JOURNAL OF combinatorial CHEMISTRY

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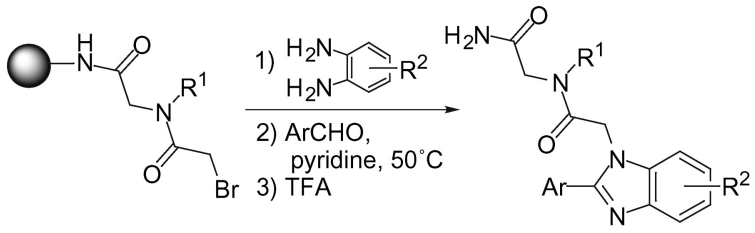
J. Comb. Chem., **2002**, 4 (5), 475-483• DOI: 10.1021/cc020006f • Publication Date (Web): 19 July 2002



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New Efficient Route for Solid-Phase Synthesis of Benzimidazole Derivatives

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Received January 31, 2002

A simple and efficient method for the solid-phase synthesis of benzimidazole libraries is described. Monoalkylation of various *o*-phenylenediamines on resin-bound bromoacetamide proceeded smoothly to give the monoalkyl resin-bound *o*-phenylenediamines in high yields. Subsequent cyclization of the diamines with various aldehydes afforded solid-supported benzimidazoles. Cleavage from the resin gave benzimidazoles in good yields. The present method enabled the introduction of the diversity on the benzene ring of imidazoles. Azabenzimidazoles, such as 4-azabenzimidazoles, 5-azabenzimidazoles, and purines, were also synthesized in good yields with high purities by the same procedure.

Solid-phase synthesis of small organic molecules has emerged as an important tool in drug discovery.[1−6] The synthetic method has helped in both expediting the preparation and increasing the diversity of the molecules.[7,8] In addition, solid-phase synthesis offers the opportunity for new synthetic routes of molecules that may be difficult to synthesize by traditional solution methods. In this paper, we report the simple and efficient solid-phase synthesis of benzimidazole library.

Benzimidazole is an important heterocyclic nucleus in medicinal chemistry.[9−16] Several solid-phase routes for the synthesis of benzimidazole libraries have therefore been reported.[17−30] In most of the cases, *o*-fluoronitrobenzene derivatives have been used as a part of the benzimidazole nucleus.[17−26,29,30] Nucleophilic addition, reduction of the nitro group, and cyclization were necessary to synthesize benzimidazoles in these routes. The yield and purity were hence moderate. Furthermore, most of the reported strategies have necessarily left the support attachment functionality (OH, $CONH_2$, or COOH) on the benzene ring of the benzimidazole nucleus and hence allowed little substituent diversity on the benzene ring.

In the present study, we investigated a new efficient route for the solid-phase synthesis of benzimidazole libraries with peptoid side chains (Scheme 1). We introduced three points of diversity in the benzimidazole library: (1) benzene ring of benzimidazole nucleus, (2) *N*-alkyl groups on the peptoid side chain, (3) 2-*C*-aryl functions on the benzimidazole.

o-Phenylenediamines were used in place of *o*-fluoronitrobenzenes in the present study. By use of this building block, a diversity can be readily introduced to the benzene ring of the benzimidazole nucleus.[31] The reaction step to reduce nitro groups can be eliminated in this route. Functional groups unstable to reductive conditions can therefore be introduced to the benzimidazole nucleus. In the present work, seven commercially available *o*-phenylenediamines were successfully used.

Selective monoalkylation of *o*-phenylenediamines with polymer-supported alkyl halides was hence the key reaction in the present route. Selective monoalkylation of diamines is generally effected by using excess diamines against alkyl halides. Removal of the excess starting diamine from the reaction mixture is tedious in traditional solution synthesis. By contrast, we expected that selective monoalkylation of diamines can be readily effected by the reaction with polymer-bound alkyl halides. After the reaction, excess diamines can be readily removed by just filtration. Site-isolation effect on solid support was also expected to prevent undesired dialkylation. In fact, monoalkylation of diamines proceeded with high selectivity.

Subsequent reaction of various aldehydes proceeded successfully with the monoalkylated *o*-phenylenediamines on polymer to afford the desired benzimidazoles in high yields (>90%) with high purities (71−100%). Furthermore, the same procedure was applicable to the synthesis of a wide range of heterocyclic nuclei, such as imidazo[4,5-*b*]pyridines (4-azabenzimidazoles), imidazo[4,5-*c*]pyridines (5-azabenzimidazoles), and purine, using the corresponding heterocyclic ortho diamines.

Benzimidazoles

Synthesis of benzimidazoles without substituents on the benzene ring was first investigated. Resin-bound monoalkylated *o*-phenylenediamines **5**, key intermediates for cyclization with aldehydes, were prepared according to Zuckermann's peptoid synthesis.[32] The reaction sequence began with deprotection of TentaGel S RAM Fmoc resin using a solution of 20% piperidine in DMF. Bromoacetic acid was then coupled onto the resin using 1,3-diisopropylcarbodiimide (DIC) in DMF to give the resin-bound bromoacetamide **2**. The bromide on resin **2** was substituted with primary amines (R^1 = propyl, isopropyl, benzyl) to give the resin-bound

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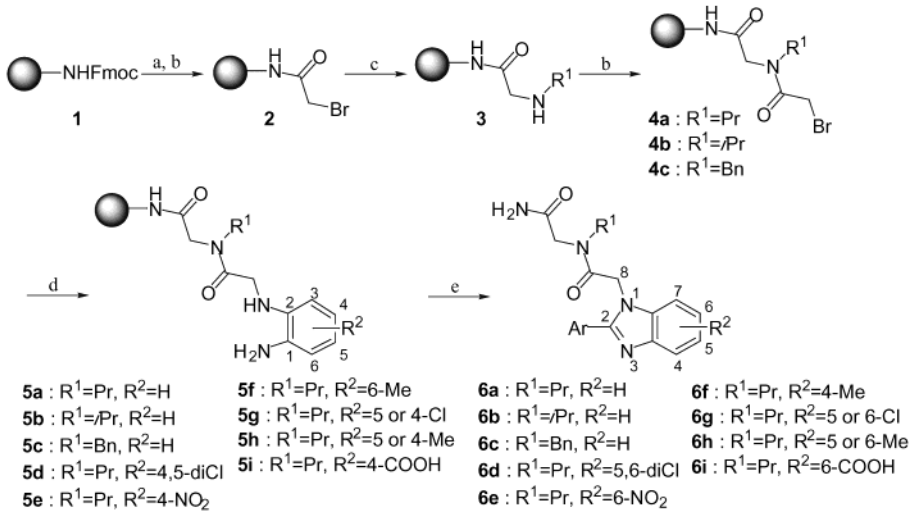
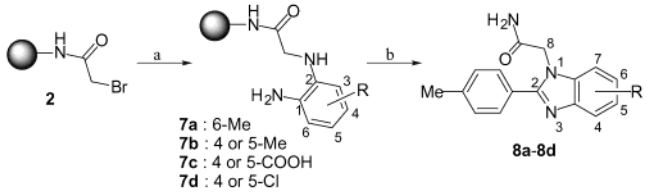
10.1021/cc020006f CCC: $22.00
Published on Web 07/19/2002

Scheme 1[a]



[a] (a) 20% piperidine/DMF; (b) bromoacetic acid, DIC, DMF; (c) R^1NH_2, DMSO; (d) *o*-phenylenediamines, DMSO; (e) ArCHO, pyridine, 50 °C, TFA.

