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_{14}N_3$ 224.1182; found 224.1184.

1-(1_H_-Benzo[_d_]imidazol-2-yl)-1,2,3,4-tetrahydroquinoline, Compound 20. Following the general method described above except that the reaction was heated at 140 °C for 3 days, the title compound was isolated in 61% yield after column chromatography with EtOAc/hexanes as the eluents. ^{1}H NMR (600 MHz, DMSO) δ 11.65 (s, 1H), 7.76 (d, J = 8.1 Hz, 1H), 7.30 (s, 2H), 7.16 (dd, J = 13.6, 7.1 Hz, 2H), 7.00 (dd, J = 5.7, 3.1 Hz, 2H), 6.93 (t, J = 7.3 Hz, 1H), 3.93−3.82 (t, J = 6.3 Hz, 2H), 2.79 (t, J = 6.3 Hz, 2H), 2.03−1.92 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 152.6, 139.6, 128.9, 127.8, 126.4, 121.5, 120.1, 119.6, 113.2, 109.5, 47.2, 26.8, 22.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{16}H_{16}N_3$ 250.1339; found 250.1335.

2-(2-Methylindolin-1-yl)-1_H_-benzo[_d_]imidazole, Compound 21. Following the general method described above except that the reaction was heated at 140 °C for 3 days, the title compound was isolated in 56% yield after column chromatography with EtOAc/hexanes as eluents. ^{1}H NMR (600 MHz, MeOD) δ 7.76 (d, J = 7.9 Hz, 1H), 7.45−7.38 (m, 2H), 7.24 (t, J = 8.3 Hz, 2H), 7.17−7.11 (m, 2H), 7.01−6.95 (m, 1H), 4.79−4.63 (m, 1H), 3.55−3.46 (m, 1H), 2.81 (dd, J = 15.7, 2.6 Hz, 1H), 1.39 (d, J = 6.3 Hz, 3H). ^{13}C NMR (151 MHz, MeOD) δ 150.6, 143.2, 137.4, 131.5, 128.6, 126.5, 123.5, 122.7, 113.7, 113.6, 59.3, 37.4, 20.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{16}H_{16}N_3$ 250.1339; found 250.1341.

1-Methyl-2-(1_H_-pyrazol-1-yl)-1_H_-benzo[_d_]imidazole, Compound 22. Following the general method described above, the title compound was isolated in 93% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.52 (d, J = 2.5 Hz, 1H), 7.98 (d, J = 1.6 Hz, 1H), 7.73−7.55 (m, 2H), 7.41−7.21 (m, 2H), 6.78−6.55 (m, 1H), 4.01 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 145.2, 142.6, 139.9, 135.5, 131.8, 122.6, 122.4, 118.6, 110.5, 107.9, 31.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{11}N_4$ 199.0978; found 199.0976.

1-(4,5-Diphenyl-1_H_-imidazol-2-yl)-1_H_-pyrazole, Compound 23. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.44 (d, J = 2.2 Hz, 1H), 7.87 (d, J = 1.3 Hz, 1H), 7.53−7.47 (m, 4H), 7.39−7.33 (m, 4H), 7.33−7.29 (m, 2H), 6.61 (dd, J = 2.3, 1.3 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 141.7, 140.9, 132.1, 128.5, 128.4, 127.8, 127.4, 108.0. * HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291; found 287.1288.

2-(1_H_-Pyrazol-1-yl)benzo[_d_]thiazole, Compound 24. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.70 (dd, J = 2.7, 0.5 Hz, 1H), 8.11 (ddd, J = 8.0, 1.2, 0.6 Hz, 1H), 7.97 (dd, J = 1.6, 0.5 Hz, 1H), 7.93 (ddd, J = 8.2, 1.1, 0.6 Hz, 1H), 7.54 (ddd, J = 8.2, 7.3, 1.3 Hz, 1H), 7.48−7.39 (m, 1H), 6.73 (dd, J = 2.7, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 160.0, 150.3, 143.9, 132.4, 128.5, 126.8, 125.0, 122.4, 121.9, 110.1. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_8N_3S$ 202.0433; found 202.0433.

