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Rhodium(II) catalyzed intermolecular double C-alkylation: a method for the synthesis of tetraindoles and indolophanes

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ABSTRACT

Double C-alkylation of cyclic diazoamides or bis-diazoamides with indoles or bis-indoles has been achieved to synthesize tetraindole derivatives using rhodium(II) acetate as a catalyst under mild reaction conditions with complete regioselectivity. The intermolecular double C-alkylation reaction strategy was successfully applied to synthesize indolophanes in moderate yield with excellent regiocontrol. The structure and stereochemistry of macrocycles were unequivocally confirmed with the help of single-crystal X-ray structure analyses.

1. Introduction

Plethora of reports are available, in which 'rhodium(II) catalysts' were highly selective for transformations, such as cyclopropanation, insertion, and ylide formation.[1] Interesting developments were seen in the past few years, particularly, the combination of transition metal-catalyzed cyclopropanation followed by other types of reactions in a single or cascade operation. Owing to the high strain of the three-membered ring system, there are many possible pathways for the ring opening of cyclopropanes. Cyclopropane rings bearing both electron-donating and -withdrawing groups are prone to undergo ring opening[2] reactions. The reactions of metallo-carbenoids with furan,[3] pyrrole[4] or indole[4] resulted in an initial cyclopropanation followed by a consecutive ring opening process. Similarly, cyclopropanation of other heterocycles including activated quinolines, isoquinolines,[5] and benzopyrylium triflates,[6] followed by the ring enlargement reaction was also reported. Many indoline alkaloids[7] were synthesized via cyclopropanation followed by ring opening strategy. The rhodium-catalyzed intramolecular reactions of pyrrolyl and indolyl diazoketones generally resulted[8] in the alkylation products via cyclopropanation. Conversely, the inter- as well as intramolecular reactions of diazo compounds with indole in the presence of copper catalysts afforded the corresponding cyclopropanation[5,9] across the indole 2,3-double bond. Our recent report indicates that the reactions of metallo-carbenoids derived from diazoamides **1** with heteroaromatic systems, such as benzofuran and benzothiophene afforded[10] the cyclopropanation products without any ring opening. However, reaction of cyclic diazoamide **1** (R^1=Me) with *N*-benzylindole **2** (R^2=Bn) in the presence of $Rh_2(OAc)_4$ afforded the corresponding 3-alkylated product[11] **5** in quantitative yields with the complete regioselectivity (Scheme 1). This process reveals that the formation of product **5** might be produced via the corresponding spirocyclopropanes **3** and followed by ring opening to zwitterions **4** as intermediate in the presence of copper or rhodium catalyst.

The design and synthesis of macrocycles containing aromatic/heteroaromatic ring systems are an intriguing branch of organic and supramolecular chemistry.[12,13] However, aromatic units present in the cyclophanes are mostly carbocyclic rings, such as benzene or naphthalene derivatives. Our enticement in developing a new synthetic strategies[14] using diazocarbonyl compounds encouraged us to investigate the application of the cyclopropane/ring opening methodology for the synthesis of indolophanes (Scheme 2). We herein report the intermolecular double C-alkylation reactions of cyclic diazoamides **6** in the presence of $Rh_2(OAc)_4$ catalyst in a single synthetic step furnishing tetraindole derivatives (indolophanes) with excellent regiocontrol via cyclopropanation followed by ring opening process.

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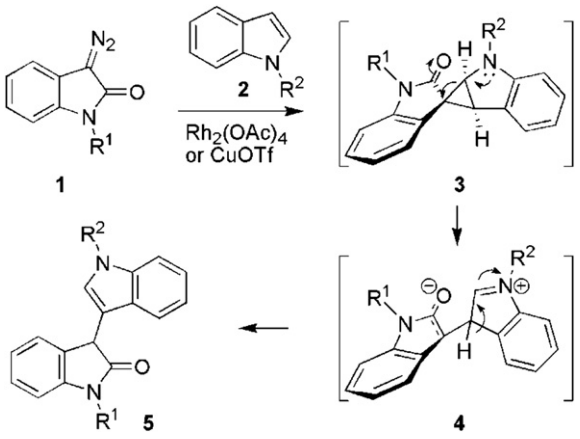
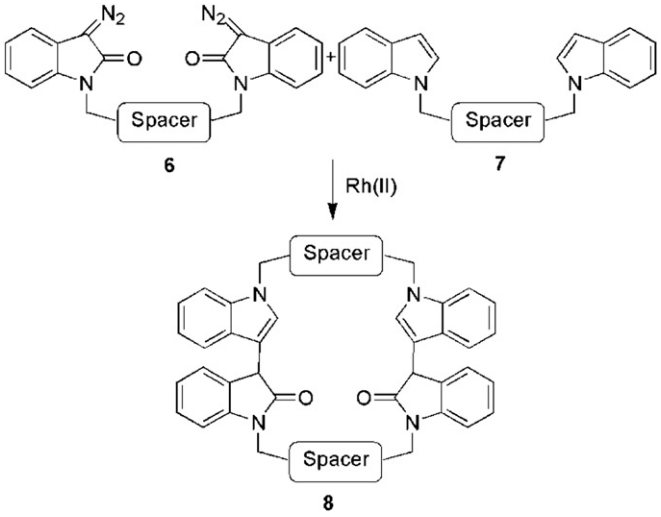


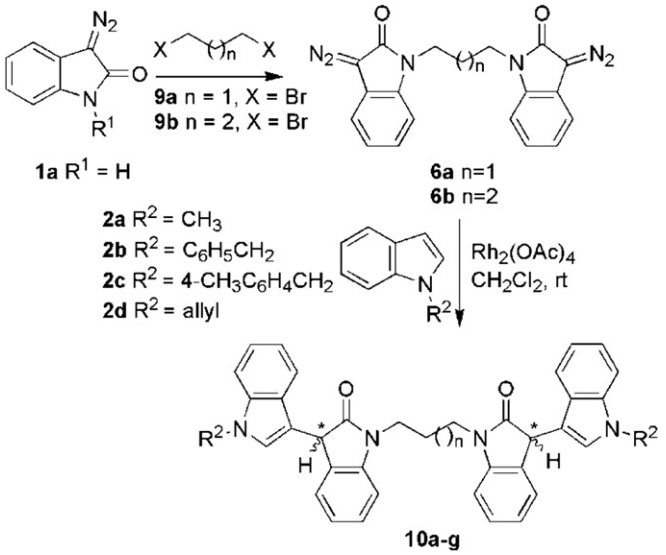
Scheme 1. Synthesis of 3-alkylated product **5**.



Scheme 2. Synthesis of indolophanes.

2. Results and discussion

With an objective to synthesize macrocycles utilizing rhodium(II) carbenoids, the selection of spacers was initially planned to interconnect the indole and diazoamide units that provide flexibility with respect to the ring size and the kind of structural units to be incorporated in the macrocycles. Based on our earlier research work[10,11,14b] on C-alkylation, we designed the double intermolecular C-alkylation reactions of bis-diazoamides **6** with indoles **2** or bis-indoles **7**. To demonstrate the double C-alkylation reaction, bis-diazoamides **6a**,**b** having aliphatic spacers were synthesized in good yield via N-alkylation of diazoamide **1a** with 1,3-dibromopropane (**9a**) or 1,4-dibromobutane (**9b**) using K_2CO_3/DMF. The double C-alkylation reaction of bis-diazoamides **6a**,**b** was investigated to determine the course of reaction. Treatment of **6a** with an excess amount of *N*-methylindole **2a** in the presence of 1 mol % of rhodium(II) acetate catalyst for 20 min at room temperature furnished the corresponding double *C*-alkylated product **10a** in 85% yield as a mixture of diastereomers in the ratio of 1:1 (Scheme 3). No mono-alkylated product was observed. The ^{1}H NMR spectrum of compound **10a** exhibited a characteristic signal at δ 4.81 and 4.85 as two separate singlets for two C*–H protons of each diastereomer. Similarly, reaction of bis-diazoamides **6a**,**b** with substituted indoles **2a**–**d** furnished the corresponding double-alkylated products **10b**–**g** as a diastereomeric mixture in very good yield and the results are delineated in Table 1.



Scheme 3. Synthesis of tetraindoles from cyclic diazoamides **6**.

Table 1
Reaction of bis-diazoamides **6** with substituted indoles **2**

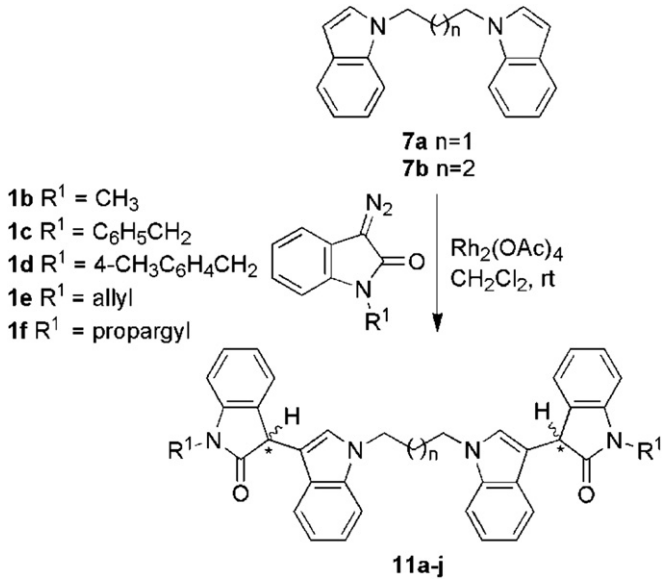
Entry	Product	*n*	R^2	Time (min)	Yield[a] %	dr[b]
1	**10a**	1	CH_3	20	85	59:41
2	**10b**	1	$C_6H_5CH_2$	20	93	56:44
3	**10c**	1	4-$CH_3C_6H_4CH_2$	30	82	58:42
4	**10d**	2	CH_3	15	89	65:35
5	**10e**	2	$C_6H_5CH_2$	15	89	61:39
6	**10f**	2	4-$CH_3C_6H_4CH_2$	15	77	59:41
7	**10g**	2	Allyl	20	80	60:40

[a] Isolated yield.
[b] Diastereomeric ratio based on the crude NMR spectra.

Having studied the reaction profile of bis-diazoamides, we next examined the double C-alkylation reaction of bis-indoles **7** with cyclic diazoamides **1b**–**f**. Thus, reaction of bis-indole **7a** with an excess amount of cyclic diazoamide **1b** in the presence of 1 mol % of rhodium(II) acetate catalyst at room temperature was performed. The reaction was completed in 25 min; concentrated and chromatographic purification of the reaction mixture delivered the tetraindole derivative **11a** as a mixture of diastereomers in quantitative yields (Scheme 4). The ^{1}H NMR spectrum of product **11a** exhibited a characteristic signal at δ 4.87 as a singlet for two C*–H protons, which indicates the presence of symmetry.

The NMR spectrum showed the complete symmetry for other protons as well as carbons because the stereocenters present in diastereomers are well separated. Thus, the diastereomeric ratio could not be determined. Spectroscopic analyses confirmed the double C-alkylation reaction of bis-indoles with complete regioselectivity. Similarly, the reaction of bis-indoles **7a**,**b** with substituted cyclic diazoamides **1b**–**f** furnished the corresponding double-alkylated products **11b**–**j** as a mixture of diastereomers in quantitative yield and the results are delineated in Table 2.

Next, double alkylation reactions of bis-indoles **7** having aromatic spacers were planned to furnish tetraindole derivatives. Reaction of bis-indole containing aromatic spacer **7c** with cyclic diazoamide **1b** afforded the alkylated product **12a** as a mixture of diastereomers (Scheme 5). However, ^{1}H NMR spectrum of product **12a** exhibited a characteristic singlet resonance at δ 4.86 for two



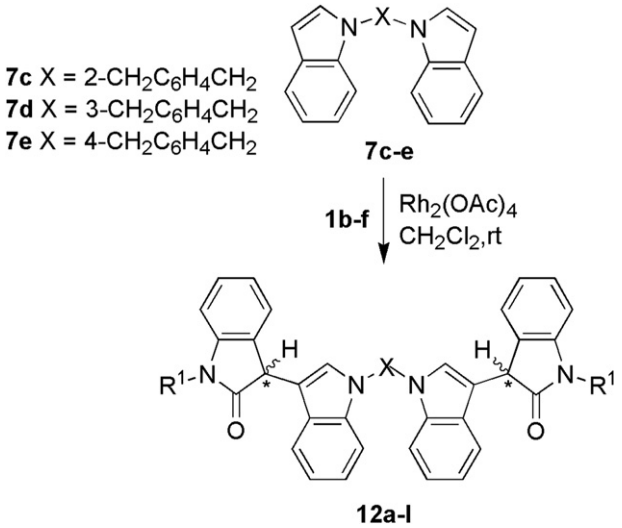
Scheme 4. Synthesis of tetraindoles from bis-indoles **7a**,**b**.

