Synthesis of Macrocyclic Bis(phenylbenzoxazole) Derivatives via Tandem Claisen Rearrangement and Their Fluorescence Behavior

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Novel macrocyclic bis(phenylbenzoxazole) derivatives were easily synthesized from macrocyclic isobutenyl bis(amide–ether)s by tandem Claisen rearrangement and subsequent intramolecular cyclization of the amide–phenol intermediates. The position of substitution of the oligoethylene glycol moiety on the phenylamido groups of the macrocycles did not have a large effect on the yields of the bis(benzoxazole)s for the *meta* and *para* derivatives. The fluorescence quantum yields of most of the macrocyclic bis(benzoxazole)s were lower than those of the corresponding nonmacrocyclic bis(benzoxazole) model compounds. The quantum yields of the *para*-substituted macrocyclic bis(benzoxazole)s were clearly lower than those of the model compounds and decreased with increasing length of the oligoethylene chain.

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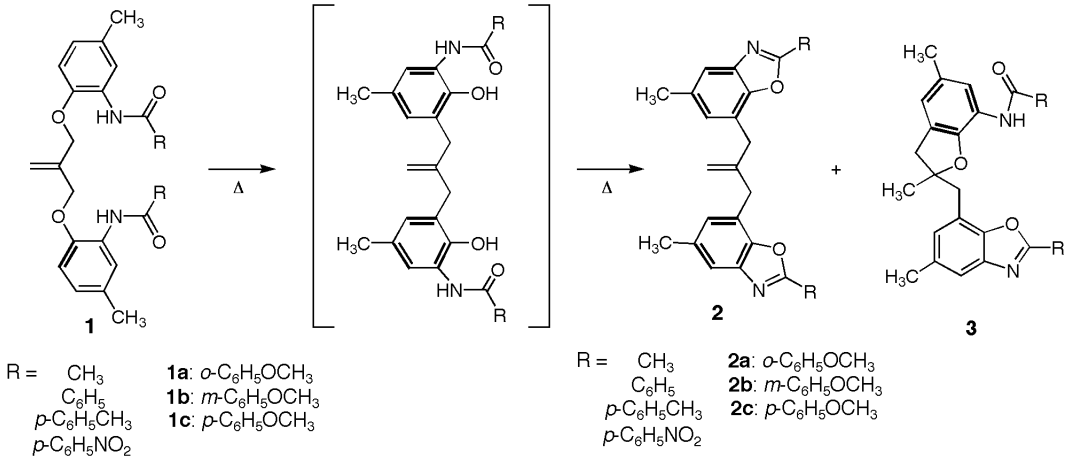
Much attention has been paid to benzoxazoles because they have a number of optical applications; they have been used as optical luminescents [1], whitening agents [2], and laser dyes [3]. Benzoxazoles also have other important uses; for example, they can serve as intermediates for organic syntheses [4] and as therapeutic materials [5].

The Claisen rearrangement has attracted interest because of its extensive applications for organic synthesis. The possibility for tandem Claisen rearrangement, that is, transposition at two reaction centers, extends the reaction's usefulness even further [6]. We have recently found that isobutenyl bis(aryl ether) derivatives are easily converted to compounds having two phenolic hydroxy groups *via* tandem Claisen rearrangement [7]. Furthermore, we have demonstrated that some noncyclic isobutenyl bis(aryl ether)s having amide groups at the *ortho* position **1** are easily converted to bis(benzoxazole)s **2** by heating and that the reaction proceeds *via* tandem Claisen rearrangement (Scheme 1) [8,9].

In this paper, we demonstrate a successful synthetic application of tandem Claisen rearrangement for a series of macrocyclic bis(phenylbenzoxazole) derivatives binding oligoethylene glycol at the *ortho*, *meta*, or *para* positions of the phenylamido groups of the macrocycles, and we investigate the effect of positional substitution on the fluorescence.

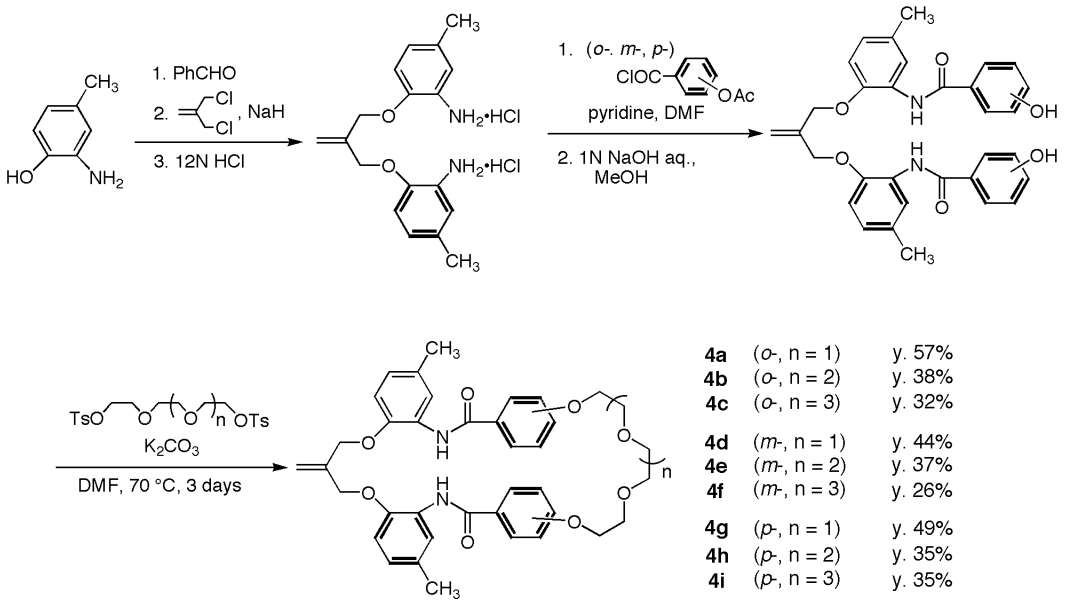
The series of macrocyclic bis(amide–ether)s **4a**–**4i** shown in Scheme 2 was prepared as follows: First, 1,3-bis(2-amino-4-methylphenoxy)-2-methylenepropane hydrochloride was prepared by a method involving a protection–deprotection process: 4-methyl-2-aminophenol was treated with benzaldehyde to form 4-methyl-2-iminophenol, which was then etherified with 3-chloro-2-(chloromethyl)-1-propene in the presence of NaH in dry dimethylformamide (DMF) and deprotected with 12 *N* aqueous HCl in chloroform. Next, macrocyclic bis(amide–ether)s **4a**–**4i** were prepared: 1,3-bis(2-amino-4-methylphenoxy)-2-methylenepropane hydrochloride was treated with *o*-, *m*-, or *p*-acetoxybenzoyl chloride in the presence of pyridine in dry DMF at 0 for 30 minutes and 20 °C for 3 hours, and the resulting intermediates were

Scheme 1



hydrolyzed in 1 *N* NaOH aqueous solution for 12 hours at room temperature. Finally, the bisphenol derivatives were treated with oligoethylene glycol ditosylate in the presence of potassium carbonate in dry DMF at 70 °C for 3 days(Scheme 2).