Scheme 2[a]



[a] (a) *o*-Phenylenediamines, DMSO; (b) *o*-tolualdehyde, pyridine, 50 °C, TFA.

secondary amines **3**, which were coupled with bromoacetic acid to give **4**. The coupling reaction of **4** with *o*-phenylenediamine was carried out under the standard conditions for peptoid synthesis to give the resin-bound monoalkylated *o*-phenylenediamines **5**. Progress of the acylation and alkylation reactions was monitored by the bromophenol blue and Beilstein tests, respectively. ESI-MS spectra of synthetic intermediates cleaved from the resins by TFA showed that the reactions proceeded almost quantitatively (data not shown).

We then examined condensation of the diamines **5** with aldehydes. Several studies for the formation of benzimidazole from *o*-phenylenediamine and aldehydes on solid support have been reported.[19,21,26,28,29] Some representative procedure are shown below: (1) resin-bound *o*-phenylenediamines were treated with aldehydes and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in DMF at room temperature;[26] (2) resin-bound *o*-phenylenediamines were treated with an aldehyde in NMP at room temperature, followed by heating at 50 °C;[29] (3) resin-bound benzaldehyde was coupled to phenylenediamines in nitrobenzene at 130 °C.[28] In the present study, we found that benzimidazole formation also proceeded smoothly in pyridine. The optimized conditions were treatment of the resin-bound diamines with benzaldehydes in pyridine at 50 °C overnight.

Finally, the resin-bound benzimidazoles were cleaved with TFA to give the desired products in good yields with high purity. The results are summarized in Table 1. Most of the products were obtained with high purity (>90%) as judged from HPLC analysis. Detection by UV at 254 nm and light scattering afforded the same results. For a particular case when we used 4-(dimethylamino)benzaldehyde and 2-pyridinecarboxaldehyde, the purity of the product fell to 70−90%. ESI-MS spectra of all the products showed the expected molecular ion peaks ($[M + H]^+$). NMR spectra of some samples also confirmed the structures, which existed as a mixture of rotational isomers at the amide bond.

Substituted Benzimidazoles

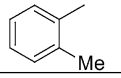
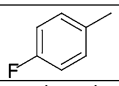
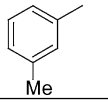
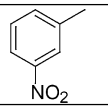
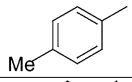
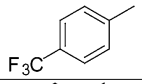
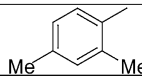
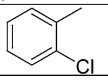
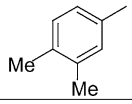
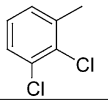
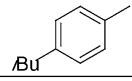
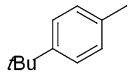
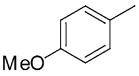
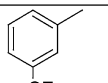
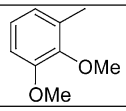
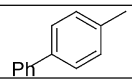
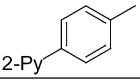
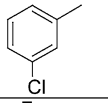
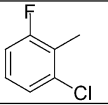
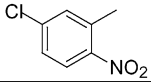
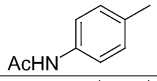
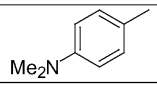
We then investigated the synthesis of substituted benzimidazoles by using substituted *o*-phenylenediamines. Since the use of unsymmetrical diamines would afford two regioisomers at the alkylation step, we estimated their ratio by using NMR after cyclization with *p*-tolualdehyde. Since *N*-substituted benzimidazoles with peptoid linker have two rotational isomers at the peptoid amide bond as described above, benzimidazoles without peptoid linker were prepared in order to simplify the NMR spectra of the products (Scheme 2), and the results are summarized in Table 2. Two regioisomers were readily distinguished by the cross signal of H-7 and H-8 in NOESY spectra. Whereas the sole product with less steric hindrance was obtained by using 2,3-diaminotoluene, mixtures of regioisomers were obtained when the other three diamines were used. The alkylation reaction did not proceed when 4-nitro-1,2-diaminobenzene was used.

We then applied this method to the preparation of a substituted benzimidazole library possessing a peptoid side chain (R^1 = Pr) (Scheme 1). As shown in Table 3, most of the products were obtained with high purity (>90%). In the present case, 6-nitrobenzimidazoles were obtained by using 4-nitro-1,2-diaminobenzene in high yields. The 4-methylbenzimidazoles, 6-nitrobenzimidazoles, and 6-carboxybenzimidazoles were obtained with high regioselectivity, whereas the selectivities were low for 5-methylbenzimidazoles and 5-chlorobenzimidazoles [(substitution at 6-position):(substitution at 5-position) = 1:2].

Imidazo[4,5-*b*]pyridines (4-Azabenzimidazoles) and Imidazo[4,5-*c*]pyridines (5-Azabenzimidazoles)

For the preparation of imidazopyridine libraries, we used 2,3-diaminopyridine or 3,4-diaminopyridine in place of

Table 1. Solid-Phase Synthesis of Benzimidazoles

Entry	Ar	Product	R_1	HPLC[a] Purity (%)	Entry	Ar	Product	R_1	HPLC[a] Purity (%)
1		**6a**{*1*}	Pr	98	16		**6a**{*16*}	Pr	90
		6b{*1*}	*i*Pr	92			**6b**{*16*}	*i*Pr	96
		6c{*1*}	Bn	93			**6c**{*16*}	Bn	99
2		**6a**{*2*}	Pr	92	17		**6b**{*17*}	*i*Pr	96
		6b{*2*}	*i*Pr	92			**6c**{*17*}	Bn	98
		6c{*2*}	Bn	92					
3		**6a**{*3*}	Pr	98	18		**6a**{*18*}	Pr	95
		6b{*3*}	*i*Pr	98			**6b**{*18*}	*i*Pr	94
		6c{*3*}	Bn	95			**6c**{*18*}	Bn	97
4		**6a**{*4*}	Pr	91	19		**6b**{*19*}	*i*Pr	95
		6b{*4*}	*i*Pr	95			**6c**{*19*}	Bn	97
		6c{*4*}	Bn	95					
5		**6a**{*5*}	Pr	96	20		**6a**{*20*}	Pr	91
		6b{*5*}	*i*Pr	97			**6b**{*20*}	*i*Pr	94
		6c{*5*}	Bn	97			**6c**{*20*}	Bn	96
6		**6a**{*6*}	Pr	91	21		**6b**{*21*}	*i*Pr	99
		6b{*6*}	*i*Pr	93			**6c**{*21*}	Bn	95
		6c{*6*}	Bn	95					
7		**6b**{*7*}	*i*Pr	93	22		**6b**{*22*}	*i*Pr	97
		6c{*7*}	Bn	94			**6c**{*22*}	Bn	96
8		**6a**{*8*}	Pr	92	23		**6b**{*23*}	*i*Pr	97
		6b{*8*}	*i*Pr	95					
9		**6a**{*9*}	Pr	94	24		**6a**{*24*}	Pr	75
		6b{*9*}	*i*Pr	94			**6b**{*24*}	*i*Pr	86
		6c{*9*}	Bn	94			**6c**{*24*}	Bn	66
10		**6a**{*10*}	Pr	92	25		**6b**{*25*}	*i*Pr	97
		6b{*10*}	*i*Pr	94			**6c**{*25*}	Bn	95
		6c{*10*}	Bn	92					
11		**6a**{*11*}	Pr	91	26		**6a**{*26*}	Pr	96
		6b{*11*}	*i*Pr	94			**6b**{*26*}	*i*Pr	96
							6c{*26*}	Bn	99
12		**6a**{*12*}	Pr	91	27		**6a**{*27*}	Pr	90
		6b{*12*}	*i*Pr	93			**6b**{*27*}	*i*Pr	90
							6c{*27*}	Bn	95
13		**6a**{*13*}	Pr	85	28		**6a**{*28*}	Pr	90
		6b{*13*}	*i*Pr	91			**6b**{*28*}	*i*Pr	94
							6c{*28*}	Bn	93
14		**6a**{*14*}	Pr	99	29		**6a**{*29*}	Pr	95
		6b{*14*}	*i*Pr	99			**6b**{*29*}	*i*Pr	97
		6c{*14*}	Bn	100			**6c**{*29*}	Bn	95
15		**6a**{*15*}	Pr	80	30		**6a**{*30*}	Pr	92
		6b{*15*}	*i*Pr	91			**6b**{*30*}	*i*Pr	96
		6c{*15*}	Bn	78			**6c**{*30*}	Bn	93

