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Catalytic amination in the synthesis of hybrid polymacrocycles comprising porphyrin and azacrown ether moieties

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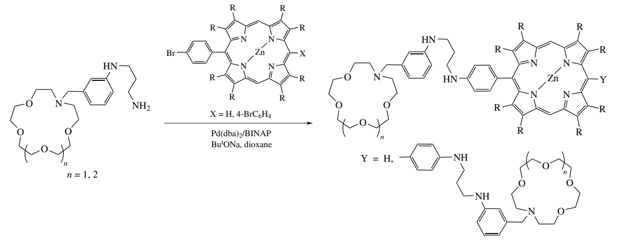
Pd^0-catalyzed amination of 3-bromobenzyl-substituted azacrown ethers with propane-1,3-diamine affords the 3-(3-aminopropyl)benzyl derivatives, whose reaction with *meso*-(bromophenyl)-substituted porphyrins leads to bis- and trismacrocyclic conjugates.



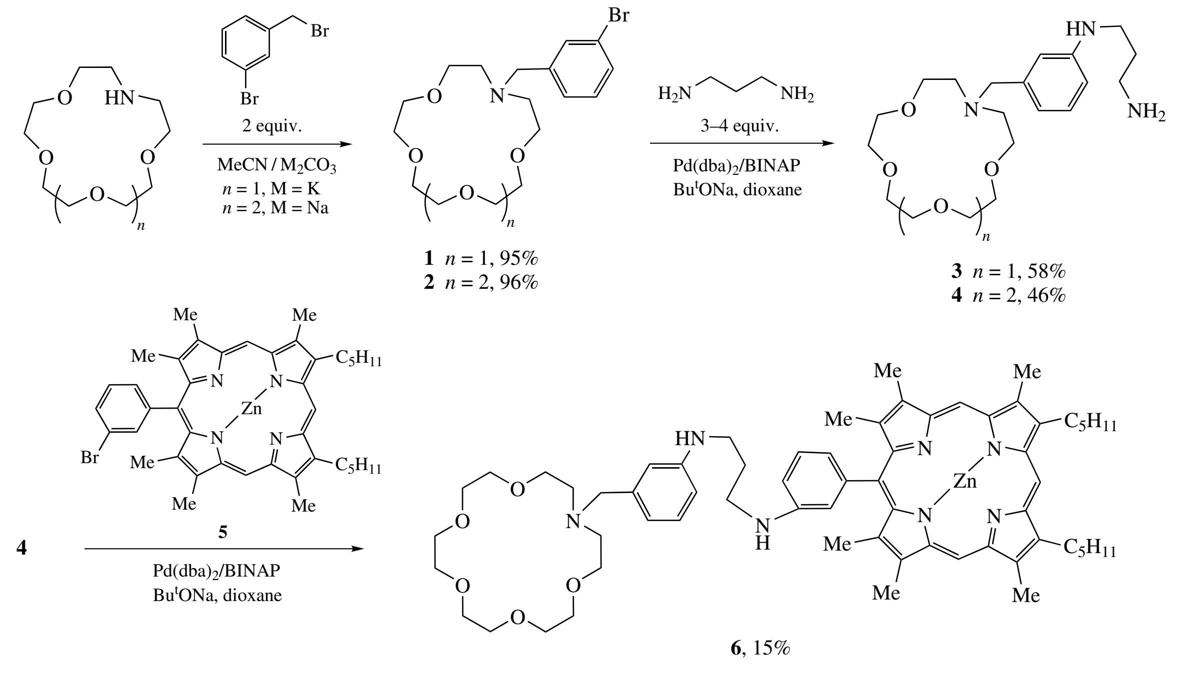
Polymacrocyclic compounds have been intensively studied during last decades soon after the elaboration of convenient synthetic approaches to macrocycles. The architecture of these compounds is often sophisticated and the purposes, for which they were obtained, vary greatly. For example, bisporphyrin systems are of constant interest as catalysts of dioxygen reduction,[1,2] model compounds for studying through-space energy transfer;[3,4] photophysical and photochemical properties of such compounds and their metal complexes have been investigated.[5,6] It is obvious that synthetic routes to bisporphyrins, especially with face-to-face organized macrocyclic moieties, are often addressed.[7–10] Another type of bismacrocyclic compounds containing two azacrown ether moieties is of interest due to their extraordinary coordination properties. Krakowiak with coauthors[11–13] were the first to elaborate a convenient and general approach to such compounds, cryptands and supercryptands, using simple nucleophilic substitution reactions. The majority of known bis(azacrown) ethers contain two isolated macrocycles symmetrically arranged around aromatic,[14,15] metallocene,[16] porphyrin[17] or calixarene[18] spacer. Crown-annelated porphyrins[19–21] and 1,3-bisporphyrin-calixarenes[22] are the examples of a smart conjugation of several ionophores, possessing not only different coordination but also electronic properties, in one assembly. Our own investigations also dealt with the synthesis of polymacrocyclic compounds incorporating either two macrocyclic moieties attached to a rigid spacer[23] or two azacrown ethers organized around the central diazacrown fragment or tetraazamacrocycle.[24,25]