Scheme 2



The bulk rearrangement of *meta*- and *para*-substituted macrocycles **4d**–**4i** was carried out at 230–240 °C for 5–7 hours under vacuum. The heating of *o*-substituted macrocycles **4a**–**4c** at 240 °C for 7 hours gave the complex mixture of the corresponding **5**, the intermediates, and other decomposed compounds. So, the thermal reaction of **4a**–**4c** was carried out under milder conditions (at 210 °C), which required more than 2 days to complete. The rearrangement of *ortho*-substituted macrocycles **4a**–**4c** proceeded very slowly compared with the rearrangements of the *meta*- and *para*-substituted macrocycles **4d**–**4i**. Previously, we studied the rearrangement of nonmacrocyclic bis(amide–ether)s **1a**–**1c**, which have methoxy groups at the *ortho*, *meta*, or *para* positions of the phenyl groups (Scheme 1) [9]. We observed a large difference in the rate of the thermal reaction among the nonmacrocyclic compounds **1a**–**1c**: the rearrangements of the *meta* and *para* compounds **1b** and **1c** were complete within 24 hours at 180 °C, whereas the rearrangement of **1a** needed heating at 210 °C for 4 days. We concluded that the rate difference was caused by the hydrogen-bonding interaction between the oxygen of the methoxy group at the *ortho* position and the OH group in the bis(amide–phenol) generated by the tandem Claisen rearrangement of **1a**, effectively inhibiting subsequent intramolecular cyclization to the corresponding nonmacrocyclic bis(benzoxazole) **2a**. This might also be the case for the macrocyclic system. The purification of **5** was carried out by silica gel column chromatography (eluent: 5:1 chloroform:ethyl acetate). The results for the rearrangements are summarized in Table 1.

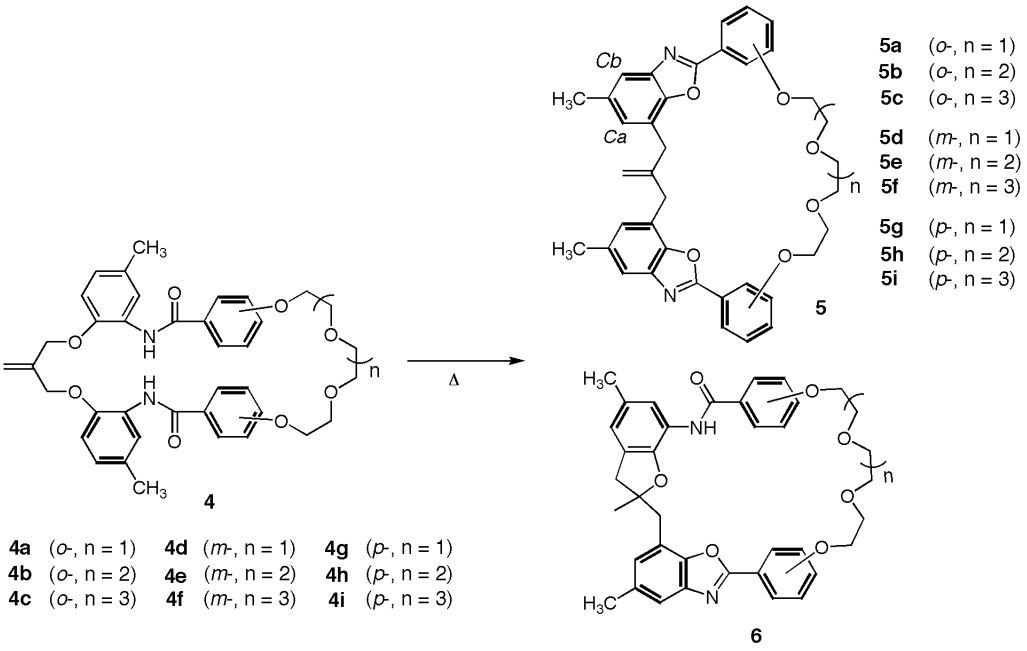
Table 1
Rearrangement of **1a–1c** and **4a–4i**[a]

Run	Compound	Time (h)	Temp (°C)	Yield of **2** (**3**) or **5** (%)
1	**4a**	48	210	20
2	**4b**	48	210	38
3	**4c**	48	210	16
4	**4d**	5	240	72
5	**4e**	5	240	71
6	**4f**	5	240	80
7	**4g**	6	230	65
8	**4h**	6	230	61
9	**4i**	7	240	72
10 [9]	**1a**	24	180	43 (16)
11 [9]	**1b**	24	180	8 (91)
12 [9]	**1c**	24	180	60 (39)

a) Conditions: without solvent, under vacuum.

The *ortho*-substituted macrocyclic bis(benzoxazole)s **5a**–**5c** were not obtained in satisfactory yields (yields of **5a**–**5c**: 16–38%). It is likely that partial decomposition occurred before the macrocyclic bis(benzoxazole)s were completely formed, since these macrocycles were heated at a high temperature (210 °C) for a long time. In contrast, the rearrangements of the *meta*- and *para*-substituted macrocycles **5d**–**5i** quantitatively gave macrocyclic bis(benzoxazole) and macrocyclic dihydrobenzofuran as a simple mixture of two products (Scheme 3). These results were consistent with the trend of the total yields for the model compounds **1a–1c** (total yield of the **2** + **3** mixture: *ortho*, 59%; *meta*, 99%; *para*, 99%).

Scheme 3



The effect of substituent on the **5**:**6** product ratio for the macrocycles was different from that for the nonmacrocyclic compounds. As described previously [9], the reactions of the *ortho*- or *para*-substituted nonmacrocyclic compounds **1a** and **1c** preferentially gave bis(benzoxazole)s **2a** and **2c** (yields: 43% and 60%) compared with **3a** and **3c** (yields: 16% and 39%), whereas the reaction of *meta*-substituted **1b** gave a drastically decreased ratio of bis(benzoxazole) **2b** (8%) to dihydrobenzofuran **3b** (91%). Interestingly, except for the *ortho*-substituted macrocycles, the macrocyclic bis(benzoxazole) derivatives **5d**–**5i** were preferentially obtained from **4d**–**4i** (61–80%). The **5**:**6** product ratios for the *ortho*-substituted macrocycles could not be determined because the thermal reaction gave complex mixtures. It is noteworthy that the oligoethylene glycol chain length had almost no effect on the yield of **5**.

