Макрогетероциклы
http://macroheterocycles.isuct.ru

DOI: 10.6060/mhc181225m

Aromatic Nucleophilic Substitution as a Side Process in the Synthesis of Alkoxy– and Crown–Substituted (Na)phthalocyanines

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This work reports on systematic survey for cyclotetramerization of crown- and butoxy-substituted phthalo- and naphthalonitriles in pentanol induced by DBU and PentOLi. It was demonstrated that these substrates undergo undesired side process of nucleophilic aromatic substitution of RO-groups with PentO-anions in dinitrile molecules. It results in cleavage of crown ether rings and leads to formation of inseparable mixture of (na)phthalocyanines with different ratios of intact and cleaved macrocyclic substituents. Butoxy-substituted substrates are notably less sensitive to nucleophilic attack. Application of magnesium pentoxide both as a base and templating agent does not result in crown ether ring opening reactions and affords target compounds in high yields. The results of work can be used as guidelines for the choice of bases and template agents in the synthesis of (na)phthalocyanines functionalized with macrocyclic substituents.

Keywords: Phthalonitrile, naphthalonitrile, phthalocyanine, naphthalocyanine, crown ether, nucleophilic substitution.

Ароматическое нуклеофильное замещение как побочный процесс в синтезе алкокси– и краун–замещенных (на)фталоцианинов

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В работе описано систематическое исследование реакций циклотетрамеризации краун- и бутокси-замещенных фтало- и нафталонитрилов в пентаноле в присутствии DBU или PentOLi. Показано, что в процессе реакции может происходить побочный процесс нуклеофильного замещения RO-групп в результате нуклеофильной атаки PentO-аниона по молекулам динитрилов. В случае краун-замещенных динитрилов это приводит к раскрытию макроциклов и последующему образованию неразделимой смеси (на)фталоцианинов с различным соотношением неповрежденных и раскрытых краун-эфирных заместителей. Дибутокси-фтало- и нафталонитрилы значительно менее склонны к участию в реакциях нуклеофильного замещения алкильных групп. Использование пентоксида магния в качестве темплата и основания в синтезе краун-замещенных (на)фталоцианинов позволяет избежать побочных процессов нуклеофильного замещения, благодаря чему целевые комплексы получаются с высоким выходом. Результаты исследования могут быть полезны при подборе оснований и темплатных агентов при синтезе новых фталоцианинов с макроциклическими заместителями.

Ключевые слова: Фталонитрил, нафталонитрил, фталоцианин, нафталоцианин, краун-эфир, нуклеофильное замещение.

Introduction

Phthalocyanines (Pc) and their π-extended analogues – naphthalocyanines (Nc) are well-known coloured compounds, which find wide applications as dyes, pigments and photoactive components of various materials and devices due to their intensive absorbance in red and near-IR ranges.[1,2]

Numerous studies of Pcs and Ncs emphasize the influence of metal centres and peripheral substituents on Pcs properties.[3–5] While the metal centres have profound influence on photophysical and redox-properties of compounds, the role of substituents also includes enhancement of solubility in comparison with the unsubstituted macrocycles, which are almost insoluble in common solvents because of their tendency to aggregation, which becomes particularly strong in the case of Nc derivatives.[6]

From the viewpoint of control of aggregation, discovery of crown-substituted phthalocyanines in middle 1980s was an important milestone.[7–9] It was demonstrated that crown-Pcs can form supramolecular assemblies of various architectures, affording material with superior characteristics.[10–17] In 2018 synthesis and characterization of first representatives of crown-substituted naphthalocyanines was reported.[18] The studies evidenced of high potential of supramolecular approach to control both aggregation and photophysics of crown-Ncs.

Phthalo- and naphthalocyanines are commonly synthesized from corresponding phthalo- and naphthalonitiles, which undergo *template* condensation in the presence of metal ion sources, which is often used for the synthesis of *d*-metal complexes. Many types of complexes are synthesized *via direct* metalation of free base macrocycles. This approach is widely used in synthesis of sandwich complexes, including double- and triple-deckers, sandwiches with low-symmetry ligands, single-atom bridged complexes, *etc.* [19–23] In turn, synthesis of free base (na)phthalocyanines can be achieved either by reductive cyclotetramerization of corresponding *o*-dinitriles in template-free conditions, or by demetalation of labile metal complexes.