[a] Purity was based on the peak area of HPLC spectra of crude products as detected at 254 nm.

o-phenylenediamine. In these cases, the nitrogen atom on the pyridine nucleus was selectively alkylated. The 4*H*-imidazo[4,5-*b*]pyridines were hence obtained by using 2,3-diaminopyridine (Scheme 3; Table 4, entry 1). The structures of 4*H*-imidazo[4,5-*b*]pyridines were confirmed by ESI-MS spectra and by the cross signal of H-5 and H-8 in NOESY spectra.

The 5*H*-imidazo[4,5-*c*]pyridines were obtained by using 3,4-diaminopyridine. The cyclization reaction of diamines with aldehydes did not occur at 50 °C but proceeded smoothly at 100 °C (Scheme 4). The structures of the products were confirmed by the cross signal of H-4 and H-8 and of H-6 and H-8 in NOESY spectra and by ESI-MS spectra (Table 4, entry 2).

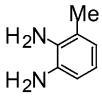
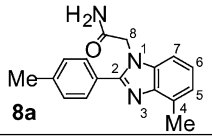
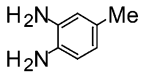
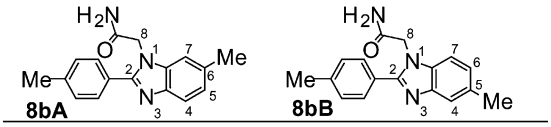
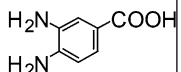
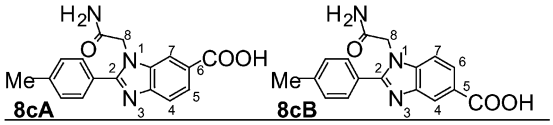
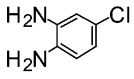
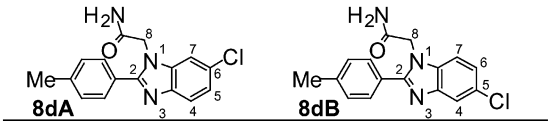
Purines

Purines were also obtained by using 4,5-diaminopyrimidine. The 1-position of pyrimidine nucleus was selectively alkylated (Scheme 5; Table 4, entry 3). The cyclization reaction of resin-bound 4,5-diaminopyrimidine with aldehydes proceeded at 100 °C. The cyclization reaction did not proceed when the resin-bound 4,5-diaminopyrimidine without peptoid linker was used.

Conclusion

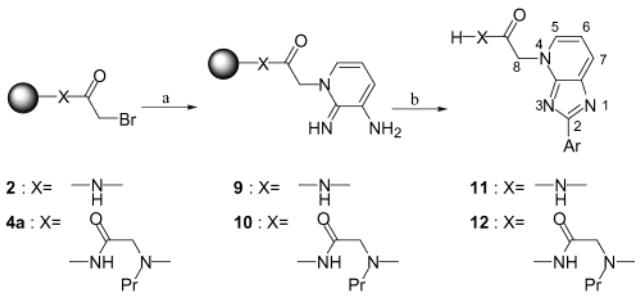
In summary, we have developed a new solid-phase method for the synthesis of benzimidazoles, 4*H*-imidazo[4,5-*b*]-pyridines, 5*H*-imidazo[4,5-*c*]pyridines, and purines. Our

Table 2. Ratio of Substituted Benzimidazoles without Peptoid Linker

diamines	Products Products ratio	HPLC purity[a] (%)
	 **8a**	85[b]
	 **8bA** 3 **8bB** 7	93[c]
	 **8cA** 9 **8cB** 1	99[c]
	 **8dA** 1 **8dB** 2	90[c]

[a] Purity was based on the peak area of HPLC spectra of crude products as detected at 254 nm. [b] Sole product was obtained. [c] Purity was determined for a mixture on the basis of the sum of the peak areas of the regioisomers.

Scheme 3[a]



[a] (a) 2,3-Diaminopyridine, DMSO; (b) ArCHO, pyridine, 50 °C, TFA.

method allows facile introduction of diversity on the benzene ring of the benzimidazole nucleus by the use of commercially available aromatic diamines.

Experimental Section

NMR spectra were measured on a Varian-Unity 600 NMR (600 MHz) spectrometer with CD_3OD as a solvent. The chemical shifts of the protons are given in δ values relative to residual CH_3OH (δ 3.5 ppm). Mass spectra were obtained on a PerSeptive Biosystem Mariner biospectrometry workstation. All reagents and solvents were obtained from commercial suppliers and used without further purification. The resin was purchased from Rapp Polymere (poly(ethylene glycol) spacer on a polystyrene bead (130 μm, 0.25 mmol/g), TentaGel S RAM Fmoc, catalog no. S30023). Agitation of all the reaction mixtures was carried out with a BURREL Wrist Action shaker.

Reverse-phase high-performance liquid chromatography (HPLC) analysis was carried out on Shiseido C-18 columns (4.6 mm × 150 mm) using a SPD-10A UV detector (SHIMAZU CORPORATION, Japan) or a PL-EMD960 evaporative light-scattering detector (Polymer Laboratories Ltd., U.K.) and a linear gradient of (A) water and (B) acetonitrile, 30−100% B in 15 min at 1.0 mL/min flow rate, a linear gradient of (A) 0.1% TFA in water and (B) acetonitrile, 10−100% B in 20 min at 1.0 mL/min flow rate, or a linear gradient of (A) 0.1% TFA in water and (B) acetonitrile, 20−100% B in 15 min at 1.0 mL/min flow rate.