We expected the molecular shapes of the macrocyclic bis(benzoxazole)s, and hence the distances between the benzoxazole units, to vary with the type of linkage (*ortho*, *meta*, or *para*) and the length of the oligoethylene glycol moiety. Thus we investigated the influence of structure on the fluorescence properties by comparing the emission spectra and quantum yields of macrocycles **5a**–**5i** with those of model compounds **2a–2c**.

The emission spectra of **2** and **5**were measured in $CHCl_3$ (1×10^{-6} *M*) at 25 °C. The fluorescence quantum yields were calculated with quinine sulfate in 1 *N* H_2SO_4 as a reference (ϕ = 0.51). Typical emission profiles are shown in Figure 1, and spectral data and quantum yields are summarized in Table 2.

Table 2
Fluorescence Spectra[a]

Compound	$\lambda_{max\,(ab)}$ (nm)	$\lambda_{max(fl)}$ (nm)	ϕ
5a	300, 312	364	0.55
5b	300, 313	364	0.51
5c	300, 313	365	0.47
5d	303, 314	353	0.33
5e	303, 311	354	0.18
5f	302, 311	354	0.18
5g	305, 311	353	0.40
5h	305	357	0.18
5i	306	358	0.17
2a	317	363	0.51
2b	303, 312	354	0.31
2c	306, 314	356	0.55

[a] Conditions; Samples were measured in $CHCl_3$ at 25 °C, and exited at 300 nm. The ϕ values were calculated with quinine sulfate in 1N H_2SO_4 as a reference, which has a quantum yield of 0.51.

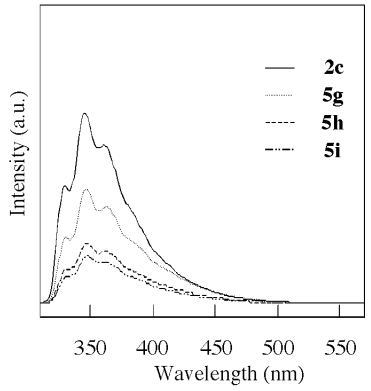


Figure 1. Fluorescence spectra of **5g** - **5i**, and **2c** in $CHCl_3$ ($1x10^{-6}$ M, at 25 °C)

The emission spectra of all model nonmacrocyclic and macrocyclic bis(benzoxazole)s showed structured emission with a strong fluorescence in the range 354–365 nm upon excitation at 300 nm (Figure 1, Table 2). Overall, there was no significant difference in the $\lambda_{max(ab)}$ and $\lambda_{max(fl)}$ values among the bis(benzoxazole) compounds with different substituted positions and oligoethylene glycol chain lengths; in compounds with the same substituted positions, the difference was especially small or there was no difference at all. Moreover, we could not confirm a peak for excimer formation between the two neighboring benzoxazoles in any of the spectra of the nonmacrocyclic or macrocyclic compounds. These results indicate that substituent position has little effect on the absorption and emission spectral shapes in spite of the proximity of the benzoxazoles in the various compounds. However, some tendencies for the fluorescence quantum yields were observed: (1) the quantum yields of the *ortho*- or *para*-substituted nonmacrocyclic **2a** and **2c** and macrocyclic bis(benzoxazole)s with triethylene glycol moieties **5a** and **5g** were higher than those of the *meta*-substituted compounds **2b** and **5d**; (2) the quantum yield decreased as the length of the oligoethylene glycol chain increased, although for the *ortho*-substituted macrocycle the decrease was relatively small, whereas for the *para*-substituted macrocycle the decrease was large; (3) the yields of the macrocycles with the shortest chain, **5a**, **5d**, and **5g**, were almost the same as those of the corresponding nonmacrocyclic compounds, although for the *para*-substituted macrocycle, the difference ($\phi_{2l} - \phi_{2g} = 0.15$) was rather large.

For the nonmacrocyclic compounds, the difference in the emission efficiencies of a single benzoxazole is expected to dominate the difference in the quantum yields, since the two benzoxazoles are bound at the same position.

Kanegae *et al*. determined the quantum yields of several 2-phenylbenzoxazole derivatives and reported that the introduction of an electron-donating group in a resonance position on the phenyl ring hindered the torsional motion of the C–C bond between the benzoxazole and the phenyl ring, resulting in an increase in the quantum yield [10]. In our case, torsional motion in the nonmacrocyclic bis(benzoxazole)s **2a** and **2c**, which have methoxy groups at the *ortho* and *para* positions, might be hindered more effectively than in the *meta*-substituted compound **2b**, thereby increasing the quantum yield. The quantum yields of the *ortho*- and *para*-substituted macrocycles, **5a** and **5g** are also higher than that of the *meta*-substituted macrocycle **5e** with triethylene glycol moiety, but this rule was not followed for macrocycles with longer chains, suggesting some other quenching mechanism.

^{13}C spin–lattice relaxation times (T_1) of *ortho*- and *para*-substituted macrocycles with tri- and pentaethylene glycol moieties, **5a**, **5c**, **5g**, and **5i**, were measured to investigate how the molecular flexibility of the benzoxazole unit contributes to the decrease in the quantum yield. The results are listed in Table 3.

Table 3
Relaxation times (T_1) of **5a**, **5c**, **5g**, and **5i**

	T_1(**5a**) (s)	T_1(**5c**) (s)	T_1(**5g**) (s)	T_1(**5i**) (s)
Ca	0.52	0.43	0.42	0.35
Cb	0.57	0.47	0.55	0.50

In both *ortho*- and *para*-substituted macrocycles, the T_1 values of the macrocycles with the pentaethylene glycol moiety were smaller than those of the macrocycles with the triethylene glycol moiety, but the decrease in the T_1 values for the *ortho*-substituted macrocycle due to the increase in the ethylene glycol chain length was greater than that for the *para*-substituted macrocycle. In general, the T_1 values of the ^{13}C nuclei decrease with increasing molecular size and decreasing molecular flexibility [11]. Thus, the enhancement of molecular flexibility with increasing chain length is greater for the *para*-substituted macrocycle than for the *ortho*-substituted macrocycle. We may, therefore, reasonably conclude that the significant decrease in quantum yield for the *para*-substituted macrocycle is mainly caused by the enhancement of the radiationless process due to the ring. However, the quantum yield of **5g** was lower than that of the model nonmacrocyclic compound **2c,** whereas the quantum yields of **5a** and **2a** were almost equal even though the T_1 value of **5g** is smaller than the T_1 value of **5a**. That is, the molecular flexibility of **5g** is larger than that of **5a**. Because of the close proximity of the two benzoxazole units in the *para*-substituted macrocycles, reabsorption and collisional quenching processes may also be involved in the quenching mechanism.

