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# Pd-catalyzed amination of isomeric dibromobiphenyls: possibilities of one-step synthesis of macrocycles

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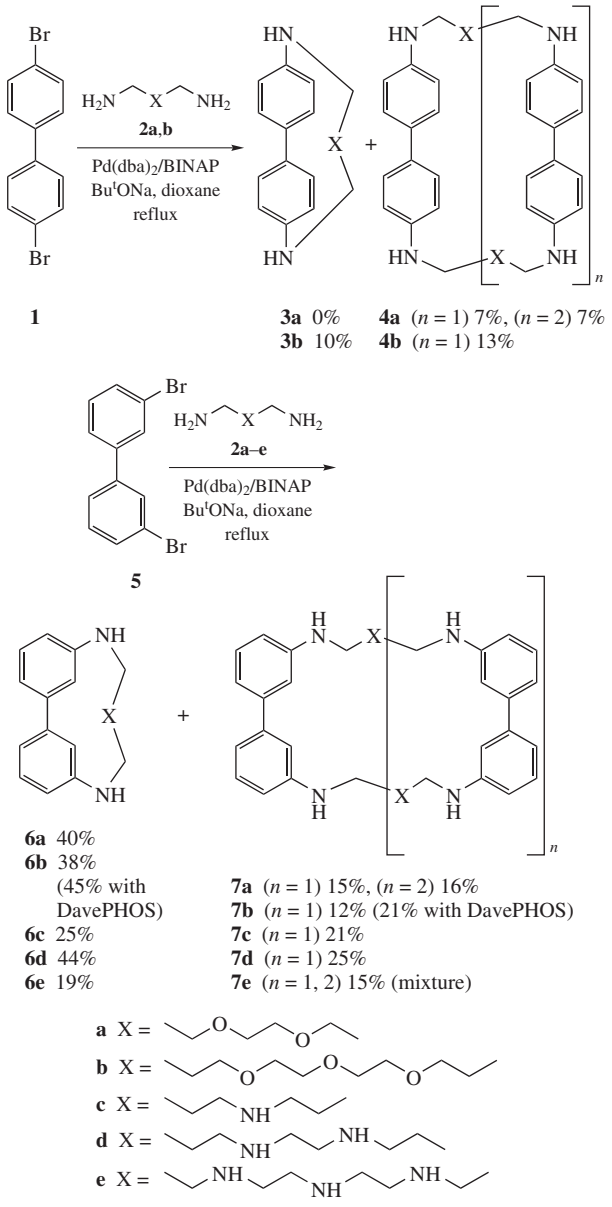
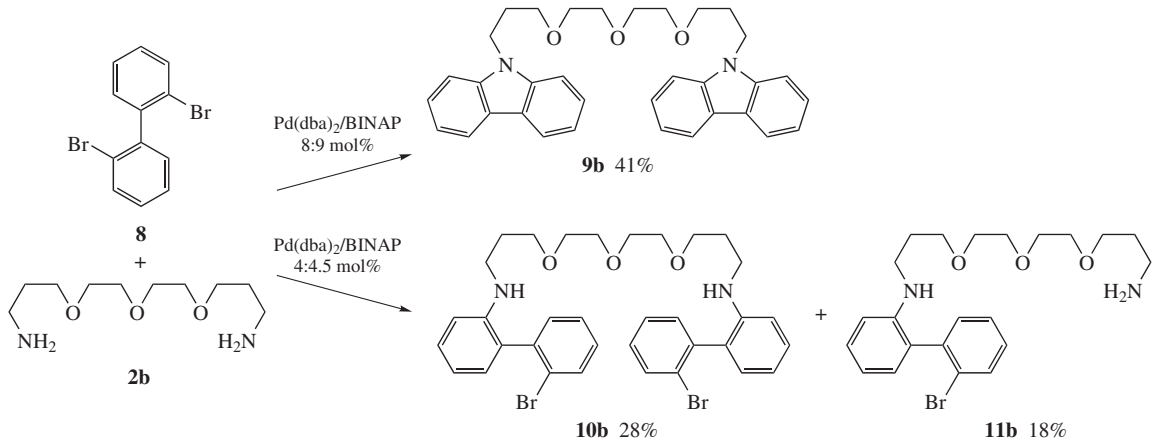
**The Pd-catalyzed amination of isomeric dibromobiphenyls using linear oxadiamines, tri-, tetra- and pentaamines was carried out. 4,4′-Dibromobiphenyl provided a macrocycle comprising one biphenyl and one oxadiamine unit in tiny yield only with the longest diamine; on contrary, 3,3′-dibromobiphenyl gave target macrocycles in good yields, while 2,2′-dibromobiphenyl afforded only acyclic products.**