2-(1_H_-Pyrazol-1-yl)quinoline, Compound 27. Following the general method described above, the title compound was isolated in 90% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.82 (dd, J = 2.6, 0.7 Hz, 1H), 8.58 (d, J = 8.7 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 8.04 (dd, J = 8.1, 1.3 Hz, 1H), 8.02−7.97 (m, 1H), 7.92 (dd, J = 1.6, 0.6 Hz, 1H), 7.82 (ddd, J = 8.4, 6.9, 1.5 Hz, 1H), 7.61 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 6.67 (dd, J = 2.6, 1.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 149.6, 145.8, 142.5, 139.8, 130.6, 128.0, 127.7, 127.1, 126.7, 126.1, 111.9, 108.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{10}N_3$ 196.0869; found 196.0874.

2-(1_H_-Pyrazol-1-yl)quinoxaline, Compound 28. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.61 (s, 1H), 8.82 (dd, J = 2.6, 0.6 Hz, 1H), 8.16 (dd, J = 8.3, 1.3 Hz, 1H), 8.06 (ddd, J = 8.3, 1.3, 0.5 Hz, 1H), 8.02 (dd, J = 1.6, 0.6 Hz, 1H), 7.92 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.84 (ddd, J = 8.3, 7.0, 1.4 Hz, 1H), 6.74 (dd, J = 2.6, 1.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 144.5, 143.5, 140.5, 139.3, 137.7, 131.4, 129.2, 128.9, 127.9, 127.8, 109.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_9N_4$ 197.0822; found 197.0824.

4-(1_H_-Pyrazol-1-yl)quinazoline, Compound 29a. Following the general method described above, the title compound was isolated in 83% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.39 (dt, J = 8.7, 1.0 Hz, 1H), 9.17 (s, 1H), 8.90 (dd, J = 2.7, 0.7 Hz, 1H), 8.13 (dd, J = 1.6, 0.6 Hz, 1H), 8.10−8.06 (m, 2H), 7.83 (ddd, J = 8.4, 5.2, 3.0 Hz, 1H), 6.76 (dd, J = 2.7, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 154.3, 153.4, 152.6, 144.7, 134.5, 131.1, 128.4, 128.1, 127.5, 115.9, 108.8. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_9N_4$ 197.0822; found 197.0815.

2,4-Di(1_H_-pyrazol-1-yl)quinazoline, Compound 29b. Following the general method described above using 2 equiv of pyrazole, the title compound was isolated in 80% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.47 (d, J = 8.7 Hz, 1H), 9.17 (d, J = 2.7 Hz, 1H), 8.99 (d, J = 2.6 Hz, 1H), 8.17 (d, J = 1.0 Hz, 1H), 8.09−8.00 (m, 2H), 7.94 (d, J = 0.9 Hz, 1H), 7.74 (ddd, J = 8.4, 6.6, 1.5 Hz, 1H), 6.81 (dd, J = 2.7, 1.6 Hz, 1H), 6.67 (dd, J = 2.6, 1.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 155.8, 154.0, 150.5, 145.3, 143.4, 135.3, 131.9, 130.3, 128.2, 127.7, 127.3, 114.3, 109.1, 108.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{14}H_{11}N_6$ 263.1039; found 263.1035.

4-(1_H_-Pyrazol-1-yl)pyrimidine, Compound 30. Following the general method described above, the title compound was isolated in 91% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.09 (d, J = 1.1 Hz, 1H), 8.89 (d, J = 5.6 Hz, 1H), 8.72 (dd, J = 2.7, 0.6 Hz, 1H), 7.98−7.96 (m, 1H), 7.94 (dd, J = 5.6, 1.3 Hz, 1H), 6.68 (dd, J = 2.7, 1.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 159.5, 158.4, 156.1, 144.1, 127.7, 109.6, 108.6. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_7H_7N_4$ 147.0665; found 147.0668.

2-(1_H_-Pyrazol-1-yl)pyrimidine, Compound 31. Following the general method described above, the title compound was isolated in 94% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.86 (d, J = 4.8 Hz, 2H), 8.65 (d, J = 2.3 Hz, 1H), 7.86 (s, 1H), 7.47 (t, J = 4.8 Hz, 1H), 6.59 (s, 1H). ^{13}C NMR (151 MHz, DMSO) δ 159.3 (2 C), 155.3, 143.2, 129.4, 119.5, 108.7.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_7H_7N_4$ 147.0665; found 147.0664.