In conclusion, we have successfully synthesized new macrocyclic bis(benzoxazole) derivatives **5a**–**5i** from novel macrocyclic bis(amide–ether) precursors *via* tandem Claisen rearrangement induced by heating under vacuum. During heating, tandem Claisen rearrangement at the isobutenyl bis(4-methylphenyl ether) units proceeded readily, followed by intramolecular cyclization between the newly generated phenol group and amide group, to give the macrocyclic bis(benzoxazole)s. The fluorescence quantum yields of the macrocyclic bis(benzoxazole)s (especially the *para*-substituted macrocycles) decreased with increasing length of the oligoethylene glycol chain. We concluded that the difference in the quantum yields was caused by the different molecular shapes of the macrocycles.

EXPERIMENTAL

Instrumentation.

^1H and ^{13}C NMR spectra were recorded on a BrukerAF-500 spectrometer using tetramethylsilane (TMS) as an internal standard

in chloroform-*d* ($CDCl_3$) or dimethyl-d_6 sulfoxide (DMSO-d_6). IR spectra were obtained with a JASCO FT/IR 420. High-resolution mass spectra (HRMS) were recorded by an ESI-TOF mass spectrometer (PE Biosystems Mariner). UV and fluorescence spectra were obtained with JASCO V-550 and FP 750 spectrophotometers, respectively.

Synthesis of 1,3-Bis(2-amino-4-methylphenoxy)-2-methylenepropane Hydrochloride.

To a dispersion of 4-methyl-2-aminophenol (5.0 g, 40.1 mmol) in MeOH (30 mL) was added benzaldehyde (4.3 g, 40.1 mmol), and the mixture was stirred for 5 hours at room temperature (rt). The mixture was filtered, and the solid protected-hydroxyarylamine obtained was dried *in vacuo*. The solid was dissolved in dry DMF (30 mL), and NaH (60% in oil, 2.0 g, 52.1 mmol) and 3-chloro-2-(chloromethyl)propene (251 g, 20.1 mmol) were added to the solution. The reaction mixture was stirred overnight at 70 °C. The solvent was removed under vacuum, and the residue was dissolved in $CHCl_3$ and washed with water. After half of the solvent was removed, 12 *N* HCl was added to the solution at rt. The precipitate obtained was collected by filtration and washed three times with acetone.

1,3-Bis(2-amino-4-methylphenoxy)-2-methylenepropane Hydrochloride.

This compound was obtained as a colorless solid, yield 82%; mp 100.7–102.0 °C; ^{1}H NMR (DMSO-d_6): δ 2.26 (s, 6H, CH_3–), 4.82 (s, 4H, –CH_2–), 5.52 (s, 2H, CH_2=), 7.12–7.13 (m, 4H, Ar), 7.23 (s, 2H, Ar), 10.12 (br s, 6H, –NH_3); ^{13}C NMR (DMSO-d_6): δ 20.36, 68.97, 113.68, 116.20, 121.06, 124.47, 129.34, 130.41, 139.51, 149.17; IR (KBr): 3398, 1637, 1508, 1273 cm^{-1}.

General Procedure for Preparation of 1,3-Bis[2-[(hydroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane.

To a solution of 1,3-bis(2-amino-4-methylphenoxy)-2-methyleneprapane hydrochloride and pyridine in dry DMF at 0 °C was added a solution of *o*-, *m*-, or *p*-acetoxybenzoyl chloride in dry DMF. The mixture was stirred at 0 °C for 30 minutes and at rt for 3 hours. The DMF was then removed under vacuum from the reaction mixture, and the residue was dissolved in $CHCl_3$. The solution was washed three times with water and then dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was purified by silica gel column chromatography (eluent: chloroform) to give 1,3-bis[2-[(acetoxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane. The resulting ester derivative was hydrolyzed in 1 *N* NaOH (aq)–methanol solution at room temperature for 12 hours. After the reaction, 1 *N* HCl aqueous solution was added to neutralize the mixture and precipitate 1,3-bis[2-[(hydroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane. The precipitate was collected by filtration, washed with water, and dried *in vacuo*.

1,3-Bis[2-[(2-hyroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane.

This compound was obtained as a colorless solid, yield 54%, mp 115.9–116.8 °C; ^{1}H NMR (DMSO-d_6): δ 2.25 (s, 6H, CH_3–Ar), 4.78 (s, 4H, –CH_2–), 5.51 (s, 2H, CH_2=), 6.77 (d, J = 8.3 Hz, 2H, Ar), 6.95 (d, J = 8.4 Hz, 2H, Ar), 6.99 (t, J = 7.8 Hz, 2H, Ar), 7.05 (d, J = 8.1 Hz, 2H, Ar), 7.43 (t, J = 8.3 Hz, 2H, Ar), 8.04 (d, J = 8.0 Hz, 2H, Ar), 8.23 (s, 2H, Ar), 10.66 (s, 2H, –NH–), 11.62 (br s, 2H, –OH); ^{13}C NMR ($CDCl_3$): δ 20.63, 68.66, 111.94, 115.22, 116.99, 118.70, 119.67, 121.59, 124.15, 127.61, 129.60, 130.71, 133.37, 139.80, 145.56, 156.34, 163.54; IR (KBr): 3427, 3313, 1629, 1593, 1543, 1489, 1236 cm^{-1}.

1,3-Bis[2-[(3-hyroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane.

This compound was obtained as a colorless solid, yield 52%, mp 148.6–149.7 °C; ^{1}H NMR (DMSO-d_6): δ 2.24 (s, 6H, CH_3–Ar), 4.68 (s, 4H, –CH_2–), 5.34 (s, 2H, CH_2=), 6.85 (dd, J_1 = 8.4, J_2 = 1.5 Hz, 2H, Ar), 6.90 (d, J = 8.4 Hz, 2H, Ar), 6.96 (dd, J_1 = 8.0, J_2 = 2.5 Hz, 2H, Ar), 7.25 (t, J = 7.9 Hz, 2H, Ar), 7.32–7.35 (m, 4H, Ar), 7.53 (d, J = 2.0 Hz, 2H, Ar), 9.33 (s, 2H, –NH–), 9.76 (br s, 2H, –OH); ^{13}C NMR ($CDCl_3$): δ 21.32, 68.44, 112.49, 114.18, 114.39, 117.68, 118.53, 125.26, 125.98, 126.75, 129.30, 129.54, 135.99, 140.33, 148.39, 157.51, 164.93; IR (KBr): 3419, 3282, 1654, 1593, 1540, 1481, 1253 cm^{-1}.

1,3-Bis[2-[(4-hyroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane.

