ИРИНА ПЕТРОВНА БЕЛЕЦКАЯ
МОСКОВСКИЙ ГОСУДАРСТВЕННЫЙ УНИВЕРСИТЕТ ИМ. М.В. ЛОМОНОСОВА, ХИМИЧЕСКИЙ ФАКУЛЬТЕТ, ЛЕНИНСКИЕ ГОРЫ, 1-3, МОСКАВА, 11991
E-mail: beletska@org.chem.msu.ru

АЛЕКСЕЙ ДМИТРИЕВИЧ АВЕРИН
ИНСТИТУТ ФИЗИЧЕСКОЙ ХИМИИ И ЭЛЕКТРОХИМИИ ИМ. А.Н. ФРУМКИНА РАН, ЛЕНИНСКИЙ ПР., 31-4, МОСКАВА, 119991
E-mail: alexaveron@yandex.ru

Мини-обзор обобщает результаты, касающиеся различных превращений порфиринов и их комплексов, осуществленных в реакциях, катализируемых комплексами палладия, и приводящих к образованию связей C-C, C-N и C-P.

Ключевые слова: порфирин, комплекс, катализ, палладий

METAL CATALYSIS IN THE TRANSFORMATIONS OF PORPHYRINS

I. P. Beletskaya, A. D. Averin

Ирина П. Белецкая
Ломоносов Московский университет, факультет химии, Ленинские Горы, 1-3, Москва, 119991 Россия
E-mail: beletska@org.chem.msu.ru

Алексей Д. Аверин
Институт физической химии и электрохимии им. А.Н. Фрумкина РАН, Ленинский пр., 31-4, Москва, 119991, Россия
E-mail: alexaveron@yandex.ru

A mini-review outlines the results considering various transformations of porphyrins and their complexes achieved in the reactions catalyzed with Pd complexes leading to C-C, C-N and C-P bonds formation.

Ключевые слова: порфирин, комплекс, катализ, палладий

INTRODUCTION

Порфиринов является важным классом органических соединений, широко распространенных в природе в виде строительных блоков в живых системах [1]. Биопорфиринов, например, магний-содержащих хлорофиллов, являются пигментами растений, в то время как гемоглобин в крови состоит из гемов. Порфирин-связанные тетрапириллактонные макrocиклы обнаружены в природе, а также искусственные порфириновидные соединения таких как фталоцианиновые даны на Fig. 1. Одна из важных задач порфириновой химии — это образование супрамолекулярных ассоциатов, потенциально полезных для различных приложений [2].

It is well known that at the end of the XXth century principally new approaches to the construction of carbon-carbon and carbon-heteroatom bonds were widely developed. The reactions, named after their discoverers and pioneers like Heck, Suzuki, Miyaura, Sonogashira, began to be actively applied in various fields of organic chemistry. The porphyrin chemistry did not stay apart from this process and began to employ the catalytic reactions though it happened later than with more simple aromatic substrates. Examples of such reactions for the construction of the \( \beta \)-meso porphyrin dimer (via Suzuki-Miyaura reaction) [3],
mono- and divinyl substituted porphyrins (via Heck reaction) [4], β-alkynyl substituted porphyrin (via Sonogashira reaction) [5] are shown on Scheme 1. The same reactions were applied for the synthesis of porphyrin dyads and triads with phenylene and acetylene bridges (Scheme 2) [6]. It is to be stressed that carrying out such reactions with porphyrin compounds is usually more difficult than with simpler aromatics and to achieve good results one needs more catalyst and ligand loadings. The development of the catalytic transformations of porphyrins before 2010 was summarized in a review [7].

Pd-catalyzed amination of bromosubstituted porphyrins

Facile and efficient synthesis of meso-arylamino- and alkylamino-substituted porphyrins via Pd-catalyzed amination was proposed by Zhang in 2003 [8], while a convenient method for the preparation of a variety of amino substituted zinc porphyrins by Pd-catalyzed intermolecular carbon-nitrogen coupling reactions between haloporphyrins and amino substituted porphyrins was reported by van Lier even earlier [9]. The successes in the application of the Buchwald-Hartwig amination to the synthesis of porphyrin derivatives were outlined in [10].

