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Synthesis of structurally diverse benzimidazolyl benzimidazolones by application of soluble polymer support

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ABSTRACT

Chemical stability and reactivity of a bifunctional polymer conjugate containing an *ortho*-amino arylamide linkage have been successfully exploited to achieve a parallel synthesis of methoxycarbonylated head–tail bis-benzimidazoles. Regioselective alkylation of the two nitrogens in the benzimidazolone moiety has been carried out by *ipso*-fluoro displacement, and N-alkylation to generate two diversities. Cleavage of the polymer support has resulted in two libraries of di- and tri-substituted benzimidazolyl benzimidazolones in high purity and high yield. All reaction steps have been monitored by ^{1}H NMR on the support directly.

1. Introduction

The main purpose of combinatorial chemistry is to create wider structural diversity in small molecules, which has been realized in practice by the application of both solid[1,2] and liquid phase[3,4] synthetic strategies. Molecular libraries of biologically active nitrogen heterocycles like quinoxalines,[5] piperazinones,[6] fused imidazoles,[7] hydantoins,[8] benzimidazoles,[9] and pyrimidinones[10] have been successfully generated by our group applying the increasingly useful soluble polymer supports under microwave conditions.

Benzimidazolin-2-ones have been found to exhibit a wide range of biological activities.[11–18] Interestingly, benzimidazolin-2-one skeleton has been a subject of crystal engineering,[19] based on which several benzimidazolin-2-ones with improved binding affinity have been designed for p-38 MAP kinase inhibiting activity.[20]

In view of their multi-dimensional activities (Fig. 1), these molecular motifs have been the targets for both solid[21,22] and liquid phase[23] synthetic methods. A survey of literature indicates that the benzimidazolyl benzimidazolone skeleton has received little attention. The 6–2′ and the 1–2′ isomers have been obtained as the photolysis products of benzimidazoles.[24,25] The recently reported bromo ter-benzimidazole possessing this skeleton was found to be an effective topoisomerase-I inhibitor.[26] A series of 6-anilino-*N*-heterocyclic benzimidazolones have been patented for their pronounced cytokinase inhibiting activity related to the inflammation process.[27] One of the reasons for the paucity of literatures also lies in the formation of mixture of regioisomers during the N,N-alkylation of benzimidazolin-2-ones, which was circumvented by protection–deprotection strategy via N-carboxyalkoxylation, under harsh reaction conditions.[28,29] Construction of bis-benzimidazole skeleton without the use of support requires use of dinitro aldehydes and 5-formyl benzimidazole,[26] and involves the use of a number of *ortho*-phenylene diamines, which again are required to be synthesized by at least a three-step sequence. Hence it is quite apparent that a systematic synthetic strategy without the need of all the above cited starting materials is required for the construction of functionalized benzimidazolyl benzimidazolones and an unambiguous method for introducing alkyl groups on the two nitrogens of the cyclic ureide moiety.

2. Results and discussion

In the present paper we have demonstrated the application of soluble polymer supports to generate a wide range of bis-benzimidazolin-2-ones and successfully addressed the issue of N-alkylation, which is in agreement with our earlier work.[9d] It can be seen that the present methodology does not make use of dinitro aldehydes and *ortho*-phenylene diamines, which are usually employed in conventional methods. Our strategy has resulted in the title compounds with two and three points of structural diversity, without any ambiguity. Various steps involved in the synthesis of benzimidazolyl benzimidazolones are shown in Scheme 1.

The starting polymer organic conjugate **1** required for the present synthetic sequence was obtained by our own established four-step procedures.[6] Initial ring closure was brought about by an acid catalyzed (5% TFA) room temperature reaction in 1,2-dichloroethane. It was found that use of anhydrous $MgSO_4$ can reduce the reaction time to 12 h from 24 h and can enhance the yields of

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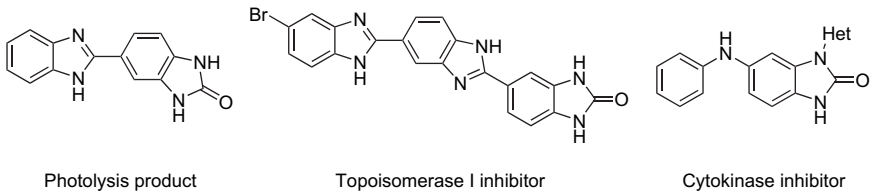
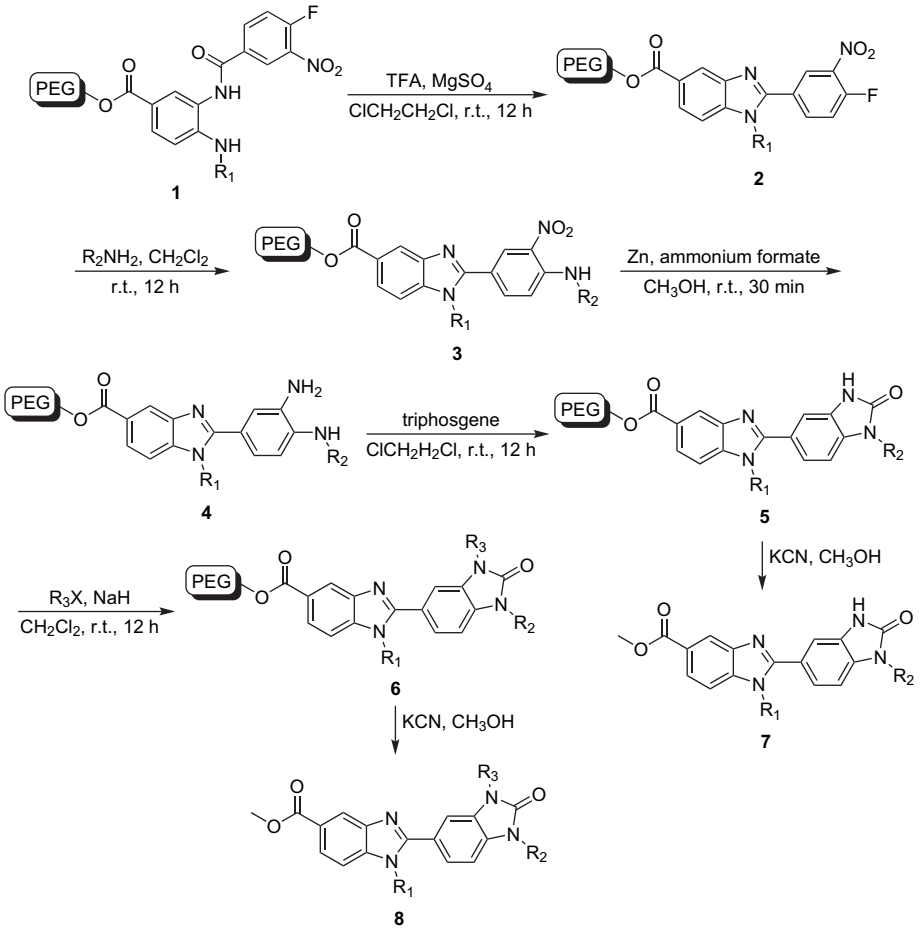


Figure 1. Structurally related benzimidazolinones.



