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# Synthesis of Macrocycles Containing Endocyclic Chiral BINAM Moieties

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*A series of nitrogen- and oxygen-containing macrocycles with endocyclic chiral BINAM moieties were synthesized using Pd(0)-catalyzed amination with a number of oxadiamines. Two alternative ways to such compounds were compared – from 1,1'-binaphthalene-2,2'-diamine (BINAM) and N,N'-bis(3-bromophenyl) substituted oxadiamine and from N,N'-bis(bromophenyl) substituted 1,1'-binaphthalene-2,2'-diamine and free oxadiamine. Macrocycles containing benzyl and 2,7-disubstituted naphthalene fragments were also successfully synthesized via the second approach, the dependence of their yields on the nature of starting compounds was demonstrated.*

**Keywords:** Macrocycles, chirality, Pd catalysis, amination, polyamines.

# Синтез макроциклов, содержащих эндоциклические хиральные BINAM фрагменты

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*Синтезирован ряд азот- и кислородсодержащих макроциклов с эндоциклическим хиральным фрагментом БИНАМ посредством Pd(0)-катализируемого аминирования с использованием ряда оксадиаминов. Произведено сравнение двух альтернативных путей получения таких соединений – из 1,1'-бинафталин-2,2'-диамина (БИНАМ) и N,N'-ди(3-бромфенил) замещенного оксадиамина и из N,N'-ди(3-бромфенил) замещенного 1,1'-бинафталин-2,2'-диамина и свободного оксадиамина. Макроциклы, содержащие бензильный и 2,7-дизамещенный нафтильный фрагменты также успешно синтезированы с использованием второго метода, показана зависимость их выходов от природы исходных соединений.*

**Ключевые слова:** Макроциклы, Pd катализ, хиральность, аминирование, полиамины.

## Introduction

Macrocyclic compounds comprising endocyclic chiral moieties attract attention of researchers as biologically active compounds, perspective chemosensors for small chiral molecules, and ligands which can be used in enantioselective metal-catalyzed transformations. Such compounds occur in nature, among them the prominent place is occupied by macrolides, cyclic oligopeptides and cyclic oligosaccharides. These compounds contain multiple carbon chiral centers, and the majority of optically active synthetic macrocycles possess the same type of chirality. Enough rare are synthetic macrocyclic compounds with another type of chirality, *i.e.* planar-chiral macrocycles,[1-3] and our previous works contributed to this field.[4,5] Also we elaborated a new type of macrocycles with endocyclic chiral cholane fragments.[6-9] Macrocyclic compounds containing fragments with *C2* chirality are known for quite a long time, and the majority

of them possess 2,2'-binaphthol (BINOL) moiety. Some of them were reported before 1991 when a comprehensive review on all types of known macrocycles emerged.[10] As this chiral moiety possesses fluorescent properties, BINOL-based chemosensors were found to be useful for detecting optically active amino alcohols, diamines, amino acids, α-hydroxyacids.[11,12] Reported are several macrocycles containing BINOL fragment which contain also additional chiral 1,2-diamine moieties.[13,14] These compounds were synthesized *via* non-catalytic approaches, and in the course of our studies of the application of the catalytic amination to the synthesis of various nitrogen-containing macrocycles we decided to elaborate a general route to the macrocyclic species containing a parent chiral 1,1'-binaphthalene-2,2'-diamine (BINAM) structural units. BINAM itself possesses interesting spectral properties, and in the combination with other aromatic and heteroaromatic groups the resulting *N*- and *O*-containing receptors could be perspective as optical chemosensors for small chiral organic molecules.

## Experimental

NMR spectra were registered using Bruker Avance 400 spectrometer in $CDCl_3$ at 298 K. MALDI-TOF spectra were obtained with Bruker Autoflex II spectrometer using 1,8,9-trihydroxyanthracene as matrix and PEGs as internal standards. Dioxa-, trioxa- and tetraoxadiamines **1a-e**, (*S*)-BINAM, 1,3-dibromobenzene, 1-(bromomethyl)-3-bromobenzene, phosphine ligands BINAP, DavePhos and Xantphos, potassium carbonate, sodium *tert*-butoxide, were purchased from Aldrich and used without further purification, $Pd(dba)_2$ was synthesized according to the method described,[15] 2,7-dibromonaphthalene was obtained *via* known procedure.[16] Dioxane was distilled over NaOH followed by the distillation over sodium under argon, acetonitrile was distilled over $CaH_2$, dichloromethane and methanol were used freshly distilled. Compound **2** was synthesized according to a procedure described.[17]

*7,14,15,17,18,21,22,28-Octahydro-13H,20H-8,12:27,23-dimethenodinaphtho[1,2-p:2',1'-n][1,4,7,13,18,24]dioxatetraazacyclohexacosine (**3a**)*. A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with compound **2** (0.1 mmol, 46 mg), $Pd(dba)_2$ (8 mol%, 4.5 mg), BINAP (9 mol%, 5.5 mg), absolute dioxane (5 ml), (*S*)-BINAM (0.1 mmol, 28.5 mg) was then added followed by sodium *tert*-butoxide (0.3 mmol, 29 mg). The reaction mixture was refluxed for 24 h, after cooling it down to ambient temperature the solvent was filtered, the precipitate was washed with $CH_2Cl_2$ (5 ml), combined organic fractions were evaporated *in vacuo*, and the residue was chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$/MeOH (200:1 – 3:1). The target compound **3a** was obtained with the eluent $CH_2Cl_2$/MeOH (100:1) as a brown solid. Yield 20 mg (34 %). In the case when DavePhos (9 mol%, mg) was used instead of BINAP, the yield was 43 %. (MALDI-TOF) found: 581.2876. $C_{38}H_{37}N_4O_2$ requires 581.2917 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.12 – 3.25 (4H, m), 3.61 (4H, s), 3.64 – 3.70 (4H, m), 5.51 (2H, s), 6.08 (2H, s), 6.19 (2H, dd, $^3J$=8.0 Hz, $^4J$=1.5 Hz), 6.35 (2H, dd, $^3J$=7.8 Hz, $^4J$=1.4 Hz), 6.97 (2H, t, $^3J$=8.0 Hz), 7.10 (2H, d, $^3J$=8.5 Hz), 7.20 – 7.24 (2H, m), 7.29 – 7.33 (2H, m), 7.68 (2H, d, $^3J$=9.0 Hz), 7.84 (2H, d, $^3J$=8.1 Hz), 7.86 (2H, d, $^3J$=9.0 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 43.8 (2C), 69.1 (2C), 70.0 (2C), 104.3 (2C), 106.1 (2C), 109.2 (2C), 117.9 (2C), 119.4 (2C), 123.5 (2C), 124.9 (2C), 126.8 (2C), 128.1 (2C), 129.2 (2C), 129.6 (2C), 130.0 (2C), 134.4 (2C), 140.0 (2C), 144.1 (2C), 149.1 (2C).

*$N^2,N^{2'}$-Bis(3-bromophenyl)-(S)-1,1'-binaphthyl-2,2'-diamine (**4**)*. A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with 1,3-dibromobenzene (0.22 mmol, 52 mg), $Pd(dba)_2$ (2 mol%, 1.2 mg), Xantphos (2.5 mol%, 1.2 mg), absolute dioxane (1 ml), (*S*)-BINAM (0.1 mmol, 28.5 mg) was then added followed by sodium *tert*-butoxide (0.3 mmol, 29 mg). The reaction mixture was refluxed for 8 h, after cooling it down to ambient temperature the solvent was filtered, the precipitate was washed with $CH_2Cl_2$ (5 ml), combined organic fractions were evaporated *in vacuo*, and the residue was chromatographed on silica gel using a sequence of eluents: hexanes/$CH_2Cl_2$ (10:1 – 1:2). The target compound **4** was obtained with the eluent hexanes/$CH_2Cl_2$ (10:1) as a light-beige solid. Yield 47 mg (68 %). (MALDI-TOF) found: 593.0251. $C_{32}H_{23}Br_2N_2$ requires 593.0228 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 5.46 (2H, br.s), 6.72 – 6.77 (2H, m), 6.94 – 6.98 (6H, m), 7.12 (2H, d, $^3J$=8.3 Hz), 7.23 – 7.27 (2H, m), 7.34 – 7.38 (2H, m), 7.65 (2H, d, $^3J$=8.8 Hz), 7.87 (2H, d, $^3J$=8.0 Hz), 7.92 (2H, d, $^3J$=8.8 Hz). $^{13}C$ NMR $\delta_c$ ppm: 117.0 (2C), 118.3 (2C), 118.9 (2C), 121.0 (2C), 123.0 (2C), 124.2 (2C), 124.4 (2C), 124.6 (2C), 127.3 (2C), 128.3 (2C), 129.7 (2C), 130.0 (2C), 130.4 (2C), 133.8 (2C), 139.0 (2C), 144.3 (2C).