Macrocycles containing biphenyl units became a constant interest of researchers due to interesting coordination possibilities of compounds with flexible and tunable polyoxa- and polyazacycles attached to a rigid non-planar aryl moiety. The most of reported macrocycles based on biphenyls were synthesized using non-catalytic approaches. Cyclic polyethers were formed starting from 2,2′-dihydroxybiphenyl,[1] and their coordination with cations like *tert*-butylammonium was studied. The transport of Li, Na and K cations[2] and $Hg(CF_3)_2$[3] through a liquid membrane was investigated using macrocycles of similar structure, in which one or two polyoxaethylene chains were attached to one biphenyl unit. Polyoxadiamino macrocycles were also synthesized on the basis of 2,2′-disubstituted biphenyl and their complexation of primary alkylammonium salts, including chiral ones, was described.[4] Polyazamacrocycles with 3, 4 and 8 nitrogen atoms were investigated as complexing agents for $Cu^{2+}$, $Zn^{2+}$ and $[PdCl_4]^{2-}$ ions.[5] More sophisticated macrocycles like peptide-biphenyl hybride[6] and hemispherand macrocycle[7] with bi- and quaterphenyl moieties have been recently reported. Cyclic triamides,[8] as well as cyclic Schiff bases (trianglimines),[9] constitute a less known class of the macrocycles with three 3,3′-disubstituted biphenyls. In some cases, macrocycles containing this fragment were synthesized using Pd-catalyzed coupling of two benzene moieties at the last step, as it was in the case of the macrocycle with diazacrown, dipeptide and biphenyl fragments.[10] Note that biphenyls are incorporated in some biologically active compounds, *e.g.*, tricyclic glucopeptides of vancomicine group.[11]

To the moment, there are no literature data on the synthesis of biphenyl-based macrocycles, which employs catalytic bond formation between aromatic and aliphatic parts of the molecule. In recent years, we have accumulated experience on the application of the Buchwald–Hartwig amination[12] in the synthesis of polyazamacrocycles starting from various dihaloarenes,[13–16] and we investigated this approach for the construction of biphenyl-based macrocycles. First, we tried 4,4′-dibromobiphenyl **1** in the Pd-catalyzed reactions with di- and trioxadiamines **2a**,**b** (Scheme 1). The reactions were run with equimolar amounts of starting compounds in enough dilute dioxane solutions ($c$ = 0.02 M) using $Pd(dba)_2$/BINAP (8:9 mol%) catalytic system, which was found to be almost universal for the synthesis of polyazamacrocycles, and the products were isolated by column chromatography on silica gel. Only trioxadiamine **2b** provided corresponding macrocycle **3b** in a poor 10% yield, while shorter




**Scheme 1**




**Scheme 2**

dioxadiamine **2a** gave only cyclic dimer and trimer **4a** ($n$ = 1, 2), both in 7% yield. Cyclodimer **4b** ($n$ = 1) was also found to be among the products in the reaction with trioxadiamine (13% yield).† The reason for the observed fact is a strict geometric demand of 4,4′-dibromobiphenyl for the polyamines with enough long chains.

Much better results were obtained when using 3,3′-dibromobiphenyl **5** under the same conditions. The reaction with dioxadiamine **2a** initially afforded 19% yield of target macrocycle **6a**, but we managed to increase it to 40% by the application of a twofold amount of the same catalytic system. Trioxadiamine **2b** provided enough high yield of the corresponding macrocycle **6b** (38%), and it was increased to 45% by the use of 2-dicyclohexylphosphino-2′-dimethylaminobiphenyl (DavePHOS) ligand instead of BINAP. We also tried linear tri-, tetra- and pentaamines **2c–e** in this process, and they also gave desired macrocycles **6c–e** in yields from moderate to good (19–44%).‡ It is to be mentioned that 40% yields of polyazamacrocycles are among the highest ever achieved by the Pd-catalyzed amination of dihaloarenes, *e.g.*, they notably surpass those synthesized recently from 2,7-dibromonaphthalene. Cyclodimers **7a–d** ($n$ = 1) were isolated as individual compounds in 12–25% yields, and in the reactions with dioxadiamine **2a** cyclotrimer **7a** ($n$ = 2) was obtained separately in 16% yield.§