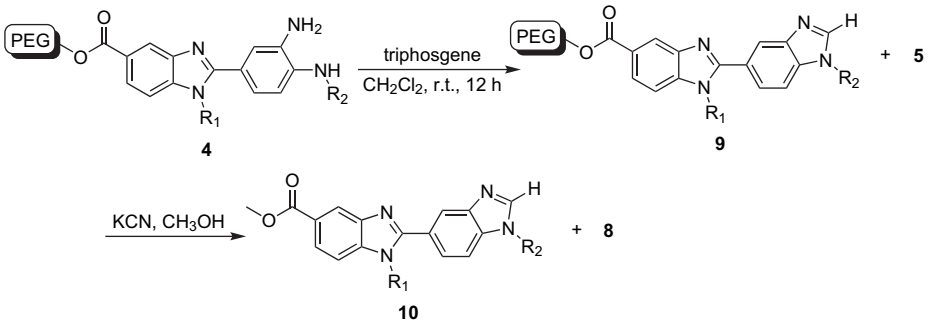
Scheme 1. Synthetic route toward the benzimidazolyl benzimidazolones **7** and **8**.

the cyclized, polymer-supported product **2**, probably by removing the eliminated water in the reaction. $MgSO_4$ was removed by passing through a thin layer of Celite before precipitation. After the reactions were completed, the reaction mixtures were subsequently purified by simple precipitation, filtration, and ether washing to remove unreacted reagents and byproducts.

The second point of structural diversity was introduced by an *ipso*-fluoro displacement, by an S_NAr reaction using various primary amines leading to the *ortho*-nitro anilines **3**. Reduction of the nitro group was achieved in half an hour under neutral conditions using zinc dust and ammonium formate in methanol at room temperature. This led to the diamine **4** leaving the polymer unaffected. The one carbon homologation to construct the benzimidazolone moiety was completed by N,N-carbonylation using triphosgene in 1,2-dichloroethane at room temperature. The time required of the cyclization was 12 h and the yields were in the range of 72–85% with excellent crude purities (80–96%). When dichloromethane was used as a reaction medium in this step, compound **10** was obtained in 40–50% after cleavage along with expected product **7**. It is clear that solvent was involved during the cyclization. However, this side reaction can be avoided by switching the solvent from dichloromethane to dichloroethane and maintained the good solubility of polymer immobilized intermediates (Scheme 2).

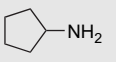
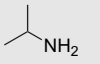
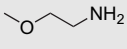
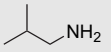
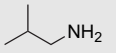
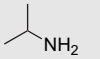
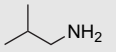
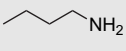
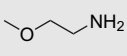
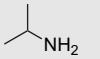
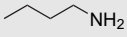
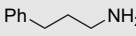
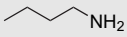
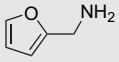
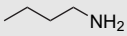
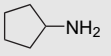
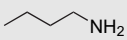
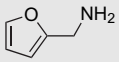
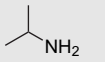
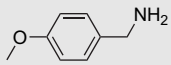
This key intermediate **5** has given rise to benzimidazolones **7** with two points of molecular diversity, after the cleavage of the polymer support by treatment with methanolic KCN at room temperature in 72 h. This led to the mono-alkylation in one of the nitrogens in the benzimidazolone part, which is the second diversity introduced after *ipso*-fluoro displacement by various amines. The HPLC purities of the crude products were analyzed by normal phase silica column with 5% methanol in dichloroethane as the eluent. For all the crude products, more than 80% purity was observed (Table 1).

Structural ambiguity and formation of mixtures of isomers have been avoided by introduction of the *N*-alkyl group by *ipso*-fluoro displacement. Furthermore, N-alkylation of **5** was affected by deprotonation of the cyclic ureide using sodium hydride in methylene chloride at room temperature. An interesting feature of this



Scheme 2. Formation of side product **9** during the cyclization in CH_2Cl_2.

Table 1
Bis-benzimidazolones with two points of structural diversity

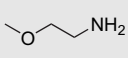
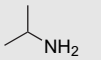
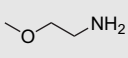
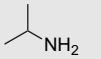
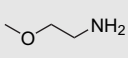
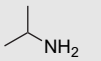
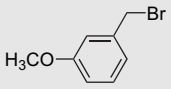
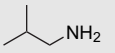
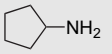
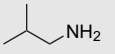
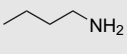
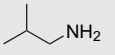
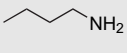
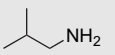
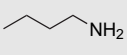
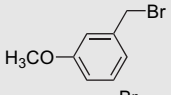
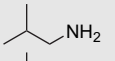
Entry	R_1NH_2	R_2NH_2	Isolated yield[a] (%)	LRMS[b]	HPLC[c]
7a			72	418	83
7b			74	422	86
7c			84	406	84
7d			80	420	92
7e			83	408	95
7f			80	482	80
7g			79	444	96
7h			83	432	78
7i			78	430	82
7j			72	484	96

[a] Yields were based on loading of soluble support.
[b] LRMS were detected with EI ionization source.
[c] Crude products were analyzed by normal phase HPLC (column: silica, 250×4.6 mm, 5 mm; eluent: 5% MeOH in CH_2Cl_2).

selective deprotonation was that the hydride ion did not attack the ester carbonyl to induce the cleavage of the polymer. Secondly, the ambident nucleophilicity of the cyclic ureide moiety was also controlled as no *O*-alkylated product was obtained. The reaction of this sodium salt with various alkyl halides lead exclusively to N-alkylation and cleavage of the polymer support using KCN in methanol led to the final bis-benzimidazolones **8** with three points of structural diversity (Table 2). The final compounds **7** and **8** were clearly distinguishable by TLC (CH_2Cl_2/CH_3OH=50:1). For bis-alkylated compounds, for example, **8a** (R_f=0.3) had higher R_f values than mono-alkylated compounds **7a** (R_f=0.2).

Conventional proton NMR (Fig. 2) was effectively used to monitor the sequence of steps in this synthetic route. The initial polymer conjugate **1h** (**8a**, Table 2) exhibited a slightly broad low field NH singlet around 9.2 (Spectrum A) and the aromatic protons H_a and H_c also displayed characteristic variations. The first ring closure leading to the benzimidazole polymer conjugate **2h** was characterized by the absence of the NH proton with the simultaneous deshielding of H_a, which has now appeared at 8.7 ppm due to the anisotropic effects of the ring nitrogen and the ester carbonyl group (Spectrum B).