*Typical procedure for the synthesis of macrocycles **3a-e**.* A two-neck flask equipped with a magnetic stirrer and reflux condenser is flushed with dry argon, charged with compound **4**, $Pd(dba)_2$, DavePhos, absolute dioxane, corresponding oxadiamine is then added followed by sodium *tert*-butoxide. The reaction mixture is refluxed for 24 h, after cooling it down to ambient temperature the solvent is filtered, the precipitate is washed with $CH_2Cl_2$ (5 ml), combined organic fractions are evaporated *in vacuo*, and the residue is chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$/MeOH (200:1 – 3:1).

*7,13,14,15,16,18,19,20,21,23,24,25,26,32-Tetradecahydro-8,12:31,27-dimethenodinaphtho[1,2-n:2',1'-l][1,26,5,11,16,22]dioxatetraazacyclotriacontine (**3b**)*. Obtained from compound **4** (0.17 mmol, 100 mg), dioxadiamine **2b** (0.17 mmol, 34 mg), in the presence of $Pd(dba)_2$ (8 mol%, 8 mg), DavePhos (8 mol%, 6 mg), and sodium *tert*-butoxide (0.51 mmol, 48 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (50:1). Yield 27 mg (25 %). (MALDI-TOF) found: 637.3590. $C_{42}H_{45}N_4O_2$ requires 637.3543 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.63-1.67 (4H, m), 1.80 (4H, quintet, $^3J$=5.9 Hz), 3.07 (4H, q, $^3J$=5.7 Hz), 3.42 – 3.46 (4H, m), 3.50 (4H, t, $^3J$=5.6 Hz), 3.94 (2H, br.s), 5.51 (2H, s), 6.03 (2H, t, $^4J$=2.0 Hz), 6.20 (2H, dd, $^3J$=8.1 Hz, $^4J$=2.0 Hz), 6.39 (2H, dd, $^3J$=7.8 Hz, $^4J$=2.0 Hz), 6.98 (2H, t, $^3J$=8.0 Hz), 7.12 (2H, d, $^3J$=8.3 Hz), 7.20 – 7.24 (2H, m), 7.28 – 7.32 (2H, m), 7.69 (2H, d, $^3J$=9.0 Hz), 7.83 (2H, d, $^3J$=8.2 Hz), 7.86 (2H, d, $^3J$=9.0 Hz). $^{13}C$ NMR $\delta_c$ ppm: 26.5 (2C), 29.3 (2C), 42.2 (2C), 69.3 (2C), 70.8 (2C), 104.2 (2C), 107.2 (2C), 108.8 (2C), 116.8 (2C), 118.9 (2C), 123.3 (2C), 124.7 (2C), 126.8 (2C), 128.1 (2C), 129.1 (2C), 129.4 (2C), 129.6 (2C), 134.1 (2C), 140.6 (2C), 143.9 (2C), 149.8 (2C).

*7,14,15,17,18,20,21,24,25,31-Decahydro-13H,23H-8,12:30,26-dimethenodinaphtho[1,2-s:2',1'-q][1,4,7,10,16,21,27]trioxatetraazacyclononacosine (**3c**)*. Obtained from compound **4** (0.2 mmol, 181 mg), trioxadiamine **2c** (0.2 mmol, 38 mg), in the presence of $Pd(dba)_2$ (16 mol%, 18 mg), DavePhos (18 mol%, 14 mg), and sodium *tert*-butoxide (0.6 mmol, 58 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 27 mg (22 %). (MALDI-TOF) found: 625.3258. $C_{40}H_{41}N_4O_3$ requires 625.3179 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.04 – 3.16 (4H, m), 3.64 (8H, s), 3.65 (4H, t, $^3J$=5.1 Hz), 5.47 (2H, s), 6.05 (2H, s), 6.23 (2H, d, $^3J$=7.7 Hz), 6.34 (2H, d, $^3J$=7.7 Hz), 6.93 (2H, t, $^3J$=8.0 Hz), 7.10 (2H, d, $^3J$=8.5 Hz), 7.20 – 7.24 (2H, m), 7.29 – 7.33 (2H, m), 7.65 (2H, d, $^3J$=9.0 Hz), 7.84 (2H, d, $^3J_{obs}$=6.8 Hz), 7.86 (2H, d, $^3J_{obs}$=8.6 Hz), two NH protons were not assigned.

*1,7,8,9,10,12,13,15,16,18,19,20,21,27-Tetradecahydro-2,6:26,22-dimethenodinaphtho[1,2-t:2',1'-r][1,4,7,11,17,22,28]trioxatetraazacyclohentriacontine (**3d**)*. Obtained from compound **4** (0.13 mmol, 77 mg), trioxadiamine **2d** (0.13 mmol, 29 mg), in the presence of $Pd(dba)_2$ (8 mol%, 6 mg), DavePhos (9 mol%, 4.5 mg), and sodium *tert*-butoxide (0.39 mmol, 38 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 22 mg (25 %). (MALDI-TOF)

found: 653.3528. $C_{42}H_{45}N_4O_3$ requires 653.3492 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.78 (4H, quintet, $^3J$=6.0 Hz), 3.06 (4H, t, $^3J$=6.3 Hz), 3.55 (4H, t, $^3J$=5.7 Hz), 3.57–3.60 (4H, m), 3.61–3.64 (4H, m), 3.70 (2H, br.s), 5.46 (2H, s), 5.98 (2H, s), 6.22 (2H, d, $^3J$=7.8 Hz), 6.33 (2H, d, $^3J$=7.8 Hz), 6.94 (2H, t, $^3J$=7.8 Hz), 7.12 (2H, d, $^3J$=8.5 Hz), 7.21–7.25 (2H, m), 7.29–7.33 (2H, m), 7.67 (2H, d, $^3J$=9.0 Hz), 7.84 (2H, d, $^3J_{obs}$=6.4 Hz), 7.86 (2H, d, $^3J_{obs}$=8.7 Hz). $^{13}C$ NMR $\delta_c$ ppm: 28.8 (2C), 42.0 (2C), 69.5 (2C), 70.2 (2C), 70.6 (2C), 103.9 (2C), 107.5 (2C), 108.8 (2C), 117.5 (2C), 119.5 (2C), 123.4 (2C), 124.8 (2C), 126.8 (2C), 128.1 (2C), 129.1 (2C), 129.5 (2C), 129.6 (2C), 134.2 (2C), 140.4 (2C), 144.2 (2C), 149.2 (2C).