At last, we also explored the possibility of 2,2′-dibromobiphenyl **8** to furnish macrocycles upon reacting it with polyamines. Under standard conditions, using trioxadimaine **2b** as an

† *General procedure.* A two-neck flask equipped with a magnetic stirrer and a condenser flushed with dry argon was charged with 4,4′- or 3,3′-dibromobiphenyl **1** or **5** (0.5 mmol), absolute dioxane (25 ml), $Pd(dba)_2$ (24 mg, 8 mol%) and BINAP (28 mg, 9 mol%). The mixture was stirred for 2 min, and then appropriate polyamine **2** (0.5 mmol) and $Bu^tONa$ (1.5 mmol) were added, and the reaction mixture was refluxed for 24 h. After cooling to ambient temperature and filtration, dioxane was evaporated *in vacuo* and the residue was chromatographed on silica gel using a sequence of eluents: $CH_2Cl_2$, $CH_2Cl_2$–MeOH (500:1–3:1), $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:1–10:4:1).

NMR spectra were measured in $CDCl_3$ solutions at 400 ($^1$H) and 100.6 ($^{13}$C) MHz.

Macrocycle **3b**: eluent $CH_2Cl_2$–MeOH (50:1), yield 19 mg (10%). $^1$H NMR, $\delta$: 1.72 (quintet, 4H, $J$ 5.5 Hz), 2.80–2.85 (m, 4H), 2.92–2.97 (m, 4H), 3.22 (t, 4H, $J$ 5.5 Hz), 3.40 (t, 4H, $J$ 5.5 Hz), 6.77 (d, 4H, $J$ 8.6 Hz), 7.43 (d, 4H, $J$ 8.6 Hz) (NH protons were not assigned). $^{13}$C NMR, $\delta$: 32.9 (2C), 42.6 (2C), 67.8 (2C), 68.5 (2C), 68.9 (2C), 115.9 (4C), 126.1 (4C), 130.5 (2C), 148.4 (2C). MS (MALDI-TOF), $m/z$: 370.2314 ($M^+$); calc. for $C_{22}H_{30}N_2O_3$: 370.2256.

Cyclodimer **4a** ($n$ = 1): eluent $CH_2Cl_2$–MeOH (50:1), yield 11 mg (7%). $^1$H NMR, $\delta$: 3.31 (t, 8H, $J$ 5.1 Hz), 3.69 (s, 8H), 3.76 (t, 8H, $J$ 5.1 Hz), 3.90 (br. s, 4H), 6.50 (d, 8H, $J$ 8.6 Hz), 7.15 (d, 8H, $J$ 8.6 Hz). $^{13}$C NMR, $\delta$: 43.9 (4C), 69.4 (4C), 70.2 (4C), 113.6 (8C), 126.8 (8C), 130.6 (4C), 146.6 (4C). MS (MALDI-TOF), $m/z$: 596.3323 ($M^+$); calc. for $C_{36}H_{44}N_4O_4$: 596.3362.

Cyclotrimer **4a** ($n$ = 2): eluent $CH_2Cl_2$–MeOH (50:1–20:1), yield 11 mg (7%). $^1$H NMR, $\delta$: 3.32 (br. s, 12H), 3.65 (s, 12H), 3.70 (t, 12H, $J$ 5.4 Hz), 3.95 (br. s, 6H), 6.67 (d, 12H, $J$ 8.6 Hz), 7.36 (d, 12H, $J$ 8.6 Hz). $^{13}$C NMR, $\delta$: 43.8 (6C), 69.5 (6C), 70.2 (6C), 113.5 (12C), 127.1 (12C), 130.9 (6C), 146.7 (6C). MS (MALDI-TOF), $m/z$: 894.5043 ($M^+$); calc. for $C_{54}H_{66}N_6O_6$: 894.4998.

