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N−H Insertion Reactions of Primary Ureas: The Synthesis of Highly Substituted Imidazolones and Imidazoles from Diazocarbonyls

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Primary ureas have been used as substrates in rhodium-catalyzed N−H insertion reactions with an array of diazocarbonyls. The insertion reaction is efficient and gives excellent selectivity and yields. The products from the insertion reaction with diazoketones cyclize readily in the presence of acid to yield the corresponding imidazolones that can be further derivatized by N-alkylation with alkyl, allyl, and benzyl halides. Alternatively, the imidazolones were treated with phosphorus oxybromide to form the corresponding 2-bromoimidazoles that were further functionalized using a Suzuki coupling reaction.

Introduction

Diazocarbonyl-functionalized molecules have a long-standing importance within synthetic organic chemistry since they form highly reactive intermediates that react by a plethora of useful pathways, including insertion (N−H, O−H, S−H, Si−H, C−H, etc.), dipolar cycloaddition, and cyclopropanation. Although some of the classical reactions of diazocarbonyls could lead to multiple or impure products, modern advances in catalysis, especially rhodium catalysts, has enabled chemists to utilize these substrates with high efficiency,[1] especially within the area of asymmetric synthesis.[2] In addition, many of the products from insertion reactions serve as very useful intermediates for the synthesis of heterocycles.[3]

In our laboratory, we have utilized diazocarbonyl functionalized substrates to prepare libraries of small heterocycles for application in combinatorial type screening programs for basic drug discovery. Thus, a series of polymer-bound α-diazo-*β*-ketoesters have been employed as key modular building blocks for these library syntheses.[4] The rhodium-catalyzed N−H insertion reaction with primary amides gave the corresponding α-acylamino-*β*-ketoesters that were subsequently converted using a cyclodehydration reaction into the corresponding oxazoles or pyrazinones.[5] Similary, reaction with *N*-alkylanilines gave the corresponding α-arylamino products that were converted into the corresponding indoles.[6] Accordingly, we sought to further investigate the potential applications of other N−H functionalized insertion partners in order to create more diverse combinatorial libraries. From initial screening, we discovered that primary ureas served as excellent substrates in N−H insertion reactions with rhodium carbenoids derived from α-diazo-*β*-ketoesters; the desired insertion products were isolated in good yields and no competing reaction was seen between the $-NH_2$ and −RNH groups.[7] Furthermore, it was discovered that these insertion products were converted easily into the corresponding 1,3-dihydro-2*H*-imidazol-2-ones (imidazolones) by acid-catalyzed cyclodehydration. Since these imidazolones presented an ideal scaffold for further elaboration and because many imidazolone-containing compounds exhibit biological activity,[8] we set out to fully investigate new reactions of these compounds. Herein the full details of our investigation of the N−H insertion reactions of primary ureas with a series of diversely functionalized diazocarbonyls and the trans-

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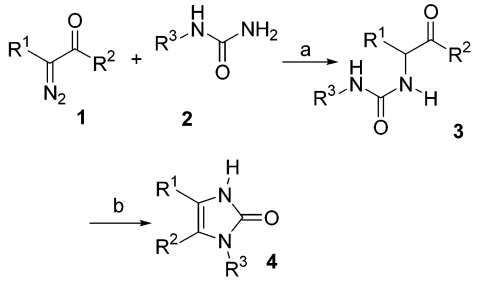
SCHEME 1[a]



[a] Reagents and conditions: (a) **2** (1.5 equiv), Rh_2Oct_4 (2 mol %), toluene/1,2-dichloroethane 1:1, 80 °C, 30 min. (b) TFA (10%−neat).

formation of these products into imidazolones and imidazoles is reported.

Results and Discussion

The general reaction scheme for the N−H insertion reaction of primary ureas and the conversion of these products into imidazolones is outlined in Scheme 1. The first objective of the study was to assess which diazocarbonyls, compounds **1**, could be reacted with primary ureas **2** in the presence of rhodium octanoate catalyst. The first problem encountered was that the ureas **2** were sparingly soluble in solvents such as chloroform or toluene which are commonly employed in N−H insertion reactions. When dimethylformamide (DMF) or *N,N*-dimethylacetamide was employed, ureas **2** were fully solublized; however, the desired reaction products were not observed by thin-layer chromatography (TLC). Upon additional experimentation, it was discovered that a 1:1 mixture of 1,2-dichloroethane and toluene gave the best results. It was also revealed that the yields of desired products were improved when the urea starting materials **2** were ground into a fine powder prior to the reaction. Finally, it should be noted that the method of addition of the catalyst is critical for the success of the reaction. When the catalyst was added in one portion, several unidentifiable side products were observed by TLC. The best method for performing the reaction required the preparation of a fine suspension of the catalyst by sonication in toluene. The diazocarbonyl **1** and urea **2** were heated to 80 °C in the mixed solvent system, and the catalyst suspension was slowly added by pipet. The results from this study are outlined in Table 1. Several diazocarbonyls **1** were employed and in some cases the insertion products **3** were isolated directly from the reaction (entries 1−3, 9, 11, and 14). However, some of the insertion products **3** were cyclized to the corresponding imidazolones **4** in the presence of even mild acid such as silica gel. In these cases, after the insertion reaction had been performed, trifluoroacetic acid was added to the reaction and the imidazolones **4** were isolated by column chromatography of the concentrated crude product.

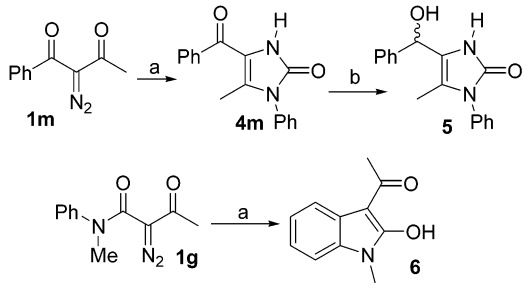
In most cases, both the insertion and imidazolone formation reactions worked well. In addition to the successful experiments where the α-diazo-*β*-ketoesters were employed (entries 4, 5, and 16), α-diazo-*β*-ketophosphonates (entries 9 and 10) and symmetrical α-diazo-1,3-diketones (entries 12 and 13) both gave modest to excellent yields of insertion and imidazolone products **3** and **4**. An interesting observation was made when the unsymmetrical 2-diazo-1-phenylbutane-1,3-dione **1m** was employed (entry 13). In this instance, the imidazolone cyclization reaction occurs selectively at the methyl carbonyl group; to validate this structure, ketone **4m** was converted into the corresponding alcohol **5** by using sodium borohydride and the structure was determined by ^{1}H NMR spectroscopic analysis, Scheme 2.