*1,8,9,11,12,14,15,17,18,21,22,28-Dodecahydro-7H,20H-2,6:27,23-dimethenodinaphtho[1,2-v:2',1'-t][1,4,7,10,13,19,24,30]tetraoxatetraazacyclodotriacontine* ***(3e)***. Obtained from compound **4** (0.1 mmol, 59 mg), tetraoxadiamine **2e** (0.1 mmol, 24 mg), in the presence of $Pd(dba)_2$ (8 mol%, 4.5 mg), DavePhos (9 mol%, 3 mg), and sodium *tert*-butoxide (0.3 mmol, 28.5 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 18 mg (27 %). (MALDI-TOF) found: 669.3493. $C_{42}H_{45}N_4O_4$ requires 669.3441 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.05–3.12 (4H, m), 3.58–3.66 (16H, m), 5.49 (2H, s), 6.09 (2H, br.s), 6.28 (2H, d, $^3J$=8.1 Hz), 6.35 (2H, dd, $^3J$=7.6 Hz, $^4J$=1.0 Hz), 6.93 (2H, t, $^3J$=8.0 Hz), 7.10 (2H, d, $^3J$=8.7 Hz), 7.21–7.25 (2H, m), 7.29–7.33 (2H, m), 7.65 (2H, d, $^3J$=9.0 Hz), 7.84 (2H, $^3J_{obs}$=7.2 Hz), 7.86 (2H, $^3J_{obs}$=8.7 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 44.0 (2C), 69.2 (2C), 70.3 (2C), 70.6 (2C), 70.7 (2C), 104.2 (2C), 108.1 (2C), 109.5 (2C), 117.3 (2C), 119.2 (2C), 123.4 (2C), 124.8 (2C), 126.8 (2C), 128.1 (2C), 129.1 (2C), 129.5 (2C), 129.8 (2C), 134.2 (2C), 140.3 (2C), 144.1 (2C), 148.8 (2C).

*N²,N²'-Bis(7-bromonaphthalen-2-yl)-(S)-1,1'-binaphthyl-2,2'-diamine* (**5**). A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with 2,7-dibromonaphthalene (1.4 mmol, 400 mg), $Pd(dba)_2$ (4 mol%, 12 mg), Xantphos (4.5 mol%, 13 mg), absolute dioxane (5 ml), (*S*)-BINAM (0.5 mmol, 142 mg) was then added followed by sodium *tert*-butoxide (2 mmol, 192 mg). The reaction mixture was refluxed for 8 h, after cooling it down to ambient temperature the solvent was filtered, the precipitate was washed with $CH_2Cl_2$ (5 ml), combined organic fractions were evaporated *in vacuo*, and the residue was chromatographed on silica gel using a sequence of eluents: hexane/$CH_2Cl_2$ (10:1–1:2). The target compound **5** was obtained with the eluent hexanes/$CH_2Cl_2$ (4:1) as a beige solid. Yield 180 mg (52 %). (MALDI-TOF) found: 693.0511. $C_{40}H_{27}Br_2N_2$ requires 693.0541 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 5.65 (2H, br.s), 6.81 (2H, d, $^3J$=8.8 Hz), 6.91 (2H, s), 7.19–7.44 (14H, m), 7.76 (2H, d, $^3J$=8.7 Hz), 7.93–7.98 (4H, m). $^{13}C$ NMR $\delta_c$ ppm: 110.4 (2C), 119.2 (2C), 119.9 (2C), 120.0 (2C), 120.4 (2C), 124.3 (2C), 124.7 (2C), 126.5 (2C), 127.2 (2C), 127.3 (2C), 128.0 (2C), 128.3 (2C), 128.9 (4C), 129.5 (2C), 130.1 (2C), 134.0 (2C), 135.2 (2C), 139.0 (2C), 141.7 (2C).

*Typical procedure for the synthesis of macrocycles* ***6a,b,d,e***. A two-neck flask equipped with a magnetic stirrer and reflux condenser is flushed with dry argon, charged with compound **5**, Pd(dba), DavePhos, absolute dioxane, corresponding oxadiamine is then added followed by sodium *tert*-butoxide. The reaction mixture is refluxed for 24 h, after cooling it down to ambient temperature the solvent is filtered, the precipitate is washed with $CH_2Cl_2$ (5 ml), combined organic fractions are evaporated *in vacuo*, and the residue is chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$/MeOH (200:1–3:1).

*Macrocycle* ***6a***. Obtained from compound **5** (0.17 mmol, 117 mg), dioxadiamine **2a** (0.17 mmol, 25 mg), in the presence of $Pd(dba)_2$ (8 mol%, 8 mg), DavePhos (9 mol%, 6 mg), and sodium *tert*-butoxide (0.51 mmol, 49 mg) in 8 ml dioxane. Eluent: $CH_2Cl_2$/MeOH (200:1). Yield 40 mg (34 %). (MALDI-TOF) found: 681.3204. $C_{46}H_{41}N_4O_2$ requires 681.3230 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.26–3.33 (4H, m), 3.69 (4H, s), 3.78 (4H, t, $^3J$=4.7 Hz), 3.98 (2H, br.s), 5.64 (2H, s), 6.30 (2H, s), 6.66 (2H, s), 6.68-6.76 (4H, m), 7.18 (2H, d, $^3J$=8.5 Hz), 7.25–7.30 (4H, m), 7.33 (2H, d, $^3J$=8.5 Hz), 7.38 (2H, t, $^3J$=7.4 Hz), 7.74 (2H, d, 9.0 Hz), 7.90 (2H, d, $^3J$=8.1 Hz), 7.94 (2H, d, $^3J$=9.0 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 53.4 (2C), 60.1 br. (2C), 69.4 (2C), 109.9 br. (2C), 114.7 (2C), 115.7 (2C), 121.1 br. (4C), 124.1 (2C), 125.1 (2C), 126.9 (2C), 128.2 (2C), 128.6 (2C), 128.7 (2C), 129.3 (2C), 130.1 (2C), 134.3 (2C), 135.4 br. (2C), 139.3 br. (2C), 142.1 (2C), six quaternary carbon atoms were not assigned due to line broadening.

*Macrocycle* ***6b***. Obtained from compound **5** (0.16 mmol, 110 mg), dioxadiamine **2b** (0.16 mmol, 33 mg), in the presence of $Pd(dba)_2$ (8 mol%, 7.5 mg), DavePhos (9 mol%, 6 mg), and sodium *tert*-butoxide (0.48 mmol, 46 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 37 mg (31 %). (MALDI-TOF) found: 737.3937. $C_{50}H_{49}N_4O_2$ requires 737.3856 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.70–1.74 (4H, m), 1.90 (4H, quintet, $^3J$=6.0 Hz), 3.13–3.26 (4H, m), 3.48–3.52 (4H, m), 3.58 (4H, t, $^3J$=5.5 Hz), 5.71 (2H, s), 6.31 (2H, br.s), 6.70 (2H, dd, $^3J$=8.3 Hz, $^4J$=1.5 Hz), 6.78 (2H, d, $^4J$=2.3 Hz), 6.83 (2H, dd, $^3J$=8.3 Hz, $^4J$=2.3 Hz), 7.17 (2H, d, $^3J$=8.0 Hz), 7.23–7.27 (2H, m), 7.32–7.36 (2H, m), 7.43 (4H, d, $^3J$=8.7 Hz), 7.72 (2H, d, $^3J$=9.0 Hz), 7.87 (2H, d, $^3J$=8.0 Hz), 7.91 (2H, d, $^3J$=8.8 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 26.5 (2C), 29.1 (2C), 42.8 br. (2C), 69.3 (2C), 70.8 (2C), 112.5 (2C), 116.2 (2C), 117.0 (2C), 117.9 (2C), 119.7 (2C), 123.6 (2C), 124.9 (2C), 126.9 (2C), 128.2 (2C), 128.4 (2C), 128.6 (2C), 129.3 (2C), 129.7 (4C), 134.2 (2C), 136.2 (2C), 140.3 (2C), 141.3 (2C), four quaternary carbon atoms were not assigned due to line broadening.