Starting from seminal papers reported by Linstead in 1930s, metal-free macrocycles are often synthesized by reactions of (na)phthalonitriles in high-boiling alcohols in the presence of lithium alkoxides.[24] These reactions yield lithium complexes with Pc/Nc ligands, which can be either demetalated *in situ* to form corresponding free bases, or isolated and used in transmetalation reactions.

Alternatively, strong organic amidine bases, especially 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) can be applied to initiate cyclotetramerization of (na)phthalonitriles in high-boiling alcohols.[25–27] In the absence of metal salts corresponding free base macrocycles can be obtained directly, while interaction of dinitriles with metal salts in the presence of DBU results in formation of corresponding complexes *via* template reactions. Up to date, the later approach is the most commonly used method in the synthesis of Pcs and Ncs.

The specific structural feature of alkoxy-(na)phthalonitriles in general and crown-substituted (na)phthalonitriles in particular is the presence of electron-withdrawing cyano-groups in *para*-positions to OR-groups which can activate these substrates towards nucleophilic substitution of alkoxy-groups in the presence of strong nucleophiles (S_N2_{Ar} mechanism).[28,29] Such conditions are often implemented during macrocyclization of phthalonitriles, and some rare examples of such nucleophilic substitution of alkoxy-groups in phthalonitriles leading to mixtures of phthalocyanines were previously reported.[30–32]

Here we firstly report systematic investigation of cyclotetramerization of various phthalo- and naphthalonitriles (Chart 1) in *n*-pentanol in the presence of DBU and PentOLi using MALDI-TOF mass-spectrometry for detection of reaction products. For this study we have chosen 15-crown-substituted phthalo- and naphthalonitriles **(15C5)Pn** and **(15C5)Nn** and their analogues bearing non-ionophoric butoxy-groups – **$(BuO)_2$Pn** and **$(BuO)_2$Nn**. It was found that crown-substituted dinitriles, particularly **(15C5)Pn** are susceptible to nucleophilic *ipso*-substitution with PentO-anion in pentanol media which results in formation of mixtures of (na)phthalocyanines with cleaved crown ether rings (Figure 1). BuO-substituted dinitriles were found to be less sensitive to nucleophilic attack.

Altogether, the obtained results can be considered as methodological guidelines for the synthesis of crown- and alkoxy-substituted (na)phthalocyanine ligands.

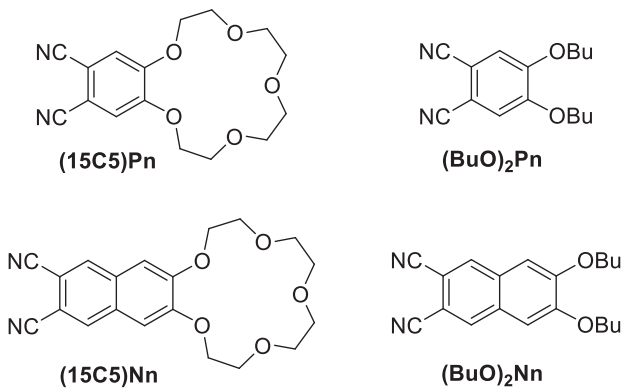


Chart 1.

Experimental

Materials and Methods

Dinitriles **(15C5)Pn**,[33] **$(BuO)_2$Pn**,[34] **(15C5)Nn**,[18] and 2,3-dibromo-6,7-dihydroxynaphthalene[35] were synthesized according to the previously reported procedures. DBU (Aldrich, 98 %) was distilled over CaH_2 in vacuum and stored under argon. *n*-Pentanol (Sigma-Aldrich, >99 %) was distilled over Mg and stored under argon. Chloroform was distilled over $NaHCO_3$. All other reagents were obtained from commercial suppliers and were used without additional purification. MALDI TOF mass-spectra were measured on Ultraflex spectrometer (Bruker Daltonics) with 2,5-dihydroxybenzoic acid (DHB), used as a matrix. ^{1}H NMR spectra were obtained using a Bruker Avance II 300 MHz NMR spectrometer. The measurements were performed using equipment of CKP FMI IPCE RAS.