This compound was obtained as a colorless solid, yield 59%, mp 205.8–206.7 °C; ^{1}H NMR (DMSO-d_6): δ 2.25 (s, 6H, CH_3–Ar), 4.68 (s, 4H, –CH_2–), 5.34 (s, 2H, CH_2=), 6.81 (d, J = 8.7 Hz, 2H, Ar), 6.81 (m, 2H, Ar), 6.91 (dd, J = 8.4 Hz, 2H, Ar), 7.56 (d, J = 1.8 Hz, 2H, Ar), 7.79 (d, J = 8.7 Hz, 2H, Ar), 9.19 (s, 2H, –NH–), 10.10 (br s, 2H, –OH); ^{13}C NMR ($CDCl_3$): δ 20.36, 68.52, 112.45, 125.05, 125.59, 127.09, 129.35, 140.38, 148.21, 160.54, 164.52; IR (KBr): 3430, 3261, 1652, 1604, 1539, 1514, 1252 cm^{-1}.

General Procedure for Preparation of Macrocyclic Isobutenyl Bis(amide–aryl ether)s (4).

To a solution of 1,3-bis[2-[(hydroxybenzoyl)amino]-4-methylphenoxy]-2-methylenepropane (1.99 g, 3.7 mmol) and triethylene glycol ditosylate (1.70 g, 3.7 mmol) in dry DMF (400 mL) was added K_2CO_3 (2.2 g, 16 mmol), and the mixture was heated at 70 °C for3 days. The mixture was evaporated, the residue was dissolved in $CHCl_3$, and the solution was washed with water. After evaporation of the solvent, the residue was purified by column chromatography on silica gel (eluent: 4:1 $CHCl_3$:ethyl acetate) to give **4**.

Macrocyclic isobutenyl bis(amide–aryl ether) (**4a**, *o*-, n = 1).

This compound was obtained as a colorless solid, yield 57%, mp 145.6–146.5 °C; ^{1}H NMR ($CDCl_3$): δ 2.30 (s, 6H, CH_3–Ar), 3.52 (s, 4H, –O–CH_2–), 3.79 (t, J = 4.9 Hz, 4H, –O–CH_2–), 4.22 (t, J = 4.9 Hz, 4H, –O–CH_2–), 4.84 (s, 4H, –CH_2–), 5.42 (s, 2H, CH_2=), 6.68 (d, J = 8.3 Hz, 2H, Ar), 6.73 (d, J = 8.3 Hz, 2H, Ar), 6.94 (d, J = 8.4 Hz, 2H, Ar), 7.14 (t, J = 7.8 Hz, 2H, Ar), 7.45 (t, J = 8.3 Hz, 2H, Ar), 8.30 (d, J = 7.8 Hz, 2H, Ar), 8.39 (s, 2H, Ar), 10.24 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 20.98, 68.80, 68.87, 69.33, 70.94, 111.94, 113.34, 115.82, 121.94, 122.36, 122.97, 124.16, 128.21, 131.02, 132.62, 132.87, 140.81, 145.57, 156.21, 163.26; IR (KBr): 3341, 1662, 1596, 1542, 1480, 1230 cm^{-1}; HRESIMS *m/z* 653.2862 $(M + H)^+$, calcd for $C_{38}H_{41}N_2O_8$ 653.2863.

Macrocyclic Isobutenyl bis(amide–aryl ether) (**4b**, *o*-, n = 2).

This compound was obtained as a colorless solid, yield 53%, mp 148.8–149.9 °C; ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 6H, CH_3–Ar), 3.45–3.50 (m, 4H, –O–CH_2–), 3.56–3.62 (m, 4H, –O–CH_2–), 3.89 (t, J = 4.8 Hz, 4H, –O–CH_2–), 4.29 (t, J = 4.8 Hz, 4H,

–O–CH_2–), 4.86 (s, 4H, –CH_2–), 5.40 (s, 2H, CH_2=), 6.65 (d, *J* = 8.3 Hz, 2H, Ar), 6.74 (d, *J* = 8.3 Hz, 2H, Ar), 6.98 (d, *J* = 8.3 Hz, 2H, Ar), 7.14 (t, *J* = 7.3 Hz, 2H, Ar), 7.46 (t, *J* = 8.3 Hz, 2H, Ar), 8.29 (d, *J* = 8.0 Hz, 2H, Ar), 8.39 (s, 2H, Ar), 10.30 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.00, 68.96, 69.15, 69.46, 70.79, 111.91, 113.39, 121.84, 122.14, 122.94, 124.14, 128.17, 130.93, 132.57, 132.88, 140.94, 145.59, 156.44, 163.21; IR (KBr): 3353, 1660, 1596, 1541, 1480, 1232 cm^{-1}; HRESIMS *m/z* 697.3162 $(M + H)^+$, calcd for $C_{40}H_{45}N_2O_9$ 697.3124.

Macrocyclic isobutenyl bis(amide–aryl ether) (**4c**, *o*-, *n* = 3).

This compound was obtained as a colorless solid, yield 32%, mp 137.0–138.1 °C; ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 6H, C*H*$_3$–Ar), 3.47–3.50 (m, 8H, –O–CH_2–), 3.58 (t, *J* = 5.2 Hz, 4H, –O–CH_2–), 3.87 (t, J = 5.2 Hz, 4H, –O–CH_2–), 4.30 (t, J = 4.9 Hz, 4H, –O–CH_2–), 4.81 (s, 4H, –CH_2–), 5.44 (s, 2H, CH_2=), 6.66 (d, J = 8.3 Hz, 2H, Ar), 6.77 (d, J = 8.4 Hz, 2H, Ar), 7.01 (d, J = 8.3 Hz, 2H, Ar), 7.14 (t, J = 7.5 Hz, 2H, Ar), 7.46 (t, J = 7.7 Hz, 2H, Ar), 8.27 (d, J = 7.8 Hz, 2H, Ar), 8.36 (s, 2H, Ar), 10.25 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 20.98, 69.03, 69.10, 69.36, 70.66, 70.81, 111.84, 113.79, 116.27, 121.93, 122.18, 123.08, 124.16, 128.06, 130.91, 132.45, 132.89, 140.58, 145.64, 156.47, 163.21; IR (KBr): 3359, 1659, 1596, 1540, 1480, 1235 cm^{-1}; HRESIMS m/z 741.3393 $(M + H)^+$, calcd for $C_{42}H_{49}N_2O_{10}$ 741.3387.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4d**, *m*-, *n* = 1).

This compound was obtained as a colorless solid, yield 44%, mp 156.3–157.0 °C; ^{1}H NMR ($CDCl_3$): δ 2.33 (s, 6H, C*H*$_3$–Ar), 3.72 (s, 4H, –O–CH_2–), 3.82 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.13 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.71 (s, 4H, –CH_2–), 5.43 (s, 2H, CH_2=), 6.80 (d, *J* = 8.4 Hz, 2H, Ar), 6.83 (d, *J* = 8.4 Hz, 2H, Ar), 7.02 (d, *J* = 8.0 Hz, 2H, Ar), 7.22 (t, *J* = 8.1 Hz, 2H, Ar), 7.29 (s, 2H, Ar), 7.32 (d, *J* = 7.8 Hz, 2H, Ar), 8.23 (s, 2H, Ar), 8.40 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.05, 67.72, 69.82, 70.17, 71.10, 112.13, 112.83, 116.80, 118.36, 119.30, 120.97, 124.24, 127.94, 129.81, 131.70, 136.57, 139.95, 145.03, 159.00, 165.17; IR (KBr): 3437, 1671, 1584, 1537, 1475, 1254 cm^{-1}; HRESIMS *m/z* 653.2910 $(M + H)^+$, calcd for $C_{38}H_{41}N_2O_8$ 653.2863.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4e**, *m*-, *n* = 2).