2-(1_H_-Pyrazol-1-yl)pyrazine, Compound 32. Following the general method described above, the title compound was isolated in 74% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.35 (d, J = 1.3 Hz, 1H), 8.52 (dd, J = 2.6, 0.6 Hz, 1H), 8.48 (d, J = 2.6 Hz, 1H), 8.36 (dd, J = 2.5, 1.5 Hz, 1H), 7.80 (d, J = 1.1 Hz, 1H), 6.52 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 147.5, 143.1, 141.8, 141.8, 135.7, 127.4, 108.6. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_7H_7N_4$ 147.0665; found 147.0663.

2-(1_H_-Pyrazol-1-yl)pyridine, Compound 33. Following the general method described above, the title compound was isolated in 96% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (dd, J = 2.6, 0.6 Hz, 1H), 8.42 (dd, J = 4.8, 1.0 Hz, 1H), 7.98 (dd, J = 4.9, 4.1 Hz, 1H), 7.82 (ddd, J = 8.3, 7.4, 1.9 Hz, 1H), 7.74 (d, J = 0.9 Hz, 1H), 7.19 (ddd, J = 7.3, 4.9, 1.0 Hz, 1H), 6.47 (dd, J = 2.5, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.1, 140.1, 136.8, 125.1, 119.5, 110.5, 105.9.* HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_8H_8N_3$ 146.0713; found 146.0708.

Methyl 2-(1_H_-Pyrazol-1-yl)-1_H_-benzo[_d_]imidazole-6-carboxylate, Compound 34. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR

(600 MHz, DMSO) δ 8.64 (dd, J = 2.6, 0.5 Hz, 1H), 8.12 (s, 1H), 8.01−7.99 (m, 1H), 7.86 (dd, J = 8.4, 1.6 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 6.70 (dd, J = 2.6, 1.7 Hz, 1H), 3.88 (s, 4H). ^{13}C NMR (151 MHz, DMSO) δ 166.6, 147.8, 143.3, 129.2, 123.5, 123.4, 109.3, 52.0. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{11}N_4O_2$ 243.0877; found 243.0875.

6-Nitro-2-(1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 35. Following the general method described above, the title compound was isolated in 95% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.83 (s, 1H), 8.66 (d, J = 2.6 Hz, 1H), 8.37 (s, 1H), 8.14 (dd, J = 8.8, 2.3 Hz, 1H), 8.04 (d, J = 1.4 Hz, 1H), 7.70 (s, 1H), 6.73 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 149.2, 143.8, 142.7, 129.5, 118.1, 109.7. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_8N_5O_2$ 230.0673; found 230.0671.

2-(1*H*-Pyrazol-1-yl)-6-(trifluoromethyl)-1*H*-benzo[*d*]imidazole, Compound 36. Following the general method described above, the title compound was isolated in 93% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.64 (dd, J = 2.6, 0.5 Hz, 1H), 8.01 (dd, J = 1.6, 0.4 Hz, 1H), 7.85 (s, 1H), 7.71 (d, J = 8.3 Hz, 1H), 7.54 (dd, J = 8.4, 1.4 Hz, 1H), 6.71 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 147.9, 143.4, 129.2, 124.9 (q, J = 271.6 Hz, 1C), 122.7 (q, J = 31.8 Hz, 1C), 118.9 (q, J = 3.5 Hz, 1C), 109.4. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_8N_4F_3$ 253.0696; found 253.0698.

2-(1*H*-Pyrazol-1-yl)-1*H*-benzo[*d*]imidazole-6-carbonitrile, Compound 37. Following the general method described above, the title compound was isolated in 92% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.66 (s, 1H), 8.64 (d, J = 2.6 Hz, 1H), 8.01 (d, J = 1.4 Hz, 2H), 7.67 (d, J = 8.3 Hz, 1H), 7.61 (dd, J = 8.3, 1.5 Hz, 1H), 6.71 (dd, J = 2.6, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 148.3, 143.5, 129.3, 125.9, 119.8, 109.5, 104.0. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_8N_5$ 210.0774; found 210.0779.

6-Methoxy-2-(1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 38. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.55 (d, J = 2.6 Hz, 1H), 7.93 (d, J = 1.2 Hz, 1H), 7.41 (d, J = 8.7 Hz, 1H), 7.03 (s, 1H), 6.83 (dd, J = 8.7, 2.5 Hz, 1H), 6.65 (dd, J = 2.5, 1.7 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 155.7, 145.5, 142.5, 128.6, 111.1, 108.7, 55.4. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_{11}N_4O$ 215.0927; found 215.0924.