Table 2
Bis-benzimidazolones with three points of structural diversity

Entry	R_1NH_2	R_2NH_2	R_3–X	Isolated yield[a] (%)	LRMS[b]
8a			CH_3I	70	422
8b				66	448
8c				68	528
8d			CH_3I	65	446
8e			CH_3I	71	434
8f				73	460
8g				68	540
8h				78	488
8i				70	536
8j			CH_3I	72	420
8k				64	446
8l				73	526
8m				70	474
8n			CH_3I	70	436
8o				70	462
8p				70	542
8q				68	554

[a] Yields were based on loading of soluble support.
[b] LRMS were detected with EI ionization source.

The *ipso*-fluoro displacement resulted in **3h** with the appearance of a D_2O exchangeable NH proton at 8.3 ppm (Spectrum C). H_e is moving to the upfield from 7.47 to 7.0 ppm because the weak electron withdrawing fluoride was replaced by electron donating amine. Reduction of the nitro group led to the diamine **4h** in which

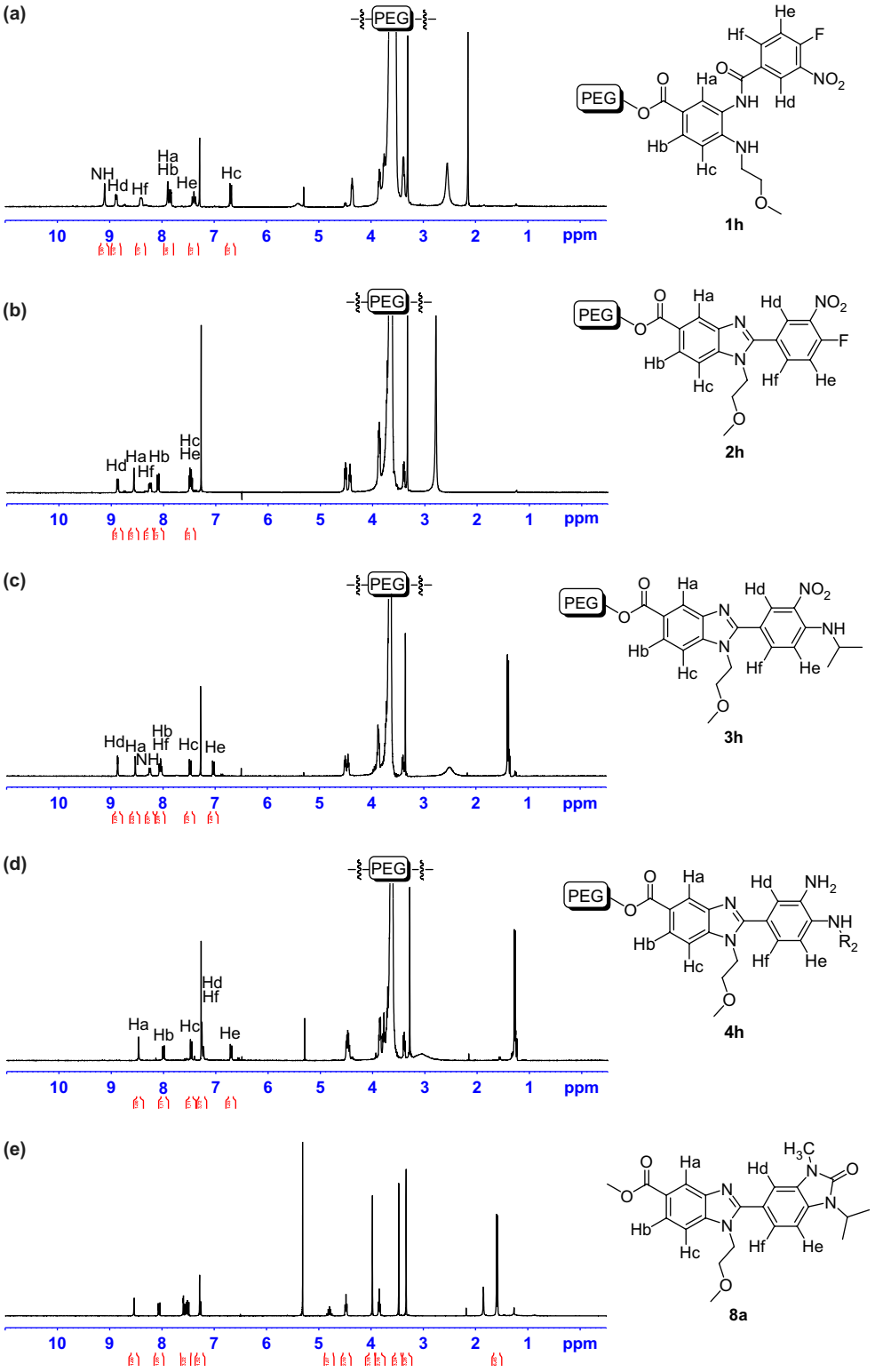


Figure 2. Formation of compound **8a** monitored by ^{1}H NMR.

the H_d observed earlier as a low field singlet around 8.9 ppm exhibited an upfield shift and was observed at 7.3 ppm (Spectrum D). H_f is also moving to upfield from 8.04 to 7.25 ppm because the nitro group was reduced to amine functionality. Formation of the benzimidazolone conjugate **5** was indicated by the low field NH proton around 10.2 ppm (not shown in Fig. 2).

Cleavage of the polymer at this stage led to benzimidazoles **7**. This was indicated by an upfield singlet at 3.9–4.00 ppm due to OCH_3 protons of the methyl ester (not shown in Fig. 2). The signal at 10.2 ppm disappeared upon alkylation and removal of the polymer resulted in bis-alkylated benzimidazoles **8** (Spectrum F).

3. Conclusion

This paper shows the first systematic approach for the benzimidazolyl benzimidazolones with a methoxycarbonyl function in

the aromatic ring. The selective N,N-bisalkylation of benzimidazolinone has been achieved by employing various substituted amines in an *ipso*-fluoro displacement and the second alkylation has been brought about using sodium hydride with different alkyl halides. All the transformations on the PEG–organic conjugates have been carried out at ambient temperature. With two stages being available for the cleavage of the polymer, the present synthetic route has facilitated the generation of two libraries of benzimidazolones with two or three points of structural diversity.