Cyclodimer **4b** ($n$ = 1): eluent $CH_2Cl_2$–MeOH (50:1), yield 25 mg (13%). $^1$H NMR, $\delta$: 1.88 (quintet, 8H, $J$ 6.1 Hz), 3.23 (t, 8H, $J$ 6.2 Hz), 3.61 (t, 8H, $J$ 5.8 Hz), 3.61–3.65 (m, 8H), 3.66–3.70 (m, 8H), 6.57 (d, 8H, $J$ 8.4 Hz), 7.29 (d, 8H, $J$ 8.4 Hz) (NH protons were not assigned). $^{13}$C NMR, $\delta$: 29.1 (4C), 42.0 (4C), 69.8 (4C), 70.2 (4C), 70.6 (4C), 113.1 (8C), 126.9 (8C), 130.2 (4C), 147.0 (4C). MS (MALDI-TOF), $m/z$: 740.4523 ($M^+$); calc. for $C_{44}H_{60}N_4O_6$: 740.4512.

‡ Macrocycle **6a**: eluent $CH_2Cl_2$–MeOH (100:1), yield 60 mg (40%). $^1$H NMR, $\delta$: 3.49 (t, 4H, $J$ 5.5 Hz), 3.70 (s, 4H), 3.71 (t, 4H, $J$ 5.6 Hz), 4.09 (br. s, 2H), 6.59 (ddd, 2H, $J$ 8.0, 1.5, 0.8 Hz), 7.06 (d, 2H, $J$ 7.7), 7.19 (t, 2H, $J$ 7.7 Hz), 7.39 (t, 2H, $J$ 1.9 Hz). $^{13}$C NMR, $\delta$: 45.2 (2C), 70.9 (2C), 72.6 (2C), 110.9 (2C), 114.2 (2C), 116.3 (2C), 128.9 (2C), 142.7 (2C), 148.9 (2C). MS (MALDI-TOF), $m/z$: 298.1681 ($M^+$); calc. for $C_{18}H_{22}N_2O_2$: 298.1706.

Macrocycle **6b**: eluent $CH_2Cl_2$–MeOH (100:1), yield 71 mg (38%). $^1$H NMR, $\delta$: 1.91 (quintet, 4H, $J$ 5.9 Hz), 3.35 (t, 4H, $J$ 6.5 Hz), 3.60–3.66 (m, 8H), 3.73–3.77 (m, 4H), 4.26 (br. s, 2H), 6.57 (d, 2H, $J$ 7.9 Hz), 6.94 (br. s, 2H), 6.97 (d, 2H, $^3J$ 7.7 Hz), 7.21 (t, 2H, $J$ 7.8 Hz). $^{13}$C NMR, $\delta$: 29.3 (2C), 42.5 (2C), 70.1 (2C), 70.7 (2C), 71.0 (2C), 111.1 (2C), 111.9 (2C), 115.9 (2C), 129.2 (2C), 142.5 (2C), 149.0 (2C). MS (MALDI-TOF), $m/z$: 370.2240 ($M^+$); calc. for $C_{22}H_{30}N_2O_3$: 370.2256.

Macrocycle **6c**: eluent $CH_2Cl_2$–MeOH (3:1), yield 35 mg (25%). $^1$H NMR, $\delta$: 1.82 (quintet, 4H, $J$ 6.7 Hz), 2.71 (t, 4H, $J$ 6.0 Hz), 3.37 (t, 4H, $J$ 7.3 Hz), 4.06 (br. s, 2H), 6.54 (dd, 2H, $J$ 8.0, 0.8 Hz), 7.03 (d, 2H, $J$ 7.5 Hz), 7.17 (t, 2H, $J$ 7.8 Hz), 7.29 (br. s, 2H) (NH proton of the dialkylamino group was not assigned). $^{13}$C NMR, $\delta$: 29.7 (2C), 41.3 (2C), 47.0 (2C), 109.6 (2C), 114.0 (2C), 114.8 (2C), 129.3 (2C), 142.1 (2C), 147.9 (2C). MS (MALDI-TOF), $m/z$: 281.1930 ($M^+$); calc. for $C_{18}H_{23}N_3$: 281.1892.

Macrocycle **6d**: eluent $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:2), yield 71 mg (44%). $^1$H NMR, $\delta$: 1.92 (quintet, 4H, $J$ 6.6 Hz), 2.82 (t, 4H, $J$ 6.0 Hz), 2.88 (s, 4H), 3.32 (t, 4H, $J$ 7.2 Hz), 3.72 (br. s, 2H), 6.53 (d, 2H, $J$ 7.6 Hz), 6.93 (s, 2H), 6.94 (d, 2H, $J$ 7.8 Hz), 7.15 (t, 2H, $J$ 7.7 Hz) (NH protons of dialkylamino groups were not assigned). $^{13}$C NMR, $\delta$: 28.1 (2C), 42.4 (2C), 47.5 (4C), 110.9 (2C), 113.3 (2C), 115.7 (2C), 129.5 (2C), 142.5 (2C), 148.3 (2C). MS (MALDI-TOF), $m/z$: 324.2264 ($M^+$); calc. for $C_{20}H_{28}N_4$: 324.2314.

