Palladium-catalyzed Amination in the Synthesis of Polyazapolyoxamacrocycles with Two and Three Anthracene or Anthraquinone Moieties: Scope and Limitations

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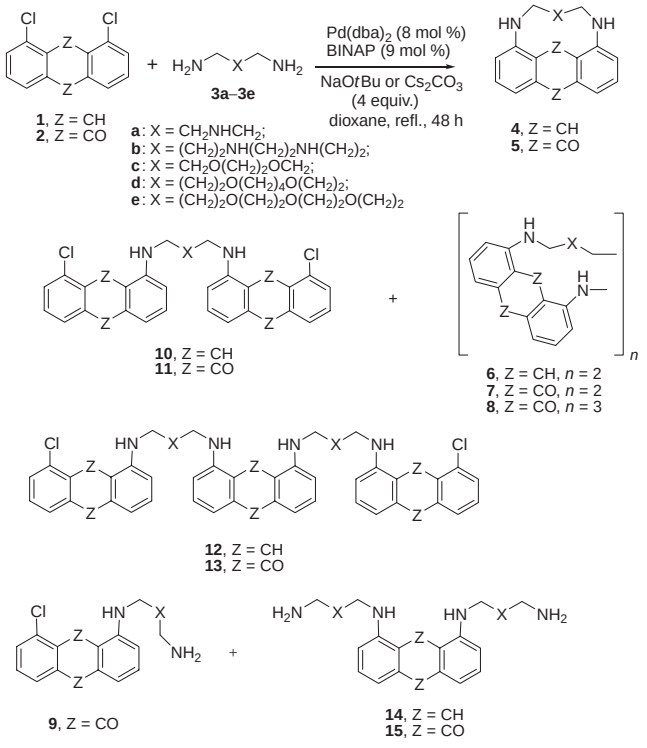
The synthesis of N^{α},N^{ω}-bis(haloaryl)polyamines and oxadiamines by Pd-catalyzed amination of 1,8-dichloroanthracene and 1,8-dichloroanthra-9,10-quinone is described, as well as the formation of 1,8-bis(polyamine)-substituted anthracenes and anthra-9,10-quinones. Scope and limitations of the application of these compounds in the synthesis of the macrocycles comprising two and three anthracene or anthraquinone moieites are shown and discussed.

Our recent investigations in the synthesis of nitrogen- and oxygen-containing macrocycles via Pd-catalyzed amination of dihalobenzenes,[1,2] dihalopyridines,[3–6] 1,8-dichloroanthracene, and 1,8-dichloroanthra-9,10-quinone,[7] as well as preparation of cholane-based macrocycles using the same technique,[8] have shown that often target polyazamacrocycles comprising one arene and one polyamine moiety are formed together with cyclic dimers and oligomers of higher masses. We noted that dichloroanthracene and anthraquinone with certain polyamines afforded "normal" macrocycles accompanied by cyclodimers and sometimes by cyclooligomers while with other polyamines only normal cycles were observed and isolated. We developed two alternative approaches to cyclic dimers with benzene and pyridine fragments using N^{α},N^{ω}-bis(haloaryl)polyamines or bis(polyamine)-substituted arenes and showed the possibilities of these methods to produce cyclodimers. However, the question has not been yet solved whether the formation of such cyclic dimers and oligomers in the course of the reactions of aryl dihalides with polyamines is irregular and accidental, or depends on the nature of starting compounds. To elucidate it, we attempted to synthesize some cyclic dimers and trimers containing anthracene and anthraquinone groups: those which were isolated as by-products and those which were not detected in the synthesis of "normal" macrocycles.

The reactions of 1,8-dichloroanthracene (**1**) and 1,8-dichloroanthraquinone (**2**) with polyamines **3** were carried out using $Pd(dba)_2$/BINAP catalytic system[9] which was found to be most suitable for polyamines and oxadiamines arylation.[7,10] Reactions were run in boiling dioxane, *t*BuONa or Cs_2CO_3 were used as bases in the case of **1** or **2**, resp. A variety of cyclic and linear products obtained is presented at Scheme 1. Equimolar amounts of starting compounds together with dilute solutions (c = 0.03–0.017 M) favored the formation of macrocycles **4** and **5** with one aryl and polyamine moiety. While macrocycles **4c** and **4e** (yields 28 and 25%), **5d** and **5e** (yields 33 and 37%) were obtained together with corresponding cyclodimers **6c** and **6e** (yields 8 and 10%), **7d** and **7e** (yields 12 and 18%) and even cyclotrimers **8d** and **8e** (yields 8 and 10%), macrocycles **4a**, **4b**, **4d**, **5b**, and **5c** were isolated as sole cyclic structures (yields 28, 24, 20, 25, and 43%, resp.).



Scheme 1.

Application of 2.5–3 equiv. of dihaloarene in more concentrated solutions (c = 0.1–0.2 M) led to preferential formation of N^{α},N^{ω}-bis(haloaryl)polyamines **10** and **11**, (yields 20–53% and 13–38%, resp.), and in some cases linear oligomers **12** and **13** (yields 3–27%) were also isolated. Diminishing the excess of 1,8-dichloroanthraquinone (**2**) (1.5–1.8 equiv.) in the reaction with trioxadiamine **3e** afforded oligomer **13e** in a reasonable yield (28%), while the same procedure with 1,8-dichloroanthracene was inefficient and produced corresponding oligomers **12d** and **12e** in very low yields (9 and 4%, resp.). To obtain 1,8-bis(polyamine)-substituted anthracene and anthraquinone **14** and **15**, we used 2.5–3 equiv. of diamines **3c**, **3e**, and obtained these derivatives in 20–40%, however, in the case of 1,8-dichloroanthraquinone mono-aminated compounds **9c** and **9e** were always formed in comparable yields (17–28%).