In the present work we studied the possibilities of the Pd^0-catalyzed amination for the synthesis of hybrid polymacrocycles combining porphyrin with azacrown ether moieties linked *via* propane-1,3-diamine. Such compounds are of interest as they possess several coordination sites differing by binding properties and thus are able to form heterobinuclear and heteropolynuclear complexes. As porphyrins are strong chromophores and fluorophores, multimodal detection of the metal cations coordination is possible. To obtain azacrown–porphyrin conjugates, 1-aza-15-crown and 1-aza-18-crown-6 ethers were first modified with 3-bromobenzyl substituents and resulting compounds **1** and **2** were subjected to the Pd^0-catalyzed amination with excess propane-1,3-diamine to give the target diamino derivatives **3** and **4** (Scheme 1).[†,26] Compound **4** was introduced in the second Pd^0-catalyzed amination reaction with Zn^{II} *meso*-(3-bromophenyl)porphyrinate **5** (reactant ratio, 1:1), and the corresponding porphyrin–azacrown conjugate **6** was isolated in 15% yield. Note that similar attempted reaction of free *meso*-(3-bromophenyl)porphyrin failed and only the catalytic hydrodebromination was observed. The UV-VIS spectrum of conjugate **6** contains a strong Soret band (λ = 409 nm, lgε 5.55) and two less intensive Q bands (λ = 539 and 574 nm, lgε 4.32 and 4.13, respectively). The comparison with the starting zinc porphyrinate **5** shows small bathochromic shifts of all bands by 2–3 nm and a notable increase in the intensity of Q bands. The fluorescence spectrum of compound **6** reveals two bands of almost equal intensities at 589 and 639 nm.

Next, we carried out the reaction of the same azacrown derivative **4** with zinc di-*meso*(4-bromophenyl)porphyrinate **7** under the similar catalytic conditions (Scheme 2) and isolated bis(azacrown)–porphyrin conjugate **9** in 15% yield.[‡] A similar coupling of free porphyrin **8** with diamino derivative of azacrown ether **3**

[†] Compounds **1**–**4** were synthesized as described.[26] Zinc porphyrinates **5**, **8** and **12** were obtained in practically quantitative yields from corresponding free porphyrins according to a standard procedure by the action of 10 equiv. of Zn(OAc)$_2$ dihydrate in minimal amount of DMF at room temperature during 24 h followed by evaporation, dissolving in CH$_2$Cl$_2$ and filtration of the residue. 3-Bromophenyl-substituted porphyrins were obtained as reported.[27]

[‡] *Conjugate* **9**. A two-necked flask flushed with dry argon, equipped with a magnetic stirrer and reflux condenser was charged with Zn porphyrinate **7** (0.11 mmol, 111 mg), azacrown derivative **4** (0.22 mmol, 94 mg), Pd(dba)$_2$ (5 mg, 8 mol%), BINAP (6 mg, 9 mol%), absolute dioxane (2 ml) and Bu^{t}ONa (0.33 mmol, 32 mg). The reaction mixture was