Table 2
Reaction of bis-indoles **7** having aliphatic spacers

Entry	Product	*n*	R^1	Time (min)	Yield[a] %
1	**11a**	1	CH_3	25	98
2	**11b**	1	$C_6H_5CH_2$	20	98
3	**11c**	1	4-$CH_3C_6H_4CH_2$	20	95
4	**11d**	1	Allyl	25	97
5	**11e**	1	Propargyl	25	95
6	**11f**	2	CH_3	25	97
7	**11g**	2	$C_6H_5CH_2$	20	98
8	**11h**	2	4-$CH_3C_6H_4CH_2$	20	96
9	**11i**	2	Allyl	25	95
10	**11j**	2	Propargyl	25	94

[a] Isolated yield.

C*–H protons indicating the presence of symmetry and the diastereomeric ratio could not be determined. In order to generalize the above reaction, a number of double-alkylated products **12b**–**l** was obtained in quantitative yields with the complete regioselectivity (Table 3) as described above. All these reactions were completed within 8–12 min.



Scheme 5. Synthesis of tetraindoles from bis-indoles **7c**–**e**.

Table 3
Reaction of bis-indoles **7** having aromatic spacers

Entry	Product	X	R^1	Time (min)	Yield[a] %
1	**12a**	2-$CH_2C_6H_4CH_2$	CH_3	10	97
2	**12b**	2-$CH_2C_6H_4CH_2$	$C_6H_5CH_2$	12	96
3	**12c**	2-$CH_2C_6H_4CH_2$	4-CH_3 $C_6H_4CH_2$	10	96
4	**12d**	2-$CH_2C_6H_4CH_2$	Allyl	10	95
5	**12e**	2-$CH_2C_6H_4CH_2$	Propargyl	10	94
6	**12f**	3-$CH_2C_6H_4CH_2$	CH_3	8	97
7	**12g**	3-$CH_2C_6H_4CH_2$	$C_6H_5CH_2$	10	96
8	**12h**	3-$CH_2C_6H_4CH_2$	4-CH_3 $C_6H_4CH_2$	10	97
9	**12i**	3-$CH_2C_6H_4CH_2$	Propargyl	10	95
10	**12j**	4-$CH_2C_6H_4CH_2$	$C_6H_5CH_2$	12	95
11	**12k**	4-$CH_2C_6H_4CH_2$	4-CH_3 $C_6H_4CH_2$	10	94
12	**12l**	4-$CH_2C_6H_4CH_2$	Allyl	10	94

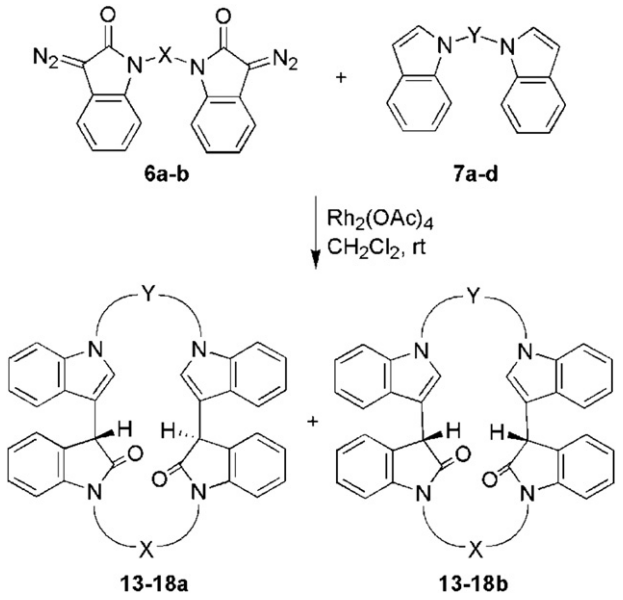
[a] Isolated yield.

The reaction was then extended to include various bis-diazoamides/bis-indoles combinations; speculation was made that if bis-indole moieties **7** were used in the double C-alkylation reaction of bis-diazoamides **6** then the resultant double *C*-alkylated product should be an interesting macrocyclic compound (Scheme 2). This will provide a new methodology for the indolophane synthesis using rhodium metal catalyst.

Macrocyclic compounds are important in modern synthetic organic chemistry in view of the fact that a large number of these compounds have shown potential biological applications and has emerged as one of the key areas in the field of molecular recognition.[15] There is currently considerable interest in the properties and applications of cyclophanes[16] and more commonly in the control of molecular architecture and crystal engineering. There is also growing interest in the development of cyclophanes as hosts for ionic guests[17] and molecular recognition as synthetic receptors.[18] For the synthesis of large ring macrocyclic lactones, catalytic metal carbene transformation emerged as an exciting tool and has been applied[19,20] to the macrocyclization process.

For the successful macrocyclization by means of intermolecular double C-alkylation reactions, 1 equiv of bis-indole **7a** was allowed to react with 1.1 equiv of bis-diazoamide **6a** under an argon atmosphere in the presence of 1 mol % of rhodium(II) acetate catalyst. As observed in double C-alkylation reactions above, the reaction was completed within 30 min. The chromatography purification of the reaction mixture afforded macrocyclic compounds **13a**,**b** as a mixture of diastereomers in moderate yield with an excellent regiocontrol (Scheme 6) and no other oligomers and mono-alkylated product were observed. The diastereomeric mixture was present in the ratio of 1:1 and separated by column chromatography. The ^{1}H NMR spectrum of product **13a** exhibited a characteristic singlet resonance at δ 4.87 for two CH protons. The ^{1}H NMR spectrum of product **13b** exhibited a characteristic singlet resonance at δ 5.02 for two CH protons. The ^{13}C, DEPT-135, and DEPT-90 NMR spectra of compounds **13a** and **13b** showed peaks for four CH_2 carbons, ten CH carbons, and six quaternary carbons. The single-crystal X-ray analyses[21] of diastereomers **13a** (*anti*) and **13b** (*syn*) were also performed (Fig. 1). The crystal packing arrangement of **13a** and **13b** showed the presence of intermolecular C–H···O and C–H···π interactions.[22] The spectroscopic and X-ray analyses confirmed the proposed macrocyclic structures of **13a**,**b**. Similarly, reaction of bis-diazoamides **6a**,**b** with bis-indole **7b** furnished the respective double *C*-alkylated macrocyclic compounds **14a**,**b** and **15a**,**b** as a mixture of diastereomers with an excellent regiocontrol and the results are summarized in Table 4.

The reaction was further extended to bis-indoles and bis-diazoamides having aromatic spacers. Reaction of bis-diazoamide



Scheme 6. Synthesis of indolophanes.

6a and bis-indole **7c** was performed as described above to afford the macrocyclic compounds **16a**,**b** as a mixture of diastereomers. The stereochemistry of the diastereomer **16b** was unequivocally demonstrated by the single-crystal X-ray analysis[21] and found as *syn*-isomer (Fig. 2). The stereochemistry of the diastereomer **16a** was tentatively assigned as an *anti*-isomer. Similarly, reaction of bis-diazoamide **6a** with bis-indole **7d** yielded the corresponding macrocyclic compounds **17a**,**b** as a mixture of diastereomers. The stereochemistry of the diastereomer **17b** was unequivocally assigned by the single-crystal X-ray analysis[21] and found as *syn*-isomer (Fig. 2). Finally, we investigated the reaction of bis-diazoamide **6c**[23] with bis-indole **7c**, both containing aromatic spacers, under similar reaction conditions as described above. The chromatographic purification of the reaction mixture led to the interesting macrocycle **18** having aryl and heteroaryl units as a mixture of diastereomers. However, numerous attempts to separate the diastereomeric mixture by crystallization or chromatography failed.

3. Conclusions

In summary, the intermolecular double C-alkylation reactions were performed for the first time using rhodium(II) acetate as catalyst to furnish tetraindole derivatives with complete regioselectivity. This methodology using rhodium(II) catalyst was successfully extended to apply for the synthesis of indolophanes with excellent regiocontrol and forms a new approach for the synthesis of macrocycles. The structure and stereochemistry of macrocycles were unequivocally confirmed with the help of single-crystal X-ray structure analyses. The cavity of the macrocycles can be varied using the different spacers. Further studies with different spacers to change the size of the cavity of macrocycles and their supramolecular chemistry are in progress.

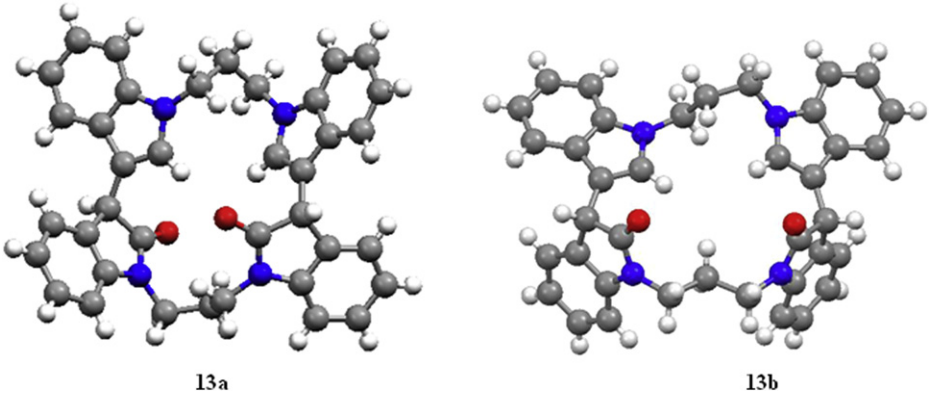


Fig. 1. X-ray structures of indolophanes **13a** and **13b** (solvent molecule was removed for clarity).

Table 4
Synthesis of macrocycles via double C-alkylation method **13**–**18**

Entry	Macrocycle	X	Y	Yield[a] %	dr[b]
1	**13**	$-(CH_2)_3-$	$-(CH_2)_3-$	50	58:42
2	**14**	$-(CH_2)_3-$	$-(CH_2)_4-$	52	53:47
3	**15**	$-(CH_2)_4-$	$-(CH_2)_4-$	55	51:49
4	**16**	$-(CH_2)_3-$	2-$CH_2C_6H_4CH_2$	63	27:73
5	**17**	$-(CH_2)_3-$	3-$CH_2C_6H_4CH_2$	54	36:64
6	**18**	3-$CH_2C_6H_4CH_2$	2-$CH_2C_6H_4CH_2$	50	56:44

[a] Isolated yield.
[b] Diastereomeric ratio based on the crude NMR spectra.

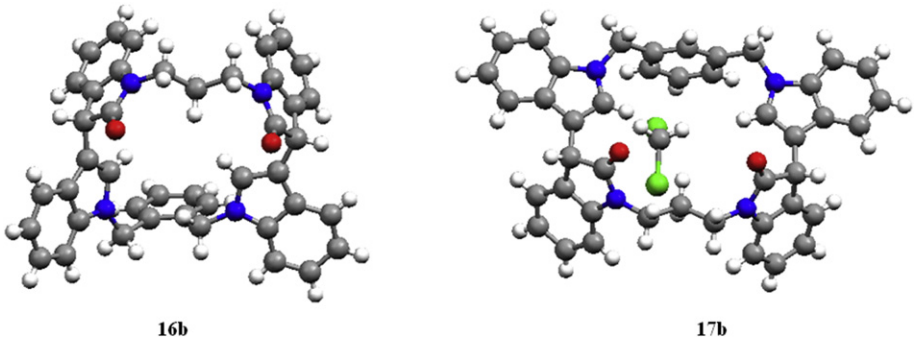


Fig. 2. X-ray structures of indolophanes **16b** (solvent molecule was removed for clarity) and **17b**.