4. Experimental section

4.1. General procedures for the synthesis of benzimidazolyl benzimidazolones (7 and 8)

To a solution of **1** (0.33 mmol, 1.0 equiv) in dichloroethane, 0.5 mL trifluoroacetic acid and 0.5 g $MgSO_4$ were added. The reaction mixture was refluxed for 12 h and after completion, the reaction mixture was passed through a thin layer of Celite to remove $MgSO_4$. The solution was concentrated by rotary evaporation and diluted with slow addition of excess of cold ether. The precipitated benzoimidazole conjugate was filtered through a fritted funnel and washed with ether to obtain polymer immobilized **2**. Compound **2** was further reacted with different amines (2.31 mmol, 7.0 equiv) in dichloroethane at ambient temperature for 12 h. After completion, the reaction mixture was washed with ether and dried to obtain compound **3**. To a solution of **3** in methanol, zinc (3.3 mmol, 30.0 equiv) and ammonium formate (3.75 mmol, 15.0 equiv) were added. The reaction mixture was allowed to stir for 30 min at room temperature. The mixture was centrifuged to remove zinc and concentrated by rotary evaporation to remove methanol. Then dichloromethane was added to salt out ammonium formate. The mixture was passed through a thin layer of Celite to remove ammonium formate and amine **4** was obtained. The polymer conjugate **4** (0.33 mmol, 1.0 equiv) and triphosgene (0.73 mmol, 2.2 equiv) were dissolved in 1,2-dichloroethane (dichloromethane for **9**) and the reaction mixtures were stirred for 12 h at room temperature. The cyclized product **5** was isolated by similar precipitation and washed with excess of ether. Compound **5** (0.33 mmol, 1.0 equiv) and sodium hydride (0.72 mmol, 2.2 equiv) were put in a 100 mL flask under nitrogen at room temperature and dry dichloromethane was added. After the reaction mixtures stirred for 10 min, appropriate halides (1.0 mmol, 3 equiv) were added and continuously stirred for 12 h. After completion, wet acetone was added to quench the excess sodium hydride. The reaction mixture was precipitated and washed several times with ether. To a solution of compound **7** in methanol, KCN (0.1 g) was added and stirred for 3 days. After the quenching procedure, the crude products **8** and **10** were obtained. The crude product was purified by column chromatography (CH_2Cl_2/MeOH=30:1) and final products were obtained in high total yields.

*4.1.1. 1-Cyclopentyl-1′-isopropyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzimidazolyl-5-carboxylic acid methyl ester (**7a**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.68 (s, 1H), 8.53 (s, 1H), 7.99 (d, J=8.5 Hz, 1H), 7.53 (d, J=8.4 Hz, 1H), 7.53 (s, 1H), 7.32 (d, J=8.2 Hz, 1H), 7.28–7.25 (m, 1H), 5.02 (quint, J=8.7 Hz, 1H), 4.78 (septet, J=6.9 Hz, 1H), 3.95 (s, 3H), 2.35–2.28 (m, 2H), 2.13–2.05 (m, 4H), 1.79–1.67 (m, 2H), 1.59 (d, J=6.9 Hz, 6H), 0.78 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.6, 155.5, 143.3, 136.7, 131.1, 129.3, 124.7, 124.0, 122.7, 122.5, 111.9, 111.3, 109.3, 58.1, 52.5, 45.3, 30.8, 25.6, 20.7; IR (KBr) 2951, 1714, 1482, 1302 cm^{-1}; EIMS m/z 418 (M^+); HRMS m/z calcd for $C_{23}H_{26}N_4O_4$ 418.2005, found 418.2007.

*4.1.2. 1′-Isobutyl-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7b**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.57 (s, 1H), 8.52 (s, 1H), 8.04 (d, J=8.5 Hz, 1H), 7.65 (s, 1H), 7.53 (d, J=8.1 Hz, 1H), 7.49 (d, J=8.5 Hz, 1H), 7.09 (d, J=8.1 Hz, 1H), 4.46 (t, J=5.4 Hz, 2H), 3.96 (s, 3H), 3.78 (t, J=5.3 Hz, 2H), 3.72 (d, J=7.4 Hz, 2H), 3.27 (s, 3H), 2.30–2.18 (m, 1H), 1.00 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.5, 156.3, 142.6, 139.4, 132.7, 128.8, 125.1, 124.7, 123.3, 122.8, 122.1, 111.5, 110.5, 108.3, 71.0, 59.5, 52.5, 48.8, 45.5, 28.4, 20.5; IR (KBr) 2925, 1708, 1486, 1302 cm^{-1}; EIMS m/z 422 (M^+); HRMS m/z calcd for $C_{24}H_{26}N_4O_3$ 422.1954, found 422.1940.

*4.1.3. 1-Isobutyl-1′-isopropyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7c**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.84 (s, 1H), 8.51 (s, 1H), 8.01 (d, J=8.4 Hz, 1H), 7.51 (s, 1H), 7.40 (d, J=8.4 Hz, 1H), 7.35 (d, J=8.4 Hz, 1H), 7.26–7.21 (m, 1H), 4.75 (septet, J=6.9 Hz, 1H), 4.13 (d, J=7.5 Hz, 2H), 3.93 (s, 3H), 2.15–2.06 (m, 1H), 1.57 (d, J=6.9 Hz, 6H), 0.73 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.4, 155.7, 142.7, 139.4, 130.9, 129.2, 124.8, 124.5, 123.3, 122.5, 122.3, 111.2, 110.6, 109.3, 52.5, 52.4, 45.3, 29.1, 20.7, 20.3; IR (KBr) 2925, 1712, 1481, 1286 cm^{-1}; EIMS m/z 406 (M^+); HRMS m/z calcd for $C_{23}H_{26}N_4O_3$ 406.2005, found 406.2023.

*4.1.4. 1′-Butyl-1-isobutyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7d**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.58 (s, 1H), 8.53 (s, 1H), 8.03 (d, J=8.5 Hz, 1H), 7.51 (s, 1H), 7.44–7.38 (m, 2H), 7.11 (d, J=8.1 Hz, 1H), 4.15 (d, J=7.5 Hz, 2H), 3.96–3.90 (m, 5H), 2.14–2.10 (m, 1H), 1.80 (quint, J=7.4 Hz, 2H), 1.45 (sextet, J=7.7 Hz, 2H), 0.99 (t, J=7.2 Hz, 3H), 0.75 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.4, 156.1, 142.6, 139.3, 132.2, 128.9, 124.9, 124.5, 123.5, 122.9, 122.3, 111.2, 110.6, 108.1, 52.6, 52.5, 41.2, 30.8, 29.2, 20.5, 20.3, 14.1; IR (KBr) 2959, 1714, 1487, 1301 cm^{-1}; EIMS m/z 420 (M^+); HRMS m/z calcd for $C_{24}H_{28}N_4O_3$ 420.2161, found 420.2163.

*4.1.5. 1′-Isopropyl-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7e**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.45 (s, 1H), 8.53 (s, 1H), 8.04 (d, J=8.5 Hz, 1H), 7.67 (s, 1H), 7.54–7.48 (m, 2H), 7.25 (d, J=8.3 Hz, 1H), 4.77 (septet, J=7.0 Hz, 1H), 4.47 (t, J=5.3 Hz, 2H), 3.96 (s, 3H), 3.79 (t, J=5.3 Hz, 2H), 3.28 (s, 3H), 1.59 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.5, 155.5, 142.4, 139.4, 131.2, 129.1, 125.1, 124.7, 123.0, 122.4, 122.1, 111.6, 110.5, 109.3, 71.0, 59.5, 52.5, 45.5, 45.3, 20.7; IR (KBr) 2935, 1711, 1482, 1301 cm^{-1}; EIMS m/z 408 (M^+); HRMS m/z calcd for $C_{22}H_{24}N_4O_4$ 408.1798, found 408.1796.