*Macrocycle* ***6d***. Obtained from compound **5** (0.26 mmol, 180 mg), trioxadiamine **2d** (0.26 mmol, 57 mg), in the presence of $Pd(dba)_2$ (8 mol%, 12 mg), DavePhos (9 mol%, 9 mg), and sodium *tert*-butoxide (0.78 mmol, 75 mg) in 8 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 29 mg (15 %). (MALDI-TOF) found: 753.3846. $C_{50}H_{49}N_4O_3$ requires 753.3805 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.81–1.95 (4H, m), 3.12–3.25 (4H, m), 3.62–3.72 (12H, m), 5.68 (2H, s), 6.15 (2H, s), 6.68 (2H, s), 6.71 (2H, d, $^3J$=9.0 Hz), 6.77 (2H, dd, $^3J$=8.6 Hz, $^4J$=1.9 Hz), 7.18 (2H, d, $^3J$=8.3 Hz), 7.24–7.28 (2H, m), 7.32–7.36 (2H, m), 7.38 (2H, d, $^3J$=8.7 Hz), 7.39 (2H, d, $^3J$=8.9 Hz), 7.71 (2H, d, $^3J$=8.8 Hz), 7.89 (2H, d, $^3J$=8.1 Hz), 7.91 (2H, d, $^3J$=9.1 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 28.3 (2C), 43.2 br. (2C), 69.7 (2C), 70.2 (2C), 70.6 (2C), 115.6 (2C), 116.3 (2C), 116.8 (2C), 120.1 (2C), 123.8 (2C), 125.0 (2C), 126.9 (2C), 128.2 (2C), 128.4 (2C), 128.6 (2C), 129.3 (2C), 129.7 (2C), 129.9 (2C), 134.3 (2C), 136.0 (2C), 140.0 (2C), 141.7 (2C), six quaternary carbon atoms were not assigned due to line broadening.

*Macrocycle* ***6e***. Obtained from compound **5** (0.1 mmol, 69 mg), tetraoxadiamine **2e** (0.1 mmol, 24 mg), in the presence of $Pd(dba)_2$ (16 mol%, 9 mg), DavePhos (18 mol%, 7 mg), and sodium *tert*-butoxide (0.3 mmol, 29 mg) in 5 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 5 mg (7 %). (MALDI-TOF) found: 769.3815. $C_{50}H_{49}N_4O_4$ requires 769.3754 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.18 (4H, br.s), 3.65–3.75 (16H, m), 5.65 (2H, s), 6.22 (2H, br.s), 6.71 (2H, s), 6.73–6.79 (4H, m), 7.17 (2H, d, $^3J$=8.0 Hz), 7.28 (2H, d, $^3J$=8.1 Hz), 7.31–7.40 (6H, m), 7.71 (2H, d, $^3J$=9.0 Hz), 7.89 (2H, d, $^3J$=8.6 Hz), 7.93 (2H, d, $^3J$=9.2 Hz), two NH protons were not assigned.

*N²,N²'-Bis(3-bromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(7)***. A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with (*S*)-BINAM (1 mmol, 284 mg), 1-(bromomethyl)-3-bromobenzene (2 mmol, 496 mg), acetonitrile (10 ml) and potassium carbonate (4 mmol, 552 mg). The reaction mixture was stirred at reflux for 24 h, after cooling it down to ambient temperature the solvent was filtered, the precipitate was washed with $CH_2Cl_2$ (5 ml), combined organic fractions were evaporated *in vacuo*, and the residue was chromatographed on silica gel using a sequence of eluents: hexanes/$CH_2Cl_2$ (4:1–1:2), $CH_2Cl_2$. The target compound **7** was obtained with the eluent hexanes/$CH_2Cl_2$ (1:1) as a yellow viscous oil. Yield 199 mg

(32 %). (MALDI-TOF) found: 621.0505. $C_{34}H_{27}Br_2N_2$ requires 621.0541 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 4.35 (2H, br.s), 4.40 (4H, s), 7.08–7.16 (8H, m), 7.24–7.30 (4H, m), 7.33 (2H, d, $^3J$=7.7 Hz), 7.40 (2H, s), 7.78–7.81 (2H, m), 7.84 (2H, d, $^3J$=9.0 Hz). $^{13}C$ NMR $\delta_c$ ppm: 46.7 (2C), 112.0 (2C), 113.9 (2C), 122.3 (2C), 122.7 (2C), 123.7 (2C), 125.3 (2C), 127.1 (2C), 127.8 (2C), 128.2 (2C), 129.6 (2C), 129.8 (2C), 130.0 (2C), 133.7 (2C), 142.3 (2C), 143.5 (2C).

*$N^2,N^{2'}$-Tris(3-bromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(9)***. Obtained as the second product in the synthesis of compound **7**. Eluent: hexanes/$CH_2Cl_2$ (2:1). Yield 117 mg (15 %). (MALDI-TOF) found: 789.0180. $C_{41}H_{32}Br_3N_2$ requires 789.0116 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.98 (2H, d, $^2J$=14.7 Hz), 4.00 (1H, br.s), 4.03 (2H, d, $^2J$=14.7 Hz), 4.25 (1H, d, $^2J$=15.8 Hz), 4.42 (1H, d, $^2J$=15.8 Hz), 6.77 (2H, d, $^3J$=7.6 Hz), 6.95–7.02 (7H, m), 7.12 (1H, d, $^3J$=8.8 Hz), 7.18–7.28 (5H, m), 7.30–7.36 (2H, m), 7.43 (1H, ddd, $^3J$=7.8 Hz, $^3J$=6.1 Hz, $^4J$=1.9 Hz), 7.48 (1H, d, $^3J$=8.9 Hz), 7.80–7.85 (2H, m), 7.92 (1H, d, $^3J$=8.1 Hz), 7.96 (1H, d, $^3J$=8.8 Hz). $^{13}C$ NMR $\delta_c$ ppm: 47.1 (1C), 56.2 (2C), 113.7 (1C), 115.5 (1C), 122.1 (1C), 122.2 (2C), 122.6 (1C), 124.1 (1C), 124.9 (1C), 125.2 (1C), 125.3 (1C), 125.8 (1C), 126.7 (1C), 127.0 (1C), 127.1 (2C), 127.7 (1C), 128.1 (1C), 128.3 (1C), 129.1 (1C), 129.4 (3C), 129.7 (1C), 129.9 br. (4C), 130.8 (1C), 131.5 (2C), 133.6 (2C), 140.5 (3C), 142.2 (1C), 142.5 (1C), 149.0 (1C).

*$N^2,N^2$-Bis(3-bromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(10)***. Obtained as the third product in the synthesis of compound **7**. Eluent: hexanes/$CH_2Cl_2$ (1:2).Yield 31 mg (5 %) (in the mixture with compound **7**). (MALDI-TOF) found: 621.0488. $C_{34}H_{27}Br_2N_2$ requires 621.0541 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.98 (2H, d, $^2J$=14.8 Hz), 4.03 (2H, d, $^2J$=14.8 Hz), 6.81 (2H, d, $^3J$=7.7 Hz), 7.00 (2H, t, $^3J$=7.8 Hz), 7.03 (1H, d, $^3J$=7.8 Hz), 7.06 (2H, s), 7.10–7.35 (10H, m), 7.24 (1H, ddd, $^3J$=8.3 Hz, $^3J$=6.8 Hz, $^4J$=1.4 Hz), 7.42–7.46 (1H, m), 7.53 (1H, d, $^3J$=8.8 Hz), 7.83–7.89 (2H, m), 7.93 (1H, d, $^3J$=8.2 Hz), 7.98 (1H, d, $^3J$=8.8 Hz), two NH protons were not assigned.

*$N^2$-(3-Bromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(11)***. Obtained as the fourth product in the synthesis of compound **7**. Eluent: $CH_2Cl_2$.Yield 100 mg (22 %). (MALDI-TOF) found: 453.0937. $C_{27}H_{22}BrN_2$ requires 453.0966 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.83 (3H, br.s), 4.36 (2H, s), 7.07–7.15 (5H, m), 7.17 (1H, d, $^3J$=8.8 Hz), 7.19–7.23 (2H, m), 7.26–7.30 (2H, m), 7.32 (1H, d, $^3J$=7.7 Hz), 7.40 (1H, s), 7.77–7.85 (4H, m). $^{13}C$ NMR $\delta_c$ ppm: 46.8, 112.0, 112.6, 113.9, 118.3, 122.1, 122.5, 122.7, 123.7, 123.9, 125.4, 126.8, 127.0, 127.7, 128.1, 128.2, 128.5, 129.6, 129.7 (2C), 130.0 (2C), 133.5, 133.9, 142.4, 142.9, 143.3.