This compound was obtained as a colorless solid, yield 37%, mp 134.5–135.3 °C; ^{1}H NMR ($CDCl_3$): δ 2.32 (s, 6H, C*H*$_3$–Ar), 3.62–3.70 (m, 8H, –O–CH_2–), 3.80 (t, *J* = 4.8 Hz, 4H, –O–CH_2–), 4.10 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.71 (s, 4H, –CH_2–), 5.43 (s, 2H, CH_2=), 6.79 (d, *J* = 8.2 Hz, 2H, Ar), 6.82 (d, *J* = 8.3 Hz, 2H, Ar), 7.01 (d, *J* = 8.2 Hz, 2H, Ar), 7.22 (t, *J* = 8.2 Hz, 2H, Ar), 7.30–7.37 (m, 4H, Ar), 8.29 (s, 2H, Ar), 8.44 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.04, 67.69, 69.61, 70.03, 70.74, 70.87, 112.01, 112.92, 116.89, 118.29, 119.06, 120.94, 124.23, 127.89, 129.79, 131.63, 136.54, 139.92, 144.99, 159.06, 165.07; IR (KBr): 3432, 1674, 1593, 1532, 1481, 1281 cm^{-1}; HRESIMS *m/z* 697.3149 $(M + H)^+$, calcd for $C_{40}H_{45}N_2O_9$ 697.3124.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4f**, *m*-, *n* = 3).

This compound was obtained as a colorless solid, yield 26%, mp 104.7–105.2 °C; ^{1}H NMR ($CDCl_3$): δ 2.32 (s, 6H, C*H*$_3$–Ar), 3.62 (s, 4H, –O–CH_2–), 3.63–3.67 (m, 8H, –O–CH_2–), 3.79 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.10 (t, *J* = 4.6 Hz, 4H, –O–CH_2–), 4.72 (s, 4H, –CH_2–), 5.43 (s, 2H, CH_2=), 6.79–6.81 (m, 4H, Ar), 7.01 (d, *J* = 8.0 Hz, 2H, Ar), 7.23 (t, *J* = 8.4 Hz, 2H, Ar), 7.32–7.35 (m, 4H, Ar), 8.27 (s, 2H, Ar), 8.43 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.03, 67.62, 69.51, 69.89, 70.61, 70.65, 70.88, 111.90, 112.92, 116.88, 118.15, 119.06, 120.94, 124.23, 127.85, 129.80, 131.58, 136.49, 139.83, 144.96, 159.03, 164.98; IR (KBr): 3428, 1656, 1586, 1537, 1481, 1287 cm^{-1}; HRESIMS *m/z* 741.3382 $(M + H)^+$, calcd for $C_{42}H_{49}N_2O_{10}$ 741.3387.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4g**, *p*-, *n* = 1).

This compound was obtained as a colorless solid, yield 49%, mp 193.2–194.7 °C; ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 6H, C*H*$_3$–Ar), 3.75 (s, 4H, –O–CH_2–), 3.91 (t, *J* = 4.6 Hz, 4H, –O–CH_2–), 4.18 (t, *J* = 4.6 Hz, 4H, –O–CH_2–), 4.70 (s, 4H, –CH_2–), 5.44 (s, 2H, CH_2=), 6.79 (d, *J* = 8.4 Hz, 2H, Ar), 6.85 (d, *J* = 8.4 Hz, 2H, Ar), 7.00 (d, *J* = 8.9 Hz, 4H, Ar), 7.85 (d, *J* = 8.9 Hz, 4H, Ar), 8.39 (s, 2H, Ar), 8.51 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.04, 67.65, 69.29, 69.47, 70.93, 111.26, 114.31, 114.61, 120.66, 123.83, 127.47, 127.91, 128.70, 131.54, 139.40, 144.75, 161.79, 164.48; IR (KBr): 3438, 1663, 1605, 1540, 1512, 1481, 1254 cm^{-1}; HRESIMS *m/z* 653.2884 $(M + H)^+$, calcd for $C_{38}H_{41}N_2O_8$ 653.2863.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4h**, *p*-, *n* = 2).

This compound was obtained as a colorless solid, yield 35%, mp 206.0–210.2 °C; ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 6H, C*H*$_3$–Ar), 3.69–3.74 (m, 8H, –O–CH_2–), 3.89 (t, *J* = 4.9 Hz, 4H, –O–CH_2–), 4.15 (t, *J* = 4.9 Hz, 4H, –O–CH_2–), 4.71 (s, 4H, –CH_2–), 5.45 (s, 2H, CH_2=), 6.80 (d, *J* = 8.3 Hz, 2H, Ar), 6.85 (d, *J* = 8.3 Hz, 2H, Ar), 6.96 (d, *J* = 8.4 Hz, 4H, Ar), 7.82 (d, *J* = 8.4 Hz, 4H, Ar), 8.38 (s, 2H, Ar), 8.48 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.06, 67.78, 69.50, 69.66, 70.84, 70.92, 111.59, 114.64, 115.28, 120.80, 123.90, 127.48, 128.00, 128.69, 131.64, 139.61, 144.81, 161.74, 164.61; IR (KBr): 3435, 1662, 1606, 1540, 1511, 1482, 1254 cm^{-1}; HRESIMS *m/z* 697.3144 $(M + H)^+$, calcd for $C_{40}H_{45}N_2O_9$ 697.3124.

Macrocyclic Isobutenyl Bis(amide–aryl ether) (**4i**, *p*-, *n* = 3).

