Synthesis of Macrocycles Comprising 2,7-Disubstituted Naphthalene and Polyamine Moieties via Pd-catalyzed Amination

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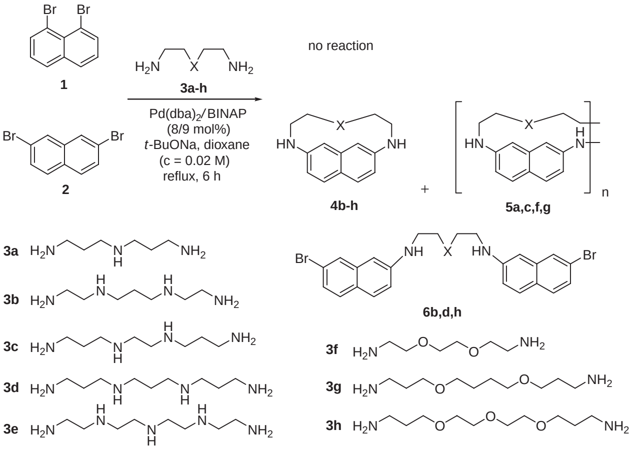
(Received August 12, 2008; CL-080784; E-mail: averin@org.chem.msu.ru)

The Pd-catalyzed reaction of equimolar amounts of 2,7-dibromonaphthalene and various polyamines led to the formation of the macrocycles comprising one naphthalene and one polyamine moieties. The same reaction also gave cyclodimers and cyclotrimers as by-products. Application of excess 2,7-dibromonaphthalene provided *N*,*N*′-bis(7-bromonaphth-2-yl)oxadiamine which was used for the synthesis of macrocycles with two naphthalene and two oxadiamine fragments.

The first simplest representatives of macrocycles containing naphthalene unit were described in the literature 70 years ago.[1] Since that time dozens of works appeared dealing with the synthesis and investigation of naphthalene-based macrocycles of different geometry and with crown ethers functionalized with naphthalene substituents in pendant arms. These macrocycles may possess structural fragments of Schiff bases,[2] diamide,[3] diimide,[4] or lactam[5] groups, naphthalene can be fused to tetraazamacrocycles,[6] the molecules may contain phosphorus atoms[7] or have only carbon atoms in the macroring.[8] Naphthalene moieties were also incorporated in more complicated structures like calixarenes,[9] catenanes,[10] and they were combined in a different manner with porphyrin units.[11] These sophisticated molecules find their application as molecular receptors, mainly of organic anions,[12] or even as molecular rotors.[13] All synthetic approaches used conventional noncatalytic methods which were unfavorable for the synthesis of macrocycles with aminonaphthalene fragments which could improve sensing properties due to an increase in optical response of the condensed aromatic system to coordination. As we acquired good experience in the synthesis of polyazamacrocycles using Pd-catalyzed amination of dihaloarenes with linear polyamines,[14] we decided to apply this method for the synthesis of naphthalene-based macrocycles.

First we tried 1,8-dibromonaphthalene (**1**) in the reaction with linear polyamines **3** catalyzed by a standard Pd(dba)$_2$/BINAP system. No reaction occured even after a long reflux in dioxane with 8 mol % of the catalyst. It was surprising because 1-bromonaphthalene earlier was shown to be very active in Pd-mediated amination.[15] Possibly in this case the second bromine atom in the peri-position totally hindered the reaction at the step of oxidative addition of 1,8-dibromonaphthalene to Pd^0. Then we ran the reaction using 2,7-dibromonaphthalene (**2**) (Scheme 1), and in this case amination proceeded normally. The same catalytic system (8 mol %) was applied, *t*-BuONa was taken as a base, and dilute dioxane solutions ($c = 0.02$ M) were employed to prevent formation of linear oligomers. Yields of target macrocycles **4b**–**4h** and of cyclic and linear by-products **5** and **6** are given in Table 1 (all compounds were isolated by column chromatography on silica gel).



Scheme 1.

Table 1. Synthesis of macrocycles **4**

Entry	Amine	Yields of **4**/%	Yields of other products/%
1	**3a**	**4a**, 0	**5a** ($n = 2$), 25
			5a ($n = 3$), 10
			5a ($n = 3$–6), 49
2	**3b**	**4b**, 9	**6b**, 5
3	**3c**	**4c**, 26	**5c** ($n = 2$), 25
4	**3d**	**4d**, 28	**6d**, 18
5	**3e**	**4e**, 19	
6	**3f**	**4f**, 10	**5f** ($n = 2$), 32
			5f ($n = 3$), 14
7	**3g**	**4g**, 29	**5g** ($n = 2$), 16
			5g ($n = 3$), 8
8	**3h**	**4h**, 17	**6h**, 10
9[a]	**3h**	**4h**, 26	

[a] 2-Dicyclohexylphosphino-2′-dimethylaminobiphenyl was used instead of BINAP.