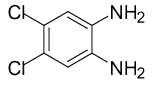
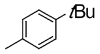
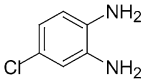
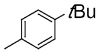
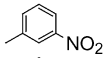
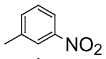
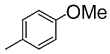
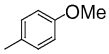
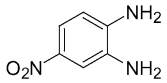
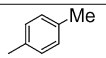
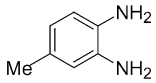
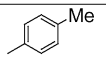
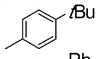
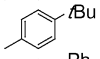
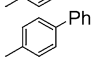
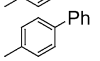
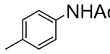
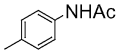
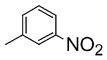
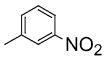
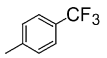
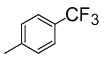
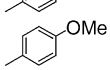
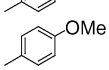
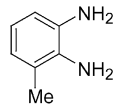
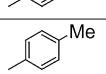
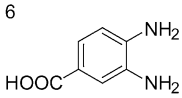
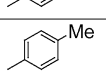
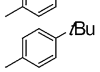
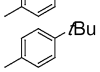
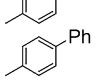
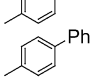
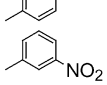
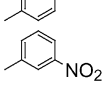
The following abbreviations were used: Fmoc = 9-fluorenylmethoxycarbonyl, DMF = *N*,*N*-dimethylformamide, THF = tetrahydrofuran, DMSO = dimethyl sulfoxide, DMA = *N*,*N*-dimethylacetamide, DIC = 1,3-diisopropylcarbodiimide, TFA = trifluoroacetic acid.

Deprotection of Fmoc Group. To TentaGel S RAM Fmoc resin **1** (1.8 g, 0.45 mmol, 0.26 mmol/g) was added a solution of 20% piperidine in DMF (10 mL). The mixture was agitated for 1 h at room temperature. The mixture was filtered, and the resin was washed with DMF (3 × 10 mL), THF/CH_2Cl_2 = 1:1 (3 × 10 mL), and CH_2Cl_2 (3 × 10 mL). The resin was dried in vacuo and then used in the following reaction.

General Amide Coupling Procedure for the Preparation of Resin-Bound Bromoacetamide (2). To the deprotected resin **1** (0.45 mmol) were added a solution of bromoacetic acid (0.63 g, 4.5 mmol) in DMF (6 mL) and a solution of DIC (0.78 mL, 5.0 mmol) in DMF (1 mL), and the mixture was agitated for 1.5 h at room temperature. The mixture was filtered, and the resin was washed with DMF (3 × 10 mL), THF/CH_2Cl_2 = 1:1 (3 × 10 mL), and CH_2Cl_2 (3 × 10 mL). The resin was dried in vacuo and then used in the following reaction.

General Alkylation Procedure for the Preparation of Resin-Bound Secondary Amines (3). To the resin-bound bromoacetamide **2** (0.45 mmol) was added a solution of primary amine (7.0 mmol) in DMSO (6.5 mL), and the mixture was agitated for 3 h at room temperature. The

Table 3. Solid-Phase Synthesis of Substituted Benzimidazoles

Entry	Diamine	Product	Ar	HPLC[a] Purity (%)	Entry	Diamine	Product	Ar	HPLC[a] Purity (%)
1		**6d**{*7*}		87	4		**6g**{*7*}		80[b]
		6d{*17*}		71			**6g**{*17*}		83[b]
		6d{*21*}		84			**6g**{*21*}		78[b]
		6d{*22*}		93			**6g**{*22*}		87[b]
2		**6e**{*3*}		93	5		**6h**{*3*}		95[b]
		6e{*7*}		95			**6h**{*7*}		91[b]
		6e{*9*}		93			**6h**{*9*}		97[b]
		6e{*14*}		83			**6h**{*14*}		98[b]
		6e{*17*}		92			**6h**{*17*}		94[b]
		6e{*18*}		89			**6h**{*18*}		97[b]
		6e{*21*}		91			**6h**{*21*}		94[b]
		6e{*22*}		91			**6h**{*22*}		96[b]
		6e{*26*}		95			**6h**{*26*}		95[b]
3		**6f**{*3*}		96	6		**6i**{*3*}		99
		6f{*7*}		77			**6i**{*7*}		99
		6f{*9*}		82			**6i**{*9*}		99
		6f{*17*}		72			**6i**{*17*}		100
		6f{*18*}		93			**6i**{*18*}		95
		6f{*21*}		96			**6i**{*21*}		100
		6f{*22*}		94			**6i**{*22*}		100
		6f{*26*}		94			**6i**{*26*}		99

[a] Purity was based on the peak area of HPLC spectra of crude products as detected at 254 nm. [b] Purity was determined for a mixture on the basis of the sum of the peak areas of the regioisomers.

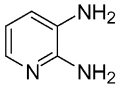
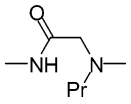
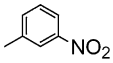
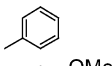
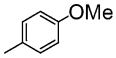
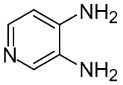
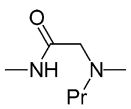
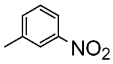
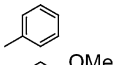
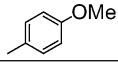
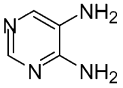
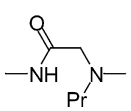
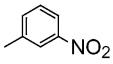
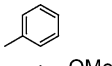
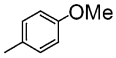
Scheme 4[a]

[a] (a) 3,4-Diaminopyridine, DMSO; (b) *p*-tolualdehyde, pyridine, 100 °C, TFA.

mixture was filtered, and the resin was washed with DMSO (3 × 10 mL), THF/CH_2Cl_2 = 1:1 (3 × 10 mL), and CH_2Cl_2 (3 × 10 mL). The resin was dried in vacuo and then used in the following reaction.

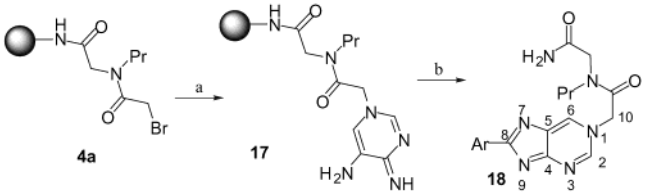
General Monoalkylation Procedure for the Preparation of Resin-Bound *o*-Phenylenediamines (5). To the resins **4a**−**c** (0.11 mmol) was added a solution of *o*-phenylenediamines (2.0 mmol) in DMSO (2 mL), and the mixture was agitated for 4 h at room temperature. The mixture was filtered, and the resin was washed with DMSO (3 × 3 mL), THF/CH_2Cl_2 = 1:1 (3 × 3 mL), and CH_2Cl_2 (3 × 3 mL) and was then dried in vacuo to give resins **5a**−**i**.