Macrocycle **6e**: eluent $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:3), yield 32 mg (19%). $^1$H NMR, $\delta$: 2.74 (t, 4H, $J$ 4.7 Hz), 2.83 (t, 4H, $J$ 4.8 Hz), 2.90 (t, 4H, $J$ 6.1 Hz), 3.34 (t, 4H, $J$ 6.1 Hz), 6.60 (d, 2H, $J$ 7.3 Hz), 6.98 (s, 2H), 6.99 (d, 2H, $J$ 6.7 Hz), 7.22 (t, 2H, $J$ 8.0 Hz) (NH protons were not assigned). $^{13}$C NMR, $\delta$: 43.7 (2C), 48.6 (2C), 49.1 (2C), 49.5 (2C), 111.6 (2C), 112.8 (2C), 116.2 (2C), 129.5 (2C), 142.6 (2C), 148.8 (2C). MS (MALDI-TOF), $m/z$: 339.2373 ($M^+$); calc. for $C_{20}H_{29}N_5$: 339.2423.

exemplary amine, only *N*,*N*′-dicarbazyl derivative **9b** was obtained in 41% yield (Scheme 2). The application of less amounts of the catalyst (2–4 mol%), use of other phosphine ligands like DavePHOS, Xanthphos, ferrocene-based Josiphos, *etc*., did not lead even to the traces of the macrocycle. We found the conditions under which N,N-diarylation process was suppressed to a certain extent [$Pd(dba)_2$/BINAP, 4 mol%, 3 equiv. of **8**], and *N*,*N*′-di(2′-bromobiphenyl)trioxadiamine **10b** was isolated in 28% yield while compound **9b** was obtained in 4% yield. Another product of this reaction was monoarylated trioxadiamine **11b** (18%).¶ However, **10b** did not react further with the second equivalent of trioxadiamine to produce cyclodimer, but rather gave *N*,*N*′-dicarbazyl derivative **9b** in an almost quantitative yield. These results are in good agreement with the literature data on the synthesis of N-substituted carbazoles *via* palladium-mediated reactions.[17]

To sum up, we investigated isomeric dibromobiphenyls in the Pd-catalyzed amination reactions with polyamines and oxadiamines, and showed that 3,3′-dibromobiphenyl can be successfully used for a facile synthesis of polyaza- and polyoxadiaza-macrocycles in rather good yields.

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§ Cyclodimer **7a** (*n* = 1): eluent $CH_2Cl_2$–MeOH (75:1), yield 22 mg (15%). $^1$H NMR, $\delta$: 3.34 (t, 8H, *J* 4.7 Hz), 3.68 (s, 8H), 3.73 (t, 8H, *J* 4.8 Hz), 4.23 (br. s, 4H), 6.60 (d, 4H, *J* 7.7 Hz), 6.79 (br. s, 4H), 6.91 (d, 4H, *J* 7.1 Hz), 7.18 (t, 4H, *J* 7.5 Hz). $^{13}$C NMR, $\delta$: 43.7 (4C), 69.6 (4C), 70.3 (4C), 111.8 (4C), 112.5 (4C), 116.8 (4C), 129.5 (4C), 142.9 (4C), 148.5 (4C). MS (MALDI-TOF), *m*/*z*: 596.3409 ($M^+$); calc. for $C_{36}H_{44}N_4O_4$: 596.3362.

Cyclotrimer **7a** (*n* = 2): eluent $CH_2Cl_2$–MeOH (20:1), yield 24 mg (16%). $^1$H NMR, $\delta$: 3.36 (br. s, 12H), 3.67 (s, 12H), 3.72 (br. s, 12H), 4.06 (br. s, 6H), 6.62 (d, 6H, *J* 7.5 Hz), 6.84 (br. s, 6H), 6.94 (d, 6H, *J* 6.8 Hz), 7.22 (t, 6H, *J* 7.4 Hz). $^{13}$C NMR, $\delta$: 43.6 (6C), 69.7 (6C), 70.3 (6C), 112.0 (6C), 112.1 (6C), 116.8 (6C), 129.5 (6C), 142.9 (6C), 148.5 (6C). MS (MALDI-TOF), *m*/*z*: 894.56 ($M^+$); calc. for $C_{54}H_{66}N_6O_6$: 894.50.