4. Experimental section

4.1. General

Melting points are uncorrected. IR spectra were recorded using KBr pellets or in CH_2Cl_2. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on 200 MHz or 400 MHz using $CDCl_3$ in parts per million (δ) related to tetramethylsilane (δ=0.00) as an internal standard. The data are reported as follows; chemical shift in parts per million (ppm, δ units), multiplicity (br=broad, s=singlet, d=doublet, m=multiplet), spin–spin coupling J (hertz), and integration. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded at 50.3 MHz or 100 MHz in $CDCl_3$. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.7 ppm for $CDCl_3$. Carbon types were determined from ^{13}C NMR and DEPT experiments. Mass analyses were performed with an ionizing voltage of 70 eV or FD^+ method or by FAB technique and reported as m/z (relative intensity). Diffraction data for the compounds are collected on a diffractometer with graphite monochromatized Mo Kα radiation (λ=0.71703 Å) at room temperature using the program SMART[24] and processed by SAINT.[25] Absorption correction was applied by SADABS.[26] The structure was solved by direct methods and refined using full-matrix least-squares/difference Fourier techniques using SHELXL 97.[27] All the non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were located from the difference Fourier map or placed at idealized positions and refined as riding atoms with the relative isotropic parameters to which they are attached. All solvents were purified by distillation following standard procedures. Thin layer chromatography was performed on silica or alumina plates and components visualized by observation under iodine/UV light. Column chromatography was performed on silica gel (100–200 mesh). All air sensitive reactions were conducted in oven-dried glassware under a positive pressure of argon with magnetic stirring. Reagents were added via syringes through septa. Synthesis of substituted diazoamides[14d] **1**, bis-diazoamides[23,14d] **6**, bis-indoles[28] **7a**–**e** were prepared by using literature methods.

4.2. General procedure for the synthesis of compounds 10

To a stirred, degassed dichloromethane (25 mL) solution of bis-diazoamide **6** (1 mmol) and indole **2** (2.50 mmol) was added rhodium(II) acetate dimer (1 mol %) catalyst at 25 °C. After the reaction was completed (15–30 min, TLC monitoring), the reaction mixture concentrated in vacuum. The residue was purified by flash chromatography (SiO_2, hexane/EtOAc 55:45) to afford the corresponding product **10** as an inseparable mixture of diastereomers. NMR data provided for the major isomer only.

*4.2.1. 1,3-Bis[(1′-methyl-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl] propane (**10a**).* Brown solid (85%); IR (KBr) ν 3055, 2931, 1711, 1612, 1486, 1467, 1359, 1265, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.03–2.20 (m, 2H, CH_2), 3.68 (s, 6H, NCH_3), 3.88–3.90 (m, 4H, CH_2), 4.81 (s, 2H, CH), 6.80–7.03 (m, 8H, ArH), 7.14–7.25 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.29 (CH_2), 33.36 (NCH_3), 38.78 (CH_2), 44.84 (*C*H), 108.75 (=*C*H), 108.82 (=*C*H), 109.94 (*quat*-C), 110.05 (=*C*H), 119.91 (=*C*H), 122.54 (=*C*H), 123.21 (=*C*H), 125.61 (=*C*H), 127.43 (*quat*-C), 128.25 (=*C*H), 128.83 (=*C*H), 130.54 (*quat*-C), 137.98 (*quat*-C), 143.86 (*quat*-C), 177.17 (*quat*-C); HRMS (ESI) calcd for $C_{37}H_{32}N_4O_2Na$ [M^++Na] 587.2423, found 587.2433.

*4.2.2. 1,3-Bis[(1′-benzyl-1,3-dihydro-1′-[3,3′]biindolyl-2-on)-1-yl] propane (**10b**).* Light brown solid (93%); IR (KBr) ν 3055, 2927, 1713, 1713, 1611, 1487, 1465, 1358, 1265, 1087, 1022, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.16–2.25 (m, 2H, CH_2), 3.85–3.92 (m, 4H, CH_2), 4.83 (s, 2H, CH), 5.20–5.25 (m, 4H, NCH_2), 6.85 (q, 2H, J=6.8 Hz, ArH), 6.97–7.02 (m, 4H, ArH), 7.03 (d, 4H, J=6.4 Hz, ArH), 7.08–7.14 (m, 8H, ArH), 7.20–7.28 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.73 (CH_2), 38.19 (CH_2), 44.35 (*C*H), 50.11 (CH_2) 108.16 (=*C*H), 108.28 (=*C*H), 109.86 (*quat*-C), 110.0 (=*C*H), 119.55 (=*C*H), 119.72 (=*C*H), 122.18 (=*C*H), 122.66 (=*C*H), 125.06 (=*C*H), 126.87 (=*C*H), 127.10 (=*C*H), 127.27 (=*C*H), 127.63 (=*C*H), 128.27 (*quat*-C), 128.77 (=*C*H), 129.24 (*quat*-C), 137.05 (*quat*-C), 137.31 (*quat*-C), 143.23 (*quat*-C), 176.92 (*quat*-C); MS (ESI) m/z 739 [M^++Na]; Anal. Calcd (%) for $C_{49}H_{40}N_4O_2$ (716.31): C, 82.10; H, 5.62; N, 7.82. Found: C, 82.36; H, 5.73; N, 7.87.

*4.2.3. 1,3-Bis[(1′-(4-methylbenzyl)-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl]propane (**10c**).* Light pink color solid (82%); IR (KBr) ν 3055, 2925, 1710, 1611, 1486, 1465, 1356, 1264, 1179, 1086, 1020, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.26–2.32 (m, 8H), 3.85–3.91 (m, 4H, CH_2), 4.85 (s, 2H, CH), 5.13–5.20 (m, 4H, NCH_2), 6.84 (q, 2H, J=6.0 Hz, ArH), 6.98–7.03 (m, 10H, ArH), 7.06 (d, 4H, J=7.6 Hz, ArH), 7.01–7.14 (m, 4H, ArH), 7.19–7.25 (m, 6H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.81 (CH_3), 22.79 (CH_2), 31.67 (CH_2), 44.30 (*C*H), 49.92 (CH_2) 108.28 (=*C*H), 109.88 (*quat*-C), 110.06 (=*C*H), 119.55 (=*C*H), 119.69 (=*C*H), 122.15 (=*C*H), 122.70 (=*C*H), 125.12 (=*C*H), 126.97 (=*C*H), 127.17 (*quat*-C), 127.33 (=*C*H), 128.31 (*quat*-C), 129.33 (*quat*-C), 129.47 (=*C*H), 134.32 (=*C*H), 137.09 (*quat*-C), 137.34 (*quat*-C), 143.24 (*quat*-C), 176.07 (*quat*-C); MS (ESI) m/z (%) 745 (M+1, 14), 744 (M^+, 21), 639 (21), 523 (14), 231 (7), 105 (100); Anal. Calcd (%) for $C_{51}H_{44}N_4O_2$ (744.35): C, 82.23; H, 5.95; N, 7.52. Found: C, 82.04; H, 5.89; N, 7.64.

*4.2.4. 1,4-Bis[(1′-methyl-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl] butane (**10d**).* Light brownish solid (89%); IR (KBr) ν 3054, 2932, 1711, 1611, 1486, 1466, 1357, 1265, 1156, 1091, 1015, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.85 (s, 4H, CH_2), 3.71 (s, 6H, NCH_3), 3.80–3.86 (m, 4H, CH_2), 4.85 (s, 2H, CH), 6.88 (d, 2H, J=7.6 Hz, ArH), 6.93 (s, 2H, ArH), 6.97–7.02 (m, 4H, ArH), 7.17–7.28 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.85 (CH_2), 29.74 (NCH_3), 39.65 (CH_2), 44.38 (*C*H), 108.43 (=*C*H), 109.36 (=*C*H), 109.46 (=*C*H), 119.38 (=*C*H), 121.96 (=*C*H), 122.51 (=*C*H), 124.96 (=*C*H), 126.89 (*quat*-C), 127.73 (=*C*H), 128.22 (=*C*H), 129.38 (*quat*-C), 129.48 (*quat*-C), 137.40 (*quat*-C), 143.43 (*quat*-C), 176.60 (*quat*-C); MS (ESI) m/z (%) 601 [M^++Na]; Anal. Calcd (%) for $C_{38}H_{34}N_4O_2$ (578.21): C, 78.87; H, 5.92; N, 9.68. Found: C, 78.65; H, 5.86; N, 9.59.

*4.2.5. 1,4-Bis[(1′-benzyl-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl] butane (**10e**).* Brown solid (89%); IR (KBr) ν 3055, 2928, 1711, 1611, 1487, 1466, 1357, 1265, 1177, 1156, 1092, 1026, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.82–1.84 (m, 4H, CH_2), 3.77–3.85 (m, 4H, CH_2), 4.86 (s, 2H, CH), 5.17–5.23 (m, 4H, NCH_2), 6.88 (d, 2H, J=8.0 Hz, ArH), 6.96–7.02 (m, 6H, ArH), 7.05–7.14 (m, 6H, ArH), 7.18–7.29 (m, 14H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.89 (CH_2), 39.67 (CH_2), 44.45 (*C*H), 50.10 (CH_2) 108.48 (=*C*H), 110.0 (=*C*H), 110.14 (*quat*-C), 119.58 (=*C*H), 122.18 (=*C*H), 122.55 (=*C*H), 124.99 (=*C*H), 126.87 (=*C*H), 127.17 (=*C*H), 127.64 (=*C*H), 128.27 (=*C*H), 128.79 (=*C*H), 129.20 (*quat*-C), 129.27 (*quat*-C), 137.06 (*quat*-C), 137.36 (*quat*-C), 143.41 (*quat*-C), 176.49 (*quat*-C); MS (ESI) m/z 753 (M^++Na); Anal. Calcd (%) for $C_{50}H_{42}N_4O_2$ (730.33): C, 82.16; H, 5.79; N, 7.67. Found: C, 82.42; H, 5.72; N, 7.82.

*4.2.6. 1,4-Bis[(1′-(4-methylbenzyl)-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl]butane (**10f**).* Light brown solid (77%); IR (KBr) ν 3054, 2929, 1710, 1612, 1487, 1466, 1357, 1265, 1178, 1093, 1020, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.80–1.83 (m, 4H, CH_2), 2.29 (s, 6H, CH_3), 3.73–3.85 (m, 4H, CH_2), 4.79 (s, 2H, CH), 5.15–5.20 (m, 4H, NCH_2), 6.87–7.21 (m, 26H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.64 (CH_3), 24.43 (CH_2), 39.19 (CH_2), 43.93 (*C*H), 49.41 (CH_2) 107.95 (=*C*H), 109.51 (=*C*H), 119.12 (=*C*H), 121.61 (=*C*H), 121.96 (=*C*H),

124.51 (=*C*H), 126.52 (=*C*H), 126.71 (=*C*H), 127.82 (=*C*H), 128.81 (*quat*-C), 128.82 (*quat*-C), 129.03 (=CH), 133.81 (*quat*-C), 136.83 (*quat*-C), 136.86 (*quat*-C), 143.04 (*quat*-C), 176.13 (*quat*-C); MS (ESI) *m*/*z* 781.3 (M^++Na), 758.3 (M^+); Anal. Calcd (%) for $C_{52}H_{46}N_4O_2$ (758.36): C, 82.29; H, 6.11; N, 7.38. Found: C, 82.42; H, 6.04; N, 7.47.