Table 4. Solid-Phase Synthesis of 4*H*-Imidazo[4,5-*b*]pyridines, 5*H*-Imidazo[4,5-*c*]pyridines, and Purines

Entry	Diamine	Product	X	Ar	HPLC[a] Purity (%)
1		**11**{*3*}			83
		12{*17*}			80
		12{*21*}			78
		12{*22*}			89
		15{*3*}			92
2		**16**{*17*}			86
		16{*21*}			91
		16{*22*}			86
		—			NR[b]
3		**18**{*17*}			87
		18{*21*}			88
		18{*22*}			82

[a] Purity was based on the peak area of HPLC spectra of crude products as detected at 254 nm. [b] The reaction did not proceed.

Scheme 5[a]



[a] (a) 4,5-Diaminopyrimidine, DMSO; (b) ArCHO, pyridine, 100 °C, TFA.

General Cyclization Procedure for the Preparation of Resin-Bound Benzimidazoles. To resins **5a**−**i** (0.031 mmol) was added a solution of benzaldehydes (1.0 mmol) in pyridine (1 mL). After the mixture was stirred at 50 °C overnight, the reaction mixture was cooled to room temperature. The mixture was filtered, and the resin was washed with pyridine (4 × 1 mL), DMA (4 × 1 mL), THF/CH_2Cl_2 = 1:1 (4 × 1 mL), CH_2Cl_2 (4 × 1 mL), and acetic acid (4 × 1 mL).

General Cleavage Procedure for the Generation of Benzimidazoles (6). The resin-bound benzimidazoles were treated with TFA (1 mL), and the mixture was agitated for 30 min at room temperature. The mixture was filtered, and the filtrate was concentrated in vacuo to give compound **6**. Imidazo[4,5-*b*]pyridines **11** and **12**, imidazo[4,5-*c*]pyridines **15** and **16**, and purines **18** were synthesized with the same procedure.

***N*²-Isopropyl-*N*²-[[2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetyl]glycinamide (6b{*3*}).** ^{1}H NMR (600 MHz, CD_3-OD mixture of rotamers, major/minor = 8:5) (major): δ 8.21−8.23 (m, 1H), 8.02−8.05 (m, 1H), 7.91−7.95 (m, 2H), 7.85−7.89 (m, 2H), 7.74−7.76 (m, 2H), 5.68 (s, 2H), 4.91−4.95 (m, 1H), 4.37 (s, 2H), 2.70 (s, 3H), 1.35 (d, 6H, *J* = 6.9 Hz). ^{1}H NMR (minor): δ 8.08−8.10 (m, 1H), 8.02−8.05 (m, 1H), 7.91−7.95 (m, 2H), 7.85−7.89 (m, 2H), 7.77−7.79 (m, 2H), 5.78 (s, 2H), 4.40−4.44 (m, 1H), 4.23 (s, 2H), 2.71 (s, 3H), 1.48 (d, 6H, *J* = 6.6 Hz). MS (ESI) *m*/*z*: 365 ([M + H]$^+$).

***N*²-Benzyl-*N*²-[[2-(2,4-dimethylphenyl)-1*H*-benzimidazol-1-yl]acetyl]glycinamide (6c{*4*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 11:10) (major): δ 8.04−8.23 (m, 2H), 7.86−7.92 (m, 2H), 7.53−7.67 (m, 2H), 7.45−7.52 (m, 4H), 7.34−7.36 (m, 1H), 7.18−7.20 (m, 1H), 5.62 (s, 2H), 4.88 (s, 2H), 4.27 (s, 2H), 2.66 (s, 3H), 2.52 (s, 3H). ^{1}H NMR (minor): δ 8.04−8.23 (m, 2H), 7.86−7.92 (m, 2H), 7.53−7.67 (m, 2H), 7.45−7.52 (m, 4H), 7.34−7.36 (m, 1H), 7.18−7.20 (m, 1H), 5.60 (s, 2H), 4.72 (s, 2H), 4.23 (s, 2H), 2.69 (s, 3H), 2.41 (s, 3H). MS (ESI) *m*/*z*: 427 ([M + H]$^+$).

***N*²-[[2-(3,4-Dimethylphenyl)-1*H*-benzimidazol-1-yl]-acetyl]-*N*²-isopropylglycinamide (6b{*5*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 3:2) (major): δ 8.20−8.22 (m, 1H), 8.01−8.05 (m, 1H), 7.85−7.89 (m, 2H), 7.79 (m, 1H), 7.68−7.78 (m, 2H), 5.68 (s, 2H), 4.92−4.96 (m, 1H), 4.38 (s, 2H), 2.62 (s, 3H), 2.61 (s, 3H), 1.35 (d, 6H, *J* = 6.9 Hz). ^{1}H NMR (minor): δ 8.08−8.10 (m, 1H), 8.01−8.05 (m, 1H), 7.85−7.89 (m, 2H), 7.79 (m, 1H), 7.68−7.78 (m, 2H), 5.79 (s, 2H), 4.40−4.44 (m, 1H), 4.22 (s, 2H), 2.63 (s, 3H), 2.62 (s, 3H), 1.48 (d, 6H, *J* = 6.6 Hz). MS (ESI) *m*/*z*: 379 ([M + H]$^+$).

***N*²-[[2-(4-*tert*-Butylphenyl)-1*H*-benzimidazol-1-yl]acetyl]-*N*²-isopropylglycinamide (6b{*7*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 8:5) (major): δ 7.85−8.25 (m, 8H), 5.70 (s, 2H), 4.91−4.95 (m, 1H), 4.38 (s, 2H), 1.60 (s, 9H), 1.35 (d, 6H, *J* = 6.6 Hz). ^{1}H NMR (minor): δ 7.85−8.25 (m, 8H), 5.78 (s, 2H), 4.40−4.44 (m, 1H), 4.23 (s, 2H), 1.60 (s, 9H), 1.48 (d, 6H, *J* = 6.6 Hz). MS (ESI) *m*/*z*: 407 ([M + H]$^+$).

***N*²-Benzyl-*N*²-[[2-(4-*tert*-butylphenyl)-1*H*-benzimidazol-1-yl]acetyl]glycinamide (6c{*7*}).** ^{1}H NMR (600 MHz, CD_3-OD mixture of rotamers, major/minor = 6:5) (major): δ 7.95−8.21 (m, 5H), 7.85−7.91 (m, 3H), 7.47−7.61 (m, 5H), 5.79 (s, 2H), 4.82 (s, 2H), 4.38 (s, 2H), 1.61 (s, 9H). ^{1}H NMR (minor): δ 7.95−8.21 (m, 5H), 7.85−7.91 (m, 3H), 7.47−7.61 (m, 5H), 5.76 (s, 2H), 4.99 (s, 2H), 4.38 (s, 2H), 1.62 (s, 9H). MS (ESI) *m*/*z*: 455 ([M + H]$^+$).