TABLE 1. N−H Insertion Reactions of Ureas 2 with a Series of Diazocarbonyls 1

entry	1	R^1	R^2	R^3	yield of **3**/%	yield of **4**/%
1	**1a**	CO_2Et	OEt	Ph	86	
2	**1b**	H	OEt	Ph	40	
3	**1c**	$PO(OEt)_2$	OEt	Ph	91	
4	**1d**	CO_2Et	Ph	Ph	*a*	85[b]
5	**1e**	CO_2Et	Me	Ph	*a*	72[b]
6	**1f**	CONH,Ph	Ph	Ph	*a*	74
7	**1g**	CONMe,Ph	Me	Ph	**6** (11)	
8	**1h**	$CON(Me)_2$	Me	Ph	*a*	93
9	**1i**	$PO(OEt)_2$	Ph	Ph	88	88
10	**1j**	$PO(OEt)_2$	Me	Ph	*a*	83
11	**1k**	PhCO	Ph	Ph	53	95
12	**1*l***	COMe	Me	Ph	*a*	49
13	**1m**	COMe	Ph	Ph	*a*	41
14	**1n**	H	Ph	Ph	38	95
15	**1o**	SO_2Me	Ph	Ph	*c*	
16	**1p**	CO_2Et	Ph	Me	*a*	85[b]

[a] Not isolated. [b] Previously published work added for comparison. [c] Product not detected.

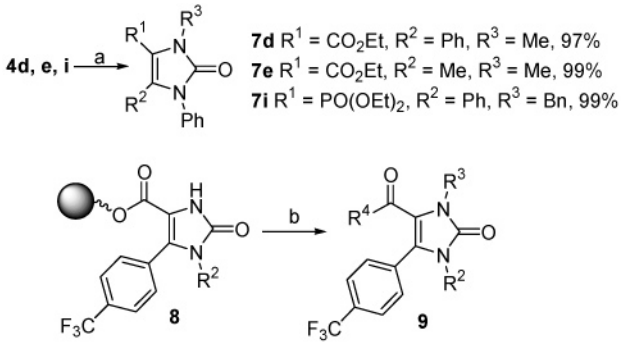
SCHEME 2[a]



[a] Reagents and conditions: (a) (i) **2** (1.5 equiv), Rh_2Oct_4 (2 mol %), toluene/1,2-dichloroethane 1:1, 80 °C, 30 min; (ii) TFA (10%−neat). (b) $NaBH_4$, MeOH, 30 min.

When α-diazo-ketone **1n** was employed, the desired insertion product **3n** was only isolated in 38% yield (entry 14). The higher reactivity associated with diazoketones led us to speculate that unwanted side reactions such as dimerization of the carbenoid resulted in this lower yield. α-Diazo-*β*-ketoamides also gave good results in the NH insertion reaction with urea **2**, with one exception. When 2-diazo-*N*-methyl-3-oxo-3-phenylpropionamide **1f** was utilized, the desired secondary amide functionalized imidazolone **4f** was isolated in 74% yield (entry 6). Similarly, when 2-diazo-*N,N*-dimethyl-3-oxo-3-phenylpropionamide **1h** was employed, the desired tertiary amide functionalized imidazolone **4h** was isolated in 93% yield (entry 8). Despite these two successful reactions, when 2-diazo-*N*-methyl-3-oxo-*N*-phenylbutyramide **1g** was employed in the reaction with urea **2**, the competing intramolecular C−H insertion reaction into the aryl ring occurred selectively to form indole **6** and no N−H insertion products were isolated (entry 7). This indole formation

SCHEME 3[a]



[a] Reagents and conditions: (a) CH_3I or BnBr (3 equiv), K_2CO_3 (3 equiv) DMF, 3 h. (b) (i) Alkyl iodide or bromide (10 equiv), tetrabutylammonium iodide (5 equiv, when $R_3X = R_3Br$), LiOtBu (5 equiv), DMF/THF 1:1, rt to 40 °C, 24 h; (ii) R,RNH (10 equiv), $AlMe_3$, (5 equiv), toluene, 50 °C, 16 h or NaOMe (2.5 equiv), THF/MeOH (4:1), 50 °C, 1 h.

reaction is well documented;[9] however, our poor yield of indole **6** was attributed to its decomposition during silica gel chromatography. Finally, it is noted that when the reaction was performed with sulfone **1o**, the corresponding N−H insertion product was not observed in the reaction products (entry 15).

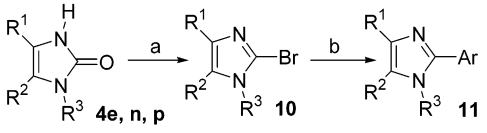
In our original report of the N−H insertion reactions of primary ureas, a series of polymer-bound α-diazo-*β*-ketoesters were utilized to prepare diverse solid-phase libraries of imidazolones. To expand this methodology, the utility of the imidazolone scaffold for further diversification was investigated.[10] The first procedure was the alkylation of the N−H of the imidazolone **4**, Scheme 3. When reactions were performed in solution, a combination of potassium carbonate and either methyl iodide or benzyl bromide in DMF provided the desired *N*-alkylimidazolones **7** in nearly quantitative yield. Since we had a number of *J*anda*J*el[11] polymer−polymer-bound imidazolones **8** on hand, whose syntheses were described in our original report,[7] we also investigated their application in this N-alkylation reaction. However, when the above conditions were applied to **8**, very poor yields of N-alkylated products **9** were observed after cleavage from the resin. After extensive optimization experiments, the selection of base proved to be crucial to the success of the reaction. Lithium *tert*-butoxide base gave the best results when used in 5-fold excess over the polymer-bound substrate. A mixed solvent system of DMF and tetrahydrofuran (THF) gave the best results and the addition of tetrabutylammonium iodide proved essential when alkyl bromide alkylating reagents were employed.

TABLE 2. N-Alkylation of Polymer-Bound Imidazolones 8

entry	R^2	R^3	R^4	product	purity/ %[a]	yield/ %[b]
1	Bn	Me	MeO	**9a**	94	74
2	Me	Bn	MeO	**9b**	95	75
3	Ph	Me	MeO	**9c**	97	77
4	Ph	Bn	MeO	**9d**	98	77
5	Ph	Allyl	MeO	**9e**	98	74
6	Ph	$PhCOCH_2$	MeO	**9f**	97	86
7	Ph	3-Ph-$(CH_2)_3$	MeO	**9g**	98	50
8	Ph	cyclopropyl-methyl	MeO	**9h**	95	40
9	Ph	Me	piperidine−	**9i**	98	67
10	Ph	Me	morpholine−	**9j**	96	69
11	Ph	Bn	PhNH−	**9k**	94	81
12	Ph	Bn	$Ph(CH_2)_2NH$−	**9l**	99	66
13	Ph	Bn	Ph,MeN−	**9m**	88	85

[a] Purity assessed by HPLC. [b] Yield of pure product after isolation by TLC.

SCHEME 4[a]



10e, $R^1 = CO_2Et$, $R^2 = Me$, $R^3 = Ph$, 76%
10n, $R^1 = H$, $R^2 = Ph$, $R^3 = Ph$, 67%
10p, $R^1 = CO_2Et$, $R^2 = Ph$, $R^3 = Me$, 87%

[a] Reagents and conditions: (a) $POBr_3$, benzene, reflux 6 h. (b) $ArB(OH)_2$ (3 equiv), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$ (3 mol %), Cs_2CO_3 (3 equiv), toluene 110 °C, 2 h.