2-(4-Chloro-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 39. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.17 (s, 1H), 8.84 (d, J = 0.6 Hz, 1H), 8.10 (d, J = 0.6 Hz, 1H), 7.53 (br s, 2H), 7.29−7.15 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 145.2, 141.1, 126.9, 122.2, 112.4. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_8N_4Cl$ 219.0432; found 219.0433.

2-(3-(4-Methoxyphenyl)-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 40. Following the general method described above, the title compound was isolated in 96% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.67 (d, J = 2.7 Hz, 1H), 8.01−7.92 (m, 2H), 7.63−7.54 (m, 2H), 7.30−7.23 (m, 2H), 7.13 (d, J = 2.7 Hz, 1H), 7.12−7.05 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 159.9, 153.9, 145.3, 136.4, 130.7, 127.4, 124.2, 122.6, 114.5, 114.3, 106.6, 55.2. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{17}H_{15}N_4O$ 291.1240; found 291.1235.

2-(3-(Trifluoromethyl)-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 41. Following the general method described above, the title compound was isolated in 88% yield. ^{1}H NMR (600 MHz, DMSO) δ 13.37 (s, 1H), 8.84 (dd, J = 2.6, 0.9 Hz, 1H), 7.58 (dd, J = 7.4, 1.6 Hz, 2H), 7.29−7.24 (m, 2H), 7.16 (d, J = 2.6 Hz, 1H). ^{13}C NMR (151 MHz, DMSO) δ 144.6, 143.7 (q, J_{C-F} = 38.0 Hz, 1C), 131.6, 122.7, 120.9 (q, J_{C-F} = 269.1 Hz, 1C), 107.2. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{11}H_8N_4F_3$ 253.0696; found 253.0699.

2-(4-(2-Chloroethyl)-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 42. Following the general method described above, the title compound was isolated in 89% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.53 (s, 1H), 7.91 (s, 1H), 7.56−7.50 (m, 2H), 7.26−7.19 (m, 2H), 3.88 (t, J = 6.9 Hz, 2H), 3.01 (t, J = 6.9 Hz, 2H). ^{13}C NMR (151 MHz, DMSO) δ 145.6, 143.2, 127.5, 122.3, 120.9, 114.6, 109.5, 44.7, 27.1. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{12}N_4Cl$ 247.0745; found 247.0747.

2-(4-Nitro-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 43. Following the general method described above, the title compound was isolated in 84% yield. ^{1}H NMR (600 MHz, DMSO) δ 9.54 (d, J = 0.36 Hz, 1H), 8.75 (d, J = 0.36 Hz, 1H), 7.60 (s, 2H), 7.34−7.19 (m, 2H). ^{13}C NMR (151 MHz, DMSO) δ 144.2, 138.2, 137.3, 128.4, 122.9, 109.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{10}H_8N_5O_2$ 230.0673; found 230.0673.

1-Methyl-2-(3-methyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 44. Following the general method described above, the title compound was isolated in 98% yield. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, J = 2.5 Hz, 1H), 7.70 (ddd, J = 3.9, 2.3, 0.5 Hz, 1H), 7.38−7.34 (m, 1H), 7.32−7.27 (m, 2H), 6.30 (d, J = 2.5 Hz, 1H), 4.11 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 152.3, 145.8, 140.6, 135.8, 131.8, 122.7, 122.6, 119.1, 109.4, 108.0, 32.1, 13.8. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{12}H_{13}N_4$ 213.1135; found 213.1133 .

1-Methyl-2-(3-phenyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 45. Following the general method described above, the title compound was isolated in 91% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.60 (s, 1H), 8.01 (d, J = 7.3 Hz, 2H), 7.67 (d, J = 7.8 Hz, 2H), 7.51 (t, J = 7.3 Hz, 2H), 7.43 (t, J = 7.0 Hz, 1H), 7.32 (dt, J = 24.9, 7.2 Hz, 2H), 7.19 (s, 1H), 4.14 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 153.5, 145.1, 140.0, 135.6, 133.2, 131.8, 128.8, 128.6, 125.7, 122.5, 122.47, 118.5, 110.5, 105.6, 31.9. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{17}H_{15}N_4$ 275.1291; found 275.1290.