***N*²-[[2-(4-Biphenylyl)-1*H*-benzimidazol-1-yl]acetyl]-*N*²-isopropylglycinamide (6b{*9*}).** ^{1}H NMR (600 MHz, CD_3-OD mixture of rotamers, major/minor = 8:5) (major): δ 8.10−8.26 (m, 5H), 8.06−8.09 (m, 1H), 7.91−7.97 (m, 2H), 7.87−7.90 (m, 2H), 7.70−7.73 (m, 2H), 7.63−7.66 (m, 1H), 5.75 (s, 2H), 4.93−4.97 (m, 1H), 4.40 (s, 2H), 1.36 (d, 6H, *J* = 6.9 Hz). ^{1}H NMR (minor): δ 8.10−8.26 (m, 5H), 8.06−8.09 (m, 1H), 7.91−7.97 (m, 2H), 7.87−7.90 (m, 2H), 7.70−7.73 (m, 2H), 7.63−7.66 (m, 1H), 5.85 (s, 2H), 4.43−4.47 (m, 1H), 4.25 (s, 2H), 1.50 (d, 6H, *J* = 6.6 Hz). MS (ESI) *m*/*z*: 427 ([M + H]$^+$).

***N*²-Isopropyl-*N*²-[[2-[4-(2-pyridyl)phenyl]-1*H*-benzimidazol-1-yl]acetyl]glycinamide (6b{*10*}).** ^{1}H NMR (600

MHz, CD_3OD mixture of rotamers, major/minor = 9:5) (major): δ 8.97−9.00 (m, 1H), 8.52−8.57 (m, 2H), 8.34−8.42 (m, 2H), 8.07−8.27 (m, 4H), 7.82−7.92 (m, 3H), 5.76 (s, 2H), 4.92−4.97 (m, 1H), 4.40 (s, 2H), 1.36 (d, 6H, J = 6.6 Hz). ^{1}H NMR (minor): δ 8.97−9.00 (m, 1H), 8.52−8.57 (m, 2H), 8.34−8.42 (m, 2H), 8.07−8.27 (m, 4H), 7.82−7.92 (m, 3H), 5.87 (s, 2H), 4.43−4.47 (m, 1H), 4.25 (s, 2H), 1.50 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 428 ([M + H]$^+$).

***N*^{2}-[[2-(4-Acetylaminophenyl)-1*H*-benzimidazol-1-yl]-acetyl]-*N*^{2}-isopropylglycinamide (6b{*14*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 8:5) (major): δ 8.21−8.23 (m, 1H), 8.12−8.14 (m, 1H), 7.97−8.04 (m, 3H), 7.84−7.88 (m, 2H), 5.69 (s, 2H), 4.92−4.96 (m, 1H), 4.38 (s, 2H), 2.38 (s, 3H), 1.35 (d, 6H, J = 6.9 Hz). ^{1}H NMR (minor): δ 8.15−8.17 (m, 1H), 8.07−8.09 (m, 1H), 7.97−8.04 (m, 3H), 7.84−7.88 (m, 2H), 5.80 (s, 2H), 4.41−4.46 (m, 1H), 4.23 (s, 2H), 2.38 (s, 3H), 1.49 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 408 ([M + H]$^+$).

***N*^{2}-[[2-(2,3-Dimethoxyphenyl)-1*H*-benzimidazol-1-yl]-acetyl]-*N*^{2}-isopropylglycinamide (6b{*23*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 7:5) (major): δ 8.20−8.23 (m, 1H), 8.03−8.06 (m, 1H), 7.85−7.90 (m, 2H), 7.65 (dd, 1H, J = 8.5, 1.4 Hz), 7.55 (t, 1H, J = 8.0 Hz), 7.39 (dd, 1H, J = 8.0, 1.4 Hz), 5.57 (s, 2H), 4.83−4.87 (m, 1H), 4.30 (s, 2H), 4.17 (s, 3H), 3.99 (s, 3H), 1.29 (d, 6H, J = 6.9 Hz). ^{1}H NMR (minor): δ 8.12−8.14 (m, 1H), 8.03−8.06 (m, 1H), 7.85−7.90 (m, 2H), 7.67 (dd, 1H, J = 8.2, 1.4 Hz), 7.59 (t, 1H, J = 8.0 Hz), 7.41 (dd, 1H, J = 8.0, 1.4 Hz), 5.66 (s, 2H), 4.33−4.37 (m, 1H), 4.17 (s, 3H), 4.14 (s, 2H), 3.95 (s, 3H), 1.43 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 411 ([M + H]$^+$).

***N*^{2}-Isopropyl-*N*^{2}-[[2-(3-pyridyl)-1*H*-benzimidazol-1-yl]-acetyl]glycinamide (6b{*25*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 2:1) (major): δ 9.22 (m, 1H), 9.13−9.15 (m, 1H), 8.54−8.56 (m, 1H), 8.22−8.24 (m, 1H), 8.07−8.10 (m, 1H), 8.00−8.05 (m, 1H), 7.84−7.89 (m, 2H), 5.70 (s, 2H), 4.89−4.92 (m, 1H), 4.37 (s, 2H), 1.33 (d, 6H, J = 6.6 Hz). ^{1}H NMR (minor): δ 9.22 (m, 1H), 9.13−9.15 (m, 1H), 8.57−8.59 (m, 1H), 8.07−8.10 (m, 2H), 8.00−8.05 (m, 1H), 7.84−7.89 (m, 2H), 5.82 (s, 2H), 4.41−4.45 (m, 1H), 4.20 (s, 2H), 1.47 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 352 ([M + H]$^+$).

***N*^{2}-Isopropyl-*N*^{2}-[[2-(4-pyridyl)-1*H*-benzimidazol-1-yl]-acetyl]glycinamide (6b{*26*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 9:5) (major): δ 9.13−9.16 (m, 2H), 8.28−8.30 (m, 2H), 8.03−8.10 (m, 2H), 7.73−7.80 (m, 2H), 5.70 (s, 2H), 4.87−4.92 (m, 1H), 4.39 (s, 2H), 1.33 (d, 6H, J = 6.9 Hz). ^{1}H NMR (minor): δ 9.13−9.16 (m, 2H), 8.28−8.30 (m, 2H), 8.03−8.10 (m, 1H), 7.96 (d, 1H, J = 7.7 Hz), 7.73−7.80 (m, 2H), 5.79 (s, 2H), 4.44−4.48 (m, 1H), 4.21 (s, 2H), 1.50 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 352 ([M + H]$^+$).

***N*^{2}-[[2-(2-Furyl)-1*H*-benzimidazol-1-yl]acetyl]-*N*^{2}-propylglycinamide (6a{*27*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 3:2) (major): δ 8.28 (d, 1H, J = 1.7 Hz), 8.06−8.11 (m, 1H), 7.80−8.02 (m, 4H), 7.08−7.10 (m, 1H), 5.94 (s, 2H), 4.55 (s, 2H), 3.57 (t, 3H, J = 7.4 Hz), 1.79−1.80 (m, 2H), 1.08 (t, 3H, J = 7.4 Hz). ^{1}H NMR (minor): δ 8.26 (d, 1H, J = 1.7 Hz), 8.06−8.11 (m, 1H), 7.80−8.02 (m, 4H), 7.08−7.10 (m, 1H), 6.00 (s, 2H), 4.31 (s, 2H), 3.77 (t, 3H, J = 7.7 Hz), 2.03−2.07 (m, 2H), 1.29 (t, 3H, J = 7.4 Hz). MS (ESI) *m*/*z*: 341 ([M + H]$^+$).