*4.1.6. 1-Butyl-2′-oxo-1′-(3-phenyl-propyl)-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7f**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 11.28 (s, 1H), 8.54 (s, 1H), 8.02 (d, J=8.4 Hz, 1H), 7.52 (s, 1H), 7.39 (d, J=8.5 Hz, 1H), 7.35 (d, J=8.2 Hz, 1H), 7.29–7.18 (m, 5H), 6.97 (d, J=8.1 Hz, 1H), 4.24 (t, J=7.2 Hz, 2H), 3.93–3.90 (m, 5H), 2.72 (t, J=7.4 Hz, 2H), 2.12 (quint, J=7.1 Hz, 2H), 1.74 (quint, J=7.0 Hz, 2H), 1.24 (sextet, J=7.6 Hz, 2H), 0.84 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.1, 142.7, 141.3, 139.2, 132.2, 129.2, 128.8, 128.7, 126.5, 124.9, 124.6, 123.2, 122.5, 122.2, 111.2, 110.2, 108.0, 52.5, 45.2, 41.0, 33.4, 32.1, 30.1, 20.3, 13.9; IR (KBr) 2953, 1712, 1486, 1301 cm^{-1}; EIMS m/z 482 (M^+); HRMS m/z calcd for $C_{29}H_{30}N_4O_3$ 482.2318, found 482.2312.

*4.1.7. 1-Butyl-1′-furan-2-ylmethyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7g**)*

^{1}H NMR (300 MHz, $CDCl_3$) δ 11.02 (s, 1H), 8.52 (s, 1H), 8.03 (d, J=8.1 Hz, 1H), 7.54 (s, 1H), 7.42–7.34 (m, 3H), 7.20 (d, J=8.1 Hz, 1H), 6.33 (m, 1H), 5.07 (s, 2H), 4.25 (t, J=7.4 Hz, 2H), 3.94 (s, 3H), 1.76

(quint, J=7.0 Hz, 2H), 1.25 (sextet, J=7.0 Hz, 2H), 0.85 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.0, 155.6, 149.6, 143.1, 142.5, 139.1, 132.0, 129.1, 125.0, 124.6, 123.1, 122.6, 122.1, 110.8, 110.9, 110.3, 109.2, 108.7, 52.5, 45.2, 37.9, 32.1, 20.3, 13.9; IR (KBr) 2955, 1712, 1484, 1301 cm^{-1}; EIMS m/z 444 (M^+); HRMS m/z calcd for $C_{25}H_{24}N_4O_4$ 444.1798, found 444.1800.

4.1.8. 1-Butyl-1′-cyclopentyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7h**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.32 (s, 1H), 8.51 (s, 1H), 8.02 (d, J=8.5 Hz, 1H), 7.52 (s, 1H), 7.41–7.34 (m, 2H), 7.15 (d, J=8.2 Hz, 1H), 4.87 (quint, J=8.8 Hz, 1H), 4.26 (t, J=8.4 Hz, 2H), 3.94 (s, 3H), 2.17–1.75 (m, 8H), 1.28–1.22 (m, 4H), 0.86 (t, J=7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.7, 155.7, 155.5, 142.5, 138.9, 130.6, 129.0, 124.6, 124.2, 122.8, 121.9, 110.8, 109.8, 108.8, 53.4, 52.1, 45.1, 44.8, 31.8, 28.9, 25.0, 19.9, 13.5; IR (KBr) 2957, 1714, 1482, 1301 cm^{-1}; EIMS m/z 432 (M^+); HRMS m/z calcd for $C_{25}H_{28}N_4O_3$ 432.2161, found 432.2167.

4.1.9. 1′-Furan-2-ylmethyl-1-isopropyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7i**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.89 (s, 1H), 8.49 (s, 1H), 7.97 (d, J=8.6 Hz, 1H), 7.62 (d, J=8.6 Hz, 1H), 7.47 (s, 1H), 7.35 (s, 1H), 7.28–7.26 (m, 1H), 7.20–7.17 (m, 1H), 6.38 (d, J=3.1 Hz, 1H), 6.32–6.30 (m, 1H), 5.05 (s, 1H), 4.92–4.83 (m, 1H), 3.93 (s, 1H), 1.62 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 155.9, 155.5, 149.5, 143.1, 137.0, 131.9, 129.0, 124.7, 124.2, 123.5, 122.9, 122.3, 112.3, 111.4, 110.9, 109.2, 108.7, 52.5, 49.5, 37.9, 21.7; IR (KBr) 2981, 1714, 1484, 1304 cm^{-1}; EIMS m/z 430 (M^+); HRMS m/z calcd for $C_{24}H_{22}N_4O_4$ 430.1641, found 430.1646.

4.1.10. 1-Isopropyl-1′-(4-methoxy-benzyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**7j**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 10.28 (s, 1H), 8.51 (s, 1H), 7.99 (d, J=8.6 Hz, 1H), 7.63 (d, J=8.6 Hz, 1H), 7.47 (s, 1H), 7.32 (d, J=8.6 Hz, 2H), 7.23 (d, J=8.1 Hz, 1H), 6.99 (d, J=8.1 Hz, 1H), 6.88 (d, J=8.6 Hz, 2H), 5.05 (s, 2H), 4.94–4.82 (m, 1H), 3.95 (s, 3H), 3.79 (s, 3H), 1.64 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 159.5, 156.1, 156.0, 143.4, 137.1, 132.0, 129.3, 129.2, 128.4, 124.5, 124.1, 123.5, 122.7, 122.4, 114.5, 112.3, 111.4, 108.6, 55.6, 52.5, 49.4, 44.5, 21.7; IR (KBr) 2951, 1713, 1484, 1303 cm^{-1}; EIMS m/z 470 (M^+); HRMS m/z calcd for $C_{27}H_{26}N_4O_4$ 470.1954, found 470.1941.

4.1.11. 1′-Isopropyl-1-(2-methoxy-ethyl)-3′-methyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8a**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.05 (d, J=8.5 Hz, 1H), 7.59 (s, 1H), 7.54 (d, J=8.1 Hz, 1H), 7.49 (d, J=8.6 Hz, 1H), 7.27 (m, 1H), 4.79 (septet, J=7.0 Hz, 1H), 4.47 (t, J=5.4 Hz, 2H), 3.97 (s, 3H), 3.84 (t, J=5.3 Hz, 2H), 3.46 (s, 3H), 3.32 (s, 3H), 1.58 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.6, 154.4, 143.0, 139.6, 131.0, 130.0, 125.0, 124.6, 123.0, 122.6, 122.4, 110.3, 109.6, 108.9, 71.1, 59.6, 52.4, 45.7, 45.6, 27.5, 20.7; IR (KBr) 2925, 1709, 1493, 1302 cm^{-1}; EIMS m/z 422 (M^+); HRMS m/z calcd for $C_{23}H_{26}N_4O_4$ 422.1954, found 422.1953.