*4.2.7. 1,4-Bis[(1′-allyl-1,3-dihydro-1′H-[3,3′]biindolyl-2-on)-1-yl]butane (**10g**).* Brown solid (80%); IR (KBr) *ν* 3055, 2926, 1711, 1611, 1487, 1466, 1356, 1263, 1178, 1156, 1092, 928, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.82–1.85 (m, 4H, CH_2), 3.81 (br s, 4H), 4.58–4.59 (m, 4H), 4.77 (s, 2H, CH), 5.01–5.15 (m, 4H, C=CH_2), 5.81–5.99 (m, 2H, allyl CH), 6.76 (d, 2H, *J*=8.1 Hz, ArH), 6.85–7.01 (m, 6H, ArH), 7.10–7.32 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 25.81 (*C*H_2), 40.13 (*C*H_2), 44.83 (*C*H), 49.33 (*C*H_2), 108.93 (=*C*H), 110.32 (=*C*H), 118.04 (=*C*H_2), 119.98 (=*C*H), 122.52 (=*C*H), 123.03 (=*C*H), 125.43 (=*C*H), 127.21 (=*C*H), 127.64 (*quat*-C), 128.76 (=*C*H), 129.83 (*quat*-C), 129.92 (*quat*-C), 133.91 (=*C*H), 137.32 (*quat*-C), 143.91 (*quat*-C), 177.06 (*quat*-C); HRMS (ESI) calcd for $C_{42}H_{38}N_4O_2Na$ [M^++Na] 653.2995, found 653.2984.

4.3. General procedure for the synthesis of compounds 11 and 12

To a stirred dichloromethane solution of bis-indole **7** (1.00 mmol) and diazoamide **1** (2.50 mmol) at 25 °C was added rhodium(II) acetate dimer (1 mol %) catalyst. The solvent was concentrated in vacuo. The residue was purified by flash chromatography (SiO_2, hexane/EtOAc 60:40) to afford the product **11** or **12** as an inseparable mixture of diastereomers.

*4.3.1. 1,3-Bis[(1′-methyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]propane (**11a**).* Colorless solid (98%); mp 121–123 °C; IR (KBr) *ν* 3054, 2927, 2855, 1713, 1612, 1492, 1468, 1373, 1347, 1265, 1173, 1125, 1087, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 2.35–2.39 (m, 2H, CH_2), 3.29 (s, 6H, NCH_3), 4.03 (t, 4H, *J*=6.8 Hz, NCH_2), 4.87 (s, 2H, CH), 6.91–6.94 (m, 4H, ArH), 7.00–7.03 (m, 4H, ArH), 7.11–7.20 (m, 6H, ArH), 7.26–7.34 (m, 4H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 26.51 (NCH_3), 29.74 (*C*H_2), 43.38 (N*C*H_2), 44.34 (*C*H), 108.12 (=*C*H), 109.56 (=*C*H), 110.01 (*quat*-C), 119.62 (=*C*H), 119.70 (=*C*H), 122.15 (=*C*H), 122.71 (=*C*H), 124.78 (=*C*H), 126.56 (=*C*H), 126.69 (*quat*-C), 128.24 (=*C*H), 129.19 (*quat*-C), 136.61 (*quat*-C), 144.26 (*quat*-C), 176.42 (*quat*-C); MS (ESI) *m*/*z* (%) 587 (M^++Na); Anal. Calcd (%) for $C_{37}H_{32}N_4O_2$ (564.25): C, 78.70; H, 5.71; N, 9.92. Found: C, 78.99; H, 5.87; N, 9.70.

*4.3.2. 1,3-Bis[(1′-benzyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]propane (**11b**).* Light yellow solid (98%); mp 115–117 °C; IR (KBr) *ν* 3045, 2925, 1710, 1611, 1486, 1465, 1348, 1178, 1010, 908, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.84 (s, 2H), 4.01–4.03 (m, 4H, NCH_2), 4.89–5.05 (m, 6H, NCH_2 and CH), 6.82 (d, 2H, *J*=8.0 Hz, ArH), 6.94–6.98 (m, 6H, ArH); 7.13–7.21 (m, 6H, ArH), 7.23–7.32 (m, 10H, ArH), 7.35 (d, 4H, *J*=6.8 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 27.77 (*C*H_2), 44.11 (*C*H_2), 44.54 (*C*H), 45.99 (*C*H_2), 109.13 (=*C*H), 109.58 (=*C*H), 109.71 (*quat*-C), 119.71 (=*C*H), 119.82 (=CH), 122.07 (=CH), 122.75 (=CH), 124.97 (=CH), 126.90 (=CH), 126.95 (=CH), 127.67 (*quat*-C), 127.71 (=*C*H), 128.14 (=*C*H), 128.82 (=*C*H), 129.22 (*quat*-C), 136.11 (*quat*-C), 136.72 (*quat*-C), 143.40 (*quat*-C), 176.58 (*quat*-C); MS (EI) *m*/*z* (%) 716 (M^+, 34), 715 (57), 493 (15), 403 (11), 351 (45), 272 (67), 231 (16), 130 (21), 91 (100); Anal. Calcd (%) for $C_{49}H_{40}N_4O_2$ (716.86): C, 82.10; H, 5.62; N, 7.82. Found: C, 82.34; H, 5.76; N, 7.69.

*4.3.3. 1,3-Bis[(1′-(4-methylbenzyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]propane (**11c**).* Brown solid (95%); mp 122–124 °C; IR (KBr) *ν* 3054, 2927, 1711, 1612, 1515, 1486, 1467, 1354, 1265, 1200, 1180, 1012, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 2.25 (s, 8H, CH_2 and $ArCH_3$), 3.94–4.09 (m, 4H, CH_2), 4.79–5.00 (m, 6H, NCH_2 and CH), 6.80 (d, 2H, *J*=7.6 Hz, ArH), 6.87–7.39 (m, 24H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.60 ($ArCH_3$), 30.56 (*C*H_2), 43.84 (*C*H_2), 44.31 (*C*H_2), 44.96 (*C*H), 109.63 (=*C*H), 110.09 (=*C*H), 110.58 (*quat*-C), 120.05 (=*C*H), 120.37 (=*C*H), 122.64 (=*C*H), 123.13 (=*C*H), 125.34 (=*C*H), 127.42 (=*C*H), 127.61 (*quat*-C), 128.12 (=*C*H), 128.60 (=*C*H), 129.67 (*quat*-C), 129.94 (=*C*H), 133.55 (*quat*-C), 137.17 (*quat*-C), 137.80 (*quat*-C), 143.94 (*quat*-C), 176.93 (*quat*-C); MS (EI) *m*/*z* (%) 744 (M^+, 34), 743 (49), 507 (19), 403 (16), 365 (34), 261 (67), 105 (100); Anal. Calcd (%) for $C_{51}H_{44}N_4O_2$ (744.35): C, 82.23; H, 5.95; N, 7.52. Found: C, 82.47; H, 6.12; N, 7.41.

*4.3.4. 1,3-Bis[(1′-allyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]propane (**11d**).* Brown solid (97%); mp 76–78 °C; IR (KBr) *ν* 3055, 2927, 1712, 1612, 1487, 1467, 1355, 1265, 1205, 738 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) *δ* 2.21 (br s, 2H), 3.88 (t, 4H, *J*=6.5 Hz, NCH_2), 4.35–4.38 (m, 4H, NCH_2), 4.86 (s, 2H, CH), 5.17–5.30 (m, 4H, C=CH_2), 5.76–5.94 (m, 2H, allyl CH), 6.86–7.05 (m, 8H, ArH), 7.09–7.29 (m, 10H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 30.41 (*C*H_2), 43.12 (*C*H_2), 43.82 (*C*H_2), 44.81 (*C*H), 109.54 (=*C*H), 110.11 (=*C*H), 110.58 (*quat*-C), 118.27 (=*C*H_2), 120.13 (=*C*H), 120.21 (=CH), 122.67 (=*C*H), 123.12 (=CH), 125.35 (=CH), 127.17 (=*C*H), 127.35 (=*C*H), 127.71 (*quat*-C), 128.60 (=CH), 129.65 (*quat*-C), 132.21 (=CH), 137.15 (*quat*-C), 143.97 (*quat*-C), 176.47 (*quat*-C); HRMS (ESI) calcd for $C_{41}H_{36}N_4O_2Na$ [M^++Na] 639.2738, found 639.2729.

*4.3.5. 1,3-Bis[(1′-(prop-2-ynyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]propane (**11e**).* Brown solid (95%); mp 161–163 °C; IR (KBr) *ν* 3285, 2929, 1715, 1611, 1487, 1466, 1351, 1164, 1010, 739 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) *δ* 2.34 (br s, 2H), 3.44 (s, 2H, CCH), 4.24–4.31 (m, 4H, CH_2), 4.60–4.70 (m, 4H, NCH_2), 5.16 (s, 2H, CH), 6.92–6.99 (m, 2H, ArH), 7.05–7.29 (m, 10H, ArH), 7.43–7.49 (m, 6H, ArH); ^{13}C NMR (100 MHz, DMSO-d_6) *δ* 28.91 (*C*H_2), 30.43 (*C*H_2), 42.97 (*C*H_2), 43.65 (*C*H), 74.34 (*C*H), 78.15 (*quat*-C), 109.18 (=*C*H), 109.29 (*quat*-C), 109.76 (=*C*H), 118.82 (=*C*H), 119.13 (=*C*H), 121.48 (=*C*H), 122.59 (=*C*H), 124.35 (=*C*H), 126.34 (*quat*-C), 127.58 (=*C*H), 127.94 (=CH), 129.18 (*quat*-C), 136.22 (*quat*-C), 142.12 (*quat*-C), 174.99 (*quat*-C); MS (ESI) *m*/*z* (%) 635 (M^++Na); Anal. Calcd (%) for $C_{41}H_{32}N_4O_2$ (612.25): C, 80.37; H, 5.26; N, 9.14. Found: C, 80.26; H, 5.33; N, 8.99.

*4.3.6. 1,4-Bis[(1′-methyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]butane (**11f**).* Colorless solid (97%); mp 168–170 °C; IR (KBr) *ν* 3055, 2928, 1713, 1612, 1492, 1469, 1371, 1347, 1265, 1160, 1087, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.81 (br s, 4H, CH_2), 3.28 (s, 6H, NCH_3), 3.99–4.00 (m, 4H, NCH_2), 4.84 (s, 2H, CH), 6.91 (d, *J*=6.0 Hz, 4H, ArH), 6.98–7.01 (m, 4H, ArH), 7.16 (q, 4H, *J*=7.6 Hz, ArH), 7.20–7.27 (m, 4H, ArH), 7.31 (t, 2H, *J*=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 26.49 (NCH_3), 27.74 (*C*H_2), 44.36 (*C*H), 45.97 (*C*H_2), 108.06 (=*C*H), 109.50 (=*C*H), 109.65 (*quat*-C), 119.45 (=*C*H), 119.64 (=*C*H), 122.0 (=*C*H), 122.66 (=*C*H), 124.80 (=*C*H), 126.64 (=*C*H), 126.68 (*quat*-C), 128.18 (=*C*H), 129.20 (*quat*-C), 136.63 (*quat*-C), 144.27 (*quat*-C), 176.40 (*quat*-C); MS (EI) *m*/*z* (%) 579 (M+1, 38), 578 (M^+, 94), 433 (13), 432 (25), 407 (11), 316 (20), 315 (16), 314 (32), 312 (18), 309 (10), 287 (28), 286 (100), 285 (28), 283 (18), 261 (90), 248 (38), 233 (31), 219 (36); HRMS (ESI) calcd for $C_{38}H_{34}N_4O_2Na$ [M^++Na] 601.2661, found 601.2661.

*4.3.7. 1,4-Bis[(1′-benzyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]butane (**11g**).* Light yellow solid (98%); mp 122–124 °C; IR (KBr) *ν* 3030, 2925, 1711, 1609, 1485, 1465, 1348, 1199, 1160, 1077, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.78–1.92 (m, 4H), 3.94 (br s, 4H, CH_2), 4.83–5.04 (m, 6H, NCH_2 and CH), 6.80 (d, 2H, *J*=7.6 Hz, ArH), 6.93–7.31 (m, 26H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 28.31 (*C*H_2), 44.70 (*C*H_2), 45.14 (*C*H), 46.52 (*C*H_2) 109.73 (=*C*H), 110.19 (=*C*H), 110.33 (*quat*-C), 120.02 (=*C*H), 120.38 (=*C*H), 122.74 (=*C*H), 123.3

(=CH), 125.65 (=CH), 127.57 (=CH), 128.32 (=CH), 128.76 (=CH), 129.41 (=CH), 129.83 (*quat*-C), 136.75 (*quat*-C), 137.28 (*quat*-C), 144.02 (*quat*-C), 177.10 (*quat*-C); MS (EI) *m/z* (%) 732 (M+2, 6), 731 (M+1, 26), 730 (M^+, 72), 639 (12), 286 (19), 247 (11), 223 (17), 222 (10), 170 (13), 91 (100); HRMS (ESI^+) calcd for $C_{50}H_{42}N_4O_2Na$ [M^++Na] 753.3208, found 753.3212.