After alkylation, the *N*-alkylimidazolones were cleaved from the resin by using either a transesterification or diversity building amide formation reaction.[12] The results from this study are presented in Table 2.

The second aspect of our study for the further derivatization of the imidazolones centered upon their conversion into imidazoles. Treatment of imidazolones **4e**, **4n**, and **4p** with phosphorus oxybromide ($POBr_3$) in benzene or toluene under reflux conditions gave the corresponding 2-bromoimidazoles **10e**, **10n**, and **10p** respectively in excellent yields, Scheme 4. After brief experimentation we discovered that the 2-bromoimidazole **10p** served as an excellent substrate in the Suzuki coupling reaction[13] with phenylboronic acid (Scheme 4 and Table 3, entries 1−4). Additionally, treatment of **10e**, **10n**, and **10p** with an array of aryl boronic acids in toluene in the presence of $Pd(dppf)Cl_2$ catalyst and cesium carbonate base at 110 °C gave the corresponding 2-arylimidazoles **11a**−**i** in excellent yields, Table 3. Since there is little methodology available for the regioselective functionalization of imidazoles at the C2 position,[14] we feel this method for the

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TABLE 3. Suzuki Coupling Reactions of 2-Bromoimidazoles 10

entry	SM	R^1	R^2	R^3	Ar	11	yield/%
1	**10p**	CO_2Et	Ph	Me	Ph	**a**	43[a,b]
2	**10p**	CO_2Et	Ph	Me	Ph	**a**	83[b]
3	**10p**	CO_2Et	Ph	Me	Ph	**a**	87[b]
4	**10p**	CO_2Et	Ph	Me	Ph	**a**	99
5	**10p**	CO_2Et	Ph	Me	4-$CF_3C_6H_4$	**b**	99
6	**10p**	CO_2Et	Ph	Me	4-Ph-C_6H_4	**c**	97
7	**10p**	CO_2Et	Ph	Me	1-naphthyl	**d**	97
8	**10p**	CO_2Et	Ph	Me	styryl	**e**	95
9	**10e**	CO_2Et	Me	Ph	4-$CH_3OC_6H_4$	**f**	90
10	**10e**	CO_2Et	Me	Ph	4-$(CO_2Et)C_6H_4$	**g**	97
11	**10e**	CO_2Et	Me	Ph	4-TBDMSOC_6H_4	**h**	93
12	**10n**	H	Ph	Ph	Ph	**i**	41

[a] $Pd(Ph_3P)_4$ catalyst used. [b] 1.5 equiv of $ArB(OH)_2$ and Cs_2CO_3 used.

regioselective synthesis of 2-functionalized imidazoles may find application in the synthesis of imidazole-containing natural products. Unfortunately, we were not able to successfully transfer these protocols to a solid-phase format for the synthesis of an imidazole library. Although the acid-stable hydroxyalkyl linker was employed, several unidentifiable cleavage products were observed by TLC analysis when polymer-bound imidazolones **8** were treated with $POBr_3$ in benzene or toluene at reflux.

Conclusion

In summary, we have demonstrated the application of primary ureas as substrates in rhodium-catalyzed N−H insertion reactions with a series of α-diazocarbonyls including diazoketones, diazodiketones, diazoketoesters, diazoketoamides, and diazoketophosphonates. The N−H insertion reaction works with great efficiency and the corresponding insertion products are easily converted into the corresponding imidazolones that can be further derivatized by N-alkylation with alkyl halides. Finally, the imidazolone products are easily converted into the corresponding 2-bromoimidazoles that serve as precursors for the synthesis of 2-arylimidazoles by using a Suzuki coupling reaction.

Experimental Section

General Methods. General methods have been reported elsewhere.[15] Ethyl diazoacetate **1b** was obtained from Aldrich Chemical Co. All α-diazo carbonyl compounds **1** were prepared according to literature precedent,[16] except for **1c**,[17] **1f**,[9] **1i**,**j**,[18] **1n**,[19] and **1o**.[20]

Rhodium-Catalyzed N−H Insertion Reaction (1 → 3). A vigorously stirred suspension of α-diazo compound **1** (2 mmol) and finely powdered phenyl urea **2** (408 mg, 3 mmol) in toluene−1,2-dichloroethane (1:1, 20 mL) was heated to 80 °C and a suspension of Rh_2Oct_4 (31 mg, 0.04 mmol) in toluene (4 mL) was added over 10 min. After addition of the catalyst, the mixture was stirred for an additional 30 min. For entries 1−3, 7, 9, 11, and 14, the solvent was removed under reduced pressure and the residue was purified by flash chromatography and/or recrystallization to give the corresponding insertion products **3**.

2-(3-Phenylureido)malonic Acid Diethyl Ester (3a). Purified by column chromatography ($CHCl_3$−CH_3CN, 15:1) and recrystallization (EtOAc−hexanes); white solid; mp 116−117 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, J = 7.0 Hz, 6H), 4.27 (m, 4H), 5.21 (s, 1H), 6.18 (br s, 1H), 7.00−7.10 (m, 1H), 7.11 (br s, 1H), 7.22−7.38 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 57.2, 62.7, 120.8, 124.0, 129.2, 138.0, 154.5, 167.3; HRMS *m/z* 295.1282 $[M + H]^+$, calcd for $C_{14}H_{19}N_2O_5$ 295.1288.

(3-Phenyluriedo)acetic Acid Ethyl Ester (3b). Purified by column chromatography ($CHCl_3$−CH_3CN, 10:1) and recrystallization (EtOAc−hexanes); colorless needles; mp 107−108 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 1.20 (t, J = 7.1 Hz, 3H), 3.85 (d, J = 6.1 Hz, 2H), 4.11 (q, J = 7.1 Hz, 2H), 6.43 (t, J = 6.1 Hz, 1H), 6.90 (t, J = 7.7 Hz, 1H), 7.22 (t, J = 8.0 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 8.78 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.1, 42.1, 61.5, 121.0, 123.8, 129.2, 138.3, 156.0, 171.3; HRMS *m/z* 223.1076 $[M + H]^+$, calcd for $C_{11}H_{15}N_2O_3$ 223.1077.

(Diethoxyphosphoryl)-(3-phenylureido)acetic Acid Ethyl Ester (3c). Purified by column chromatography ($CHCl_3$−acetone, 9:1) and recrystallization (EtOAc−hexanes); white solid; mp 93−94 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.19−1.29 (m, 9H), 4.05−4.25 (m, 6H), 4.84 (dd, J = 8.8, 22.7 Hz, 1H), 6.86 (dd, J = 4.3, 8.8 Hz, 1H), 6.94 (t, J = 7.3 Hz, 1H), 7.25 (t, J = 7.9 Hz, 2H), 7.37 (dd, J = 1.1, 8.5 Hz, 2H), 8.89 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 13.9, 16.1 (d, J = 5.7 Hz), 16.2 (d, J = 5.7 Hz), 51.0 (d, J = 150.0 Hz), 61.6, 63.1 (d, J = 6.7 Hz), 63.2 (d, J = 5.7 Hz), 117.6, 121.7, 128.8, 139.6, 154.2 (d, J = 9.5 Hz), 167.5 (d, J = 2.9 Hz); HRMS *m/z* 359.1371 $[M + H]^+$, calcd for $C_{15}H_{24}N_2O_6P_1$ 359.1366.