4.1.12. 3′-Allyl-1′-isopropyl-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8b**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.05 (d, J=8.5 Hz, 1H), 7.57–7.54 (m, 2H), 7.49 (d, J=8.4 Hz, 1H), 7.29–7.26 (m, 1H), 5.93 (tdd, J=11.2, 10.2, 5.4 Hz, 1H), 5.27–5.20 (m, 2H), 4.80 (septet, J=7.0 Hz, 1H), 4.56 (d, J=5.3 Hz, 2H), 4.44 (t, J=5.4 Hz, 2H), 3.96 (s, 3H), 3.82 (t, J=5.3 Hz, 2H), 3.31 (s, 3H), 1.59 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.5, 154.0, 142.8, 139.7, 132.2, 130.3, 130.2, 125.1, 124.8, 123.3, 122.7, 122.4, 118.1, 110.4, 110.2, 109.2, 71.1, 59.6, 52.5, 40.9, 40.7, 44.9, 20.8; IR (KBr) 2981, 1713, 1699, 1488, 1302 cm^{-1}; EIMS m/z 448 (M^+); HRMS m/z calcd for $C_{25}H_{28}N_4O_4$ 448.2111, found 448.2112.

4.1.13. 1′-Isopropyl-3′-(3-methoxy-benzyl)-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8c**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.02 (d, J=8.5 Hz, 1H), 7.55 (d, J=8.2 Hz, 1H), 7.46 (d, J=8.5 Hz, 1H), 7.46 (s, 1H), 7.29–7.19 (m, 2H), 6.92–6.88 (m, 2H), 6.78 (d, J=8.1 Hz, 1H), 5.10 (s, 2H), 4.83 (septet, J=6.9 Hz, 1H), 4.32 (t, J=5.2 Hz, 2H), 3.95 (s, 3H), 3.75 (s, 3H), 3.70 (t, J=5.2 Hz, 2H), 3.22 (s, 3H), 1.61 (d, J=6.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 160.3, 156.4, 142.7, 139.4, 138.0, 130.2, 129.9, 125.0, 124.6, 123.6, 122.5, 122.2, 120.0, 113.8, 11.3.1, 110.5, 110.1, 109.3, 70.9, 59.5, 55.5, 52.4, 45.9, 45.5, 45.1, 30.0, 20.7; IR (KBr) 2935, 1711, 1489, 1303 cm^{-1}; EIMS m/z 528 (M^+); HRMS m/z calcd for $C_{30}H_{32}N_4O_5$ 528.2373, found 528.2374.

4.1.14. 1′-Cyclopentyl-1-isobutyl-3′-methyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8d**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.03 (d, J=8.5 Hz, 1H), 7.44 (d, J=8.5 Hz, 1H), 7.41 (s, 1H), 7.37 (d, J=8.1 Hz, 1H), 7.18 (d, J=8.1 Hz, 1H), 4.93 (quint, J=8.8 Hz, 1H), 4.17 (d, J=7.6 Hz, 2H), 3.97 (s, 3H), 3.48 (s, 3H), 2.23–1.95 (m, 5H), 1.84–1.70 (m, 4H), 0.78 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.4, 154.7, 142.9, 139.5, 131.1, 129.8, 124.9, 124.5, 123.4, 122.4, 122.3, 110.5, 109.2, 108.8, 54.1, 52.6, 52.5, 29.3, 29.2, 27.6, 25.4, 20.4; IR (KBr) 2956, 1710, 1493, 1302 cm^{-1}; EIMS m/z 446 (M^+); HRMS m/z calcd for $C_{26}H_{30}N_4O_3$ 446.2318, found 446.2315.

4.1.15. 1′-Butyl-1-isobutyl-3′-methyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8e**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.93 (d, J=8.5 Hz, 1H), 7.35–7.27 (m, 3H), 7.01 (d, J=8.4 Hz, 1H), 4.07 (d, J=7.5 Hz, 2H), 3.86–3.81 (m, 5H), 3.38 (s, 3H), 1.93 (m, 1H), 1.68 (quint, J=7.5 Hz, 2H), 1.33 (sextet, J=7.8 Hz, 2H), 0.88 (t, J=7.2 Hz, 3H), 0.67 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 156.3, 154.9, 142.6, 139.4, 131.2, 130.9, 124.9, 124.5, 123.3, 122.7, 122.3, 110.6, 109, 107.7, 52.6, 52.5, 41.5, 30.9, 29.2, 27.7, 20.4, 20.4, 14.1; IR (KBr) 2958, 1711, 1496, 1302 cm^{-1}; EIMS m/z 434 (M^+); HRMS m/z calcd for $C_{25}H_{30}N_4O_3$ 434.2318, found 434.2307.

4.1.16. Methyl-3′-allyl-1′-butyl-1-isobutyl-2′-oxo-2,5′-bi-(1H-benzo[d]imidazole)-5-carboxylate (**8f**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.02 (d, J=8.5 Hz, 1H), 7.43–7.33 (m, 2H), 7.33 (s, 1H), 7.12 (d, J=8.1 Hz, 1H), 5.92 (tdd, J=11.1, 10.4, 5.3 Hz), 5.29–5.17 (m, 2H), 4.57 (d, J=5.3 Hz, 2H), 4.11 (d, J=7.6 Hz, 2H), 3.93–3.92 (m, 5H), 2.12 (m, 1H), 1.79 (quint, J=7.3 Hz, 2H), 1.43 (sextet, J=7.6 Hz, 2H), 0.98 (t, J=7.2 Hz, 3H), 0.75 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 156.3, 154.4, 142.7, 139.4, 132.1, 131.3, 129.9, 124.9, 124.5, 123.4, 123.1, 122.4, 118.0, 110.5, 109.7, 108.0, 52.6, 52.4, 43.9, 41.6, 30.8, 29.2, 20.4, 20.3, 14.1; IR (KBr) 2957, 1710, 1492, 1301 cm^{-1}; EIMS m/z 460 (M^+); HRMS m/z calcd for $C_{27}H_{32}N_4O_3$ 460.2474, found 460.2429.

4.1.17. 1′-Butyl-1-isobutyl-3′-(3-methoxy-benzyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8g**)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.01 (d, J=8.5 Hz, 1H), 7.43–7.37 (m, 2H), 7.28–7.11 (m, 3H), 6.88 (d, J=7.6 Hz, 1H), 6.84 (s, 1H), 6.78 (d, J=8.1 Hz, 1H), 5.10 (s, 2H), 4.01–3.93 (m, 7H), 3.74 (s, 3H), 1.99 (m, 1H), 1.82 (quint, J=7.4 Hz, 2H), 1.45 (sextet, J=7.7 Hz, 2H), 1.00 (t, J=7.2 Hz, 3H), 0.63 (d, J=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 160.3, 156.2, 154.8, 142.5, 139.3, 137.9, 131.3, 130.2, 129.7, 124.9, 124.5, 123.4, 123.3, 122.3, 120.0, 113.5, 113.4, 110.5,

109.7, 108.1, 55.5, 52.4, 52.4, 45.2, 41.7, 30.8, 29.0, 20.4, 20.2, 14.1; IR (KBr) 2958, 1712, 1492, 1302 cm^{-1}; EIMS *m*/*z* 540 (M^+); HRMS *m*/*z* calcd for $C_{32}H_{36}N_4O_4$ 540.2737, found 540.2713.

