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Synthesis of new tetraazamacrocycles by Pd-catalyzed amination of 1,8-dichloroanthracene and 1,8-dichloroanthra-9,10-quinone

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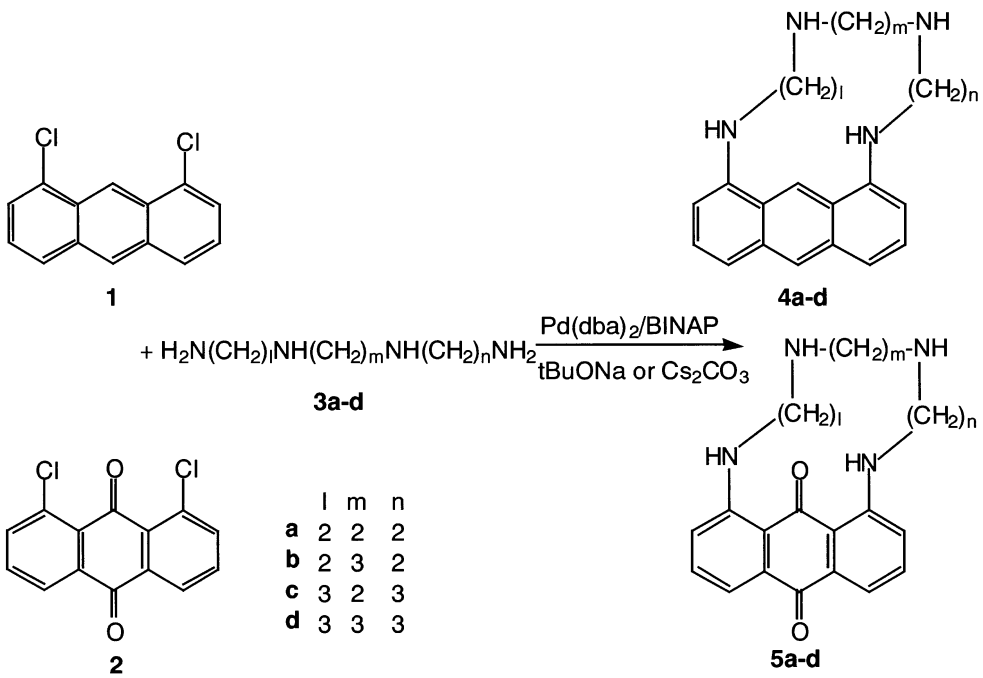
Abstract—Pd-catalyzed amination of 1,8-dichloroanthracene and 1,8-dichloroanthra-8,10-quinone leads to new tetraazamacrocycles containing anthracene or anthraquinone moiety. © 2001 Elsevier Science Ltd. All rights reserved.

Saturated and tetrapyrrolic macrocyclic ligands, which contain anthracene or anthraquinone fragments as a component of a macrocycle or as a substituent in a cycle, present a significant interest for chemists since their free ligands and metal complexes possess a number of relevant physico–chemical properties. The use of these compounds as bioinorganic models of biological systems, redox-active ligands, fluoro and luminosensors, and anion-binding agents has already been demonstrated.[1] Nowadays, studying such compounds is strictly limited owing to difficulties of synthetic approaches to these compounds. Other molecular systems, whose biphenyl[2] or dibenzacridine[3] moieties are incorporated in polyazamacrocycles, have also been



Scheme 1.

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reported. Together with various substituted porphyrins and related compounds,[4] including famous face-to-face porphyrins bound via an anthracene spacer, all these compounds were produced either by conventional non-catalytic methods or by Pd-catalyzed cross-coupling reactions leading to C–C bond formation. Here, we report the synthesis of new tetraazamacrocycles that are based on anthracene or anthraquinone moiety by means of Pd-catalyzed amination reaction[5] of aryl-halides. For the first time, the formation of a direct bonding arene–nitrogen in the synthesis of macrocycles is achieved starting from molecules with non-activated chlorine atoms.

The reaction of equimolar quantities of linear tetra-amines **3a–d** and anthracene **1** or anthraquinone **2** has also been studied. The $Pd(dba)_2$/BINAP catalytic system (8 mol%) was utilized with *t*BuONa base in the case of dichloroanthracene and Cs_2CO_3 for the reactions with dichloroanthraquinone. Diluted solutions of reagents in dioxane were used (0.025–0.017 mol/l) to eliminate any undesirable formation of oligomers while prolonged reflux (48–103 h) was required to accomplish cyclization (Scheme 1).