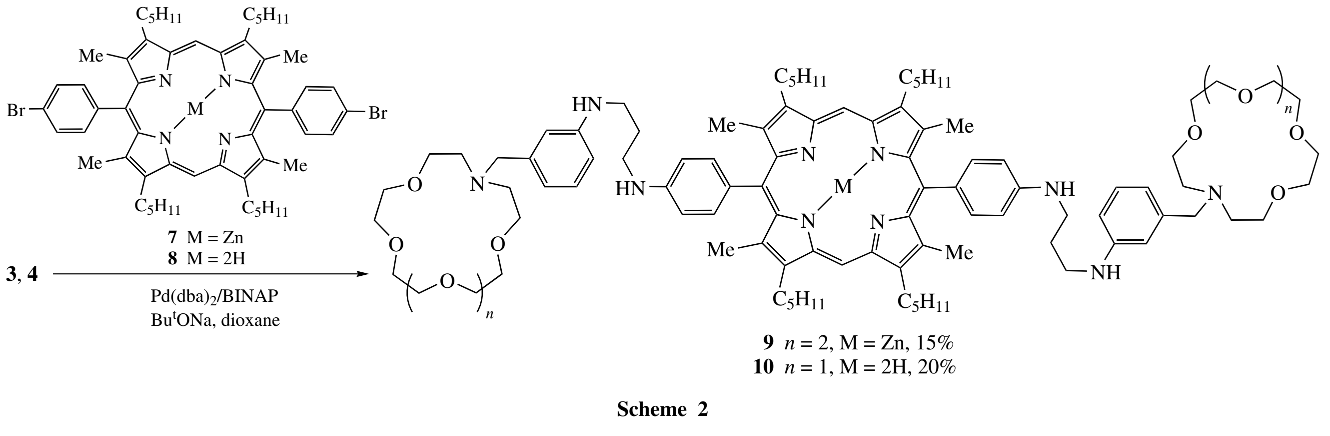


Scheme 1

produced conjugate **10** in 20% yield. The UV-VIS spectrum of conjugate **9** contains a strong Soret band (λ = 417 nm, lgε 4.80) and two less intensive Q bands (λ = 546 and 578 nm, lgε 3.45 and 3.17, respectively). The comparison with the starting zinc porphyrinate **7** shows small bathochromic shifts of all bands by 3–6 nm and a small increase in the intensity of the Soret band and one Q band. The fluorescence spectrum of compound **9** exhibits two bands at 594 and 648 nm, the first being more intensive. The UV-VIS spectrum of trismacrocycle **10** is characterized by a strong Soret band (λ = 409 nm, lgε 5.02) and the fluorescence spectrum possesses two emission bands at 638 and 704 nm, the second being more intensive. Thus, emission maxima in a free porphyrin derivative **10** are red-shifted by *ca.* 50 nm compared to zinc porphirynate **9**.

We explored the possibility of the alternative synthesis of azacrown–porphyrin conjugate. For this purpose bis(diamino) derivative of porphyrin **11** was prepared from compound **7** by coupling with excess diamine under Pd^0 catalysis conditions, the yield being 49% (Scheme 3). This compound was subjected to Pd^0-catalyzed reactions with 3-bromobenzyl azacrown ether **1**. However, this approach turned to be inefficient as only the partial reduction of the carbon–bromine bond occurred and no product of conjugation was formed. This result was unexpected in view of successful amination *via* an alternative way (see Schemes 1 and 2) and the explanation is to be found in future. Thus, it has been established that only the route employing amino derivatives of azacrown ethers and bromophenyl-substituted porphyrins can lead to the formation of azacrown–porphyrin conjugates.

Coordination studies of compounds **6**, **9** and **10** are underway now. The first results are as follows. We investigated the dependence of the spectral properties of compounds **9** and **10** bearing two 1-aza-18-crown-6 moieties in their structures on the presence of 18 metal cations (Li^{I}, Na^{I}, K^{I}, Mg^{II}, Ca^{II}, Ba^{II}, Al^{III}, Mn^{II}, Fe^{II}, Cr^{III}, Co^{II}, Ni^{II}, Cu^{II}, Zn^{II}, Cd^{II}, Pb^{II}, Ag^{I}, Hg^{II}) in order to find perspective optical chemosensors. For this purpose we measured UV-VIS and fluorescence spectra of these polymacrocycles in MeCN adding 0.5, 1, 2.5, and 5 equiv. of the corresponding metal perchlorates (see Figures S1–S6, Online Supplementary Materials). Excitation of trismacrocycle **9** was carried out at 418 nm and of trismacrocycle **10** at 410 nm. The addition of



Scheme 2

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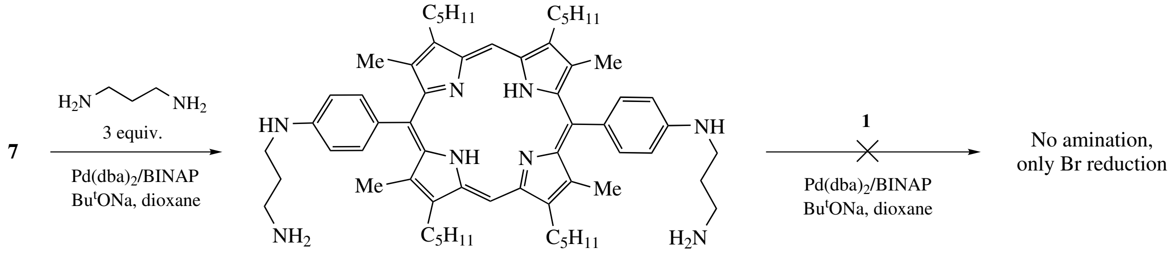
refluxed for 24 h, cooled to ambient temperature and diluted with CH$_2$Cl$_2$ (5 ml). The residue was filtered off, washed with CH$_2$Cl$_2$ (5 ml), combined organic fractions were evaporated *in vacuo*, dissolved in CH$_2$Cl$_2$, washed with water (5 ml) and dried over molecular sieves. Solvent was again evaporated *in vacuo* and the residue was chromatographed on silica gel using a gradient of eluents: CH$_2$Cl$_2$–CH$_2$Cl$_2$/MeOH (3:1). The target compound was eluted with CH$_2$Cl$_2$/MeOH/NH$_{3\,aq}$ 100:35:6–10:4:1. Yield 28 mg (15%), deep-red solid.