***N*^{2}-[[2-(2-Furyl)-1*H*-benzimidazol-1-yl]acetyl]-*N*^{2}-isopropylglycinamide (6b{*27*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 11:5) (major): δ 8.29 (m, 1H), 8.10−8.14 (m, 1H), 8.06 (d, 1H, J = 3.6 Hz), 7.98−8.01 (m, 1H), 7.81−7.86 (m, 2H), 7.09−7.11 (m, 1H), 5.92 (s, 2H), 4.87−4.91 (m, 1H), 4.50 (s, 2H), 1.36 (d, 6H, J = 6.9 Hz). ^{1}H NMR (minor): δ 8.27−8.28 (m, 1H), 8.10−8.14 (m, 1H), 7.98−8.01 (m, 1H), 7.81−7.86 (m, 3H), 7.09−7.11 (m, 1H), 6.03 (s, 2H), 4.57−4.61 (m, 1H), 4.21 (s, 2H), 1.60 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 341 ([M + H]$^+$).

***N*^{2}-Benzyl-*N*^{2}-[[2-(2-furyl)-1*H*-benzimidazol-1-yl]acetyl]-glycinamide (6c{*27*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 9:5) (major): δ 8.25 (dd, 1H, J = 1.7, 0.55 Hz), 7.46−8.10 (m, 10H), 7.09 (dd, 1H, J = 3.7, 1.8), 5.99 (s, 2H), 4.80 (s, 2H), 4.48 (s, 2H). ^{1}H NMR (minor): δ 8.12 (dd, 1H, J = 1.9, 0.55 Hz), 7.46−8.10 (m, 10H), 7.03 (dd, 1H, J = 3.7, 1.8), 5.97 (s, 2H), 5.10 (s, 2H), 4.36 (s, 2H). MS (ESI) *m*/*z*: 389 ([M + H]$^+$).

***N*^{2}-Isopropyl-*N*^{2}-[[2-(2-pyrrolyl)-1*H*-benzimidazol-1-yl]-acetyl]glycinamide (6b{*28*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 9:5) (major): δ 8.06−8.08 (m, 1H), 7.93−7.96 (m, 1H), 7.75−7.81 (m, 2H), 7.57 (dd, 1H, J = 2.7, 1.4 Hz), 7.41 (dd, 1H, J = 4.1, 1.4 Hz), 6.71−6.73 (m, 1H), 5.80 (s, 2H), 4.90−4.94 (m, 1H), 4.48 (s, 2H), 1.37 (d, 6H, J = 6.6 Hz). ^{1}H NMR (minor): δ 8.02−8.03 (m, 1H), 7.93−7.96 (m, 1H), 7.75−7.81 (m, 2H), 7.58 (dd, 1H, J = 2.5, 1.4 Hz), 7.32 (dd, 1H, J = 3.8, 1.4 Hz), 6.71−6.73 (m, 1H), 5.85 (s, 2H), 4.52−4.56 (m, 1H), 4.27 (s, 2H), 1.56 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 340 ([M + H]$^+$).

***N*^{2}-Isopropyl-*N*^{2}-[[2-(2-thienyl)-1*H*-benzimidazol-1-yl]-acetyl]glycinamide (6b{*29*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 2:1) (major): δ 8.31−8.32 (m, 1H), 8.15−8.19 (m, 2H), 7.99−8.03 (m, 1H), 7.82−7.87 (m, 2H), 7.63−7.66 (m, 1H), 5.80 (s, 2H), 4.91−4.95 (m, 1H), 4.45 (s, 2H), 1.37 (d, 6H, J = 6.9 Hz). ^{1}H NMR (minor): δ 8.31−8.32 (m, 1H), 8.15−8.19 (m, 1H), 8.08−8.11 (m, 1H), 7.99−8.03 (m, 1H), 7.82−7.87 (m, 2H), 7.63−7.66 (m, 1H), 5.91 (s, 2H), 4.49−4.53 (m, 1H), 4.24 (s, 2H), 1.54 (d, 6H, J = 6.6 Hz). MS (ESI) *m*/*z*: 357 ([M + H]$^+$).

***N*^{2}-[[6-Nitro-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]-acetyl]-*N*^{2}-propylglycinamide (6e{*3*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 11:10) (major): δ 8.86 (d, 1H, J = 2.2 Hz), 8.52 (dd, 1H, J = 8.8, 2.2 Hz), 8.09 (d, 1H, J = 8.8 Hz), 7.83−7.88 (m, 2H), 7.66−7.68 (m, 2H), 5.67 (s, 2H), 4.29 (s, 2H), 3.59 (t, 2H, J = 7.6 Hz), 2.67 (s, 3H), 1.75−1.86 (m, 2H), 1.10 (t, 3H, J = 7.4 Hz). ^{1}H NMR (minor): δ 8.94 (d, 1H, J = 2.2 Hz), 8.55 (dd, 1H, J = 9.1, 2.2 Hz), 8.07 (d, 1H, J = 9.1 Hz), 7.83−7.88 (m, 2H), 7.66−7.68 (m, 2H), 5.64 (s, 2H), 4.42 (s, 2H), 3.62 (t, 2H, J = 7.8 Hz), 2.67 (s, 3H), 1.75−1.86 (m, 2H), 1.12 (t, 3H, J = 7.4 Hz). MS (ESI) *m*/*z*: 410 ([M + H]$^+$).

***N*^{2}-[[4-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetyl]-*N*^{2}-propylglycinamide (6f{*3*}).** ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 6:5)

(major): δ 7.84−7.98 (m, 2H), 7.84−7.88 (m, 1H), 7.72−7.78 (m, 3H), 7.66−7.67 (m, 1H), 5.65 (s, 2H), 4.42 (s, 2H), 3.56−3.59 (m, 2H), 2.89 (s, 3H), 2.71 (s, 3H), 1.74−1.87 (m, 2H), 1.09 (t, 3H, $J = 7.4$ Hz). ^{1}H NMR (minor): δ 7.84−7.98 (m, 2H), 7.84−7.88 (m, 1H), 7.72−7.78 (m, 3H), 7.66−7.67 (m, 1H), 5.70 (s, 2H), 4.29 (s, 2H), 3.61−3.63 (m, 2H), 2.89 (s, 3H), 2.71 (s, 3H), 1.74−1.87 (m, 2H), 1.12 (t, 3H, $J = 7.4$ Hz). MS (ESI) *m*/*z*: 379 ([M + H]$^+$).

N^2-[[2-(4-*tert*-Butylphenyl)-4-methyl-1*H*-benzimidazol-1-yl]acetyl]-N^2-propylglycinamide (6f{*7*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 11:10) (major): δ 7.84−8.02 (m, 5H), 7.73−7.77 (m, 1H), 7.66−7.67 (m, 1H), 5.67 (s, 2H), 4.30 (s, 2H), 3.57−3.63 (m, 2H), 2.89 (s, 3H), 1.75−1.86 (m, 2H), 1.60 (s, 9H), 1.07−1.13 (m, 3H). ^{1}H NMR (minor): δ 7.84−8.02 (m, 5H), 7.73−7.77 (m, 1H), 7.66−7.67 (m, 1H), 5.70 (s, 2H), 4.42 (s, 2H), 3.57−3.63 (m, 2H), 2.89 (s, 3H), 1.75−1.86 (m, 2H), 1.60 (s, 9H), 1.07−1.13 (m, 3H). MS (ESI) *m*/*z*: 421 ([M + H]$^+$).