*Typical procedure for the synthesis of macrocycles* ***12a***,***b***,***d***. A two-neck flask equipped with a magnetic stirrer and reflux condenser is flushed with dry argon, charged with compound **7**, $Pd(dba)_2$, BINAP, absolute dioxane, corresponding oxadiamine is then added followed by sodium *tert*-butoxide. The reaction mixture is refluxed for 24 h, after cooling it down to ambient temperature the solvent is filtered, the precipitate is washed with $CH_2Cl_2$ (5 ml), combined organic fractions are evaporated *in vacuo*, and the residue is chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$/MeOH (200:1–3:1).

*7,8,15,16,18,19,22,23,29,30-Decahydro-14H,21H-9,13:28,24-dimethenodinaphtho[1,2-q:2',1'-o][1,4,7,14,19,26]dioxatetraazacyclooctacosine* ***(12a)***. Obtained from compound **7** (0.13 mmol, 82 mg), dioxadiamine **2a** (0.13 mmol, 19 mg), in the presence of $Pd(dba)_2$ (8 mol%, 6 mg), BINAP (9 mol%, 8 mg), and sodium *tert*-butoxide (0.39 mmol, 40 mg) in 4 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 32 mg (41 %). (MALDI-TOF) found: 609.3180. $C_{40}H_{41}N_4O_2$ requires 609.3230 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.11 (4H, t, $^3J$=4.9 Hz), 3.53 (4H, t, $^3J$=4.9 Hz), 3.54 (4H, s), 4.22 (2H, d, $^2J$=15.3 Hz), 4.34 (2H, d, $^2J$=15.3 Hz), 4.68 (2H, s), 6.47 (2H, d, $^3J$=8.5 Hz), 6.49 (2H, s), 6.56 (2H, d, $^3J$=7.2 Hz), 6.99–7.05 (4H, m), 7.14–7.22 (4H, m), 7.24 (2H, d, $^3J$=7.5 Hz), 7.73-7.76 (2H, m), 7.82 (2H, d, $^3J$=9.0 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 43.7 (2C), 48.3 (2C), 69.3 (2C), 70.2 (2C), 111.6 (2C), 112.1 (4C), 114.6 (2C), 116.5 (2C), 121.9 (2C), 123.9 (2C), 126.7 (2C), 127.8 (2C), 128.1 (2C), 129.3 (2C), 129.6 (2C), 133.8 (2C), 141.0 (2C), 144.7 (2C), 148.1 (2C).

*1,2,8,9,10,11,13,14,15,16,18,19,20,21,27,28-Hexadecahydro-3,7:26,22-dimethenodinaphtho[1,2-o:2',1'-m][1,28,5,12,17,24]dioxatetraazacyclodotriacontine* ***(12b)***. Obtained from compound **7** (0.13 mmol, 82 mg), dioxadiamine **2b** (0.13 mmol, 26 mg), in the presence of $Pd(dba)_2$ (8 mol%, 6 mg), BINAP (9 mol%, 8 mg), and sodium *tert*-butoxide (0.39 mmol, 40 mg) in 4 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (200:1). Yield 38 mg (44 %). (MALDI-TOF) found: 665.3817. $C_{44}H_{49}N_4O_2$ requires 665.3856 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.62–1.66 (4H, m), 1.77 (4H, quintet, $^3J$=5.7 Hz), 3.09 (4H, t, $^3J$=6.0 Hz), 3.38–3.42 (4H, m), 3.46 (4H, t, $^3J$=5.4 Hz), 4.19–4.38 (6H, m), 6.40 (2H, d, $^3J$=7.5 Hz), 6.46 (2H, s), 6.50 (2H, d, $^3J$=8.0 Hz), 6.98 (2H, t, $^3J$=7.7 Hz), 7.01–7.05 (2H, m), 7.15–7.21 (6H, m), 7.73–7.77 (2H, m), 7.80 (2H, d, $^3J$=8.9 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 26.7 (2C), 29.2 (2C), 42.1 (2C), 47.7 (2C), 69.5 (2C), 70.8 (2C), 110.8 (2C), 111.1 (2C), 111.9 (2C), 114.3 (2C), 115.4 (2C), 121.8 (2C), 123.9 (2C), 126.6 (2C), 128.0 (2C), 129.3 (2C), 129.5 (2C), 133.9 (2C), 140.9 (2C), 144.4 (2C), 148.9 (2C).

*1,2,8,9,10,11,13,14,16,17,19,20,21,22,28,29-Hexadecahydro-3,7:27,23-dimethenodinaphtho[1,2-u:2',1'-s][1,4,7,11,18,23,30]trioxatetraazacyclotritriacontine* ***(12d)***. Obtained from compound **7** (0.13 mmol, 82 mg), trioxadiamine **2d** (0.13 mmol, 29 mg), in the presence of $Pd(dba)_2$ (8 mol%, 6 mg), BINAP (9 mol%, 8 mg), and sodium *tert*-butoxide (0.39 mmol, 40 mg) in 4 ml of dioxane. Eluent: $CH_2Cl_2$/MeOH (100:1). Yield 39 mg (45 %). (MALDI-TOF) found: 681.3759. $C_{44}H_{49}N_4O_3$ requires 681.3805 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 1.74 (4H, quintet, $^3J$=6.0 Hz), 3.08 (4H, t, $^3J$=6.3 Hz), 3.52 (4H, t, $^3J$=5.8 Hz), 3.54–3.57 (4H, m), 3.60–3.63 (4H, m), 4.25 (2H, d, $^2J$=15.7 Hz), 4.30 (2H, br.s), 4.44 (2H, d, $^2J$=15.7 Hz), 6.48 (2H, d, $^3J$=7.7 Hz), 6.52 (2H, s), 6.56 (2H, d, $^3J$=7.6 Hz), 6.99–7.04 (4H, m), 7.14–7.20 (6H, m), 7.73–7.77 (2H, m), 7.81 (2H, d, $^3J$=9.0 Hz), two NH protons were not assigned. $^{13}C$ NMR $\delta_c$ ppm: 28.6 (2C), 42.3 (2C), 47.7 (2C), 69.8 (2C), 70.1 (2C), 70.6 (2C), 111.6 (4C), 111.8 (2C), 114.2 (2C), 116.0 (2C), 121.8 (2C), 123.9 (2C), 126.6 (2C), 127.7 (2C), 128.1 (2C), 129.3 (2C), 129.6 (2C), 133.9 (2C), 141.0 (2C), 144.4 (2C), 148.2 (2C).

*$N^2,N^{2'}$-Bis(3,5-dibromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(13)***. A two-neck flask equipped with a magnetic stirrer and reflux condenser, flushed with dry argon, was charged with (*S*)-BINAM (2.4 mmol, 674mg), 1,3-dibromo-5-(bromomethyl)benzene (4.8 mmol, 1551 mg), acetonitrile (24 ml) and potassium carbonate (9.6 mmol, 1325 mg). The reaction mixture was stirred at reflux for 24 h, after cooling it down to ambient temperature the solvent was filtered, the precipitate was washed with $CH_2Cl_2$ (10 ml), combined organic fractions were evaporated *in vacuo*, and the residue was chromatographed on silica gel using a sequence of eluents: hexanes/$CH_2Cl_2$ (10:1–1:1). The target compound **13** was obtained with the eluent hexanes/$CH_2Cl_2$ (2:1) as a yellow viscous oil. Yield 1424 mg (76 %). (MALDI-TOF) found: 776.8662. $C_{34}H_{25}Br_4N_2$ requires 776.8751 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 4.41 (4H, s), 4.45 (2H, br.s), 7.11 (2H, d, $^3J$=9.0 Hz), 7.21 (2H, d, $^3J$=8.3 Hz), 7.23 (2H, ddd, $^3J$=8.1 Hz, $^3J$=7.0 Hz, $^4J$=1.3 Hz), 7.37 (4H, d, $^4J$=1.8 Hz), 7.38 (2H, ddd, $^3J$=8.3 Hz, $^3J$=7.0 Hz, $^4J$=1.4 Hz), 7.55 (2H, t, $^4J$=1.8 Hz), 7.86 (2H, d, $^3J$=7.8 Hz), 7.90 (2H, $^3J$=9.0 Hz). $^{13}C$ NMR $\delta_c$ ppm: 46.0 (2C), 111.9 (2C), 113.5 (2C), 122.5 (2C), 123.1 (4C), 123.6 (2C), 127.4 (2C), 127.8 (2C), 128.3 (6C), 130.0 (2C), 132.5 (2C), 133.6 (2C), 142.9 (2C), 144.1 (2C).