Synthesis

2,3-Dibromo-6,7-butoxynaphthalene. 2,3-Dibromo-6,7-dihydroxynaphthalene (4.81 g, 15 mmol) and dry K_2CO_3 (8.35 g, 61 mmol) were suspended in 100 mL of dry DMF in a two-neck

flask equipped with a reflux condenser. The mixture was degassed and heated to 90 °C under argon atmosphere, then *n*-BuBr (9.8 ml, 91 mmol) was added with a syringe through the septum. The mixture was stirred at 90 °C overnight. After cooling the mixture was filtered, the solids were washed with *N*,*N*-dimethylformamide. The combined filtrates were evaporated to give a brown solid. Column chromatography on silica (elution with hexane + 0→50 vol.% acetone) and recrystallization from hexane afforded 4.81 g of target dibromide as a pale yellow crystalline solid (yield 75 %). ^{1}H NMR (300 MHz, acetone-d_6) δ_H ppm: 8.08 (s, 2H, H_{Ar}), 7.25 (s, 2H, H_{Ar}), 4.11 (t, *J*=6.4 Hz, 4H, OCH_2), 1.88–1.79 (m, 4H, 2-CH_2), 1.61–1.49 (m, 4H, 3-CH_2), 0.99 (t, *J*=7.4 Hz, 6H, CH_3). ^{13}C NMR (75 MHz, acetone-d_6) δ_C ppm: 151.71, 131.42, 130.47, 119.17, 107.24, 69.09, 31.89, 19.97, 14.13.

6,7-Dibutoxynaphthalene-2,3-dicarbonitrile ***(BuO)$_2$Nn***. 2,3-Dibromo-6,7-butoxynaphthalene (4.30 g, 10 mmol), zinc cyanide (1.76 g, 15 mmol), tris(dibenzylideneacetone)dipalladium – $Pd_2(dba)_3$ (183 mg, 0.20 mmol) and 1,1'-bis(diphenylphosphino) ferrocene – dppf (149 mg, 0.27 mmol) were placed into a two-neck flask equipped with a reflux condenser. The mixture of solids was degassed with three vacuum/argon cycles and 20 mL of dry *N*,*N*-dimethylacetamide was added with a syringe. The mixture was heated to 120 °C under argon atmosphere. Control over reaction by TLC (hexane/acetone 4:1 vol) evidenced a complete conversion of starting dibromide (dark spot at 256 nm UV light, R_f=0.64) into the dinitrile (blue luminescent spot at 256 nm UV light, R_f=0.18). After cooling the reaction mixture was filtered through the layer of silica, solids were washed with acetone and the combined filtrate was evaporated with silica. Resulting solid was loaded onto the column, packed with silica in hexane and eluted with hexane + 0→50 vol. % acetone. Combined fractions containing target dinitrile were evaporated and the solid was washed with boiling hexane, yielding 3.04 g of **(BuO)$_2$Nn** as a pale yellow solid (yield 95 %). ^{1}H NMR (300 MHz, acetone-d_6) δ_H ppm: 8.34 (s, 2H, H_{Ar}), 7.50 (s, 2H, H_{Ar}), 4.20 (t, *J*=6.4 Hz, 4H, OCH_2), 1.92–1.83 (m, 4H, 2-CH_2), 1.63–1.51 (m, 4H, 3-CH_2), 1.01 (t, *J*=7.4 Hz, 6H, CH_3). ^{13}C NMR (75 MHz, acetone-d_6) δ_C ppm: 153.84, 134.44, 130.93, 117.41, 108.54, 108.08, 69.48, 31.71, 19.90, 14.10.

Reaction of ***(15C5)Pn*** *with DBU.* **(15C5)Pn** (95 mg, 0.3 mmol) was suspended in 2 mL of PentOH and DBU (45 μL, 0.3 mmol) was added. The mixture was degassed and refluxed under argon for 15 h. After cooling the product was precipitated with the mixture of 20 mL of EtOAc and 30 mL of hexane, the solid was filtered, washed with EtOAc and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→4 % MeOH. Yield of mixture of phthalocyanines 25 mg (yield *ca*. 26 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for tetra-15-crown-5-phthalocyanine): found 1274.4 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{64}H_{74}N_8O_{20}$ 1274.5; found 1362.5 $[M+PentOH]^+$ ($I_{rel.}$=6 a.u.), calculated for $C_{69}H_{86}N_8O_{21}$ 1362.6.

Reaction of ***(15C5)Nn*** *with DBU.* **(15C5)Nn** (110 mg, 0.3 mmol) was suspended in 2 mL of PentOH and DBU (45 μL, 0.3 mmol) was added. The mixture was degassed and refluxed under argon for 15 h. After cooling the product was precipitated with the mixture of 20 mL of EtOAc and 30 mL of hexane, the solid was filtered, washed with EtOAc and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→8 % MeOH. Yield – 11 mg (10 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for tetra-15-crown-5-naphthalocyanine): found 1474.6 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{80}H_{82}N_8O_{20}$ 1474.6.