This compound was obtained as a colorless solid, yield 35%, mp 179.0–180.0 °C; ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 6H, C*H*$_3$–Ar), 3.66 (s, 4H, –O–CH_2–), 3.67–3.69 (m, 4H, –O–CH_2–), 3.62–3.70 (m, 4H, –O–CH_2–), 3.87 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.14 (t, *J* = 4.7 Hz, 4H, –O–CH_2–), 4.72 (s, 4H, –CH_2–), 5.46 (s, 2H, CH_2=), 6.82 (d, *J* = 8.4 Hz, 2H, Ar), 6.85 (d, *J* = 8.4 Hz, 2H, Ar), 6.93 (d, *J* = 8.8 Hz, 2H, Ar), 7.79 (d, *J* = 8.9 Hz, 2H, Ar), 8.38 (s, 2H, Ar), 8.47 (br s, 2H, –NH–); ^{13}C NMR ($CDCl_3$): δ 21.07, 67.73, 69.54, 69.78, 70.74, 70.79, 70.94, 111.78, 114.68, 119.71, 120.77, 123.91, 127.42, 128.10, 128.64, 128.74, 131.71, 144.83, 161.72, 164.63; IR (KBr): 3431, 1654, 1605, 1540, 1513, 1252 cm^{-1}; HRESIMS *m/z* 741.3352 $(M + H)^+$, calcd for $C_{42}H_{49}N_2O_{10}$ 741.3387.

General Procedure for Preparation of **5a–c** by Thermal Reaction of **4a–c**.

Typical Procedure **4a**.

Compound **4a** (0.06 g, 0.092 mmol) was heated at 210 °C for 2 days under vacuum. The crude mixture was purified by silica gel chromatography (eluent: 2:1 chloroform:ethylacetate) to give **5a**.

Macrocyclic Bis(benzoxazole) (**5a**).

This compound was obtained as acolorless solid, yield 20%, mp 227.0–228.5 °C; ^{1}H NMR ($CDCl_3$): δ 2.40 (s, 6H, C*H*$_3$–Ar), 3.70 (s, 4H, –CH_2–), 3.71 (s, 4H, –O–CH_2–), 3.81 (t, *J* = 4.4 Hz, 4H, –O–CH_2–), 4.19 (t, *J* = 4.3 Hz, 4H, –O–CH_2–), 5.00 (s, 2H,

CH_2=), 6.88 (s, 2H, Ar), 7.00 (d, J = 8.3 Hz, 2H, Ar), 7.07 (t, J = 7.6 Hz, 2H, Ar), 7.40 (s, 2H, Ar), 7.45 (dt, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 2H, Ar), 8.11 (dd, J_1 = 7.7 Hz, J_2 = 1.7 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.49, 36.15, 69.02, 69.70, 70.86, 113.11, 114.62, 116.99, 117.62, 120.99, 121.87, 126.46, 131.64, 132.53, 134.16, 141.50, 144.82, 148.54, 157.53, 162.70; IR (KBr): 1610, 1500, 1258 cm^{-1}; HRESIMS *m/z* 617.2699 $(M + H)^+$, calcd for $C_{38}H_{37}N_2O_6$ 617.2651.

Macrocyclic Bis(benzoxazole) (**5b**).

This compound was obtained as a colorless solid, yield 38%, mp 146.1–146.9 °C; ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 6H, C*H*$_3$–Ar), 3.43–3.45 (m, 4H, –O–CH_2–), 3.49–3.50 (m, 4H, –O–CH_2–), 3.70 (s, 4H, –CH_2–), 3.78 (t, J = 4.7 Hz, 4H, –O–CH_2–), 4.18 (t, J = 4.6 Hz, 4H, –O–CH_2–), 5.09 (s, 2H, CH_2=), 6.92 (s, 2H, Ar), 6.98 (d, J = 8.3 Hz, 2H, Ar), 7.05 (t, J = 7.8 Hz, 2H, Ar), 7.40 (s, 2H, Ar), 7.43 (t, J = 7.7 Hz, 2H, Ar), 8.03 (dd, J_1 = 7.7 Hz, J_2 = 1.6 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.44, 36.14, 68.76, 69.48, 70.26, 70.91, 113.16, 114.85, 116.93, 117.69, 120.88, 121.92, 126.55, 128.55, 129.53, 131.45, 132.43, 134.02, 141.71, 144.69, 148.17, 157.52, 162.25; IR (KBr): 1602, 1582, 1533, 1478, 1449, 1266 cm^{-1}; HRESIMS *m/z* 661.2907 $(M + H)^+$, calcd for $C_{40}H_{41}N_2O_7$ 661.2913.

Macrocyclic Bis(benzoxazole) (**5c**).

This compound was obtained as a colorless solid, yield 16%, mp 46.6–48.0 °C; ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 6H, C*H*$_3$–Ar), 3.43 (s, 4H, –CH_2–), 3.48 (t, J = 4.9 Hz, 4H, –O–CH_2–), 3.59 (t, J = 4.9 Hz, 4H, –O–CH_2–), 3.68 (s, 4H, –CH_2–), 3.81 (t, J = 5.1 Hz, 4H, –O–CH_2–), 4.20 (t, J = 4.9 Hz, 4H, –O–CH_2–), 5.07 (s, 2H, CH_2=), 6.94 (s, 2H, Ar), 6.99 (d, J = 8.3 Hz, 2H, Ar), 7.02 (t, J = 7.5 Hz, 2H, Ar), 7.39 (s, 2H, Ar), 7.41 (dt, J_1 = 7.9 Hz, J_2 = 1.7 Hz, 2H, Ar), 7.98 (dd, J_1 = 7.8 Hz, J_2 = 1.7 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.46, 36.25, 68.82, 69.58, 70.52, 70.93, 113.36, 114.54, 116.90, 117.75, 120.91, 121.93, 126.62, 131.32, 132.39, 134.00, 141.78, 145.00, 148.05, 157.55, 162.06; IR (KBr): 1602, 1583, 1538, 1480, 1451 cm^{-1}; HRESIMS *m/z* 705.3160 $(M + H)^+$, calcd for $C_{42}H_{43}N_2O_8$ 705.3176.

General Procedure for Preparation of **5d–i** by Thermal reaction of **4d–i**.

Typical Procedure **4d**.

Compound **4d** (0.06 g, 0.092 mmol) was heated at 240 °C for 5 hours under vacuum. The crude mixture was purified by gel permeation chromatography (GPC, eluent: chloroform) to obtain a mixture of **5d** and **6d**, and the product ratio was determined by ^{1}H NMR spectrum. Then, the mixture was purified by silica gel chromatography (eluent: 4:1 chloroform:ethyl acetate) to give **5d**.

Macrocyclic Bis(benzoxazole) (**5d**).

This compound was obtained as a colorless solid, yield 72%, mp 186.9–187.9 °C; ^{1}H NMR ($CDCl_3$): δ 2.44 (s, 6H, C*H*$_3$–Ar), 3.63 (s, 4H, –CH_2–), 3.82 (s, 4H, –CH_2O–), 3.92 (t, J = 4.8 Hz, 4H, –O–CH_2–), 4.15 (t, J = 4.8 Hz, 4H, –O–CH_2–), 5.15 (s, 2H, CH_2=), 6.93 (s, 2H, Ar), 7.00 (d, J = 7.8 Hz, 2H, Ar), 7.26 (t, J = 7.8 Hz, 2H, Ar), 7.32 (s, 2H, Ar), 7.44–7.47 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.53, 36.02, 67.64, 69.71, 71.16, 112.31, 114.76, 117.78, 118.34, 119.98, 121.86, 126.57, 128.15, 129.70, 134.23, 141.91, 145.06, 147.89, 158.84, 162.44; IR (KBr): 1587, 1556, 1487, 1452, 1289 cm^{-1}; HRESIMS *m/z* 617.2661 $(M + H)^+$, calcd for $C_{38}H_{37}N_2O_6$ 617.2651.