*$N^2,N^2,N^{2'}$-Tris(3,5-dibromobenzyl)-(S)-1,1'-binaphthyl-2,2'-diamine* ***(14)***. Obtained as the second product in the synthesis of compound **13**. Eluent: hexanes/$CH_2Cl_2$ (10:1). Yield 150 mg (9 %). (MALDI-TOF) found: 1022.71. $C_{41}H_{29}Br_6N_2$ requires 1022.74 $[M+H]^+$. $^1H$ NMR $\delta_H$ ppm: 3.95 (1H, br.s), 3.97 (4H, s), 4.22 (1H, dd, $^2J$=16.8 Hz, $^3J$=4.8 Hz), 4.43 (1H, dd, $^2J$=16.8 Hz, $^3J$=6.8 Hz), 6.81 (4H, d, $^4J$=1.5 Hz), 6.89–6.92 (1H, m), 7.06 (1H, d, $^3J$=9.0 Hz), 7.15 (2H, d, $^4J$=1.3 Hz), 7.19–7.27 (2H, m), 7.31 (1H, d, $^3J$=8.2 Hz),

7.37 (2H, t, $^4J$=1.5 Hz), 7.37-7.41 (1H, m), 7.43 (1H, t, $^3J$=1.3 Hz), 7.45–7.49 (1H, m), 7.53 (1H, d, $^3J$=9.0 Hz), 7.80–7.83 (1H, m), 7.86 (1H, d, $^3J$=9.1 Hz), 7.94 (1H, $^3J$=8.1 Hz), 8.02 (1H, $^3J$=8.8 Hz). $^{13}$C NMR $\delta_c$ ppm: 46.5 (1C), 57.5 (2C), 113.5, 115.4, 121.6, 122.5, 123.1, 123.7, 125.3, 125.5, 126.4, 127.1, 127.6, 127.8, 128.2, 128.4, 128.6, 129.7, 129.9, 130.1, 131.2, 132.5, 132.6, 133.5, 133.6, 141.9, 142.1, 143.9, 148.9 (integration of the aromatic carbons is ambiguous).

*N²-(3,5-Dibromobenzyl)-1,1'-binaphthyl-2,2'-diamine* ***(15)***. Obtained as the third product in the synthesis of compound **13**. Eluent: hexanes/$CH_2Cl_2$ (2:1). Yield 200 mg (16 %). (MALDI-TOF) found: 531.0029. $C_{27}H_{21}Br_2N_2$ requires 531.0072 $[M+H]^+$. $^1$H NMR $\delta_H$ ppm: 3.73 (2H, br.s), 4.31 (2H, s), 4.32 (1H, br.s), 7.03 (1H, d, $^3J$=9.0 Hz), 7.11–7.16 (2H, m), 7.18 (1H, d, $^3J$=8.7 Hz), 7.20–7.25 (2H, m), 7.28–7.34 (2H, m), 7.35 (2H, d, $^4J$=1.5 Hz), 7.51 (1H, t, $^4J$=1.5 Hz), 7.78–7.87 (4H, m). $^{13}$C NMR $\delta_c$ ppm: 46.1 (1C), 111.8 (1C), 112.7 (1C), 113.6 (1C), 118.3 (1C), 122.3 (1C), 122.6 (2C), 123.1 (1C), 123.7 (1C), 123.8 (1C), 126.9 (1C), 127.2 (1C), 127.8 (1C), 128.1 (1C), 128.2 (1C), 128.4 (3C), 129.7 (2C), 132.5 (1C), 133.4 (1C), 133.8 (1C), 142.8 (1C), 142.9 (1C), 144.2 (1C).

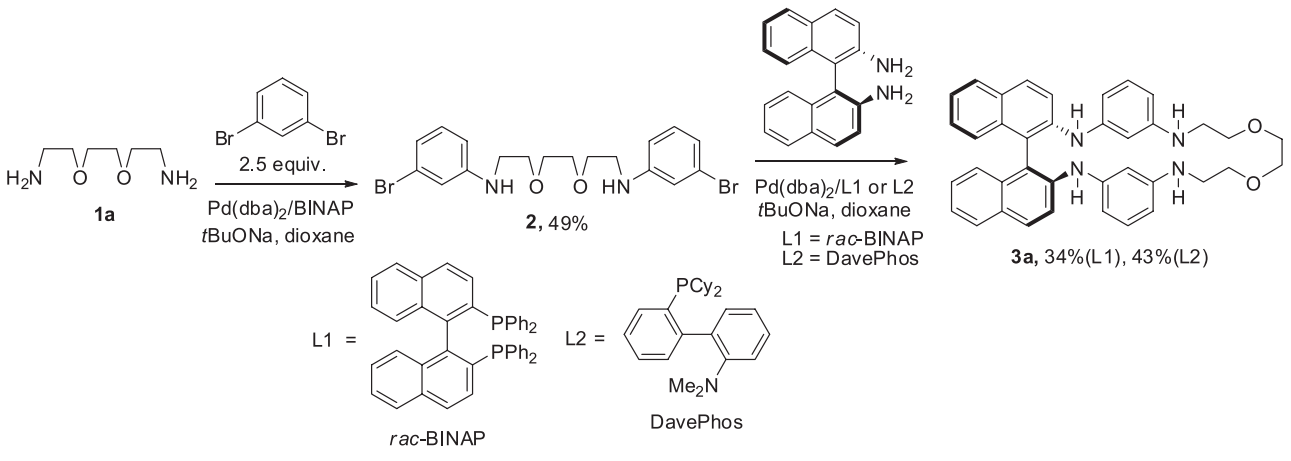
*Macrocycle* ***16***. A two-neck flask equipped with a magnetic stirrer and reflux condenser is flushed with dry argon, charged with compound **13** (0.25 mmol, 194 mg), $Pd(dba)_2$ (16 mol%, 23 mg), BINAP (18 mol%, 28 mg), absolute dioxane (12 ml), trioxadiamine **2d** (0.5 mmol, 110 mg) is then added followed by sodium *tert*-butoxide (0.75 mmol, 72 mg). The reaction mixture is refluxed for 24 h, after cooling it down to ambient temperature the solvent is filtered, the precipitate is washed with $CH_2Cl_2$ (5 ml), combined organic fractions are evaporated *in vacuo*, and the residue is chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$/MeOH (200:1–50:1). The macrocycle **16** was obtained with $CH_2Cl_2$/MeOH (100:1) as a yellow viscous oil, yield 28 mg (13 %). (MALDI-TOF) found: 837.1954. $C_{44}H_{47}Br_2N_4O_3$ requires 837.2015 $[M+H]^+$. $^1$H NMR $\delta_H$ ppm: 1.68 (4H, quintet, $^3J$=5.3 Hz), 2.97–3.02 (4H, m), 3.48–3.52 (4H, m), 3.54–3.57 (4H, m), 3.60–3.63 (4H, m), 4.19 (2H, dd, $^2J$=15.5 Hz, $^3J$=4.5 Hz), 4.27 (2H, dd, $^3J$=5.4 Hz, $^3J$=4.5 Hz), 4.34 (2H, dd, $^2J$=15.5 Hz, $^3J$=5.4 Hz), 6.35 (2H, s), 6.53 (2H, s), 6.64 (2H, s), 7.01–7.05 (2H, m), 7.14 (2H, d, $^3J$=9.1 Hz), 7.18–7.23 (4H, m), 7.76–7.80 (2H, m), 7.83 (2H, d, $^3J$=9.1 Hz). $^{13}$C NMR $\delta_c$ ppm: 28.5 (2C), 41.7 (2C), 47.1 (2C), 69.7 (2C), 70.0 (2C), 70.5 (2C), 109.5 (2C), 111.9 (2C), 113.5 (2C), 114.0 (2C), 117.8 (2C), 122.1 (2C), 123.3 (2C), 123.8 (2C), 126.9 (2C), 127.8 (2C), 128.1 (2C), 129.8 (2C), 133.8 (2C), 142.8 (2C), 144.0 (2C), 150.1 (2C).