Cyclodimer **7b** (*n* = 1): eluent $CH_2Cl_2$–MeOH (50:1), yield 22 mg (12%). $^1$H NMR, $\delta$: 1.84 (quintet, 8H, *J* 6.0 Hz), 3.23 (t, 8H, *J* 6.4 Hz), 3.55 (t, 8H, *J* 5.8 Hz), 3.55–3.60 (m, 8H), 3.63–3.67 (m, 8H), 4.18 (br. s, 4H), 6.54 (dd, 4H, *J* 7.7, 1.9 Hz), 6.73 (br. s, 4H), 6.85 (d, 4H, *J* 7.4 Hz), 7.17 (t, 4H, *J* 8.0 Hz). $^{13}$C NMR, $\delta$: 29.0 (4C), 41.7 (4C), 69.7 (4C), 70.2 (4C), 70.6 (4C), 111.3 (4C), 111.8 (4C), 116.1 (4C), 129.3 (4C), 143.0 (4C), 148.8 (4C). MS (MALDI-TOF), *m*/*z*: 740.4473 ($M^+$); calc. for $C_{44}H_{60}N_4O_6$: 740.4512.

Cyclodimer **7c** (*n* = 1): eluent $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:1), yield 30 mg (21%). $^1$H NMR, $\delta$: 1.80 (quintet, 8H, *J* 6.7 Hz), 2.68 (t, 8H, *J* 5.9 Hz), 3.29 (t, 8H, *J* 5.1 Hz), 3.90 (br. s, 4H), 6.53 (d, 4H, *J* 8.0 Hz), 7.02 (d, 4H, *J* 7.4 Hz), 7.16 (t, 4H, *J* 7.7 Hz), 7.17 (br. s, 4H) (NH proton of the dialkylamino group was not assigned). $^{13}$C NMR, $\delta$: 28.4 (4C), 41.1 (4C), 48.0 (4C), 109.8 (4C), 114.0 (4C), 114.8 (4C), 129.3 (4C), 142.3 (4C), 147.7 (4C). MS (MALDI-TOF), *m*/*z*: 562.3701 ($M^+$); calc. for $C_{36}H_{46}N_6$: 562.3784.

Cyclodimer **7d** (*n* = 1): eluent $CH_2Cl_2$–MeOH–aqueous $NH_3$ (100:20:3), yield 41 mg (25%). $^1$H NMR, $\delta$: 1.73 (quintet, 8H, *J* 6.3 Hz), 2.71 (t, 8H, *J* 6.3 Hz), 2.72 (s, 8H), 3.15 (t, 8H, *J* 6.3 Hz), 6.53 (dd, 4H, *J* 7.8, 1.7 Hz), 6.76 (t, 4H, *J* 1.7 Hz), 6.87 (d, 4H, *J* 7.5 Hz), 7.17 (t, 4H, *J* 7.7 Hz) (NH protons of the dialkylamino groups were not assigned). $^{13}$C NMR, $\delta$: 29.1 (4C), 42.9 (4C), 48.1 (4C), 48.9 (4C), 111.3 (4C), 111.9 (4C), 116.2 (4C), 129.3 (4C), 142.9 (4C), 148.8 (4C). MS (MALDI-TOF), *m*/*z*: 648.4612 ($M^+$); calc. for $C_{40}H_{56}N_8$: 648.4628.

¶ *9,9′-{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}-bis(9*H*-carbazole)* **9b** was obtained from 2,2′-dibromobiphenyl **8** (0.5 mmol) and trioxadiamine **2b** (0.5 mmol), in the presence of $Pd(dba)_2$ (24 mg, 8 mol%), BINAP (28 mg, 9 mol%) and $Bu^tONa$ (1.5 mmol) in dioxane (25 ml). Reflux time, 24 h. Eluent $CH_2Cl_2$–MeOH (200:1), yield 53 mg (41%). $^1$H NMR, $\delta$: 2.15 (quintet, 4H, *J* 6.1 Hz), 3.39 (t, 4H, *J* 5.8 Hz), 3.58 (t, 4H, *J* 4.8 Hz), 3.75 (t, 4H, *J* 4.8 Hz), 4.46 (t, 4H, *J* 6.5 Hz), 7.23–7.28 (m, 4H), 7.45–7.50 (m, 8H), 8.12 (d, 4H, *J* 7.9 Hz). $^{13}$C NMR, $\delta$: 29.0 (2C), 39.4 (2C), 67.6 (2C), 70.2 (2C), 70.6 (2C), 108.7 (4C), 118.7 (4C), 120.2 (4C), 122.7 (4C), 125.6 (4C), 140.5 (4C). MS (MALDI-TOF), *m*/*z*: 520.2726 ($M^+$); calc. for $C_{34}H_{36}N_2O_3$: 520.2769.