*4.1.18. 1′-Butyl-1-isobutyl-3′-(3-methyl-but-2-enyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8h**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.05 (d, *J*=8.5 Hz, 1H), 7.46–7.40 (m, 2H), 7.31 (s, 1H), 7.12 (d, *J*=8.1 Hz, 1H), 5.29 (t, *J*=6.6 Hz, 1H), 4.55 (d, *J*=6.6 Hz, 2H), 4.14 (d, *J*=7.5 Hz, 2H), 3.99–3.92 (m, 5H), 2.02–1.97 (m, 1H), 1.84 (s, 3H), 1.84–1.72 (m, 2H), 1.72 (s, 3H), 1.44 (sextet, *J*=7.6 Hz, 2H), 0.99 (t, *J*=7.4 Hz, 3H), 0.77 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 156.4, 154.5, 139.3, 137.3, 131.4, 130.0, 125.0, 124.6, 123.0, 122.3, 118.9, 110.6, 109.4, 107.9, 52.6, 52.5, 41.6, 39.6, 30.9, 29.2, 26.0, 20.5, 20.3, 18.5, 14.1; IR (KBr) 2958, 1712, 1492, 1301 cm^{-1}; EIMS *m*/*z* 488 (M^+); HRMS *m*/*z* calcd for $C_{29}H_{36}N_4O_3$ 488.2787, found 488.2759.

*4.1.19. 1′-Butyl-1-isobutyl-2′-oxo-3′-(3-phenyl-allyl)-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8i**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.01 (d, *J*=8.5 Hz, 1H), 7.44–7.21 (m, 8H), 7.14 (d, *J*=8.0 Hz, 1H), 6.63 (d, *J*=15.9 Hz, 1H), 6.28 (dt, *J*=15.9, 5.9 Hz, 1H), 4.74 (d, *J*=5.9 Hz, 2H), 4.03 (d, *J*=7.5 Hz, 2H), 4.00–3.95 (m, 5H), 1.99 (m, 1H), 1.81 (quint, *J*=7.3 Hz, 2H), 1.45 (sextet, *J*=7.6 Hz, 2H), 1.00 (t, *J*=7.2 Hz, 3H), 0.62 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 156.3, 154.4, 142.7, 139.4, 136.3, 133.7, 131.3, 129.8, 128.9, 128.3, 126.8, 124.9, 124.5, 123.4, 123.4, 123.2, 122.3, 110.6, 109.6, 108.1, 52.5, 52.4, 43.6, 41.6, 30.9, 29.1, 20.5, 20.2; IR (KBr) 2958, 1711, 1492, 1301 cm^{-1}; EIMS *m*/*z* 536 (M^+); HRMS *m*/*z* calcd for $C_{33}H_{36}N_4O_3$ 536.2787, found 536.2832.

*4.1.20. 1-Isobutyl-1′-isopropyl-3′-methyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8j**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.02 (d, *J*=8.5 Hz, 1H), 7.42 (d, *J*=8.6 Hz, 1H), 7.38 (s, 1H), 7.35 (d, *J*=8.1 Hz, 1H), 7.23 (d, *J*=8.6 Hz, 1H), 4.76 (septet, *J*=6.9 Hz, 1H), 4.15 (d, *J*=7.5 Hz, 2H), 3.94 (s, 3H), 3.45 (s, 3H), 2.11 (m, 1H), 1.57 (d, *J*=6.9 Hz, 6H), 0.76 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.3, 154.3, 142.7, 139.5, 131.0, 130.0, 124.9, 124.5, 123.2, 122.4, 122.3, 110.6, 109.1, 108.9, 52.6, 52.4, 45.7, 29.2, 27.6, 20.7, 20.3; IR (KBr) 2959, 1711, 1493, 1302 cm^{-1}; EIMS *m*/*z* 420 (M^+); HRMS *m*/*z* calcd for $C_{24}H_{28}N_4O_3$ 420.2161, found 420.2144.

*4.1.21. 3′-Allyl-1-isobutyl-1′-isopropyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8k**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 8.02 (d, *J*=8.5 Hz, 1H), 7.43–7.37 (m, 2H), 7.33 (s, 1H), 7.26 (d, *J*=8.2 Hz, 1H), 5.92 (tdd, *J*=11.1, 10.4, 5.3 Hz, 1H), 5.24–5.17 (m, 2H), 4.79 (septet, *J*=6.9 Hz, 1H), 4.55 (d, *J*=5.3 Hz, 2H), 4.12 (d, *J*=7.6 Hz, 2H), 3.95 (s, 3H), 2.08 (m, 1H), 1.59 (d, *J*=6.9 Hz, 6H), 0.76 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.3, 153.9, 142.7, 139.4, 132.1, 130.1, 130.1, 124.9, 124.5, 123.1, 122.8, 122.4, 118.0, 110.5, 109.6, 109.2, 52.6, 52.4, 45.8, 43.8, 29.2, 20.7, 20.3; IR (KBr) 2960, 1712, 1489, 1302 cm^{-1}; EIMS *m*/*z* 446 (M^+); HRMS *m*/*z* calcd for $C_{26}H_{30}N_4O_3$ 446.2318, found 446.2339.

*4.1.22. 1-Isobutyl-1′-isopropyl-3′-(3-methoxy-benzyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8l**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.02 (d, *J*=8.4 Hz, 1H), 7.40 (d, *J*=8.3 Hz, 1H), 7.29–7.17 (m, 3H), 6.91–6.78 (m, 3H), 5.10 (s, 1H), 4.84 (septet, *J*=6.8 Hz, 1H), 3.96–3.94 (m, 2H), 3.76 (s, 3H), 2.07–1.96 (m, 1H), 1.63 (d, *J*=6.9 Hz, 6H), 0.65 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 160.3, 156.2, 154.3, 142.7, 139.4, 137.9, 130.2, 130.2, 129.9, 124.9, 124.5, 123.1, 123.0, 122.4, 120.0, 113.6, 113.3, 110.5, 109.7, 109.3, 55.5, 52.4, 45.9, 45.2, 30.0, 29.1, 20.7, 20.2; IR (KBr) 2957, 1708, 1489, 1301 cm^{-1}; EIMS *m*/*z* 526 (M^+); HRMS *m*/*z* calcd for $C_{31}H_{34}N_4O_4$ 526.2580, found 526.2582.