Corresponding macrocycles **4** were formed in all cases except for the shortest triamine **3a**, in this case only cyclooligomers **5a** ($n = 2$–6) were obtained (Entry 1). Amines **3b** and **3g** (Entries 2 and 6) provided low yields of corresponding macrocycles **4b** and **4g** due to insufficiently long chains, other polyamines gave comparable results. In the case of trioxadiamine **3h** we supposed that 17% yield (Entry 8) could be improved by the application of more active ligand: 2-dicyclohexylphosphino-2′-dimethylaminobiphenyl instead of BINAP, and this was the case (Entry 9). However, in other cases this ligand did not increase the yields of compounds **4**. No regularities were observed for the formation of cyclic and linear by-products **5** and **6**. X-ray structure was obtained for the macrocycle **4c** (solvate with methanol, Figure 1).[16]

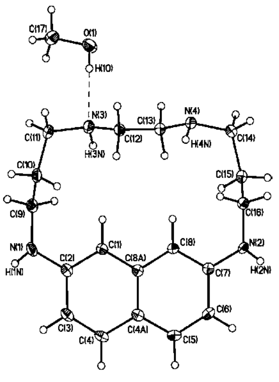
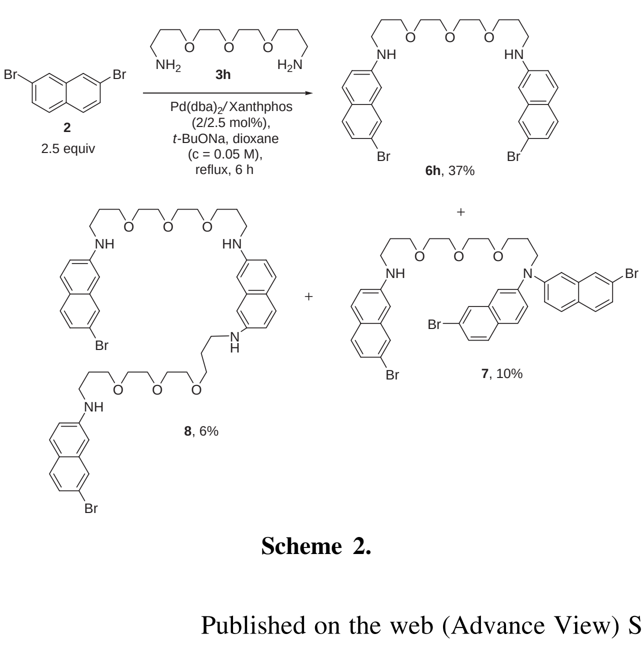


Figure 1.

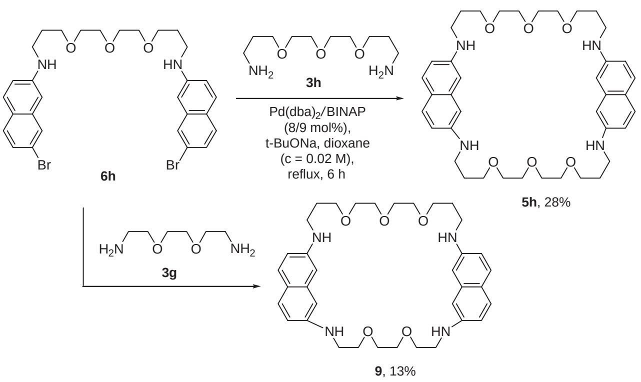
In accordance with our interest in the pathways of cyclic oligomers formation[17] we studied the possibility of the synthesis of cyclodimers **5** via bis(bromonaphthyl)-substituted polyamines **6**. The reaction of excess **2** with trioxadiamine **3h** catalyzed by Pd(dba)$_2$/BINAP at $c = 0.1$ M led only to an inseparable mixture of linear oligomers, possibly owing to a high reactivity of the bromine atoms in **2**. The use of a less active complex with Xanthphos (2 mol %) at $c = 0.05$ M provided the formation of target **6h** in 37% yield, though by-products: triarylated diamine **7** and oligomer **8** were also isolated (Scheme 2).

N,N′-Diarylated diamine **6h** was then introduced in the reaction with a free trioxadiamine **3h**, this reaction was carried in conditions similar to that used for the synthesis of "normal" macrocycles **4** (Scheme 3). While the "symmetrical" cyclodimer **5h** (not obtained in the synthesis of **4h**, Entries 8 and 9) was isolated in a reasonable 28% yield, cyclodimer **9** with two different dioxadiamine linkers, formed in the reaction of **6h** with dioxadiamine **3g**, was obtained in 13% yield. This fact can be explained by a less favorable geometry of the intermediary linear compound for ring closure. Indeed, a number of linear oligomeric by-products were isolated in this case (63% yield in total).

To sum up, we have elaborated a convenient one-step method[18] for the synthesis of nitrogen- and oxygen-containing macrocycles comprising 2,7-disubstituted naphthalene unit and showed its applicability to the synthesis of macrocycles with two naphthalene and two polyamine moieties.



Scheme 2.



Scheme 3.

This work was supported by RFBR grants N 06-03-32376, 08-03-00628, and by the Russian Academy of Sciences program P-8 "Development of methods of organic synthesis and construction of compounds with valuable properties."

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16 Crystallographic data reported in this manuscript have been deposited with Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-699653. Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).
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18 Experimental procedures and spectral data are given in Supporting Information. It is also available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.