N,N′-*{3,3′-[2,2′-Oxybis(ethane-2,1-diyl)bis(oxy)]bis(propane-3,1-diyl)}-bis(2′-bromobiphenyl-2-amine)* **10b** was synthesized from 2,2′-dibromobiphenyl **8** (1.5 mmol) and trioxadiamine **2b** (0.5 mmol), in the presence of $Pd(dba)_2$ (12 mg, 4 mol%), BINAP (14 mg, 4.5 mol%) and $Bu^tONa$ (1.5 mmol) in dioxane (5 ml). Reflux time, 6 h. Eluent $CH_2Cl_2$–MeOH (200:1–100:1), yield 95 mg (28%). $^1$H NMR, $\delta$: 1.82 (quintet, 4H, *J* 6.3 Hz), 3.24 (t, 4H, *J* 6.1 Hz), 3.46–3.54 (m, 10H), 3.58 (br. s, 2H), 6.74 (d, 2H, *J* 8.4 Hz), 6.76 (t, 2H, *J* 7.4 Hz), 6.99 (dd, 2H, *J* 7.3, 1.1 Hz), 7.23 (td, 2H, *J* 7.7, 1.4 Hz), 7.29 (td, 2H, *J* 7.4, 1.3 Hz), 7.32 (dd, 2H, *J* 7.7, 1.5 Hz), 7.39 (td, 2H, *J* 7.4, 0.9 Hz), 7.70 (d, 2H, *J* 8.0 Hz). $^{13}$C NMR, $\delta$: 29.1 (2C), 41.1 (2C), 69.1 (2C), 70.0 (2C), 70.4 (2C), 110.2 (2C), 116.2 (2C), 124.5 (2C), 126.6 (2C), 127.8 (2C), 129.0 (2C), 129.1 (2C), 129.9 (2C), 132.0 (2C), 133.0 (2C), 139.9 (2C), 145.1 (2C). MS (MALDI-TOF), *m*/*z*: 680.1282 ($M^+$); calc. for $C_{34}H_{38}Br_2N_2O_3$: 680.1249.

N-*(3-{2-[2-(3-Aminopropoxy)ethoxy]ethoxy}propyl)-2′-bromobiphenyl-2-amine* **11b** was obtained as a by-product in the synthesis of **10b**. Eluent $CH_2Cl_2$–MeOH (10:1), yield 40 mg (18%). $^1$H NMR, $\delta$: 1.80 (quintet, 2H, *J* 6.3 Hz), 2.00 (quintet, 2H, *J* 5.7 Hz), 3.15 (t, 2H, *J* 6.0 Hz), 3.21 (t, 2H, *J* 6.6 Hz), 3.47–3.53 (m, 6H), 3.56 (br. s, 4H), 3.62 (t, 2H, *J* 5.5 Hz), 6.72 (d, 1H, *J* 8.3 Hz), 6.73 (t, 1H, *J* 6.9 Hz), 6.95 (dd, 1H, *J* 7.5, 1.5 Hz), 7.20–7.26 (m, 2H), 7.28 (dd, 1H, *J* 7.5, 1.2 Hz), 7.37 (t, 1H, *J* 7.5 Hz), 7.67 (d, 1H, *J* 7.7 Hz) (NH protons were not assigned). $^{13}$C NMR, $\delta$: 26.2, 29.0, 39.4, 41.3, 69.1, 69.6, 69.7 (2C), 69.9, 70.1, 110.5, 116.4, 124.4, 126.7, 127.8, 129.1 (2C), 129.8, 132.0, 133.0, 139.7, 145.0. MS (MALDI-TOF), *m*/*z*: 450.1557 ($M^+$); calc. for $C_{22}H_{31}BrN_2O_3$: 450.1518.