6. Purified by column chromatography (EtOAc−hexanes, 1:4); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.42 (s, 3H), 3.31 (s, 3H), 6.92 (d, J = 7.3 Hz, 1H), 7.05−7.14 (m, 1H), 7.17−7.25 (m, 1H), 7.33 (d, J = 7.3 Hz, 1H), 13.65 (br s, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 20.2, 25.5, 101.6, 108.3, 119.6, 122.0, 122.1, 125.1, 138.8, 170.9, 172.8; HRMS *m/z* 190.0864 $[M + H]^+$, calcd for $C_{11}H_{12}N_1O_2$ 190.0863.

[2-Oxo-2-phenyl-1-(3-phenylureido)ethyl]phosphonic Acid Diethyl Ester (3i). Reaction time 1.5 h; purified by column chromatography ($CHCl_3$−CH_3CN, 5:1); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08 (t, J = 7.4 Hz, 3H), 1.35 (t, J = 7.4 Hz, 3H), 3.94−4.14 (m, 2H), 4.28−4.46 (m, 2H), 6.29 (dd, J = 9.2, 22.0 Hz, 1H), 6.95−7.02 (m, 1H), 7.12 (br d, J = 8.5 Hz, 1H), 7.20−7.65 (m, 7H), 7.98−8.07 (m, 2H), 8.29 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9 (d, J = 6.7 Hz), 16.5 (d, J = 5.7 Hz), 53.5 (d, J = 147.9 Hz), 63.3 (d, J = 7.6 Hz), 65.0 (d, J = 7.6 Hz), 118.8, 122.4, 128.5, 128.8, 129.3, 133.9, 135.4 (d, J = 1.9 Hz), 139.5, 154.7 (d, J = 6.7 Hz), 194.0 (d, J = 3.8 Hz); HRMS *m/z* 391.1433 $[M + H]^+$, calcd for $C_{19}H_{24}N_2O_4P_1$ 391.1417.

1-(1-Benzoyl-2-oxo-2-phenylethyl)-3-phenylurea (3k). Purified by column chromatography ($CHCl_3$−CH_3CN, 125:1); white solid; mp 195−196 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.74 (s, 1H), 7.05−7.13 (m, 1H), 7.24−7.31 (m, 2H), 7.32−7.48 (m, 9H), 7.52−7.60 (m, 1H), 7.92−8.02 (m, 2H), 9.69 (br s, 1H), 10.38 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 60.9, 120.3, 124.4, 128.7, 128.92, 128.97, 129.03, 129.7, 132.5, 134.1, 135.3, 136.9, 150.7, 170.2, 194.5; HRMS *m/z* 359.1390 $[M + H]^+$, calcd for $C_{22}H_{19}N_2O_3$ 359.1390.

1-(2-Oxo-2-phenylethyl)-3-phenylurea (3n). Purified by column chromatography ($CHCl_3$−acetone, 10:1); white solid; mp 146−147 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 4.69 (d, J = 5.5 Hz, 2H), 6.52 (d, J = 5.5 Hz, 1H), 6.90 (t, J = 7.7 Hz, 1H), 7.23 (t, J = 7.7 Hz, 2H), 7.42 (d, J = 7.7 Hz, 2H), 7.56 (t, J = 7.7 Hz, 2H), 7.67 (t, J = 7.7 Hz, 1H), 8.01 (d, J = 7.1 Hz, 2H), 8.91 (s, 1H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 46.8, 117.6,

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121.2, 127.8, 128.7, 128.9, 133.6, 134.9, 140.4, 155.2, 196.2; HRMS *m/z* 255.1134 $[M + H]^+$, calcd for $C_{15}H_{15}N_2O_2$ 255.1128.

TFA-Promoted Cyclization Reaction (3 → 4). For entries 4−6, 8, 10, 12, and 13, to the cooled insertion reaction mixture was added TFA (1 mL), and the resulting solution was stirred for 1 h at room temperature. For entry 10, insertion mixture was evaporated, and then treated with neat TFA (10 mL) for 3 h at 50 °C. After removal of solvent under reduced pressure, the residue was purified by flash chromatography to give corresponding 2-imidazolone **4**. For entries 9, 11, and 14, the insertion product **2** (1 mmol) was treated with neat TFA (10 mL) (entries 9, 11) or 10% TFA in 1,2-dichloroethane (10 mL) (entry 14), and the resulting solution was stirred for several hours (see below). After removal of solvent under reduced pressure, the residue was purified by flash chromatography and/or recrystallization to give corresponding 2-imidazolone **4**.

Oxo-1,5-diphenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (4d). Purified by column chromatography ($CHCl_3$−CH_3CN, 5:1). An analytical sample was obtained by recrystallization (EtOAc); white solid; mp 237−238 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.16 (t, J = 7.4 Hz, 3H), 4.19 (q, J = 7.4 Hz, 2H), 7.08−7.16 (m, 2H), 7.18−7.34 (m, 8H), 9.83 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 60.9, 110.6, 127.4, 127.5, 127.7, 127.8, 128.8, 129.1, 130.6, 132.4, 134.0, 152.0, 159.3; HRMS *m/z* 309.1235 $[M + H]^+$, calcd for $C_{18}H_{17}N_2O_3$ 309.1234.

5-Methyl-2-oxo-1-phenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (4e). Purified by column chromatography ($CHCl_3$−CH_3CN, 5:1). An analytical sample was obtained by recrystallization (EtOAc−hexanes); white solid; mp 182−183 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34 (t, J = 7.4 Hz, 3H), 2.26 (s, 1H), 4.32 (q, J = 7.4 Hz, 2H), 7.27−7.33 (m, 2H), 7.39−7.54 (m, 3H), 8.29 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.0, 14.3, 60.7, 109.8, 127.7, 128.7, 129.5, 130.7, 133.6, 151.9, 160.0; HRMS *m/z* 247.1077 $[M + H]^+$, calcd for $C_{13}H_{15}N_2O_3$ 247.1077.

2-Oxo-1,5-diphenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methylphenylamide (4f). Purified by column chromatography ($CHCl_3$−CH_3CN, 4:1) and recrystallization ($CHCl_3$−hexanes); white solid; mp 275−278 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.01−7.08 (m, 1H), 7.09−7.15 (m, 2H), 7.20−7.40 (m, 10H), 7.42−7.52 (m, 2H), 9.28 (s, 1H), 11.07 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 114.1, 119.5, 123.6, 127.5, 127.8, 127.9, 128.11, 128.14, 128.5, 128.70, 128.73, 130.5, 134.6, 138.5, 151.6, 157.1; HRMS *m/z* 356.1385 $[M + H]^+$, calcd for $C_{22}H_{18}N_3O_2$ 356.1393.