*4.3.8. 1,4-Bis[(1′-(4-methylbenzyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]butane (**11h**).* Colorless solid (96%); mp 134–136 °C; IR (KBr) *ν* 3054, 2927, 1712, 1612, 1486, 1467, 1355, 1265, 1180, 908, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.83 (br s, 4H), 2.30 (s, 6H, $ArCH_3$), 3.93–3.96 (m, 4H, CH_2), 4.85–5.00 (m, 6H, NCH_2 and CH), 6.82 (d, 2H, *J*=8.0 Hz, ArH), 6.91–6.97 (m, 6H, ArH), 7.09 (d, 4H, *J*=8.0 Hz, ArH), 7.13–7.25 (m, 14H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.19 ($ArCH_3$), 27.76 (CH_2), 43.87 (CH_2), 44.52 (*C*H), 46.00 (CH_2) 109.14 (=CH), 109.55 (=CH), 109.74 (*quat*-C), 119.43 (=CH), 119.84 (=CH), 122.04 (=CH), 122.66 (=CH), 124.91 (=CH), 126.88 (=CH), 126.93 (=CH), 126.98 (=CH), 127.67 (=CH), 128.10 (=CH), 129.21 (*quat*-C), 129.46 (=CH), 133.08 (*quat*-C), 136.70 (*quat*-C), 137.36 (*quat*-C), 143.44 (*quat*-C), 176.51 (*quat*-C); MS (EI) *m/z* (%) 758 (M^+, 13), 653 (10), 539 (8), 435 (8), 434 (23), 352 (11), 247 (21), 231 (7), 219 (8), 218 (9), 170 (14), 106 (21), 104 (10); Anal. Calcd (%) for $C_{52}H_{46}N_4O_2$ (758.36): C, 82.29; H, 6.11; N, 7.38. Found: C, 82.47; H, 6.18; N, 7.47.

*4.3.9. 1,4-Bis[(1′-allyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl] butane (**11i**).* Colorless solid (95%); mp 178–180 °C; IR (KBr) *ν* 3055, 2928, 1709, 1610, 1485, 1465, 1353, 1266, 1206, 1186, 1159, 923, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.83 (br s, 4H), 4.00–4.01 (m, 4H), 4.41 (d, *J*=4.0 Hz, 4H), 4.88 (s, 2H, CH), 5.22–5.31 (m, 4H, C=CH_2), 5.83–5.91 (m, 2H, allyl CH), 6.91–6.93 (m, 4H), 7.00 (t, *J*=7.6 Hz, 4H), 7.16 (q, 4H, *J*=7.6 Hz, ArH), 7.21–7.30 (m, 6H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 27.76 (CH_2), 42.62 (CH_2), 44.36 (*C*H), 45.98 (CH_2), 108.98 (=CH), 109.54 (=CH), 109.65 (*quat*-C), 117.75 ($=CH_2$), 119.46 (=CH), 119.69 (=CH), 122.02 (=CH), 122.63 (=CH), 124.92 (=CH), 126.70 (=CH), 127.01 (*quat*-C), 128.08 (=CH), 129.14 (*quat*-C), 131.65 (=CH), 136.65 (*quat*-C), 143.44 (*quat*-C), 176.08 (*quat*-C); HRMS (ESI) calcd for $C_{42}H_{38}N_4O_2Na$ [M^++Na] 653.2995, found 653.2992.

*4.3.10. 1,4-Bis[(1′-(prop-2-ynyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl]butane (**11j**).* Colorless solid (94%); mp 137–139 °C; IR (KBr) *ν* 3285 (CCH), 3055, 2929, 1715, 1611, 1487, 1466, 1351, 1164, 1010, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.83 (br s, 4H), 2.25–2.27 (m, 2H, CCH), 4.01–4.02 (m, 2H, CH_2), 4.56–4.58 (m, 4H, NCH_2), 4.89 (s, 2H, CH), 6.92 (d, 2H, *J*=7.6 Hz, ArH), 6.97–7.06 (m, 4H, ArH), 7.06–7.25 (m, 12H, ArH), 7.32 (t, 2H, *J*=7.4 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 28.20 (CH_2), 29.62 (CH_2), 44.83 (*C*H), 46.09 (CH_2), 74.19 (*quat*-C), 78.68 (*C*H), 109.85 (=CH), 110.43 (*quat*-C), 110.69 (=CH), 119.52 (=CH), 120.16 (=CH), 122.23 (=CH), 123.34 (=CH), 125.30 (=CH), 127.54 (*quat*-C), 128.53 (=CH), 128.71 (=CH), 130.42 (*quat*-C), 137.54 (*quat*-C), 143.28 (*quat*-C), 175.93 (*quat*-C); HRMS (ESI) calcd for $C_{42}H_{34}N_4O_2Na$ [M^++Na] 649.2682, found: 649.2678.

*4.3.11. 1,2-Bis[((1′-methyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12a**).* Light brown solid (97%); mp 108–110 °C; IR (KBr) *ν* 3052, 2929, 1710, 1611, 1492, 1468, 1372, 1344, 1248, 1123, 1085, 1017, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 3.29 (s, 6H, NCH_3), 4.86 (s, 2H, CH), 5.16 (s, 4H, $ArCH_2N$), 6.89–6.92 (m, 6H, ArH), 6.98–7.03 (m, 4H, ArH), 7.10–7.11 (m, 4H, ArH), 7.18 (d, 2H, *J*=7.2 Hz, ArH) 7.20–7.25 (m, 4H, ArH), 7.31 (t, 2H, *J*=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 26.54 (NCH_3), 44.46 (*C*H), 47.53 (CH_2), 108.14 (=CH), 110.83 (=CH), 110.53 (*quat*-C), 119.70 (=CH), 119.91 (=CH), 122.41 (=CH), 122.73 (=CH), 124.77 (=CH), 126.96 (=CH), 127.08 (*quat*-C), 128.26 (=CH), 128.30 (=CH), 128.42 (=CH), 129.13 (*quat*-C), 134.61 (*quat*-C), 137.06 (*quat*-C), 144.26 (*quat*-C), 176.35 (*quat*-C); MS (ESI) *m/z* (%) 649 (M^++Na); Anal. Calcd (%) for $C_{42}H_{34}N_4O_2$ (626.26): C, 80.49; H, 5.47; N, 8.94. Found: C, 80.68; H, 5.34; N, 8.99.

*4.3.12. 1,2-Bis[((1′-benzyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12b**).* Light brown solid (96%); mp 126–128 °C; IR (KBr) *ν* 3054, 2923, 1710, 1611, 1486, 1465, 1347, 1177, 1098, 1008, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 4.87–5.04 (m, 6H, NCH_2 and CH), 5.15 (s, 4H, $ArCH_2N$), 6.81 (d, 2H, *J*=7.6 Hz, ArH), 6.89 (t, 2H, *J*=4 Hz, ArH), 6.91–6.97 (m, 5H, ArH), 7.07–7.28 (m, 19H, ArH), 7.32 (d, 4H, *J*=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 44.11 (CH_2), 45.57 (*C*H), 47.58 (CH_2), 109.16 (=CH), 109.86 (=CH), 110.63 (*quat*-C), 119.87 (=CH), 119.90 (=CH), 122.47 (=CH), 122.77 (=CH), 124.92 (=CH), 127.02 (=CH), 127.12 (=CH), 127.64 (=CH), 127.71 (=CH), 128.18 (=CH), 128.38 (=CH), 128.49 (=CH), 128.82 (*quat*-C), 129.12 (*quat*-C), 134.67 (*quat*-C), 136.07 (*quat*-C), 137.14 (*quat*-C), 143.38 (*quat*-C), 176.47 (*quat*-C); HRMS (ESI) calcd for $C_{54}H_{42}N_4O_2Na$ [M^++Na] 801.3205, found 801.3210.

*4.3.13. 1,2-Bis[((1′-(4-methylbenzyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl] benzene (**12c**).* Brown solid (96%); mp 116–118 °C; IR (KBr) *ν* 3054, 2926, 1713, 1612, 1486, 1466, 1354, 1265, 1180, 1012, 908, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 2.28 (s, 6H, $ArCH_3$), 4.82–5.00 (m, 6H, NCH_2 and CH), 5.13 (s, 4H, $ArCH_2N$), 6.81 (d, 2H, *J*=7.6 Hz, ArH), 6.88 (q, 2H, *J*=4.4 Hz, ArH), 6.92–6.97 (m, 6H, ArH), 7.06–7.23 (m, 20H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 21.20 ($ArCH_3$), 43.89 (CH_2), 44.60 (*C*H), 47.58 (CH_2), 109.21 (=CH), 109.88 (=CH), 110.67 (*quat*-C), 119.91 (=CH), 122.46 (=CH), 122.72 (=CH), 124.89 (=CH), 127.05 (=CH), 127.15 (=CH), 127.18 (=CH), 127.66 (*quat*-C), 128.17 (=CH), 128.36 (=CH), 128.48 (=CH), 129.16 (=CH), 129.50 (=CH), 133.06 (*quat*-C), 134.70 (*quat*-C), 137.16 (*quat*-C), 137.37 (*quat*-C), 143.45 (*quat*-C), 176.46 (*quat*-C); MS (ESI) *m/z* 829 (M^++Na); Anal. Calcd (%) for $C_{56}H_{46}N_4O_2$ (806.36): C, 83.36; H, 5.75; N, 6.94. Found: C, 83.51; H, 5.68; N, 6.99.

*4.3.14. 1,2-Bis[((1′-allyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl) methyl]benzene (**12d**).* Brown solid (95%); mp 97–99 °C; IR (KBr) *ν* 3055, 2926, 1711, 1612, 1487, 1466, 1355, 1265, 1204, 1184, 929, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 4.39 (s, 4H, $ArCH_2$), 4.88 (s, 2H, CH), 5.06 (s, 4H), 5.17–5.30 (m, 4H), 5.78–5.92 (m, 2H, allyl CH), 6.80–7.27 (m, 22H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 43.15 (CH_2), 44.95 (*C*H), 47.95 (CH_2), 109.54 (=CH), 110.41 (=CH), 111.04 (*quat*-C), 118.24 ($=CH_2$), 120.24 (=CH), 120.39 (=CH), 122.89 (=CH), 123.15 (=CH), 125.37 (=CH), 127.58 (=CH), 128.59 (=CH), 128.63 (=CH),128.84 (=CH), 129.59 (*quat*-C), 132.13 (=CH), 135.15 (*quat*-C), 137.63 (*quat*-C), 143.95 (*quat*-C), 176.46 (*quat*-C); HRMS (ESI) calcd for $C_{46}H_{38}N_4O_2Na$ [M^++Na] 701.2908, found 701.2910.

*4.3.15. 1,2-Bis[((1′-(prop-2-ynyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12e**).* Brown solid (94%); mp 144–146 °C; IR (KBr) *ν* 3302 (CCH), 3055, 2924, 1714, 1613, 1487, 1467, 1351, 1265, 1182, 1012, 909, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 2.23 (s, 2H, CCH), 4.55–4.56 (m, 4H, NCH_2), 4.87 (s, 2H, CH), 5.09 (s, 4H, $ArCH_2N$), 6.81–7.35 (m, 22H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 30.08 (CH_2), 45.04 (*C*H), 48.13 (CH_2), 72.93 (*quat*-C), 77.72 (*C*H), 109.73 (=CH), 110.41 (=CH), 110.89 (*quat*-C), 120.33 (=CH), 120.53 (=CH), 123.04 (=CH), 123.69 (=CH), 125.54 (=CH), 127.52 (*quat*-C), 127.71 (=CH), 128.84 (=CH), 129.04 (=CH), 129.48 (*quat*-C), 135.18 (=CH), 137.55 (*quat*-C), 142.86 (*quat*-C), 175.90 (*quat*-C); MS (ESI) *m/z* 697 (M^++Na); Anal. Calcd (%) for $C_{46}H_{34}N_4O_2$ (674.27): C, 81.88; H, 5.08; N, 8.30. Found: C, 81.71; H, 5.01; N, 8.38.