For characteristics of conjugate **9** as well as synthesis and characteristics of conjugates **6**, **10** and porphyrin **11**, see Online Supplementary Materials.



11, 49%

Scheme 3

2.5 equiv. of different metal perchlorates to the solution of trismacrocycle **9** did not result in significant changes in its absorption and emission spectra, except for Cu(ClO$_4$)$_2$ which dramatically decreased the intensity of absorption and led to a bathochromic shift of its maximum (from 417 to 432 nm). The quenching of emission with Cu$^{\mathrm{II}}$ was almost total, while Pb$^{\mathrm{II}}$ decreased it only by 25%, and the ligand was quite insensitive for other metal cations. It is interesting that the addition of 0.5 or 1 equiv. of Cu$^{\mathrm{II}}$ gradually decreased the absorption, however, it did not result in the shift of the absorption maximum of both Soret and Q bands. The addition of the second equivalent gave rise to above mentioned bathochromic shift of the Soret band and simultaneously the Q band almost totally disappeared. Also, upon the addition of 0.5 and 1 equiv. of Cu$^{\mathrm{II}}$ emission gradually decreased (*ca.* 2 and 6 times, respectively), whereas with the second equivalent it was fully quenched. These facts might be explained by the formation of a non-emissive dicopper complex with trismacrocycle **9** bearing two azacrown fragments each capable of complexing with one Cu$^{\mathrm{II}}$ cation. Special experiments have been undertaken to verify cross-selectivity of the ligand **9** towards Cu$^{\mathrm{II}}$ using Na$^{\mathrm{I}}$, K$^{\mathrm{I}}$, Mg$^{\mathrm{II}}$, Ca$^{\mathrm{II}}$, Ba$^{\mathrm{II}}$, Zn$^{\mathrm{II}}$, Pb$^{\mathrm{II}}$ and Hg$^{\mathrm{II}}$ perchlorates which can be viewed as the most expected interfering ions. The UV-VIS and fluorescence spectra in all cases were absolutely the same as in the presence of sole copper perchlorate (weak maximum at 432 nm and no emission). Therefore, conjugate **9** can be proposed as a perspective two-channel fluorimetric and colorimetric chemosensor for Cu$^{\mathrm{II}}$ ions.

Different results were obtained with a free porphyrin tricyclic derivative **10**. The addition of the majority of cations except Al$^{\mathrm{III}}$ resulted in insignificant changes of the spectrum, addition of Cu$^{\mathrm{II}}$ led to somewhat narrowing of the absorption band in UV spectra without prominent enhancement of the absorption or shift of the maximum. Only with Zn$^{\mathrm{II}}$ the enhancement was *ca.* twofold along with a bathochromic shift by 6 nm. The addition of 1 or 2 equiv. of aluminium perchlorate resulted in the attenuation of the absorption band, and with 5 equiv. two absorptions of almost the same intensity were clearly seen in the spectrum with maxima at 411 and 494 nm. In the fluorescence spectra (excitation at 409 nm) many cations led to emission quenching: addition of 5 equiv. of Al$^{\mathrm{III}}$, Cu$^{\mathrm{II}}$, 10 equiv. of Cr$^{\mathrm{III}}$ quenched it totally, while 10 equiv. of Pb$^{\mathrm{II}}$ diminished the emission intensity *ca.* 30 times, and 10 equiv. of Mn$^{\mathrm{II}}$ – *ca.* 4 times. Only in the presence of 5 equiv. of Zn$^{\mathrm{II}}$ emission bands shifted to 594 and 648 nm, that envisages the formation of the Zn porphyrinate complex as trismacrocycle **9** possesses exactly the same emission bands. Thus, compound **10** can be viewed as a colorimetric molecular probe for Al$^{\mathrm{III}}$ and fluorimetric probe for Zn$^{\mathrm{II}}$ cations.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.04.006.

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