5-Methyl-2-oxo-1-phenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Dimethylamide (4h). Purified by column chromatography (acetone−hexanes, 1:1). An analytical sample was obtained by recrystallization ($CHCl_3$−hexanes); yellow solid; mp 220−222 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.04 (s, 3H), 3.05 (s, 6H), 7.26−7.32 (m, 2H), 7.36−7.43 (m, 1H), 7.44−7.51 (m, 2H), 10.31 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.1, 37.2, 113.0, 124.3, 127.7, 128.4, 129.4, 133.9, 152.9, 162.5; HRMS *m/z* 246.1235 $[M + H]^+$, calcd for $C_{13}H_{16}N_3O_2$ 246.1237.

(2-Oxo-1,5-diphenyl-2,3-dihydro-1*H*-imadazol-4-yl)phosphonic Acid Diethyl Ester (4i). Reaction conditions, neat TFA, 40 °C, 3 h; purified by column chromatography (EtOAc−hexanes, 4:5); white solid; mp 203−205 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.13 (t, J = 7.0 Hz, 6H), 3.90−4.10 (m, 4H), 7.09−7.15 (m, 2H), 7.19−7.31 (m, 8H), 9.53 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.9 (d, J = 6.7 Hz), 62.8 (d, J = 5.7 Hz), 107.1 (d, J = 235.6 Hz), 127.4, 127.5, 127.8, 128.0, 128.8, 129.0, 129.9, 133.3 (d, J = 20.0 Hz), 134.4, 153.2 (d, J = 12.4 Hz); HRMS *m/z* 373.1296 $[M + H]^+$, calcd for $C_{19}H_{22}N_2O_4P_1$ 373.1312.

(5-Methyl-2-oxo-1-phenyl-2,3-dihydro-1*H*-imidazol-4-yl)phosphonic Acid Diethyl Ester (4j). Reaction conditions, neat TFA, 40 °C, 3 h; purified by column chromatography (EtOAc−acetone, 11:4); yellow solid; mp 123−125 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.27 (t, J = 7.2 Hz, 6H), 2.09 (d, J = 1.9 Hz, 3H), 3.80−4.20 (m, 4H), 7.30−7.60 (m, 5H), 10.54 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 10.5, 16.1 (d, J = 6.7 Hz), 61.8 (d, J = 4.8 Hz), 103.9 (d, J = 233.7 Hz), 127.9, 128.1, 129.1, 131.9 (d, J = 23.9 Hz), 134.3, 153.0 (d, J = 12.4 Hz); HRMS *m/z* 311.1161 $[M + H]^+$, calcd for $C_{14}H_{20}N_2O_4P_1$ 311.1155.

4-Benzoyl-1,5-diphenyl-1,3-dihydroimidazol-2-one (4k). Reaction conditions, neat TFA, 70 °C, 18 h; purified by column chromatography ($CHCl_3$−CH_3CN, 9:2); white solid; mp >300 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82−6.87 (m, 2H), 6.92−7.25 (m, 13H), 8.75 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.6, 127.2, 127.6, 127.7, 128.4, 128.5, 128.8, 129.4, 129.8, 131.1, 132.2, 132.3, 136.8, 150.6, 153.1, 162.5; HRMS *m/z* 341.1277 $[M + H]^+$, calcd for $C_{22}H_{17}N_2O_2$ 341.1284.

4-Acetyl-5-methyl-1-phenyl-1,3-dihydroimidazol-2-one (4*l*). Purified by column chromatography ($CHCl_3$−CH_3CN, 2:1) and recrystallization (EtOAc−hexanes); white solid; mp 250−251 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 2.20 (s, 3H), 2.33 (s, 3H), 7.35 (d, J = 7.8 Hz, 2H), 7.46 (t, J = 7.8 Hz, 1H), 7.53 (t, J = 7.8 Hz, 2H), 10.73 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 11.5, 28.2, 119.0, 128.0, 128.4, 129.2, 130.1, 133.7, 151.6, 186.7; HRMS *m/z* 217.0970 $[M + H]^+$, calcd for $C_{12}H_{13}N_2O_2$ 217.0971.

4-Benzoyl-5-methyl-1-phenyl-1,3-dihydroimidazol-2-one (4m). Purified by column chromatography ($CHCl_3$−CH_3CN, 4:1); white solid; mp 235−237 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.94 (s, 3H), 7.30−7.35 (m, 2H), 7.42−7.60 (m, 6H), 7.65−7.75 (m, 2H), 8.09 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.6, 118.9, 127.8, 128.2, 128.6, 129.0, 129.6, 132.0, 132.1, 133.3, 138.5, 151.9, 184.7; HRMS *m/z* 279.1132 $[M + H]^+$, calcd for $C_{17}H_{15}N_2O_2$ 279.1128.

1,5-Diphenyl-1,3-dihydroimidazol-2-one (4n). Reaction conditions, 10% TFA in $ClHC_2CH_2Cl$, room temperature, 1 h; purified by recrystallization ($CHCl_3$−hexanes); white solid; mp 228−230 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.85 (d, J = 2.2 Hz, 1H), 6.96−7.07 (m, 2H), 7.08−7.25 (m, 5H), 7.29 (t, J = 7.4 Hz, 1H), 7.37 (t, J = 7.7 Hz, 2H), 10.55 (br s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 108.1, 123.5, 126.3, 126.80, 126.82, 127.3, 128.3, 128.7, 129.8, 135.8, 153.6; HRMS *m/z* 237.1018 $[M + H]^+$, calcd for $C_{15}H_{13}N_2O_1$ 237.1022.

4-(Hydroxyphenylmethyl)-5-methyl-1-phenyl-1,3-dihydroimidazol-2-one (5). To a stirred solution of imidazolone **4m** (20 mg, 0.072 mmol) in MeOH (2 mL) was added $NaBH_4$ (2.7 mg, 0.285 mmol) at room temperature, and the mixture was stirred for an additional 30 min. After removal of solvent under reduced pressure, the residue was purified by preparative TLC ($CHCl_3$−MeOH, 7:3) to afford alcohol **5** (19 mg, 0.068 mmol, 94%) as a white solid; mp 185−186 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.91 (s, 3H), 5.64 (d, J = 3.7 Hz, 1H), 5.77 (d, J = 3.7 Hz, 1H), 7.21−7.30 (m, 3H), 7.31−7.38 (m, 3H), 7.41−7.51 (m, 4H), 10.03 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 9.4, 65.8, 113.8, 120.0, 126.1, 126.9, 127.0, 127.5, 128.0, 128.9, 135.2, 143.4, 152.7; HRMS *m/z* 281.1280 $[M + H]^+$, calcd for $C_{17}H_{17}N_2O_2$ 281.1284.

General Solution-Phase Procedure for the Alkylation at the N-3 Position of 2-Imidazolones (4 → 7). To a vigorously stirred mixture of 2-imidazlone **4** (1 mmol) and K_2CO_3 (346 mg, 2.5 mmol) in DMF (5 mL) was added alkyating agent (5 mmol) at room temperature under argon, and the resulting suspension was stirred for 3 h. After removal of solvent under reduced pressure, the residue was suspended in EtOAc−$CHCl_3$ (1:1, 20 mL) and then passed through a short silica gel plug (~5 cm^3) and further eluted with EtOAc−$CHCl_3$ (1:1, 30 mL). The combined filtrate was concentrated under reduced pressure to afford analytically pure, imidazolone **7** in nearly quantitative yield.