Fig. 1. Naturally occurring and artificial porphyrinoids

Рис. 1. Природные и синтетические порфириноиды
The investigations conducted in the Laboratory of Organoelement Compounds of the Department of Chemistry of the Lomonosov MSU were at first focused at the application of the Pd(0)-catalyzed amination of meso-(bromophenyl)substituted porphyrins due to our vast experience in the application of this method to the chemistry of macrocyclic compounds. 5-(4-Bromophenyl)- and 5,15-di(4-bromophenyl)porphyrins were involved in the catalytic amination and compounds containing chiral hydroxypiperidine fragments were thus obtained (Scheme 3) [11, 12]. This was one of the first rare examples of the Pd-catalyzed amination reactions in porphyrin series using Buchwald (2-(dicyclohexylphosphino)-2'-diphenylbiphenyl, DavePhos) and Fu (tris(tert-butyl)phosphine) ligands.
Previously unknown 5,10,15,20-tetrakis(4-bromophenyl) substituted tetrabenzo- and tetranaphthoporphyrins with extended π-system were successfully obtained in our laboratory and their Pd-catalyzed polyamination was carried out using BINAP or DavePhos ligands (Scheme 4) [13]. The same approach was applied for the synthesis of polymacrocyclic compounds featuring one central porphyrin and several surrounding azacrown moieties.

Scheme 4

Scheme 5
The diamination reactions of Zn(II) 5,15-bis(4-bromophenyl)porphyrinate with various nitrogen-containing compounds (Scheme 5) was carried out in order to obtain polydentate ligands which possess three coordination sites: one electrophilic site where Zn can coordinate nucleophiles, and two nucleophilic sites to form complexes with metal cations [14, 15].

Scheme 6

Scheme 7
The diamination of this porphyrinate with diazacrown ether or DMEDA \((N,N'\text{-dimethyl-1,2-ethanediamine})\) proceeded with good yields of the desired products (50-63%) though it was complicated with a usual hydrodebromination side process which led to corresponding products of monoamination in 32-36% yields. In the case of the amination with piperazine monoamination with the reduction of the second C-Br bond became the predominant process, and with \(N,N',N''\text{-triBOCcyclen}\) only monoaminated product was formed in 50% yield. Interesting conjugates of metalloporphyrins with the lanthanide complexes of triamidocyclen were synthesized according to a three-step procedure starting from triBoccyclen derivative of Zn(II) porphyrinate (Scheme 6).

Catalytic diamination of 5,15-bis(3- or 4-bromophenyl)porphyrins taken as free bases with excess 1,3-propanediamine and trioxadiamine gave corresponding bis(dimaino) derivatives of porphyrins (Scheme 7). More sophisticated conjugates possessing several coordination sites were obtained via the reactions of diamino derivatives of \(N\)-benzylazacrown ethers [16].

The synthesis of the porphyrin dimers linked by various diamines like 1,2-ethanediame, DMEDA, piperazine, diazacrown ether can be carried out either in a stepwise mode, via intermediate diamino derivatives of corresponding metal porphyrinates, or directly from the diamines and porphyrinates taken in 1:2 ratio [17]. A similar approach using bis(diamino) derivatives of Zn(II) porphyrinates and 5-(4-bromophenyl)-porphyrinate taken in 1:2 ratio allows to create more sophisticated porphyrin trimers in which three porphyrin units are linked with two diamine moieties (Scheme 8).
We demonstrated the possibility to create another porphyrin trimer in which macrocycles are linked via simple NH units (Scheme 9), for this purpose 2 equiv. of Zn(II) 5-(4-bromophenyl)porphyrinate were reacted with 1 equiv. of Zn(II) 5,15-(4-aminophenyl)porphyrinate [17].

Using previously developed naphthalene- and biphenyl-based diazacrown ethers, we successfully applied Pd(0)-catalyzed amination to the synthesis of interesting trimacrocyclic compounds comprising either two porphyrin and one diazacrown or two diazacrown and one porphyrin moieties (Scheme 10) [18, 19].
Important conjugates of macrobicyclic compounds based on diazacrown ethers with porphyrins were synthesized via Pd-catalyzed amination using 2 equiv. of Zn(II) 5-(4-bromophenyl)porphyrinate (Scheme 11) [20, 21]. The aim of the synthesis of such molecules was to obtain fluorescent sensors for metal cations employing receptor abilities of macrobicyclic cryptands and fluorescent properties of the attached porphyrin units.