Our preliminary computational studies of synthesized compounds did not provide unambiguous data due to the absence of conformational rigidity of the molecules, thus we have undertaken the experimental search for the cyclodimer formation pathway. To synthesize cyclodimers and cyclotrimers first we used the reaction of N^{α},N^{ω}-bis(haloaryl)polyamines with corresponding polyamines which is presented at Scheme 2. The reactions of

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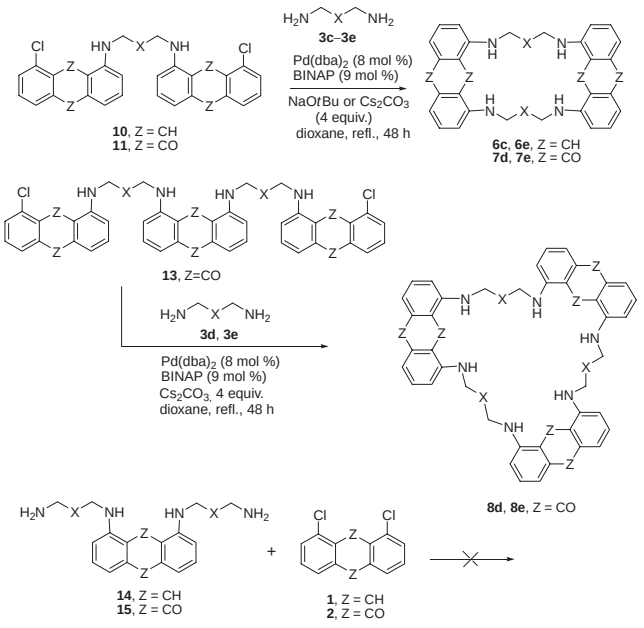

Scheme 2.

Table 1. Synthesis of cyclic oligomers **6–8**

Entry	Aryl halide	Amine	Pd/BINAP (mol %) (Conc., M)	Yields of isolated products/%
1	**10c**	**3c**	8/9 (0.027)	**6c**, 34
2	**11c**	**3c**	8/9 (0.02)	0
3	**10d**	**3d**	8/9 (0.02)	**6d**, traces
4	**11d**	**3d**	8/9 (0.02)	**7d**, 21
5	**10e**	**3e**	8/9 (0.03)	**6e**, 15
6	**11e**	**3e**	8/9 (0.03)	**7e**, 37
7	**13d**	**3d**	8/9 (0.01)	**8d**, 25
8	**13e**	**3e**	8/9 (0.02)	**8e**, 40

compounds **11a** and **11b** with corresponding amines were all unsuccessful and did not provide desired cyclodimers. The reaction between **10c** with **3c** was efficient and afforded target cyclodimer **6c** in 34% yield (Table 1, Entry 1); the same was obtained in 8% yield in the synthesis of macrocycle **4c**. However, compound **11c** with the same amine did not give any corresponding cyclodimer (Table 1, Entry 2), which corresponds to the absence of such by-product in the synthesis of macrocycle **5c**. Similar situation was observed in the reaction between **10d** and **3d** where cyclodimer **6d** was detected only in the mass spectrum of the reaction mixture (Table 1, Entry 3); it was neither isolated as a by-product in the synthesis of **4d**. On the contrary, cyclodimer **7d** was obtained in 21% yield (Table 1, Entry 4), as were cyclodimers **6e** and **7e** (yields 15% and 37%, resp., Table 1, Entries 5 and 6). All these cyclodimers were also isolated in the synthesis of corresponding macrocycles **5d**, **4e**, and **5e**. At last, starting from linear oligomers **13d** and **13e** we managed to synthesize cyclotrimers **8d** and **8e** in 25 and 40% yields, resp. (Table 1, Entries 7 and 8) which were obtained as by-products in the synthesis of compounds **5d** and **5e** in lower yields. As we noted perfect coincidence between cyclodimers formation both as by-products and as target compoounds, we abstained from the attempt to synthesize cyclotrimers comprising anthracene units which were not detected at all in the synthesis of "normal" macrocycles **4**.

When we introduced 1,8-bis(diamine)-substituted anthracene and anthraquinone **14c**, **14e** and **15c**, **15e** in the reactions with **1** or **2** no formation of cyclodimers was observed (Scheme 2). This fact contrasts with our previous results obtained with bis(polyamine) derivatives of pyridine and cholane where at least in some cases cyclodimers were successfully obtained using this approach.[4–6,8]

All these facts led us to a conclusion that cyclic dimers and oligomers in the case of 1,8-dichloroanthracene and anthraquinone amination were formed via intermediate N^{α},N^{ω}-bis(haloaryl)polyamines **10** and **11** or similar linear oligomers like **12** and **13**, and not via their bis(polyamine) derivatives. Moreover, there are strict restrictions for the formation of such cyclic oligomers even according to the first route, and with the same amine anthracene and anthraquinone derivatives can give quite different results. Probably this is caused by a preferable geometry of polyaza(polyoxa) chains and/or by reciprocal orientation of two large fused ring systems.

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