3-Methyl-2-oxo-1,5-diphenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (7d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, J = 7.0 Hz, 3H), 3.64 (s, 3H), 4.10 (q, J = 7.0 Hz, 2H), 7.03−7.12 (m, 2H), 7.14−7.32 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 30.2, 60.4, 112.4, 127.6,

127.7, 128.5, 128.8, 130.7, 132.4, 134.2, 152.5, 160.1; HRMS *m/z* 323.1380 $[M + H]^+$, calcd for $C_{19}H_{19}N_2O_3$ 323.1390.

3,5-Dimethyl-2-oxo-1-phenyl-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (7e). Colorless needles; mp 114−115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (t, J = 7.0 Hz, 3H), 2.25 (s, 3H), 3.54 (s, 3H), 4.33 (q, J = 7.0 Hz, 2H), 7.21−7.32 (m, 2H), 7.38−7.55 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 14.4, 30.2, 60.4, 111.6, 127.9, 128.7, 129.4, 130.7, 133.9, 152.6, 160.7; HRMS *m/z* 261.1235 $[M + H]^+$, calcd for $C_{14}H_{17}N_2O_3$ 261.1234.

(3-Benzyl-2-oxo-1,5-diphenyl2,3-dihydro-1*H*-imidazol-4-yl)phosphonic Acid Diethyl Ester (7i). White solid; mp 92−93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (t, J = 7.2 Hz, 6H), 3.63−3.75 (m, 2H), 3.88−4.01 (m, 2H), 5.41 (s, 2H), 7.15−7.21 (m, 2H), 7.23−7.37 (m, 9H), 7.38−7.45 (m, 2H), 7.53−7.60 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.7 (d, J = 7.6 Hz), 46.3, 62.2 (d, J = 5.7 Hz), 108.4 (d, J = 233.7 Hz), 127.3, 127.50, 127.53, 127.7, 128.18, 128.26, 128.28, 128.7, 128.9, 130.7, 134.0 (d, J = 21.0 Hz), 134.5, 137.8, 153.4 (d, J = 12.4 Hz); HRMS *m/z* 463.1768 $[M + H]^+$, calcd for $C_{26}H_{28}N_2O_4P_1$ 463.1781.

General Solid-Phase Procedure for the Alkylation at the N-3 Position of Polymer-Bound 2-Imidazolones (8 → 9), Scheme 3. LiO^tBu (1 M in THF, 0.75 mL, 0.75 mmol) was added to a stirred suspension of polymer-bound 2-imidazolone **8** (200 mg, ∼ 0.15 mmol) and DMF−THF (2 mL:1.25 mL) in a 6-mL vial at 0 °C under argon, and then the resulting mixture was stirred for 1 h at room temperature. The alkylating agent (1.5 mmol) was added, and the mixture was stirred for 24 h at room temperature, after which time, acetic acid (1 mL) was added to quench the reaction. In the cases of using alkyl bromide as alkylating agents (entries 7 and 8), anhydrous tetrabutylammonium iodide (276 mg, 0.747 mmol) was added to the reaction mixture after the addition of alkylating agent, and the reaction was carried out at 45 °C. The resin was collected in a plastic syringe equipped with a polyethylene frit and washed several times with DMF, DMF−water (1:1), THF, methanol, ether, $CHCl_3$, and hexanes, then dried in vacuo to give N-3 alkylated 2-imidazolone resin as a brown powder.

1-Benzyl-3-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9a). Colorless oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.56 (s, 3H), 3.63 (s, 3H), 4.73 (s, 2H), 6.87−6.94 (m, 2H), 7.15−7.28 (m, 5H), 7.60 (d, J = 8.3 Hz, 2H); HRMS *m/z* 391.1267 $[M + H]^+$, calcd for $C_{20}H_{18}F_3N_2O_3$ 391.1264.

3-Benzyl-1-methyl-2-oxo-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9b). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.13 (s, 3H), 3.51 (s, 3H), 5.31 (s, 2H), 7.23−7.29 (m, 1H), 7.30−7.35 (m, 2H), 7.37−7.42 (m, 2H), 7.46 (d, J = 8.1 Hz, 2H), 7.72 (d, J = 8.1 Hz, 2H); HRMS *m/z* 391.1264 $[M + H]^+$, calcd for $C_{20}H_{18}F_3N_2O_3$ 391.1264.

3-Methyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9c). Brown solid; mp 137−139 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.66 (s, 3H), 7.01−7.08 (m, 2H), 7.20−7.33 (m, 5H), 7.50 (d, J = 8.8 Hz, 2H); HRMS *m/z* 377.1109 $[M + H]^+$, calcd for $C_{19}H_{16}F_3N_2O_3$ 377.1107.

3-Benzyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9d). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (s, 3H), 5.38 (s, 2H), 7.04−7.11 (m, 2H), 7.23−7.32 (m, 6H), 7.33−7.39 (m, 2H), 7.44−7.53 (m, 4H); HRMS *m/z* 453.1411 $[M + H]^+$, calcd for $C_{25}H_{20}F_3N_2O_3$ 453.1420.

3-Allyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9e). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.64 (s, 3H), 4.78 (dddt, J = 1.1, 1.5, 5.5 Hz, 2H), 5.23 (ddt, J = 10.3, 1.1, 1.5 Hz, 1H), 5.27 (ddt, J = 16.9, 1.1, 1.5 Hz, 1H), 6.01 (ddt, J = 16.9, 10.3, 5.5 Hz, 1H), 7.02−7.10 (m, 2H), 7.21−7.35 (m, 5H), 7.50 (d, J = 8.1 Hz, 2H); HRMS *m/z* 403.1263 $[M + H]^+$, calcd for $C_{21}H_{18}F_3N_2O_3$ 403.1264.

2-Oxo-3-(2-oxo-2-phenylethyl)-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9f). Yellow solid; mp 163−165 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.51 (s, 3H), 5.64 (s, 2H), 7.08−7.15 (m, 2H), 7.24−7.32 (m, 3H), 7.34−7.41 (m, 2H), 7.48−7.58 (m, 4H), 7.59−7.68 (m, 1H), 7.98−8.08 (m, 2H); HRMS *m/z* 481.1358 $[M + H]^+$, calcd for $C_{26}H_{20}F_3N_2O_4$ 481.1370.

2-Oxo-1-phenyl-3-(3-phenylpropyl)-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9g). White solid; mp 100−102 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15 (quint, J = 7.6 Hz, 2H), 2.77 (t, J = 7.8 Hz, 2H), 3.59 (s, 3H), 4.21 (t, J = 7.5 Hz, 2H), 7.01−7.06 (m, 2H), 7.16−7.21 (m, 1H), 7.22−7.32 (m, 9H), 7.49 (d, J = 8.0 Hz, 2H); HRMS *m/z* 481.1722 $[M + H]^+$, calcd for $C_{27}H_{24}F_3N_2O_3$ 481.1733.