Macrocyclic Bis(benzoxazole) (**5e**).

This compound was obtained as a colorless solid, yield 71%, mp 143.5–144.5 °C; ^{1}H NMR ($CDCl_3$): δ 2.43 (s, 6H, C*H*$_3$–Ar), 3.62 (s, 4H, –CH_2–), 3.77 (m, 8H, –CH_2O–), 3.93 (t, J = 4.7 Hz, 4H, –O–CH_2–), 4.10 (t, J = 4.9 Hz, 4H, –O–CH_2–), 5.18 (s, 2H, CH_2=), 6.92 (s, 2H, Ar), 6.97 (d, J = 7.9 Hz, 2H, Ar), 7.21 (t, J = 7.9 Hz, 2H, Ar), 7.31 (s, 2H, Ar), 7.33–7.38 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.54, 35.89, 67.75, 69.73, 70.80, 71.08, 111.89, 114.99, 117.77, 118.69, 119.80, 121.87, 126.50, 128.09, 129.66, 134.23, 141.86, 145.08, 147.89, 158.85, 162.50; IR (KBr): 1588, 1554, 1484, 1232 cm^{-1}; HRESIMS *m/z* 661.2935 $(M + H)^+$, calcd for $C_{40}H_{41}N_2O_7$ 661.2913.

Macrocyclic Bis(benzoxazole) (**5f**).

This compound was obtained as a colorless solid, yield 80%, mp 102.5–104.0 °C; ^{1}H NMR ($CDCl_3$): δ 2.42 (s, 6H, C*H*$_3$–Ar), 3.61 (s, 4H, –CH_2–), 3.72 (s, 4H, –CH_2O–), 3.75–3.77 (m, 8H, –CH_2O–), 3.91 (t, J = 4.9 Hz, 4H, –O–CH_2–), 4.11 (t, J = 5.0 Hz, 4H, –O–CH_2–), 5.18 (s, 2H, CH_2=), 6.93 (s, 2H, Ar), 6.95 (d, J = 8.2 Hz, 2H, Ar), 7.19 (t, J = 8.0 Hz, 2H, Ar), 7.32 (d, J = 7.7 Hz, 2H, Ar), 7.34 (d, J = 7.5 Hz, 2H, Ar) , 7.35 (s, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.51, 35.85, 67.63, 69.69, 70.79, 70.89, 70.93, 112.05, 114.99, 117.75, 118.52, 119.75, 121.88, 126.51, 128.01, 129.66, 134.23, 141.83, 145.08, 147.87, 158.73, 162.52; IR (KBr): 1585, 1553, 1486, 1455 cm^{-1}; HRESIMS *m/z* 705.3179 $(M + H)^+$, calcd for $C_{42}H_{43}N_2O_8$ 705.3176.

Macrocyclic Bis(benzoxazole) (**5g**).

This compound was obtained as a colorless solid, yield 65%, mp 219.5–221.7 °C; ^{1}H NMR ($CDCl_3$): δ 2.39 (s, 6H, C*H*$_3$–Ar), 3.70 (s, 4H, –CH_2–), 3.79 (s, 4H, –O–CH_2–), 3.90 (t, J = 4.6 Hz, 4H, –O–CH_2–), 4.08 (t, J = 4.5 Hz, 4H, –O–CH_2–), 5.04 (s, 2H, CH_2=), 6.75 (d, J = 8.9 Hz, 4H, Ar), 6.87 (s, 2H, Ar), 7.24 (s, 2H, Ar), 7.87 (d, J = 8.7 Hz, 4H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.47, 37.32, 67.72, 69.53, 71.18, 114.65, 114.81, 117.47, 119.79, 121.76, 126.31, 128.92, 129.25, 133.93, 142.00, 144.70, 147.66, 161.18, 162.91; IR (KBr): 1610, 1500, 1258 cm^{-1}; HRESIMS *m/z* 617.2567 $(M + H)^+$, calcd for $C_{38}H_{37}N_2O_6$ 617.2651.

Macrocyclic Bis(benzoxazole) (**5h**).

This compound was obtained as a colorless solid, yield 61%, mp 248.2–248.9 °C; ^{1}H NMR ($CDCl_3$): δ 2.40 (s, 6H, CH_3–Ar), 3.67 (s, 4H, –CH_2–), 3.94 (s, 4H, –CH_2O–), 5.05 (s, 2H, CH_2=), 6.95 (s, 2H, Ar), 7.01–7.04 (m, 4H, Ar), 7.43–7.45 (m, 4H, Ar), 7.96 (d, J = 6.3 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.08, 67.80, 69.52, 69.68, 70.86, 70.94, 111.61, 114.66, 115.04, 115.29, 120.82, 123.93, 127.50, 128.02, 128.71, 131.66, 139.64, 144.84, 161.76, 164.63; IR (KBr): 1611, 1500, 1258 cm^{-1}; HRESIMS *m/z* 661.2908 $(M + H)^+$, calcd for $C_{40}H_{41}N_2O_7$ 661.2913.

Macrocyclic Bis(benzoxazole) (**5i**).

This compound was obtained as a colorless solid, yield 72%, mp 169.4–171.8 °C; ^{1}H NMR ($CDCl_3$): δ 2.41 (s, 6H, C*H*$_3$–Ar), 3.65 (s, 4H, –CH_2–), 3.72 (s, 4H, –O–CH_2–), 3.74–3.77 (m, 8H, –O–CH_2–),3.92 (t, J = 5.2 Hz, 4H, –O–CH_2–), 4.07 (t, J = 5.0 Hz, 4H, –O–CH_2–), 5.11 (s, 2H, CH_2=), 6.72 (d, J = 8.9 Hz, 4H, Ar), 6.91 (s, 2H, Ar), 7.27 (s, 2H, Ar), 7.87 (d, J = 8.9 Hz, 4H, Ar); ^{13}C NMR ($CDCl_3$): δ 21.50, 36.64, 67.64, 69.63, 70.81, 70.95, 71.04, 114.58, 114.76, 117.46, 119.76, 121.78, 126.16, 128.81, 133.99, 142.06, 145.03, 147.73, 161.07, 162.82; IR (KBr): 1611,

1501, 1257 cm^{-1}; HRESIMS *m/z* 705.3201 $(M + H)^+$, calcd for $C_{42}H_{43}N_2O_8$ 705.3176.

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