N^2-[[5-Chloro-2-(4-methoxyphenyl)-1*H*-benzimidazol-1-yl]acetyl]-N^2-propylglycinamide and N^2-[[6-Chloro-2-(4-methoxyphenyl)-1*H*-benzimidazol-1-yl]acetyl]-N^2-propylglycinamide (6g{*22*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers and isomers): δ 7.78−8.25 (m, 5H), 7.43−7.48 (m, 2H), 5.65−5.70 (m, 2H), 4.32−4.43 (m, 2H), 4.13 (s, 3H), 3.58−3.65 (m, 2H), 1.75−1.90 (m, 2H), 1.07−1.17 (m, 3H). MS (ESI) *m*/*z*: 415 ([M + H]$^+$).

N^2-[[5-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetyl]-N^2-propylglycinamide and N^2-[[6-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetyl]-N^2-propylglycinamide (6h{*3*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers and isomers): δ 7.69−8.04 (m, 7H), 5.65−5.71 (m, 2H), 4.30−4.43 (m, 2H), 3.57−3.65 (m, 2H), 2.69−2.80 (m, 6H), 1.74−1.90 (m, 2H), 1.08−1.15 (m, 3H). MS (ESI) *m*/*z*: 379 ([M + H]$^+$).

1-[2-[*N*-(2-Amino-2-oxoethyl)]propylamino-2-oxoethyl]-2-(4-methylphenyl)-1*H*-benzimidazole-6-carboxylic Acid (6i{*3*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers, major/minor = 27:25) (major): δ 8.66 (m, 1H), 8.43−8.47 (m, 1H), 8.06−8.08 (m, 1H), 7.89−7.92 (m, 2H), 7.72−7.75 (m, 2H), 5.76 (s, 2H), 4.30 (s, 2H), 3.60 (t, 2H, $J =$ 7.4 Hz), 2.69 (s, 3H), 1.77−1.80 (m, 2H), 1.10 (t, 3H, $J =$ 7.4 Hz). ^{1}H NMR (minor): δ 8.72 (m, 1H), 8.43−8.47 (m, 1H), 8.06−8.08 (m, 1H), 7.89−7.92 (m, 2H), 7.72−7.75 (m, 2H), 5.73 (s, 2H), 4.44 (s, 2H), 3.63 (t, 2H, $J = 7.7$ Hz), 2.69 (s, 3H), 1.85−1.88 (m, 2H), 1.14 (t, 3H, $J = 7.4$ Hz). MS (ESI) *m*/*z*: 409 ([M + H]$^+$).

2-[4-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]-acetamide (8a). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers): δ 7.94−7.96 (m, 2H), 7.81−7.83 (m, 1H), 7.75−7.77 (m, 3H), 7.66−7.68 (m, 1H), 5.37 (s, 2H), 2.89 (s, 3H), 2.71 (s, 3H). MS (ESI) *m*/*z*: 280 ([M + H]$^+$).

2-[6-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]-acetamide (8bA) and 2-[5-Methyl-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetamide (8bB) (3:7). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers) (**8bA**): δ 7.92−7.94 (m, 2H), 7.88−7.91 (m, 1H), 7.82−7.83 (m, 1H), 7.75−7.76 (m, 2H), 7.70−7.72 (m, 1H), 5.37 (s, 2H), 2.77 (s, 3H), 2.71 (s, 3H). ^{1}H NMR (**8bB**): δ 7.92−7.94 (m, 2H), 7.88−7.91 (m, 1H), 7.82−7.83 (m, 1H), 7.75−7.76 (m, 2H), 7.70−7.72 (m, 1H), 5.37 (s, 2H), 2.78 (s, 3H), 2.71 (s, 3H). MS (ESI) *m*/*z*: 280 ([M + H]$^+$).

1-(2-Amino-2-oxoethyl)-2-(4-methylphenyl)-1*H*-benzimidazole-6-carboxylic Acid (8cA) and 1-(2-Amino-2-oxoethyl)-2-(4-methylphenyl)-1*H*-benzimidazole-5-carboxylic Acid (8cB) (9:1). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers): δ 8.61 (d, 1H, $J = 1.4$ Hz), 8.46 (dd, 1H, $J = 8.8$, 1.4 Hz), 8.08 (d, 1H, $J = 8.8$ Hz), 7.94−7.95 (m, 2H), 7.73−7.75 (m, 2H), 5.42 (s, 2H), 2.70 (s, 3H). MS (ESI) *m*/*z*: 310 ([M + H]$^+$).

2-[6-Chloro-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]-acetamide (8dA) and 2-[5-Chloro-2-(4-methylphenyl)-1*H*-benzimidazol-1-yl]acetamide (8dB) (1:2). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers) (**8dA**): δ 8.03 (d, 1H, $J = 1.6$ Hz), 7.93 (d, 1H, $J = 8.2$ Hz), 7.90−7.91 (m, 2H), 7.77−7.80 (m, 1H), 7.72−7.73 (m, 2H), 5.33 (s, 2H), 2.69 (s, 3H). ^{1}H NMR (**8dB**): δ 8.06 (d, 1H, $J = 1.9$ Hz), 7.99 (d, 1H, $J = 8.8$ Hz), 7.90−7.91 (d, 2H), 7.77−7.80 (m, 1H), 7. 72−7.73 (m, 2H), 5.33 (s, 2H), 2.69 (s, 3H). MS (ESI) *m*/*z*: 300 ([M + H]$^+$).

2-[2-(4-Methylphenyl)-4*H*-imidazo[4,5-*b*]pyridin-4-yl]-acetamide (11{*3*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers): δ 8.77−8.80 (m, 2H), 8.38−8.39 (m, 2H), 7.94 (dd, 1H, $J = 8.0$, 6.3 Hz), 7.66−7.67 (m, 2H), 5.89 (s, 2H), 2.67 (s, 3H). MS (ESI) *m*/*z*: 267 ([M + H]$^+$).

2-[2-(4-Methylphenyl)-5*H*-imidazo[4,5-*c*]pyridin-5-yl]-acetamide (15{*3*}). ^{1}H NMR (600 MHz, CD_3OD mixture of rotamers): δ 9.44 (d, 1H, $J = 0.5$ Hz), 8.71 (dd, 1H, $J =$ 6.6, 1.4 Hz), 8.34−8.35 (m, 2H), 8.26 (d, 1H, $J = 6.6$ Hz), 7.66 (d, 2H, $J = 8.5$ Hz), 5.68 (s, 2H), 2.67 (s, 3H). MS (ESI) *m*/*z*: 267 ([M + H]$^+$).

Acknowledgment. The authors thank Dr. Keonil Lee for NMR measurements. The present study was financially supported in part by Special Coordination Funds of the Ministry of Education, Culture, Sports, Science and Technology and Grant-in-Aid for Creative Scientific Research of Japan Society for the Promotion of Science "In vivo Molecular Science for Discovery of New Biofunctions and Pharmaceutical Drugs" Grant No. 13NP0401.

Supporting Information Available. Spectra and listing of additional data for the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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CC020006F