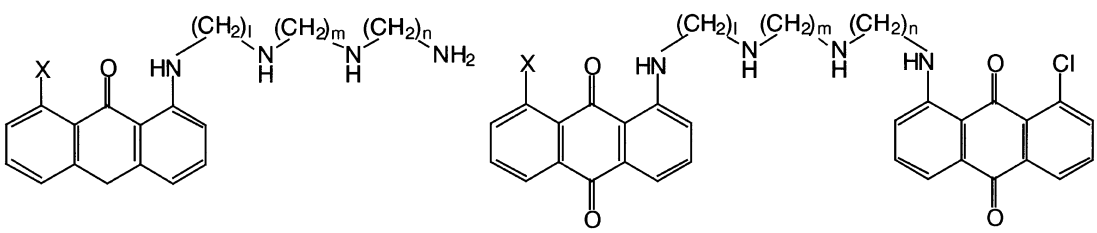
Yields of macrocycles **4a–d** ranged from 21 to 36% whereas, for compounds (**5a–d**), lower yields (10–25%) have generally been observed (Table 1). Macrocycles **4a–d** were obtained as brown solids after column chromatography on silica, compounds **5a**,**b** and **5c**,**d** turned red and lilac solids, respectively. The consumption of dichloroanthracene in these reactions was quantitative whereas dichloroanthraquinone estimated consumption, based on ^{1}H NMR spectra of isolated products, reached 90–95%. Indeed, a noticeable reduction of the chlorine atoms of dichloroanthraquinone has been observed. Besides, no oligomers were detected among the products of the reaction of dichloroanthracene **1** with tetraamines. On the contrary, reactions of dichloroanthraquinone **2** with polyamines provided a substantial formation of linear compounds: a mixture of 1-amino- and 1-amino-8-chloroanthraquinones **6a–d**, **7a–d** (yields up to 30%) as well as compounds with a higher molecular weight for an anthraquinone/amine ratio 2:1 (**8a**,**d**, **9a**,**d**). These by-products can be easily isolated by column chromatography and then analyzed. As for the reactions with triamines,[6] an arylation of only primary nitrogen atoms has been observed (Scheme 2).

We have previously established[7] that 1,8-dichloro-anthraquinone could react more easily with monoamines and, as a result, could provide excellent yields of diamines, due to its more pronounced electron-deficient character. As compared to 1,8-dichloroanthracene, the lower reactivity of this compound, which is being observed in the present case, is to some extent very surprising; this could probably be explained by the fact that, unlike most isolated compounds **6–9**, the lower

Table 1. Reaction conditions and yields of the products **4–9**

Product	Reaction time, h (reflux)	Amount of catalyst, mol%	Concentration of reagents, M	Yield, %[a]
4a	74	8	0.017	33
4b	48	8	0.025	36
4c	48	8	0.025	24
4d	75	8	0.02	21
5a	73	8	0.017	14
5a	103	16	0.01	10
5b	96	8	0.025	8
5b	76	16	0.017	19
5c	96	8	0.025	25
5d	73	8	0.017	3
5d	102	16	0.01	10
6a+**7a**[b]	73	8	0.017	25
6b+**7b**[b]	76	16	0.017	18
8a+**9a**[b]	103	16	0.01	5
8d+**9d**[b]	102	16	0.01	10

[a] Yields after column chromatography.
[b] Isolated mixture of two compounds.



6, X = Cl
7, X = H

8, X = Cl
9, X = H

Scheme 2.

yields could be due to the formation of undesired linear oligomers for a higher tetraamine/anthraquinone ratio (Scheme 2).

Typical experimental procedure:

A two-necked round flask filled with dry argon is charged with a mixture of 247 mg (1 mmol) of 1,8-dichloroanthracene[8] (or 277 mg of 1,8-dichloroanthraquinone), 1 mmol of tetraamine, 46 mg (0.098 mmol) of $Pd(dba)_2$,[9] 55 mg (0.084 mmol) of BINAP, 400 mg (4 mmol) of *t*BuONa (1.4 g (4 mmol) of Cs_2CO_3 in case of **2**), and 40–100 ml of absolute dioxane. Amounts of catalyst and ligand may be increased two-fold in order to achieve better yields. The reaction mixture is refluxed for 48–103 h. Then after filtration, dioxane is evaporated in vacuum and produces a dark brown residue (deep-red in case of **2**). The solid is dissolved in 30 ml of dichloromethane and extracted with 15 ml of water. Diethyl ether may be added so as to destroy the newly formed emulsion. The water layer is extracted with 3×25 ml of dichloromethane, organic fractions are combined, dried over Na_2SO_4, and the solvent is evaporated. Finally, the obtained dark brown solid is chromatographed on silica using subsequently dichloromethane, CH_2Cl_2/MeOH (3:1) and CH_2Cl_2/MeOH/NH_3 = 30:6:1 eluents. All compounds were characterized by ^1H and ^{13}C NMR spectroscopies, MALDI-TOF spectroscopy and elemental analysis.