Another type of the conjugates with porphyrins as fluorophore groups are those based on diaminocalix[4]arenes taken in cone and 1,3-alternate forms (Scheme 12). The dependence of the yields of the target trimacrocyclic derivatives on the structure of the starting diaminocalix[4]arene was clearly demonstrated.

**Coordination studies of porphyrin-derived polymacrocycles**

Many polymacroyclic compounds containing porphyrin moieties were studied in the complexation with metal cations. For example, spectrophotometric titration of the bis(azacrown) derivative of Zn(II) porphyrinate at \( \lambda = 419 \) nm with NaBr in CHCl/MeOH showed the formation of the complex with two sodium cations (Fig. 2). On the other hand the titration of the same trimacrocyclic compounds with KI resulted in the formation of the complex with 2:2 stoichiometry due to a larger ionic radius of K(I) cation (Fig. 3) [15].
Fig. 2. Coordination of bis(azacrown) derivative of Zn(II) porphyrinate with Na(I) cations
Рис. 2. Координация бис (азакраун) производного порфирината Zn (II) c катионами Na (I)
Interesting coordination between a porphyrin dyad in which two Zn(II) porphyrinates are linked via ethylenediamine bridge and a molecule of DABCO was studied. Spectrophotometric titration at $\lambda = 406$ nm revealed the formation of the 1:1 complex with co-facial arrangement of the porphyrin macrocycles at the first stage after the addition of 0.5 equiv. of the organic base. More DABCO led to the formation of the complex with two DABCO molecules (Fig. 4).
Similar coordination mode was established in the case of titration of the Zn(II)-Sn(II) bisporphyrinate with CuBr (Fig. 5). The porphyrin dyad acts as a tweezer forming a 1:1 complex with Cu(I) [22]. The driving force of this process is the formation of the chelate complex involving ethylenediamine and copper as well as the axial coordination of Zn cation with the hydroxyl group of the Sn(II) porphyrinate unit of the dyad. After the addition of either a more strong ligand (phenanthroline) or acid (HCl), which protonates two nitrogen atoms in the ethylenediamine fragment, a linear structure of the porphyrin dyad is recovered.

Several porphyrin-azacrown conjugates were tested as fluorescent chemosensors for metal cations [18]. The investigations revealed that bisporphyrinate derivative of the biphenyl-based diazacrown ether could be regarded as a fluorescent molecular probe for Cu(II), Al(III) and Cr(III) as only these cations quenched emission (Fig. 6a). Interestingly, a quite similar trimacrocycle, the derivative of the naphthalene-based diazacrown ether containing the same prophyrinate units, was found to be much more selective towards Cu(II) as only the addition of this cation led to full quenching of the emission (Fig. 6b).
More sophisticated tetra-macroyclic conjugate containing two Zn(II) porphyrinate units and a central macrobicyclic cryptand was also efficient in the fluorescent detection of Cu(II) [19] as only this cation among other 17 led to almost full quenching of fluorescence (Fig 7).

Copper-catalyzed synthesis of porphyrin dyads and triads

Cu(I)-catalyzed 1,3-dipolar cycloaddition reactions were successfully used for the synthesis of non-linear porphyrin triads containing 1,2,3-triazole linkers. Two alternative approaches were developed for this purpose, the first employing the reaction of 5,15-bis(ethynylphenyl) derivative of porphyrin with 2 equiv. of meso-(4-azidophenyl)substituted porphyrinate (Scheme 13) [23]. The application of Cul/DIPEA in THF-MeCN was advantageous over a classical system (CuSO₄/sodium ascorbate in DMF). The second approach involved Zn(II) 5,15-bis-(4-azidophenyl) substituted porphyrinate with 2 equiv. of meso-(4-ethylphenyl)porphyrinate in the presence of Cul/DIPEA in THF-MeCN (Scheme 14) and it produced an isomeric porphyrin triad also in a high 70% yield.
Scheme 13

2 equiv.