*4.3.16. 1,3-Bis[((1′-methyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12f**).* Colorless solid (97%); mp 144–146 °C; IR (KBr) *ν* 3055, 2935, 1713, 1612, 1469, 1347, 1265, 1171, 1125, 1087,

1018, 909, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.28 (s, 6H, NCH_3), 4.88 (s, 2H, CH), 5.19 (s, 4H, $ArCH_2N$), 6.91 (d, 2H, J=8 Hz, ArH), 6.94–7.03 (m, 8H, ArH), 7.11 (t, 2H, J=7.6 Hz, ArH), 7.17 (d, 2H, J=8.8 Hz, ArH), 7.20 (t, 2H, J=3.6 Hz, ArH), 7.24 (s, 2H, ArH), 7.28 (dd, 2H, J_1=8 Hz, J_2=3.2 Hz, ArH), 7.32 (d, 2H, J=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.15 (NCH_3), 44.85 (*C*H), 49.95 (CH_2), 108.72 (=*C*H), 110.51 (=CH), 110.79 (*quat*-C), 120.33 (=*C*H), 122.87 (=CH), 123.21 (=*C*H), 125.44 (=*C*H), 126.03 (=*C*H), 126.79 (=*C*H), 127.83 (=*C*H), 128.81 (=CH), 129.73 (*quat*-C), 129.92 (=*C*H), 137.61 (*quat*-C), 138.64 (*quat*-C), 144.93 (*quat*-C), 176.90 (*quat*-C); MS (ESI) *m*/*z* 649 (M^++Na); Anal. Calcd (%) for $C_{42}H_{34}N_4O_2$ (626.27): C, 80.49; H, 5.47; N, 8.94. Found: C, 80.61; H, 5.38; N, 8.99.

*4.3.17. 1,3-Bis[((1′-benzyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12g**).* Brown solid (96%); mp 132–134 °C; IR (KBr) ν 3055, 2926, 1713, 1612, 1486, 1466, 1356, 1265, 1179, 1011, 909, 738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.84–5.06 (m, 6H, NCH_2 and CH), 5.15 (s, 4H, $ArCH_2N$), 6.80 (d, 2H, J=7.6 Hz, ArH), 6.93–7.31 (m, 30H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.71 (CH_2), 45.14 (*C*H), 50.62 (CH_2), 109.73 (=*C*H), 110.59 (=*C*H), 110.92 (*quat*-C), 120.29 (=*C*H), 120.42 (=*C*H), 122.89 (=*C*H), 123.28 (=*C*H), 125.64 (=*C*H), 126.12 (=*C*H), 126.93 (=*C*H), 127.72 (*quat*-C), 128.02 (=*C*H), 128.29 (=*C*H), 128.83 (=*C*H), 129.41 (=*C*H), 130.04 (=*C*H), 136.72 (*quat*-C), 137.74 (*quat*-C), 138.73 (*quat*-C), 143.88 (*quat*-C), 177.15 (*quat*-C); MS (EI) *m*/*z* (%) 778 (M^+, 2), 339 (15), 338 (95), 247 (100), 219 (16), 105 (29), 91 (64); HRMS (ESI) calcd for $C_{54}H_{42}N_4O_2Na$ [M^++Na] 801.3208, found: 801.3213.

*4.3.18. 1,3-Bis[((1′-(4-methylbenzyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl] benzene (**12h**).* Light brown solid (97%); mp 124–126 °C; IR (KBr) ν 3054, 2926, 1713, 1612, 1486, 1466, 1354, 1265, 1180, 1012, 908, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.27 (s, 6H, $ArCH_3$), 4.82–5.00 (m, 6H, NCH_2 and CH), 5.15 (s, 4H, $ArCH_2N$), 6.80–6.82 (m, 2H, ArH), 6.93–6.97 (m, 8H, ArH), 7.03–7.18 (m, 16H, ArH), 7.22 (d, 4H, J=6.8 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.23 ($ArCH_3$), 43.90 (CH_2), 44.60 (*C*H), 50.01 (CH_2), 109.20 (=*C*H), 110.00 (=*C*H), 110.32 (*quat*-C), 119.71 (=*C*H), 119.87 (=*C*H), 122.31 (=*C*H), 122.71 (=*C*H), 124.96 (*quat*-C), 125.49 (=*C*H), 126.27 (=*C*H), 127.14 (=*C*H), 127.44 (=*C*H), 127.52 (=*C*H), 127.71 (=*C*H), 128.17 (=*C*H), 129.20 (=*C*H), 129.42 (*quat*-C), 129.51 (*quat*-C), 133.10 (=*C*H), 137.13 (*quat*-C), 137.39 (*quat*-C), 138.10 (*quat*-C), 144.39 (*quat*-C), 176.51 (*quat*-C); MS (EI) *m*/*z* (%) 806 (M^+, 7), 702 (9), 701 (17), 587 (20), 482 (22), 456 (12), 353 (12), 352 (62), 351 (33), 247 (100), 235 (10); Anal. Calcd (%) for $C_{56}H_{46}N_4O_2$ (806.36): C, 83.35; H, 5.75; N, 6.94. Found: C, 83.48; H, 5.69; N, 6.81.

*4.3.19. 1,3-Bis[((1′-(prop-2-ynyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12i**).* Colorless solid (95%); mp 188–190 °C; IR (KBr) ν 3303, 3055, 2927, 1714, 1612, 1487, 1467, 1351, 1265, 1181, 1098, 909, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.25 (s, 2H, CCH), 4.56–4.57 (m, 4H, NCH_2CCH), 4.90 (s, 2H, CH), 5.18 (s, 4H, $ArCH_2N$), 6.77–7.37 (m, 22H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.05 (CH_2), 45.14 (*C*H), 50.48 (CH_2), 72.86 (*quat*-C), 77.75 (*C*H), 109.73 (=*C*H), 110.52 (=*C*H), 120.31 (=*C*H), 122.89 (=*C*H), 123.56 (=*C*H), 125.45 (=*C*H), 125.89 (=*C*H), 126.79 (=*C*H), 127.64 (*quat*-C), 127.86 (=*C*H), 128.82 (=*C*H), 129.47 (*quat*-C), 129.87 (=*C*H), 137.61 (*quat*-C), 138.63 (*quat*-C), 142.92 (*quat*-C), 175.91 (*quat*-C); MS (ESI) *m*/*z* 675 (M^++Na); Anal. Calcd (%) for $C_{46}H_{34}N_4O_2$ (674.27): C, 81.88; H, 5.08; N, 8.30. Found: C, 82.03; H, 5.13; N, 8.42.

*4.3.20. 1,4-Bis[((1′-benzyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12j**).* Brown solid (95%); mp 138–140 °C; IR (KBr) ν 3055, 2927, 1712, 1612, 1487, 1466, 1354, 1265, 1179, 1013, 909, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.87–5.04 (m, 6H, NCH_2 and CH), 5.19 (s, 4H, $ArCH_2N$), 6.81 (d, 2H, J=7.6 Hz, ArH), 6.95 (t, 4H, J=7.6 Hz, ArH), 7.02–7.04 (m, 6H, ArH), 7.11 (t, 2H, J=7.6 Hz, ArH), 7.19 (d, 8H, J=8.0 Hz, ArH), 7.22–7.29 (m, 6H, ArH), 7.33 (d, 4H, J=6.8 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.11 (CH_2), 44.55 (*C*H), 49.79 (CH_2), 109.14 (=*C*H), 109.96 (=*C*H), 110.23 (*quat*-C), 119.69 (=*C*H), 119.69 (=*C*H), 119.82 (=*C*H), 122.29 (=*C*H), 122.75 (=*C*H), 125.00 (=CH), 127.09 (*quat*-C), 127.33 (=CH), 127.67 (=*C*H), 127.72 (=*C*H), 128.17 (=*C*H), 128.82 (=CH), 129.13 (*quat*-C), 136.10 (*quat*-C), 136.88 (*quat*-C), 137.05 (*quat*-C), 143.42 (*quat*-C), 176.50 (*quat*-C); MS (ESI) *m*/*z* (%) 779 (M+1, 48), 778 (M^+, 100), 687 (19), 556 (17), 440 (29), 337 (38), 307 (25), 222 (40), 154 (83); Anal. Calcd (%) for $C_{54}H_{42}N_4O_2$ (778.37): C, 83.26; H, 5.43; N, 7.19. Found: C, 83.47; H, 5.34; N, 7.11.

*4.3.21. 1,4-Bis[((1′-(4-methylbenzyl)-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12k**).* Colorless solid (94%); mp 136–138 °C; IR (KBr) ν 3054, 2926, 1713, 1612, 1515, 1486, 1466, 1354, 1265, 1179, 1014, 909, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 6H, $ArCH_3$), 4.83–5.00 (m, 6H, NCH_2 and CH), 5.19 (s, 4H, $ArCH_2N$), 6.82 (d, 2H, J=8.0 Hz, ArH), 6.94 (t, 4H, J=7.6 Hz, ArH), 7.03 (s, 6H, ArH), 7.09 (d, 6H, J=7.6 Hz, ArH), 7.17–7.19 (m, 8H, ArH), 7.23 (d, 4H, J=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.84 ($ArCH_3$), 44.54 (CH_2), 45.13 (*C*H), 50.41 (CH_2), 109.72 (=*C*H), 110.51 (=*C*H), 110.89 (*quat*-C), 120.21 (=*C*H), 120.43 (=*C*H), 122.85 (=*C*H), 123.21 (=*C*H), 125.53 (=*C*H), 127.72 (*quat*-C), 127.91 (=*C*H), 128.38 (=*C*H), 128.69 (=*C*H), 129.79 (*quat*-C), 130.12 (=*C*H), 133.73 (*quat*-C), 137.51 (*quat*-C), 137.71 (*quat*-C), 137.92 (*quat*-C), 144.12 (*quat*-C), 177.01 (*quat*-C); MS (ESI) *m*/*z* (%) 829 (M^++Na); Anal. Calcd (%) for $C_{56}H_{46}N_4O_2$ (806.36): C, 83.35; H, 5.75; N, 6.94. Found: C, 83.19; H, 5.81; N, 6.98.

*4.3.22. 1,4-Bis[((1′-allyl-1′,3′-dihydro-1′H-[3,3′]biindolyl-2′-on)-1-yl)methyl]benzene (**12l**).* Colorless solid (94%); mp 123–125 °C; IR (KBr) ν 3054, 2924, 1711, 1613, 1482, 1469, 1265, 1200, 1189, 921, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (s, 4H, $ArCH_2$), 4.87 (s, 2H, CH), 4.97–5.29 (m, 8H), 5.78–5.91 (m, 2H, allyl CH), 6.73–7.43 (m, 22H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.10 (CH_2), 44.93 (*C*H), 50.21 (CH_2), 109.49 (=*C*H), 110.46 (=*C*H), 110.70 (*quat*-C), 118.23 (=CH_2), 120.19 (=*C*H), 122.72 (=*C*H), 123.13 (=*C*H), 125.45 (=*C*H), 127.76 (=*C*H), 128.62 (=CH), 129.61 (*quat*-C), 132.17 (=*C*H), 137.351 (*quat*-C), 137.52 (*quat*-C), 143.98 (*quat*-C), 176.49 (*quat*-C); HRMS (ESI) for $C_{46}H_{38}N_4O_2Na$ [M^++Na] 701.2973, found: 701.2965.

4.4. Synthesis of macrocycles 13a and 13b

A solution of bis-indole **6a** (100 mg, 0.37 mmol), bis-diazoamide **7a** (143 mg, 0.40 mmol), and rhodium(II) acetate (1.6 mg) in dichloromethane (50 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated in vacuo and purified on silica (hexane/acetone, 65:35) to yield **13a** and **13b** as a mixture of diastereomers (ratio 58:42) in 50% yield.