Selected spectroscopic data:

Compound **4a**: ^1H NMR (200 MHz, $CDCl_3$): δ_H, ppm (*J*, Hz): 2.74 s (4H), 2.87 dd (4H, 5.7, 5.3), 3.25 dd (4H, 5.7, 5.3), 6.59 d (2H, 6.9), 7.29 dd (2H, 8.3, 6.9), 7.42 d (2H, 8.3), 8.25 s (1H), 9.16 s (1H). ^{13}C NMR (50 MHz, $CDCl_3$): δ_C 46.5 (2C), 48.1 (2C), 48.9 (2C), 106.9 (2C), 114.8 (1C), 118.5 (2C), 124.1 (1C), 126.1 (2C), 126.3 (2C), 132.7 (2C), 145.2 (2C). MALDI-TOF: [M^+] 320.65 (calc. 320.20)

Compound **5b**: ^1H NMR: 1.64 q (2H, 6.5), 1.86 s (2H, broad), 2.91 t (4H, 6.5), 2.97 dd (4H, 5.8, 5.0), 3.26 dt (4H, broad, 5.4, 4.2), 6.87 m (2H), 7.28–7.45 m (4H), 10.08 t (2H, 4.2). ^{13}C NMR: 31.3 (1C), 44.0 (2C), 48.3 (2C), 49.20 (2C), 114.4 (2C), 115.3 (2C), 118.0 (2C), 133.9 (2C), 134.4 (2C), 150. 9 (2C), 185.2 (1C), 188.2 (1C). MALDI-TOF: [M+H^+] 365.01 (calcd 365.19).

Compound **6a**: ^1H NMR: 1.95 s (4H, broad), 2.65–2.70 m (2H), 2.72–2.82 m (6H), 2.99 t (2H, 6.0), 3.44 q (2H, 5.8), 7.07 dd (1H, 7.0, 2.5), 7.47–7.51 m (2H), 7.54 t (1H, 7.7), 7.72 dd (1H, 8.0, 1.4), 8.20 dd (1H, 7.4, 1.4), 9.70 t (1H, 4.6). ^{13}C NMR: 42.1, 43.3, 48.7, 49.4, 49.6, 52.7, 115.6, 118.7, 124.7, 126.1, 126.8, 133.0, 134.4, 135.4, 135.7, 135.9, 138.4, 151.9, 183.4, 184.5. MALDI-TOF: [M^+] 386.61 (calcd 386.15).

Compound **7b**: ^1H NMR: 1.72 q (2H, 6.4), 2.38 s (4H, broad), 2.50–2.82 m (8H), 2.87 t (2H, 6.2), 3.43 q (2H, 5.7), 7.03–7.11 m (1H), 7.47–7.60 m (4H), 7.69 dd (1H, 7.5, 1.6), 8.24 dd (1H, 7.5, 1.6), 9.83 s (1H, broad). ^{13}C NMR: 29.8, 41.2, 42.6, 48.2, 48.3, 52.2, 52.2, 113.8, 115.7, 117.9, 126.4, 126.6, 132.6, 133.9, 135.3, 184.9, 184.0 (3 quaternary carbons of anthraquinone cycle were not unambiguously assigned). MALDI-TOF: [M^+] 366.93 (calcd 366.21).

Compound **8d**: ^1H NMR: 1.81 q (2H, 6.2), 1.94 q (4H, 6.6), 2.72 s (2H, broad), 2.82 t (8H, 6.4), 3.37 q (4H, 6.0), 6.93–7.10 m (2H), 7.37–7.55 m (4H), 7.50 t (2H, 7.6), 7.67 dd (2H, 7.6, 1.3), 8.12 dd (2H, 7.6, 1.3), 9.58 t (2H, 5.1). MALDI-TOF: [M^+] 668.73 (calcd 668.20).

Compound **9d**: ^1H NMR: 1.81 q (2H, 6.2), 1.94 q (4H, 6.6), 2.72 s (2H, broad), 2.82 t (8H, 6.4), 3.37 q (4H, 6.0), 6.93–7.10 m (2H), 7.37–7.55 m (6H), 7.50 t (1H, 7.6), 7.67 dd (1H, 7.6, 1.3), 7.70 dd (1H, 8.0, 1.3), 8.12 dd (1H, 7.6, 1.3), 8.17 dd (1H, 7.6, 1.6), 9.58 t (2H, 5.1). MALDI-TOF: [M+] 634.87 (calcd 634.23).

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