*4.1.23. 1-Isobutyl-1′-isopropyl-3′-(3-methyl-but-2-enyl)-2′-oxo-2′,3′-dihydro-1,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8m**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.04 (d, *J*=8.5 Hz, 1H), 7.44 (d, *J*=8.5 Hz, 1H), 7.39 (d, *J*=8.1 Hz, 1H), 7.30–7.24 (m, 2H), 5.29 (t, *J*=6.6 Hz, 1H), 4.80 (septet, *J*=6.9 Hz, 1H), 4.54 (d, *J*=6.6 Hz, 1H), 4.13 (d, *J*=7.6 Hz, 2H), 3.97 (s, 3H), 2.04 (m, 1H), 1.84 (s, 3H), 1.73 (s, 3H), 1.59 (d, *J*=6.9 Hz, 6H), 0.78 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.4, 153.9, 142.7, 139.4, 137.2, 130.1, 125.0, 124.6, 122.7, 122.4, 118.9, 110.6, 109.4, 109.1, 52.6, 52.5, 45.7, 39.6, 29.2, 26.0, 20.7, 20.3, 18.5; IR (KBr) 2927, 1709, 1488, 1301 cm^{-1}; EIMS *m*/*z* 474 (M^+); HRMS *m*/*z* calcd for $C_{28}H_{34}N_4O_3$ 474.2631, found 474.2637.

*4.1.24. 1′-Isobutyl-1-(2-methoxy-ethyl)-3′-methyl-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8n**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.04 (d, *J*=8.5 Hz, 1H), 7.59 (s, 1H), 7.55 (d, *J*=8.1 Hz, 1H), 7.48 (d, *J*=8.5 Hz, 1H), 7.11 (d, *J*=8.0 Hz, 1H), 4.47 (t, *J*=5.3 Hz, 2H), 3.96 (s, 3H), 3.83 (t, *J*=5.3 Hz, 2H), 3.73 (d, *J*=7.4 Hz, 2H), 3.48 (s, 3H), 3.31 (s, 3H), 2.22 (m, 1H), 0.99 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.9, 156.5, 155.2, 142.7, 139.4, 131.7, 130.7, 125.1, 124.7, 123.3, 122.7, 122.2, 110.4, 109.6, 108.0, 71.0, 59.5, 52.5, 49.2, 45.6, 28.4, 27.7, 20.5; IR (KBr) 2956, 1712, 1496, 1302 cm^{-1}; EIMS *m*/*z* 436 (M^+); HRMS *m*/*z* calcd for $C_{24}H_{28}N_4O_4$ 436.2111, found 436.2121.

*4.1.25. 3′-Allyl-1′-isobutyl-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8o**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.04 (d, *J*=8.5 Hz, 1H), 7.58–7.55 (m, 2H), 7.49 (d, *J*=8.5 Hz, 1H), 7.13 (d, *J*=8.5 Hz, 1H), 5.93 (tdd, *J*=11.0, 10.7, 5.3 Hz, 1H), 5.24–5.18 (m, 2H), 4.58 (d, *J*=5.2 Hz, 2H), 4.44 (t, *J*=5.3 Hz, 2H), 3.96 (s, 3H), 3.82 (t, *J*=5.3 Hz, 2H), 3.75 (d, *J*=7.4 Hz, 2H), 3.30 (s, 3H), 2.24 (septet, *J*=6.8 Hz, 1H), 1.00 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.5, 154.7, 142.8, 139.4, 132.1, 131.7, 129.8, 125.1, 124.6, 123.6, 122.8, 122.3, 118.0, 110.4, 110.1, 108.2, 71.0, 59.5, 52.5, 49.2, 45.6, 43.9, 28.3, 20.5; IR (KBr) 2956, 1711, 1493, 1302 cm^{-1}; EIMS *m*/*z* 462 (M^+); HRMS *m*/*z* calcd for $C_{26}H_{30}N_4O_4$ 462.2267, found 462.2277.

*4.1.26. 1′-Isobutyl-3′-(3-methoxy-benzyl)-1-(2-methoxy-ethyl)-2′-oxo-2′,3′-dihydro-1H,1′H-[2,5′] bisbenzoimidazolyl-5-carboxylic acid methyl ester (**8p**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.02 (d, *J*=8.5 Hz, 1H), 7.56 (d, *J*=8.1 Hz, 1H), 7.47–7.44 (m, 2H), 7.28–7.19 (m, 1H), 7.13 (d, *J*=8.1 Hz, 1H), 6.92–6.87 (m, 2H), 6.78 (d, *J*=8.1 Hz, 1H), 5.12 (s, 2H), 4.31 (t, *J*=5.2 Hz, 2H), 3.95 (s, 3H), 3.79 (d, *J*=7.4 Hz, 2H), 3.74 (s, 3H), 3.70 (t, *J*=5.2 Hz, 2H), 3.22 (s, 3H), 2.28 (septet, *J*=6.7 Hz, 1H), 1.02 (d, *J*=6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 160.3, 156.4, 155.1, 142.7, 139.4, 138.0, 131.7, 130.2, 129.6, 125.0, 124.6, 123.9, 122.8, 122.2, 120.0, 113.6, 113.3, 110.4, 110.1, 108.4, 70.9, 59.5, 55.5, 52.4, 49.2, 45.5, 45.1, 28.3, 20.5; IR (KBr) 2957, 1710, 1491, 1302 cm^{-1}; EIMS *m*/*z* 542 (M^+); HRMS *m*/*z* calcd for $C_{31}H_{34}N_4O_5$ 542.2529, found 542.2523.

*4.1.27. (E)-Methyl-1-cyclopentyl-3′-(3,7-dimethylocta-2,6-dienyl)-1′-isopropyl-2′-oxo-2,5′-bi(1H-benzo[d]imidazole)-5-carboxylate (**8q**)*

^1H NMR (300 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.98 (d, *J*=8.5 Hz, 1H), 7.51 (d, *J*=8.6 Hz, 1H), 7.34–7.24 (m, 3H), 5.30–5.26 (m, 1H), 5.04–4.93 (m, 2H), 4.78 (quint, *J*=6.9 Hz, 1H), 4.54 (d, *J*=6.3 Hz, 2H), 3.94

(s, 3H), 2.34–2.29 (m, 2H), 2.15–2.01 (m, 8H), 1.82 (s, 3H), 1.77–1.73 (m, 2H), 1.62–1.51 (m, 9H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.0, 156.7, 153.9, 143.6, 140.6, 136.9, 132.1, 130.2, 130.1, 124.6, 124.0, 123.0, 122.7, 122.6, 118.8, 111.8, 109.5, 109.1, 58.1, 52.4, 45.7, 39.8, 39.6, 30.8, 26.7, 25.9, 25.6, 20.7, 18.0, 16.9; IR (KBr) 2972, 1712, 1489, 1304 cm^{-1}; EIMS m/z 554 (M^+); HRMS m/z calcd for $C_{34}H_{42}N_4O_3$ 554.3257, found 554.3255.

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Supplementary data

Representative ^{1}H NMR and ^{13}C NMR spectrum of compounds **7** and **8**. This information is available free of charge via the internet at <http://pubs.acs.org>. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.081.

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