3-Cyclopropylmethyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Methyl Ester (9h). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.45−0.58 (m, 4H), 1.28−1.38 (m, 1H), 3.65 (s, 3H), 4.02 (d, J = 7.0 Hz, 2H), 7.04−7.10 (m, 2H), 7.21−7.30 (m, 3H), 7.33 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H); HRMS *m/z* 417.1420 $[M + H]^+$, calcd for $C_{22}H_{20}F_3N_2O_3$ 417.1420.

1-Methyl-3-phenyl-5-(piperidine-1-carbonyl)-4-(4-(trifluoromethyl)phenyl)-1,3-dihydroimidazol-2-one (9i). Brown solid; mp 117−119 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.50−0.85 (br s, 1H), 1.12−1.34 (br s, 1H), 1.35−1.70 (m, 4H), 2.72−3.02 (br s, 1H), 3.07−3.30 (br s, 1H), 3.36 (s, 3H), 3.42−3.78 (m, 2H), 7.09−7.19 (m, 4H), 7.24−7.35 (m, 3H), 7.46 (d, J = 8.8 Hz, 2H); HRMS *m/z* 430.1739 $[M + H]^+$, calcd for $C_{23}H_{23}F_3N_3O_2$ 430.1737.

1-Methyl-5-(morpholine-4-carbonyl)-3-phenyl-4-(4-(trifluoromethyl)phenyl)-1,3-dihydroimidazol-2-one (9j). Brown solid; mp 178−180 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.60−3.90 (m, 8H), 3.39 (s, 3H), 7.07−7.12 (m, 2H), 7.16 (d, J = 8.8 Hz, 2H), 7.26−7.36 (m, 3H), 7.50 (d, J = 8.8 Hz, 2H); HRMS *m/z* 432.1532 $[M + H]^+$, calcd for $C_{22}H_{21}F_3N_3O_3$ 432.1529.

3-Benzyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazole-4-carboxylic Acid Phenylamide (9k). Brown solid; mp 151−154 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.35 (s, 2H), 6.83 (br s, 1H), 6.94−7.13 (m, 5H), 7.18−7.39 (m, 10H), 7.48−7.62 (m, 4H); HRMS *m/z* 514.1737 $[M + H]^+$, calcd for $C_{30}H_{23}F_3N_3O_2$ 514.1737.

3-Benzyl-2-oxo-1-phenyl-5-(4-(trifluoromethyl)phenyl)-2,3-dihydro-1*H*-imidazolecarboxylic Acid (3-Phenylpropyl)amide (9*l*). Yellow solid; mp 141−143 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.55 (t, J = 6.5 Hz, 2H), 3.41 (dt, J = 6.2, 6.5 Hz, 2H), 5.16 (br t, J = 5.5 Hz, 1H), 5.28 (s, 2H), 6.77−6.87 (m, 2H), 7.04 (d, J = 7.4 Hz, 2H), 7.12−7.20 (m, 5H), 7.23−7.31 (m, 4H), 7.34 (t, J = 7.5 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H), 7.48 (d, J = 7.0 Hz, 2H); HRMS *m/z* 542.2043 $[M + H]^+$, calcd for $C_{32}H_{27}F_3N_3O_2$ 542.2050.

2-Bromo-1-methyl-5-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (10p). A round-bottomed flask fitted with a reflux condenser was charged with imidazolone **4p** (R^1 = CO_2Et, R^2 = Ph, R^3 = Me; 3.20 g, 13.0 mmol) and toluene (70 mL). After complete dissolution of **4p**, phosphorus oxybromide (4.48 g, 15.6 mmol) was added, the apparatus was purged with argon, and the mixture was heated to reflux for 6 h. After cooling, the mixture was slowly added to a separating funnel that contained saturated sodium hydrogen carbonate (100 mL). The mixture was extracted three times with ethyl acetate, and the extracts were combined, dried over magnesium sulfate, and concentrated under reduced pressure to give the crude product. Column chromatography (40−60% ethyl acetate in hexanes) gave 2-bromoimidazole **10p** (3.51 g, 87%) as a white solid; mp 93−94 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.22 (t, J = 8.0 Hz, 2H), 3.44 (s, 3H), 4.23 (q, J = 7, 14 Hz, 2H), 7.35−7.36 (m, 2H), 7.48 (m, 3H); ^{13}C (125 MHz) 14.1, 33.2, 60.4, 121.6, 128.3, 128.6, 129.5, 130.2, 130.3, 140.8, 161.8; HRMS *m/z* 309.0231 $[M + H]^+$, calcd for $C_{13}H_{13}BrN_2O_2$ 309.0233.

2-Bromo-5-methyl-1-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (10e). White solid; mp 119−120 °C; ^{1}H NMR (600 MHz) δ 1.41 (t, J = 7 Hz, 3H), 2.37 (s, 3H), 4.41 (q, J = 7, 14, 2H), 7.23 (m, 2H), 7.56−7.57 (m, 3H); ^{13}C NMR (125 MHz) 11.2, 14.3, 60.4, 120.0, 127.7, 129.6, 129.9, 134.8, 139.2, 162.6; HRMS *m/z* 299.0186 [M + H]$^+$, calcd for $C_{15}H_{11}BrN_2$ 299.0178.

2-Bromo-1,5-diphenyl-1*H*-imidazole (10n). White solid; mp 121−123 °C; ^{1}H NMR (500 MHz) δ 7.05−7.07 (m, 2H), 7.19−7.22 (m, 5H), 7.25 (s, 3H), 7.42−7.44 (m, 2H); ^{13}C (125 MHz) δ 121.7, 127.7, 127.8, 128.3, 128.4, 129.1, 129.3, 129.4, 136.3, 136.6; HRMS *m/z* 309.0232 [M + H]$^+$, calcd for $C_{13}H_{13}BrN_2O_2$ 309.0233.

General Procedure for the Suzuki Coupling of 2-bromoimidazole 10 with Aryl Boronic Acids. Anhydrous toluene (0.5 mL) was added to a flask charged with 2-bromoimidazole **10** (0.1 mmol), aryl boronic acid (0.3 mmol), [Pd(dppf)Cl$_2$]·CH$_2$Cl$_2$ (2.4 mg, 3 mol %), and Cs_2CO_3 (98 mg, 0.3 mmol) and flushed with argon. The flask was immersed in a oil bath maintained at 110 °C and stirred for 2 h. After cooling to room temperature, saturated $NaHCO_3$ (1 mL) was added to the suspension and extracted with EtOAc (5 mL × 3). The combined extract was dried over $MgSO_4$, filtered, and concentrated in vacuo, and then the residue was purified by preparative TLC (EtOAc−hexanes) to give the corresponding arylimidazole **11**.

1-Methyl-2,5-diphenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11a). White solid; mp 117−118 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.22 (t, J = 7.0 Hz, 3H), 3.48 (s, 3H), 4.26 (q, J = 7.0 Hz, 2H), 7.42−7.53 (m, 8H), 7.70 (d, J = 6.5 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 14.2, 33.4, 60.3, 128.3, 128.5, 129.1, 129.29, 129.33, 129.46, 129.48, 130.0, 130.4, 140.1, 148.4, 163.1; mp 113−115 °C; HRMS *m/z* 307.1430 [M + H]$^+$, calcd for $C_{19}H_{18}N_2O_2$ 307.1441.