*4.4.1. Macrocycle **13a**.* Colorless solid; mp 255–257 °C; IR (KBr) ν 3052, 2933, 1700, 1609, 1484, 1467, 1359, 1340, 1184, 759 cm^{-1}; ^1H NMR (200 MHz, CD_2Cl_2) δ=2.23 (t, 2H, J=6.8 Hz, CH_2), 2.38 (t, 2H, J=6.5 Hz, CH_2), 3.50–3.67 (m, 4H), 4.06–4.256 (m, 4H), 4.87 (s, 2H, CH), 6.80 (s, 2H, ArH), 6.93–7.01 (m, 4H, ArH), 7.16–7.40 (m, 10H, ArH), 7.79–7.82 (m, 2H, ArH); ^{13}C NMR (50.3 MHz, CD_2Cl_2) δ 28.74 (CH_2), 29.53 (CH_2), 38.43 (CH_2), 43.72 (*C*H, observed in DEPT-90 NMR) 109.10 (=*C*H), 110.82 (=*C*H), 112.00 (*quat*-C), 119.45 (=*C*H), 120.46 (=*C*H), 122.67 (=*C*H), 123.14 (=*C*H), 125.30 (=*C*H), 127.75 (=*C*H), 128.65 (=*C*H), 129.84 (*quat*-C), 131.65 (*quat*-C), 136.9 (*quat*-C), 144.31 (*quat*-C), 177.90 (*quat*-C); HRMS (ESI) calcd for $C_{38}H_{32}N_4O_2Na$ [M^++Na] 599.2423, found 599.2417. Crystal data for compound **13a**: (CCDC-832919) Colorless plate crystal. $C_{38}H_{32}N_4O_2$, M=576.68, 0.15×0.12×0.08 mm^3, monoclinic, space group $C2/c$ with a=43.37(2) Å, b=8.517(4) Å, c=16.561(7) Å, α=90°, β=104.126(15)°, γ=90°, V=5932(4) $Å^3$, T=273(2) K, R_1=0.0641,

wR_2=0.1085 on observed data, z=8, D_{calcd}=1.291 g cm^{-3}, F(000)=2432, Absorption coefficient=0.081 mm^{-1}, λ=0.71073 Å, 14,489 reflections were collected on a Smart Apex CCD single-crystal diffractometer, 5219 observed reflections ($I\geq 2\sigma$ (I)). The largest difference peak and hole=0.182 and −0.148 e Å^{-3}, respectively.

*4.4.2. Macrocycle **13b**.* Colorless solid; mp 220–222 °C; IR (KBr) ν 3050, 2938, 1694, 1611, 1487, 1466, 1368, 1209, 1125, 743 cm^{-1}; ^{1}H NMR (200 MHz, DMSO-d_6) δ=1.25–1.27 (m, 1H), 1.73–1.76 (m, 1H), 2.04–2.09 (m, 2H), 3.66–3.97 (overlapping m, 8H), 5.02 (s, 2H, CH), 6.37 (s, 2H, ArH), 7.05 (t, 2H, J=6.8 Hz, ArH), 7.13–7.34 (m, 10H, ArH), 7.51 (d, 2H, J=8.1 Hz, ArH), 7.93 (d, 2H, J=7.7 Hz, ArH); ^{13}C NMR (50.3 MHz, DMSO-d_6) δ 26.60 (*C*H$_2$), 32.13 (*C*H$_2$), 37.04 (*C*H$_2$), 42.50 (*C*H$_2$), 43.00 (*C*H), 109.22 (=*C*H), 110.21 (=*C*H), 113.23 (*quat*-C), 119.69 (=*C*H), 119.87 (=*C*H), 122.39 (=*C*H), 122.83 (=*C*H), 123.97 (=*C*H), 124.90 (=*C*H), 127.51 (*quat*-C), 128.46 (=*C*H), 130.74 (*quat*-C), 136.73 (*quat*-C), 142.95 (*quat*-C), 176.78 (*quat*-C); HRMS (ESI) calcd for $C_{38}H_{32}N_4O_2Na$ [M$^+$+Na] 599.2423, found 599.2439. Crystal data for compound **13b**: (CCDC-832920) Colorless plate crystal. $C_{39}H_{32}Cl_3N_4O_2$, 695.04, 0.14×0.10×0.06 mm^3, Monoclinic, space group P with a=8.6282(9) Å, b=17.7685(19) Å, c=21.078(2) Å, α=90°, β=95.647(2)°, γ=90°, V=3215.8(6) Å^3, T=273(2) K, R_1=0.1173, wR_2=0.3723 on observed data, z=4, D_{calcd}=1.436 g cm^{-3}, F(000)=1444, Absorption coefficient=0.329 mm^{-1}, λ=0.71073 Å, 12,773 reflections were collected on a smart apex CCD single-crystal diffractometer, 4200 observed reflections ($I\geq 2\sigma$ (I)). The largest difference peak and hole=0.731 and −1.852 e Å^{-3}, respectively.

4.5. Synthesis of macrocycles 14a and 14b

A solution of bis-indole **7b** (100 mg, 0.37 mmol), bis-diazoamide **6a** (136 mg, 0.40 mmol), and rhodium(II) acetate (1.6 mg) in dichloromethane (50 mL) was stirred at room temperature for 45 min. The reaction mixture was concentrated in vacuo and purified on silica (hexane/acetone, 65:35) to furnish **14a** and **14b** as a mixture of diastereomers (ratio 53:47) in 52% yield.

*4.5.1. Macrocycle **14a**.* Colorless solid; mp 202–203 °C; IR (neat) ν 3053, 2940, 1708, 1611, 1466, 1357, 1264, 1175, 1086, 1018, 728 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.36–1.42 (m, 2H, CH$_2$), 1.51–1.55 (m, 2H, CH$_2$), 1.86–1.89 (m, 2H, CH$_2$), 3.35–3.41 (m, 2H, N–CH$_2$), 3.55–3.59 (m, 2H, N–CH$_2$), 3.85–3.90 (m, 2H, OCH$_2$), 4.07–4.13 (m, 2H, OCH$_2$), 4.75 (s, 2H, CH), 6.25 (s, 2H, ArH), 6.80 (d, 2H, J=8.0 Hz, ArH,), 6.93 (t, 2H, J=7.6 Hz, ArH,), 7.08–7.23 (m, 10H, ArH), 7.75 (d, 2H, J=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.19 (*C*H$_2$), 27.76 (*C*H$_2$), 37.45 (*C*H$_2$), 43.17 (*C*H, observed in DEPT-135 NMR), 45.90 (*C*H$_2$), 108.27 (=*C*H), 109.31 (=*C*H), 111.26 (*quat*-C), 119.56 (=*C*H), 119.72 (=*C*H), 122.05 (=*C*H), 122.58 (=*C*H), 125.06 (=*C*H), 125.33 (=*C*H), 128.0 (*quat*-C), 128.39 (=*C*H), 129.38 (*quat*-C), 135.99 (*quat*-C), 143.40 (*quat*-C), 176.76 (*quat*-C); HRMS (ESI) calcd for $C_{39}H_{34}N_4O_2Na$ [M$^+$+Na] 613.2579, found 613.2563.

*4.5.2. Macrocycle **14b**.* Colorless solid; mp 225–227 °C; IR (neat) ν 3054, 2933, 1708, 1610, 1465, 1356, 1264, 1175, 1086, 1021, 729 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.43–1.60 (m, 2H, CH$_2$), 1.92 (br s, 2H, CH$_2$), 1.93–1.95 (m, 2H, CH$_2$), 3.42–3.49 (m, 2H, N–CH$_2$), 3.61–3.64 (m, 2H, N–CH$_2$), 3.91–3.99 (m, 2H, OCH$_2$), 4.13–4.17 (m, 2H, OCH$_2$), 4.81 (s, 2H, CH), 6.32 (s, 2H, ArH), 6.87 (d, 2H, J=8.0 Hz, ArH), 6.97–7.01 (m, 2H, ArH), 7.14–7.29 (m, 10H, ArH), 7.82 (d, 2H, J=7.2 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.17 (*C*H$_2$), 27.76 (*C*H$_2$), 37.43 (*C*H$_2$), 43.17 (*C*H, observed in DEPT-135 NMR), 45.90 (*C*H$_2$), 108.25 (=*C*H), 109.28 (=*C*H), 111.26 (*quat*-C), 119.55 (=*C*H), 119.71 (=*C*H), 122.03 (=*C*H), 122.56 (=*C*H), 125.04 (=*C*H), 125.30 (=*C*H), 128.00 (*quat*-C), 128.37 (=*C*H), 129.35 (*quat*-C), 135.97 (*quat*-C), 143.39 (*quat*-C), 176.74 (*quat*-C); HRMS (ESI) calcd for $C_{39}H_{34}N_4O_2Na$ [M$^+$+Na] 613.2579, found 613.2573.

4.6. Synthesis of macrocycles 15a and 15b

A solution of bis-indole **7b** (100 mg, 0.37 mmol), bis-diazoamide **6b** (140 mg, 0.40 mmol), and rhodium(II) acetate (1.6 mg) in dichloromethane (50 mL) was stirred at room temperature for 45 min. The reaction mixture was concentrated in vacuo and purified on silica (hexane/acetone, 65:35) to obtain **15a** and **15b** as a mixture of diastereomers (ratio 51:49) in 55% yield.

*4.6.1. Macrocycle **15a**.* Colorless solid; mp 150–154 °C; IR (neat) ν 3050, 2932, 1702, 1609, 1463, 1349, 1237, 1154, 1091, 1014, 870 cm^{-1}; ^{1}H NMR (400 MHz, CD_2Cl_2) δ=1.64–1.66 (m, 8H, CH$_2$), 3.28–3.42 (m, 2H, N–CH$_2$), 3.56–3.60 (m, 2H, N–CH$_2$), 3.83–3.89 (m, 2H, OCH$_2$), 4.07–4.10 (m, 2H, OCH$_2$), 4.69 (s, 2H, CH), 6.21 (s, 2H, ArH), 6.74–6.79 (m, 3H, ArH), 6.92–6.98 (m, 3H, ArH) 7.12–7.15 (m, 3H, ArH) 7.20–7.25 (m, 7H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.72 (*C*H$_2$), 28.02 (*C*H$_2$), 39.69 (*C*H$_2$), 43.41 (*C*H, observed in DEPT-135 NMR), 46.18 (*C*H$_2$), 108.78 (=*C*H), 109.23 (=*C*H), 109.83 (*quat*-C), 119.65 (=*C*H), 120.14 (=*C*H), 122.14 (=*C*H), 122.50 (=*C*H), 124.80 (=*C*H), 125.14 (=*C*H), 128.21 (=*C*H), 128.42 (*quat*-C), 136.09 (*quat*-C), 143.59 (*quat*-C), 176.89 (*quat*-C); HRMS (ESI) calcd for $C_{40}H_{36}N_4O_2Na$ [M$^+$+Na] 627.2771, found 627.2780.

*4.6.2. Macrocycle **15b**.* Colorless solid; mp 220–224 °C; IR (neat) ν 3052, 2935, 1704, 1610, 1486, 1464, 1352, 1264, 1155, 1091, 1014, 876 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ=1.54–1.65 (m, 8H, CH$_2$), 3.26–3.30 (m, 2H, N–CH$_2$), 3.57–3.60 (m, 2H, N–CH$_2$), 4.11–4.18 (m, 4H, OCH$_2$), 4.79 (s, 2H, CH), 6.35 (s, 2H, ArH), 6.79 (d, 2H, J=7.6 Hz, ArH), 6.98 (t, 2H, J=7.2 Hz, ArH), 7.09–7.86 (m, 10H, ArH), 7.88 (d, 2H, J=7.6 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.73 (*C*H$_2$), 27.98 (*C*H$_2$), 39.70 (*C*H$_2$), 43.41 (*C*H, observed in DEPT-135 NMR), 46.16 (*C*H$_2$), 108.74 (=*C*H), 109.20 (=*C*H), 109.92 (*quat*-C), 119.64 (=*C*H), 120.13 (=*C*H), 122.13 (=*C*H), 122.48 (=*C*H), 124.79 (=*C*H), 125.12 (=*C*H), 128.41 (=*C*H), 128.40 (*quat*-C), 136.12 (*quat*-C), 143.59 (*quat*-C), 175.88 (*quat*-C); HRMS (ESI) calcd for $C_{40}H_{36}N_4O_2Na$ [M$^+$+Na] 627.2771, found 627.2766.