## Results and Discussion

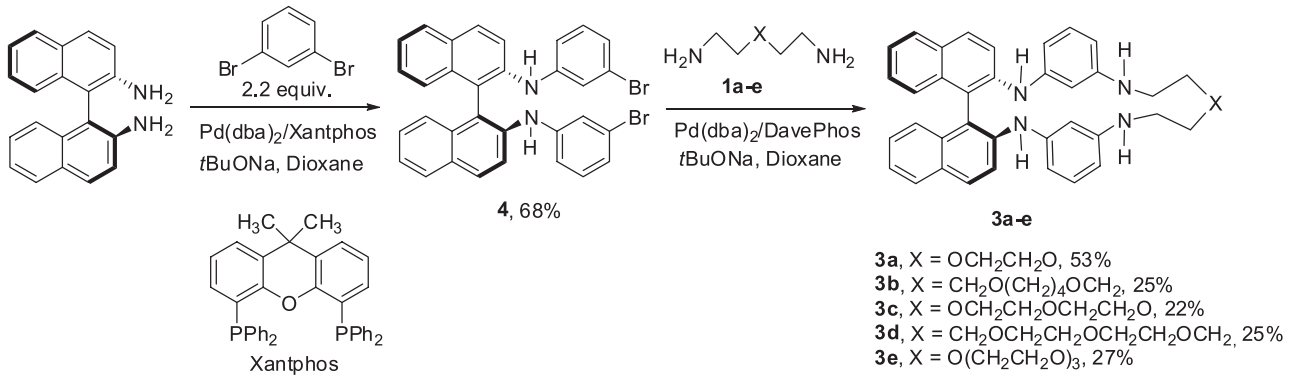
As BINAM molecule contains two identical primary amino groups, to furnish a macrocyclic structure with polyamine chain by means of Pd(0)-catalyzed amination, one needs to introduce the aromatic spacer between nitrogen atoms of BINAM and polyamine. At first we compared two approaches for introducing such spacer, the first one employing the reaction of BINAM with *N,N'*-bis(bromophenyl) substituted oxadiamine, the second one using the coupling of *N,N'*-bis(bromophenyl) substituted binaphthalene-2,2'-diamine with free oxadiamine. According to the first method, we synthesized *N,N'*-di(3-bromophenyl) substituted dioxadiamine **2** starting from dioxadiamine **1a** according to the known procedure,[17] and then introduced it in the macrocyclization reaction with (*S*)-BINAM using two catalytic systems: $Pd(dba)_2$/BINAP and $Pd(dba)_2$/DavePhos (Scheme 1). The reactions were run in boiling dioxane with equimolar amounts of the reagents ($c$=0.02 M) in the presence of sodium *tert*-butoxide taken as a base.

The target macrocycle **3a** was obtained by the column chromatography on silica gel and it was found that DavePhos provided slightly better results than BINAP (43 % compared to 34 %). Here and further all compounds were isolated by column chromatography and reported yields correspond to isolated products. Using the second method, at first *N,N'*-di(3-bromophenyl) substituted BINAM **4** was synthesized in 68 % yield by reacting BINAM with 2.2 equiv. 1,3-dibromobenzene in the presence of $Pd(dba)_2$/Xantphos catalytic system (Scheme 2). The necessity to use Xantphos instead of more universal BINAP ligand is explained by a high reactivity of the amino groups in BINAM that results in the formation of a considerable amount of linear oligomers caused by the diamination of 1,3-dibromobenzene. The second macrocyclization step with dioxadiamine **1a** was run using $Pd(dba)_2$/DavePhos catalytic system and gave the target macrocycle **3a** in 53 % yield (Scheme 2) what is a good result for the catalytic macrocyclization reactions. The overall yield of the macrocycle according to the first method was 21 % while in the second method it attained 36 % thus we chose it for the synthesis of other oxadiazamacrocycles. Moreover, the chromatographic isolation of the intermediate compound **4** is much easier than that of oxadiamine derivative **2**.

The reactions of other oxadiamines **3b-d** differing in the number of the oxygen atoms and chain length were conducted under stated conditions and produced similar results: the yields of the macrocyclization products ranged




**Scheme 1.**




**Scheme 2.**

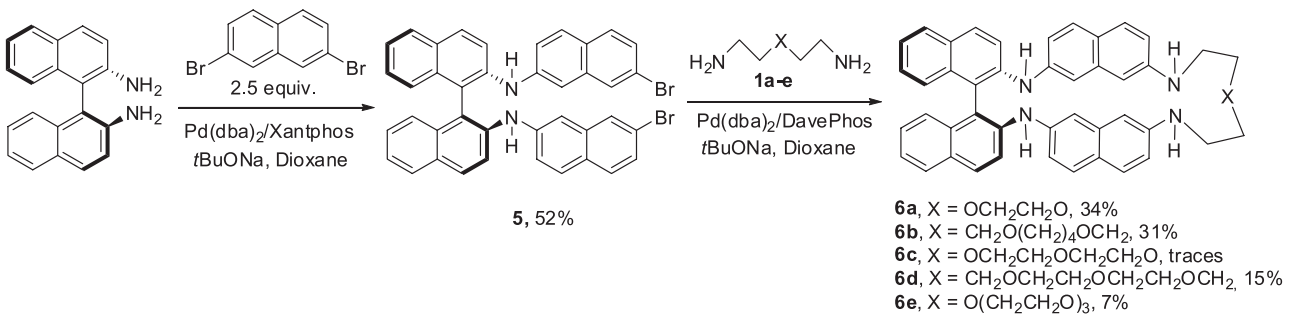
from 22 to 27 %, thus only the diamine with the shortest chain provided two times higher yield, probably due to a better adjustment of its two amino groups to two bromine atoms in the compound **4**.

A similar approach was used for the synthesis of the macrocycles possessing two 2,7-disubstituted naphthalene moieties. The reaction of BINAM with 2.5 equiv. of 2,7-dibromonaphthalene afforded *N,N'*-di(7-bromonaphth-2-yl) derivative **5** in 52 % yield, and this compound was introduced in the series of catalytic macrocyclization reactions with the same oxadiamines **1a-e** (Scheme 3). Again the best result was obtained with the shortest oxadiamine **1a** (34 % yield of the corresponding macrocycle **6a**), rather good yield was also provided by another oxadiamine **1b** with a longer chain, (31 % yield of **6b**). However, the results with other oxadiamines were less encouraging: trioxadiamine **1d** gave 15 % yield of the macrocyclization poroduct **6d**, tetraoxadiamine **1e** cyclized into the target product only in 7 % yield, while trioxadiamine **6c** provided corresponding macrocycle **6c** only in trace amounts in the reaction mixture. We may propose the same explanation for the observing effect of the chain length as in the case with macrocycles **3**, but in the reaction of oxadiamines with dinaphthyl derivative **5** this dependence is more pronounced due to a longer distance between two bromine atoms participating in the intramolecular cyclization.