1-Methyl-5-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11b). White solid; mp 128−129 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.21 (t, J = 7.0 Hz, 3H), 3.51 (s, 3H), 4.26 (q, J = 7.0 Hz, 2H), 7.42−7.45 (m, 2H), 7.48−7.54 (m, 3H), 7.75 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 7.9 Hz, 2H), 7.86 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 7.9 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 14.2, 33.6, 60.4, 123.0, 124.8, 125.50, 125.53, 125.55, 125.57, 128.4, 129.1, 129.4, 129.6, 129.9, 130.4, 131.1, 131.3, 133.4, 140.6, 146.8, 162.9; mp 124−126 °C; HRMS *m/z* 375.1312 [M + H]$^+$, calcd for $C_{20}H_{17}F_3N_2O_2$ 375.1315.

2-Biphenyl-4-yl-1-methyl-5-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11c). White solid; 146−147 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.23 (t, J = 7.0 Hz, 3H), 3.52 (s, 3H), 4.27 (q, J = 7.0 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.44−7.54 (m, 7H), 7.64 (d, J = 7.4 Hz, 2H), 7.71 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 8.3 Hz, 2H), 7.79 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 14.2, 33.6, 60.3, 127.1, 127.2, 127.8, 128.3, 128.8, 128.9, 129.1, 129.5, 129.6, 129.7, 130.5, 140.2, 140.3, 142.0, 148.1, 163.1; mp 122−124 °C; HRMS *m/z* 383.1743 [M + H]$^+$, calcd for $C_{25}H_{22}N_2O_2$ 383.1754.

1-Methyl-2-naphthalen-1-yl-5-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11d). Brown oil; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.25 (t, J = 7.0 Hz, 3H), 3.23 (s, 3H), 4.29 (q, J = 7.0 Hz, 2H), 7.46−7.55 (m, 7H), 7.57 (t, J = 7.9 Hz, 1H), 7.65−7.70 (m, 2H), 7.90−7.94 (m, 1H), 7.98 (d, J = 8.3 Hz, 1H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 14.3, 32.6, 60.3, 125.1, 125.2, 126.3, 127.1, 127.6, 128.3, 128.5, 129.1, 129.2, 129.4, 129.5, 130.2, 130.5, 132.4, 133.5, 139.5, 147.2, 163.2; HRMS *m/z* 357.1589 [M + H]$^+$, calcd for $C_{23}H_{20}N_2O_2$ 357.1597.

1-Methyl-5-phenyl-2-styryl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11e). Yellow solid; mp 101−102 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.22 (t, J = 7.0 Hz, 3H), 3.51 (s, 3H), 4.26 (q, J = 7.0 Hz, 2H), 6.94 (d, J = 16.2 Hz, 1H), 7.31 (t, J = 7.4 Hz, 1H), 7.35−7.40 (m, 4H), 7.45−7.50 (m, 3H), 7.56 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 15.8 Hz, 1H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 14.2, 31.3, 60.4, 112.7, 127.0, 128.3, 128.7, 128.8, 129.1, 129.3, 129.7, 130.5, 135.2, 136.2, 139.5, 147.0, 163.1; mp 94−96 °C; HRMS *m/z* 333.1587 [M + H]$^+$, calcd for $C_{21}H_{20}N_2O_2$ 333.1597.

2-(4-Methoxyphenyl)-5-methyl-1-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11f). Brown solid; mp 127−129 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.43 (t, J = 7.0 Hz, 3H), 2.39 (s, 3H), 3.75 (s, 3H), 4.44 (q, J = 7.0 Hz, 2H), 6.71 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 8.8 Hz, 2H), 7.15−7.18 (m, 2H), 7.27−7.30 (m, 2H), 7.46−7.49 (m, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 11.1, 14.6, 55.2, 60.4, 113.4, 122.3, 128.0, 128.8, 129.2, 129.8, 130.2, 136.6, 137.9, 146.8, 159.8, 164.2; HRMS *m/z* 333.1541 [M + H]$^+$, calcd for $C_{20}H_{20}N_2O_3$ 337.1547.

2-(4-(Ethoxycarbonyl)phenyl)-5-methyl-1-phenyl-1-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11g). White solid; mp 93−94 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 1.36 (t, J = 7.0 Hz, 3H), 1.44 (t, J = 7.0 Hz, 3H), 2.42 (s, 3H), 4.33 (q, J = 7.0 Hz, 2H), 4.45 (q, J = 7.0 Hz, 2H), 7.17−7.20 (m, 2H), 7.44 (d, J = 8.3 Hz, 2H), 7.48−7.52 (m, 3H), 7.87 (d, J = 8.3 Hz, 2H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 11.1, 14.3, 14.5, 60.5, 61.1, 127.8, 128.5, 129.2, 129.5, 129.6, 130.0, 130.2, 133.7, 136.2, 138.8, 145.7, 163.8, 166.1; mp 78−81 °C; HRMS *m/z* 379.1643 [M + H]$^+$, calcd for $C_{22}H_{22}N_2O_4$ 379.1652.

2-[4-(*tert*-Butyldimethylsilanoxy)phenyl]-5-methyl-1-phenyl-1*H*-imidazole-4-carboxylic Acid Ethyl Ester (11h). Brown solid; mp 58−63 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 0.13 (s, 6H), 0.93 (s, 9H), 1.43 (t, J = 7.0 Hz, 3H), 2.40 (s, 3H), 4.43 (q, J = 7.0 Hz, 2H), 6.65 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 8.8 Hz, 2H), 7.15−7.18 (m, 2H), 7.22 (apparent d of a AA′BB system, $J_{ab} + J_{ab'}$ = 8.8 Hz, 2H), 7.44−7.47 (m, 3H); ^{13}C NMR (150 MHz, CDCl$_3$) δ −4.5, 11.1, 14.6, 18.2, 25.61, 60.4, 119.8, 123.0, 127.9, 128.8, 129.2, 129.7, 130.2, 136.5, 137.8, 146.9, 156.1, 164.2; mp 88−90 °C; HRMS *m/z* 437.2248 [M + H]$^+$, calcd for $C_{25}H_{32}N_2O_3Si_1$ 437.2255.

1,2,5-Triphenyl-1*H*-imidazole (11i). White solid; mp 247−248 °C; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.06−7.12 (m, 4H), 7.18−7.28 (m, 6H), 7.32−7.40 (m, 6H); ^{13}C NMR (150 MHz, CDCl$_3$) δ 127.4, 128.1, 128.21, 128.27, 128.29, 128.30, 128.5, 128.6, 128.8, 129.4, 129.8, 130.6, 135.1, 137.2, 148.0; mp 237−239 °C; HRMS *m/z* 297.1379 [M + H]$^+$, calcd for $C_{21}H_{16}N_2$ 297.1386.

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Supporting Information Available: ^{1}H NMR spectra for all novel compounds **3**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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