1-Methyl-2-(3-methyl-4-phenyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 46. Following the general method described above, the title compound was isolated in 95% yield. ^{1}H NMR (600 MHz, DMSO) δ 8.70 (s, 1H), 7.67−7.63 (m, 2H), 7.63−7.60 (m, 2H), 7.49−7.44 (m, 2H), 7.37−7.27 (m, 3H), 4.08 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 149.1, 145.0, 139.9, 135.6, 131.7, 129.9, 128.8, 127.4, 126.9, 122.7, 122.6, 122.5, 118.5, 110.5, 31.8, 13.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{17}N_4$ 289.1448; found 289.1447.

1-Methyl-2-(5-methyl-3-phenyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 47. Following the general method described above except that it took 4 days for the reaction to complete, the title compound was isolated in 60% yield after column chromatography with EtOAc/hexanes as eluents. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.89−7.82 (m, 2H), 7.77 (dd, J = 6.7, 1.8 Hz, 1H), 7.44−7.37 (m, 2H), 7.37−7.27 (m, 4H), 6.55 (d, J = 0.7 Hz, 1H), 3.87 (s, 3H), 2.57 (d, J = 0.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 153.2, 145.1, 144.0, 140.8, 135.2, 132.7, 128.7, 128.4, 125.9, 123.3, 122.7, 119.9, 109.7, 105.0, 31.4, 12.5. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{17}N_4$ 289.1448; found 289.1452.

1-Methyl-2-(3-methyl-5-phenyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 48. The title compound was isolated as a minor product in 6% yield after column chromatography with EtOAc/hexanes as eluents. ^{1}H NMR (600 MHz, DMSO) δ 7.62 (dd, J = 8.9, 8.2 Hz, 2H), 7.38−7.34 (m, 1H), 7.32−7.26 (m, 4H), 7.25−7.21 (m, 2H), 6.69 (s, 1H), 3.62 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (151 MHz, DMSO) δ 151.0, 146.5, 144.9, 139.9, 134.5, 128.9, 128.7, 128.6, 127.3, 123.3, 122.5, 119.6, 110.8, 107.4, 29.9, 13.3. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{18}H_{17}N_4$ 289.1448; found 289.1451.

2-(3,5-Diisopropyl-1*H*-pyrazol-1-yl)-1*H*-benzo[*d*]imidazole, Compound 49. Following the general method described above except that the reaction was performed at 140 °C for 1 d, the title compound was isolated in 55% yield after column chromatography with EtOAc/hexanes as eluents. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.14 (s, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.36−7.10 (m, 3H), 6.19 (s, 1H), 4.42−4.18 (m, 1H), 3.13−2.90 (m, 1H), 1.40 (d, J = 6.8 Hz, 6H), 1.31 (d, J = 7.0 Hz, 6H). ^{13}C

NMR (151 MHz, $CDCl_3$) δ 161.4, 154.0, 146.7, 142.6, 132.0, 122.5, 122.1, 119.1, 110.3, 102.8, 28.0, 25.9, 22.5, 22.4. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{16}H_{21}N_4$ 269.1761; found 269.1763.

2-(3,5-Diisopropyl-1*H*-pyrazol-1-yl)-1′*H*-1,2′-bibenzo[*d*]-imidazole, Compound 50. The title compound was isolated as a byproduct in 18% yield after column chromatography with EtOAc/hexanes as eluents. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.10 (s, 1H), 8.42−8.36 (m, 1H), 7.85−7.78 (m, 2H), 7.50 (ddd, J = 8.3, 7.3, 1.2 Hz, 1H), 7.43 (ddd, J = 8.3, 7.3, 1.2 Hz, 1H), 7.40−7.35 (m, 1H), 7.33−7.26 (m, 2H), 6.14 (s, 1H), 3.49−3.30 (m, 1H), 3.13 (hept, J = 6.9 Hz, 1H), 1.43 (d, J = 7.0 Hz, 6H), 1.12 (d, J = 6.9 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2, 157.2, 142.6, 142.0, 141.7, 140.3, 133.7, 132.2, 125.7, 124.5, 123.4, 122.7, 120.2, 119.7, 114.5, 110.8, 102.8, 28.1, 25.6, 22.4, 22.2. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{23}H_{25}N_6$ 385.2135; found 385.2127.

* Denotes that some of the C signals do not show up even at very high concentration.

■ ASSOCIATED CONTENT

Supporting Information. ^{1}H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

We wish to thank Ms. Heather McAllister for analytical support and Dr. Daniel J. Pippel for proofreading the manuscript.

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