4.7. Synthesis of macrocycles 16a and 16b

A solution of bis-indole **7c** (100 mg, 0.30 mmol), bis-diazoamide **6a** (120 mg, 0.33 mmol), and rhodium(II) acetate (1.3 mg) in dichloromethane (50 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated in vacuo and purified on silica (hexane/acetone, 65:35) to yield **16a** and **16b** as a mixture of diastereomers (ratio 27:73) in 63% yield.

*4.7.1. Macrocycle **16a**.* Colorless solid; mp 210–212 °C; IR (neat) ν 3055, 2929, 1707, 1610, 1485, 1463, 1356, 1179, 729 cm^{-1} ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.05–2.10 (m, 2H), 3.50–3.56 (m, 2H), 3.87–3.94 (m, 2H), 4.71 (d, 2H, J=16.0 Hz, NCH$_2$), 4.73 (s, 2H, CH), 5.00 (d, 2H, J=16.0 Hz, NCH$_2$), 6.77 (s, 1H, ArH), 6.83 (d, 2H, J=7.6 Hz, ArH), 6.91–6.94 (m, 3H, ArH), 7.02–7.23 (m, 14H, ArH), 7.40 (d, 2H, J=8.0 Hz, ArH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26 (*C*H$_2$), 37.97 (*C*H$_2$), 43.3 (*C*H), 48.1 (*C*H$_2$), 108.1 (=*C*H), 109.7 (=*C*H), 111.5 (*quat*-C), 118.9 (=*C*H), 119.9 (=*C*H), 122.0 (=*C*H), 122.6 (=*C*H), 125.0 (=*C*H), 126.7 (=*C*H), 128.0 (*quat*-C), 128.1 (=*C*H), 128.3 (=*C*H), 128.8 (=*C*H), 130.0 (*quat*-C), 134.5 (*quat*-C), 136.5 (*quat*-C), 143.4 (*quat*-C), 177.5 (*quat*-C); MS (EI) m/z (%) 639 (M+1, 7), 638 (M$^+$, 17), 421 (6), 306 (5), 220 (6), 219 (25), 218 (74), 217 (100), 189 (5), 117 (11); HRMS (ESI$^+$) calcd for $C_{43}H_{34}N_4O_2Na$ [M$^+$+Na] 661.2682, found 661.2674.

*4.7.2. Macrocycle **16b**.* Colorless solid; mp 216–218 °C; IR (neat) ν 3057, 3019, 2934, 1708, 1612, 1486, 1466, 1359, 1265, 1216, 909,

757 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.87–1.94 (m, 1H, CH_2), 2.60–2.67 (m, 1H, CH_2), 3.42–3.57 (m, 2H), 3.99–4.13 (m, 2H), 4.85 (s, 2H, CH), 4.93 (d, 2H, J=15.8 Hz, NCH_2), 5.03 (d, 2H, J=15.8 Hz, NCH_2), 6.82–7.23 (m, 20H, ArH), 7.42 (d, 2H, J=7.8 Hz, ArH); ^{13}C NMR (50 MHz, $CDCl_3$) δ 25.6 (CH_2), 37.8 (CH_2), 43.7 (*C*H), 47.4 (CH_2), 107.7 (=*C*H), 109.5 (=*C*H), 111.1 (*quat*-C), 119.2 (=*C*H), 119.6 (=*C*H), 121.9 (=*C*H), 122.2 (=*C*H), 124.9 (=*C*H), 126.6 (=*C*H), 127.6 (*quat*-C), 127.8 (=*C*H), 128.3 (=*C*H), 128.9 (=*C*H), 129.9 (*quat*-C), 134.4 (*quat*-C), 136.9 (*quat*-C), 143.2 (*quat*-C), 176.5 (*quat*-C); MS (EI) *m*/*z* (%) 639 (M+1, 7), 638 (M^+, 17), 421 (6), 306 (5), 220 (6), 219 (25), 218 (74), 217 (100), 189 (5), 117 (11); HRMS (ESI) calcd for $C_{43}H_{34}N_4O_2Na$ [M^++Na] 661.2682, found 661.2670. Crystal data for compound **16b**: (CCDC-832921) Colorless plate crystal. $C_{45}H_{34}Cl_6N_4O_2$, 875.46, 0.14×0.10×0.08 mm^3, Triclinic, space group *P*–1 with *a*=10.9507(19) Å, *b*=12.664(2) Å, *c*=15.465(3) Å, α=97.505(4)°, β=92.949(3)°, γ=98.717(4)°, *V*=2096.1(6) $Å^3$, *T*=273(2) K, R_1=0.1280, wR_2=0.3429 on observed data, *z*=2, D_{calcd}=1.387 g cm^{-3}, *F*(000)=900, Absorption coefficient=0.453 mm^{-1}, λ=0.71073 Å, 8409 reflections were collected on a smart apex CCD single-crystal diffractometer, 5440 observed reflections ($I \geq 2\sigma$ (I)). The largest difference peak and hole=0.710 and −0.775 e $Å^{-3}$, respectively.

4.8. Synthesis of macrocycles 17a and 17b

A solution of bis-indole **7d** (93 mg, 0.28 mmol), bis-diazoamide **6a** (110 mg, 0.31 mmol), and rhodium(II) acetate (1.2 mg) in dichloromethane (50 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated under reduced pressure and purified on silica (hexane/acetone, 65:35) to furnish **17a** (32 mg) and **17b** (64 mg) (diastereomeric ratio 36:64) in 54% yield.

*4.8.1. Macrocycle **17a**.* Colorless solid; mp 296–298 °C; IR (KBr) ν 3055, 2927, 1710, 1612, 1487, 1466, 1360, 1265, 1180, 1180, 1021, 738 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.68–1.95 (m, 1H), 2.11–2.25 (m, 1H), 3.48–3.66 (m, 2H), 3.99–4.20 (m, 2H), 4.85 (d, 2H, J=14.5 Hz, NCH_2), 4.93 (s, 2H, CH), 5.15 (d, 2H, J=14.5 Hz, NCH_2), 6.60–6.76 (m, 2H, ArH), 6.84–7.00 (m, 4H, ArH), 7.16–7.39 (m, 14H, ArH), 7.71 (d, 2H, J=6.5 Hz, ArH); ^{13}C NMR (50.3 MHz, $CDCl_3$), δ 25.9 (CH_2), 37.7 (CH_2), 43.2 (*C*H), 50.0 (CH_2), 108.0 (=*C*H), 109.7 (=*C*H), 111.0 (*quat*-C), 118.8 (=*C*H), 119.6 (=*C*H), 121.9 (=*C*H), 122.4 (=*C*H), 124.6 (=*C*H), 126.1 (=*C*H), 126.4 (=*C*H), 127.2 (=*C*H), 127.9 (=*C*H), 128.7 (=*C*H), 128.5 (*quat*-C), 130.1 (*quat*-C), 136.6 (*quat*-C), 137.9 (*quat*-C), 142.9 (*quat*-C), 176.6 (*quat*-C); HRMS (ESI) calcd for $C_{43}H_{34}N_4O_2Na$ [M^++Na] 661.2682, found: 661.2665.

*4.8.2. Macrocycle **17b**.* Colorless solid; mp 290–292 °C; IR (KBr) ν 3048, 2921, 1706, 1617, 1481, 1461, 1355, 1261, 1173, 1019, 735 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.59–1.83 (m, 1H), 2.01–2.17 (m, 1H), 3.35–3.60 (m, 2H), 3.90–4.16 (m, 2H), 4.92 (d, 2H, J=14.5 Hz, NCH_2), 5.12 (s, 2H, CH), 5.25 (d, 2H, J=14.5 Hz, NCH_2), 6.65–7.82 (m, 2H, ArH), 6.90–7.08 (m, 4H, ArH), 7.23–7.46 (m, 14H, ArH), 7.75 (d, 2H, J=6.5 Hz, ArH); ^{13}C NMR (50.3 MHz, $CDCl_3$), δ 25.5 (CH_2), 36.7 (CH_2), 43.4 (*C*H), 49.5 (CH_2), 107.8 (=*C*H), 109.4 (=*C*H), 111.2 (*quat*-C), 118.9 (=*C*H), 119.4 (=*C*H), 122.0 (=*C*H), 122.4 (=*C*H), 124.8 (=*C*H), 125.1 (=*C*H), 126.1 (=*C*H), 127.0 (=*C*H), 127.7 (=*C*H), 128.1 (*quat*-C), 130.2 (*quat*-C), 136.8 (*quat*-C), 138.1 (*quat*-C), 142.6 (*quat*-C), 176.2 (*quat*-C); HRMS (ESI) calcd for $C_{43}H_{34}N_4O_2Na$ [M^++Na] 661.2682, found: 661.2671. Crystal data for compound **17b**: (CCDC-832922) Colorless plate crystal. $C_{44}H_{36}Cl_2N_4O_2$, 722.22, 0.18×0.10×0.07 mm^3, Orthorhombic, space group *Pnma* with *a*=21.794(3) Å, *b*=18.955(2) Å, *c*=8.8502(10) Å, α=90°, β=90°, γ=90°, *V*=3656.1(7) $Å^3$, *T*=273(2) K, R_1=0.0778, wR_2=0.1577 on observed data, *z*=4, D_{calcd}=1.315 g cm^{-3}, *F*(000)=1512, Absorption coefficient=0.222 mm^{-1}, λ=0.71073 Å, 17,541 reflections were collected on a smart apex CCD single-crystal diffractometer, 3325 observed reflections ($I \geq 2\sigma$ (I)). The largest difference peak and hole=0.247 and −0.220 e $Å^{-3}$, respectively.

4.9. Synthesis of macrocycle 18

A solution of bis-indole **7c** (90 mg, 0.27 mmol), bis-diazoamide **6c** (105 mg, 0.30 mmol), and rhodium(II) acetate (1.2 mg) in dichloromethane (50 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated in vacuo and purified on silica (hexane/acetone, 60:35) to obtain the product **18** (50%) as an inseparable mixture of diastereomers (diastereomeric ratio 56:44). Colorless solid; IR (KBr) ν 3055, 2987, 1711, 1611, 1486, 1466, 1422, 1358, 1265, 1180, 1187, 1016, 896, 740 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.43–4.73 (m, 2H), 4.90 (s, 2H, CH), 4.98–5.28 (m, 6H), 6.85–7.04 (m, 9H, ArH), 7.08–7.34 (m, 15H, ArH), 7.52–7.70 (m, 2H, ArH); ^{13}C NMR (50.3 MHz, $CDCl_3$, The * symbol represents signals due to the minor amount of diastereomer) δ 44.8 (CH_2), 45.0 (CH), 45.2* (CH_2), 48.6 (CH_2), 48.8* (CH_2), 108.9* (=*C*H), 109.0 (=*C*H), 110.3 (=*C*H), 110.5* (=*C*H), 110.8 (*quat*-C), 119.7 (=*C*H), 120.4 (=*C*H), 122.7 (=*C*H), 123.1* (=*C*H), 123.2 (=*C*H), 125.4* (=*C*H), 125.5 (=*C*H), 127.5 (=*C*H), 128.1 (=*C*H)*, 128.2 (=*C*H), 128.5 (=*C*H), 128.6* (=*C*H), 129.0* (=*C*H), 129.1 (=*C*H), 129.5 (=*C*H), 129.7* (=*C*H), 130.5 (*quat*-C), 130.6* (*quat*-C), 131.1 (*quat*-C), 135.4 (*quat*-C), 135.6* (*quat*-C), 137.0 (*quat*-C), 137.4* (*quat*-C), 137.8 (*quat*-C), 143.7 (*quat*-C), 177.3 (*quat*-C); MS (FAB) *m*/*z* 700 (M^+); HRMS(ESI) calcd for $C_{48}H_{36}N_4O_2Na$ (M^++Na) 723.2738, found 723.2722.

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Supplementary data

Single-crystal X-ray analyses and packing diagram of compounds **13a**,**b**,**16b**,**17b**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.11.073.

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21. CCDC-832919 (for **13a**), 832920 (for **13b**), 832921 (for **16b**), and 832922 (for **17b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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