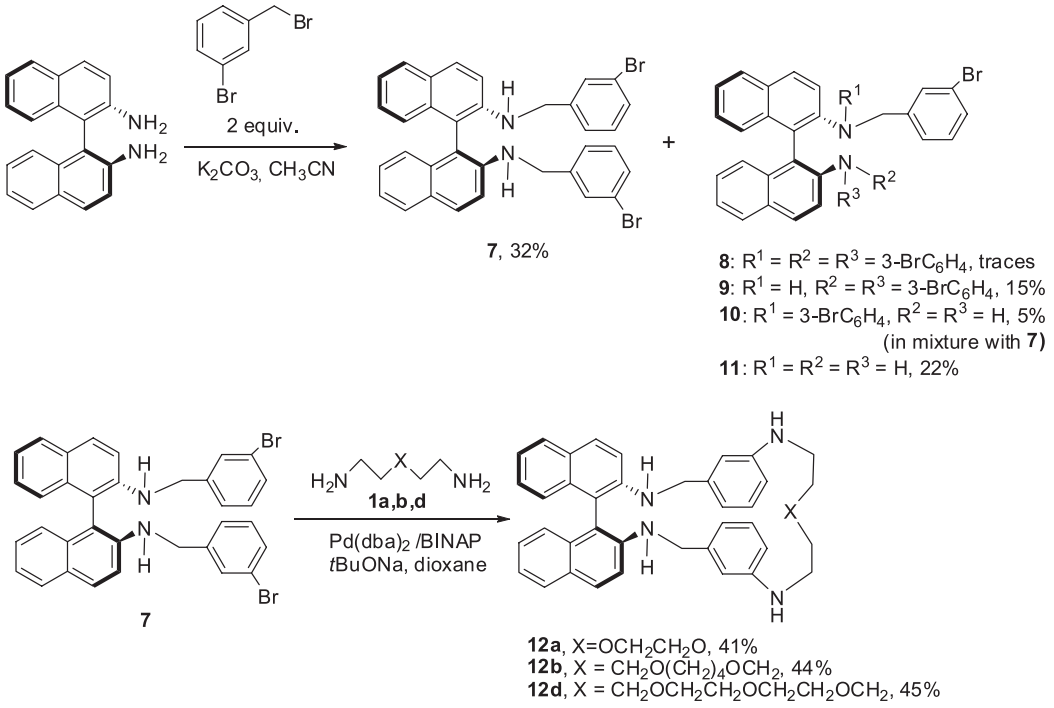
In our previous works dealing with the synthesis of macrocycles by Pd(0)-catalyzed intramolecular diamination of dihaloarenes we found out that in many cases the substitution of the second halogen atom proceeded with difficulties.[18-21] On the other hand, catalytic macrocyclization of di(bromobenzyl) derivatives afforded enough high yields. [22-25] We attempted the synthesis of *N,N'*-di(3-bromobenzyl) substituted BINAM by the reaction with 2 equiv. of 3-bromobenzyl bromide in boiling MeCN in the presence of potassium carbonate and isolated the target compound **7** in 32 % yield (Scheme 4). This modest result is explained by the inevitable formation of the side products of tetra- and tribenzylation **8** and **9**, the isomeric *N,N*-di(3-bromobenzyl) derivative **10** and monobenzylated BINAM **11**. Compounds **9** and **11** were isolated in pure state (yields 15 and 22 %), isomer **10** was obtained and characterized in the mixture with the target compound **7**.

Compound **7** was introduced in the macrocyclization reaction with oxadiamines **1a**,**b**,**d**, in this case $Pd(dba)_2$/BINAP catalytic system was applied as it was observed earlier that BINAP is more helpful for the amination reactions of bromobenzyl derivatives. As it was expected, the macrocyclization reactions proceeded more successfully than in the previous cases, and all target macrocycles **12a**,**b**,**d** were obtained in 41 – 45 % yields (Scheme 4). It is supposed that two factors make the reaction in this case easier: the amination of bromobenzyl moiety proceeds smoother than that of aminobromophenyl moiety, and conformational factors are more favorable in the case of bromobenzyl amination.

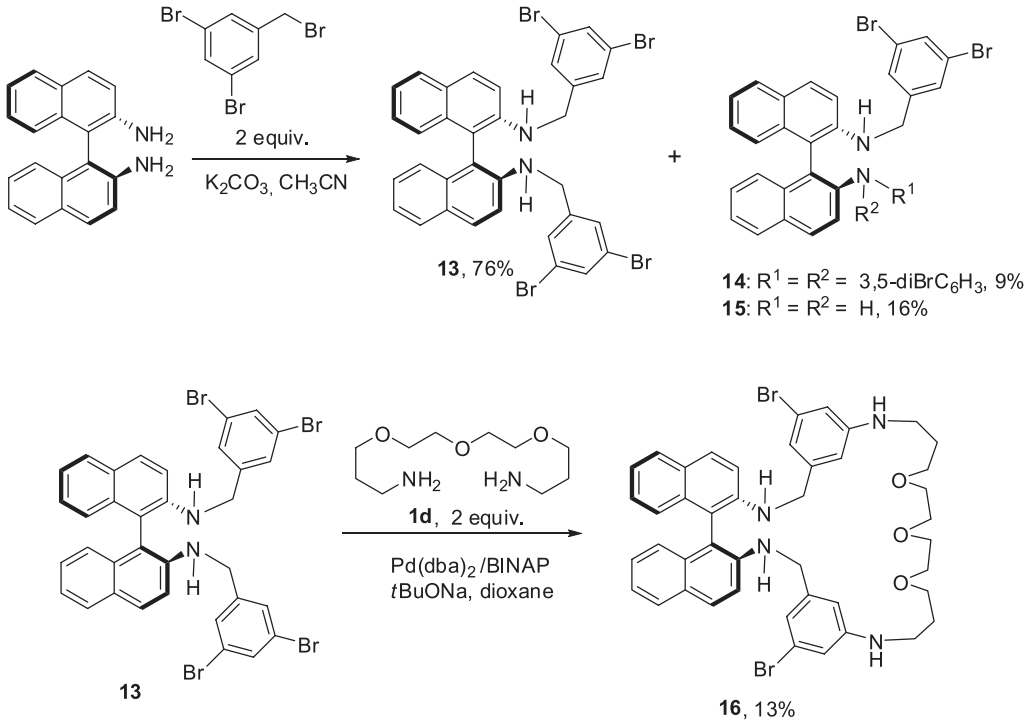
At the last step of our investigation we synthesized *N,N'*-di(3,5-dibromobenzyl) substituted BINAM **13** via a similar reaction with 3,5-dibromobenzyl bromide (Scheme 5), in this process the yield of the target product attained 76 % while




**Scheme 3.**




**Scheme 4.**




**Scheme 5.**

tribenzylated and monobenzylated by-products **14** and **15** were isolated in 9 and 16 %, respectively. The compound **13** was introduced in the reaction with 2 equiv. of trioxadiamine **1d** using $Pd(dba)_2$/BINAP catalytic system in view of the synthesis of macrobicyclic compound, however, only macrocycle **16** was obtained in 13 % yield. The substitution of one bromine atom in each benzyl substituent took place and no evidence of the diamination of the phenyl ring could be received from the $^1$H NMR spectrum of the reaction mixture. We tried another donor phosphine ligand, RuPhos which was thought to promote diamination, and in the reaction mixture weak signals of 3,5-diaminobenzyl group were observed in $^1$H NMR spectrum, but no product could be isolated by chromatography in this case.

## Conclusions

To sum up, we developed the catalytic approach to a previously unknown class of *N*- and *O*-containing macrocycles comprising chiral BINAM fragment. The method consists of two subsequent Pd(0)-catalyzed amination reactions – the first step is the synthesis of corresponding *N,N'*-di(bromoaryl) substituted BINAM, the second is Pd(0)-mediated macrocyclization with linear oxadiamines. This approach was demonstrated to be enough general for the synthesis of macrocycles possessing various aryl spacers (phenyl, benzyl and naphthalene) and oxadiamine chains. The dependence of the compounds yields on the structure of starting compounds was established. The reaction of *N,N'*-di(3,5-dibromobenzyl) substituted BINAM with trioxadiamine led to substitution of one bromine atom in each benzyl moiety and formation of a similar macrocyclic compound.

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