Scheme 14

2 equiv.

CuI/DIPEA in THF/MeCN, 70%
Porphyran triad of a star shape [24] was obtained using the similar approach in which 1,3,5-tri(ethynyl)benzene was reacted with 3 equiv. of meso-(4-azidophenyl) substituted porphyrinate. The target star-shaped triad was isolated in 30% yield (Scheme 15).

All these porphyrin trimers possess very interesting photophysical properties important for studying femtosecond processes occurring in nature [25].

**Scheme 15**

**CH-activation reactions for porphyrins transformations**

Application of palladium catalysis to the synthesis of phosphorylated porphyrins in view of their coordination and versatile physico-chemical studies is much addressed in the works by Bessmertnykh-Lemeune and Gorbunova [26-32]. Another approach to P-containing porphyrins, namely, Pd(II)-catalyzed oxidative phosphonation of the *meso*-position of porphyrins and their metal complexes was studied using 5-mesityl-, 5,15-dimesityl- and 5,10,15-trimesitylsulfurated porphyrins in the reactions with diethyl phosphate in the presence of K$_2$S$_2$O$_8$ and bipyridyl [33]. It was disclosed that an accurate adjustment of the amount of catalyst, base and oxidant was important to obtain good yields of the desired compounds. Also, the dependence of the nature of starting porphyrins was crucial for a success of the synthesis. Thus, monophosphonation of 5-mesitylporphyrin taken as a free base gave only a moderate yield of the *trans*-monophosphonated product (Scheme 16).

**Scheme 16**
The application of Ni(II) 5-mesitylporphyrinate produced the product of cis-phosphonation in a high yield (Scheme 17).

The diphosphonation of 5,15-dimesitylporphyrin was shown to proceed with the free base and Ni(II) porphyrinate, the formation of the monophosphonated products in comparable yields was observed in all cases (Scheme 18).

The phosphonation of the isomeric 5,10-dimesitylporphyrin and 5,10,15-trimesitylporphyrin was a more difficult task and only Ni complexes could be successfully involved in this process (Scheme 19). It is interesting that if Zn(II) porphyrinate was employed, full demetallation was observed and a free phosphonated porphyrin was obtained in a rather good yield.
Heteroarylation of Zn(II) 5-(bromophenyl)porphyrinates with the heterocycles possessing an “acidic” C-H bond (benzoxazole, benzothiazole and N-methylbenzimidazole) was carried out in the presence of Pd(II)/Cu(II) catalytic system. Corresponding heterocyclic derivatives were obtained in yields from good to high, up to 95% (Scheme 20) [34].

In the case of Zn(II) 5,15-di(bromophenyl)porphyrinate the possibility of diheteroarylation was shown with benzoxazole while other heterocycles could produce only monoheterocyclic derivatives (Scheme 21).

Benzoxazole was also the sole heterocycle helpful in the formation of tri- and tetraheteroaryl derivatives in the reaction with Zn(II) 5,10,15,20-tetrakis-(4-bromophenyl)porphyrinate (Scheme 22).
CONCLUSIONS

We demonstrated wide possibilities of the Pd(0)-catalyzed amination for various modifications of meso-(bromophenyl)substituted porphyrins using monoamines, linear di- and polyamines, azacrown ethers, more sophisticated nitrogen-containing macrocycles and macrobicycles and diaminocalix[4]arenes. It was shown that porphyrins taken as free bases as well as their metal complexes could participate in such reactions. As a result novel polytopic ligands were elaborated and their coordination studies were done. Some of them were shown to be suitable as potential fluorescent chemosensors for Cu(II) cations. Cu-catalyzed synthesis of the porphyrin triads was elaborated. Novel approaches to phosphonated porphyrins and heterocyclic derivatives via CH-activation reactions catalyzed by Pd(II) or Pd(II)/Cu(II) were worked out.

Acknowledgements. This work was financially supported by the RSF grant 14-23-00186P (catalytic modification of porphyrins) and the RFBR grant 16-29-10685 (coordination and spectral studies of the porphyrins conjugates).

REFERENCES


Поступила в редакцию 27.11.2018
Принята к опубликованию 04.12.2018

Received 27.11.2018
Accepted 04.12.2018