Reaction of ***(BuO)$_2$Pn*** *with DBU.* **(BuO)$_2$Pn** (82 mg, 0.3 mmol) was suspended in 2 mL of PentOH and DBU (45 μL, 0.3 mmol) was added. The mixture was degassed and refluxed under argon for 15 h. After cooling the product was precipitated with 50 mL of 50 % aqueous EtOH, the solid was filtered, washed with EtOH and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 40→20 % hexane. Yield of mixture of phthalocyanines 26 mg (yield *ca*. 31 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for octabutoxyphthalocyanine): found 1090.7 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{64}H_{82}N_8O_8$ 1090.6; found 1104.7 $[M\text{-}BuO+PentO]^+$ ($I_{rel.}$=4 a.u.), calculated for $C_{65}H_{84}N_8O_8$ 1104.6.

Reaction of ***(BuO)$_2$Nn*** *with DBU.* **(BuO)$_2$Nn** (97 mg, 0.3 mmol) was suspended in 2 mL of PentOH and DBU (45 μL, 0.3 mmol) was added. The mixture was degassed and refluxed under argon for 15 h. After cooling the product was precipitated with 50 mL of 50 % aqueous EtOH, the solid was filtered, washed with EtOH and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→2 % MeOH. Yield 15 mg (15 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for octabutoxynaphthalocyanine): found 1290.8 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{80}H_{90}N_8O_8$ 1290.7.

Reaction of ***(15C5)Pn*** *with PentOLi.* **(15C5)Pn** (95 mg, 0.3 mmol) was suspended in 2 mL of 0.8 M solution of PentOLi in PentOH. The mixture was degassed, refluxed under argon for 3 h and quenched with 100 μL AcOH. After cooling the product was precipitated with the mixture of 20 mL EtOAc and 30 mL of hexane, the solid was filtered, washed with EtOAc and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→4 % MeOH. Yield of mixture of phthalocyanines 69 mg (yield *ca*. 72 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for tetra-15-crown-5-phthalocyanine): found 1274.3 $[M]^+$ (I_{rel}=11 a.u.), calculated for $C_{64}H_{74}N_8O_{20}$ 1274.5; found 1362.4 $[M+PentOH]^+$ ($I_{rel.}$=34 a.u.), calculated for $C_{69}H_{86}N_8O_{21}$ 1362.6; found 1450.5 $[M+2PentOH]^+$ ($I_{rel.}$=67 a.u.), calculated for $C_{74}H_{98}N_8O_{22}$ 1450.7; found 1538.5 $[M+3PentOH]^+$ ($I_{rel.}$=100 a.u.), calculated for $C_{79}H_{110}N_8O_{23}$ 1538.8; found 1627.6 $[M+4PentOH]^+$ ($I_{rel.}$=73 a.u.), calculated for $C_{84}H_{122}N_8O_{24}$ 1626.9.

Reaction of ***(15C5)Nn*** *with PentOLi.* **(15C5)Nn** (110 mg, 0.3 mmol) was suspended in 2 mL of 0.8 M solution of PentOLi in PentOH. The mixture was degassed, refluxed under argon for 3 h and quenched with 100 μL AcOH. After cooling the product was precipitated with the mixture of 20 mL of EtOAc and 30 mL of hexane, the solid was filtered, washed with EtOAc and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→8 % MeOH. Yield of mixture of phthalocyanines 61 mg (yield *ca*. 55 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for tetra-15-crown-5-naphthalocyanine): found 1474.4 $[M]^+$ (I_{rel}=60 a.u.), calculated for $C_{80}H_{82}N_8O_{20}$ 1474.6; found 1582.5 $[M+PentOH]^+$ (I_{rel}=100 a.u.), calculated for $C_{85}H_{94}N_8O_{21}$ 1562.7; found 1650.5 $[M+2PentOH]^+$ (I_{rel}=74 a.u.), calculated for $C_{90}H_{106}N_8O_{22}$ 1650.7; found 1738.6 $[M+3PentOH]^+$ (I_{rel}=36 a.u.), calculated for $C_{95}H_{118}N_8O_{23}$ 1738.8; found 1826.7 $[M+4PentOH]^+$ (I_{rel}=4 a.u.), calculated for $C_{100}H_{130}N_8O_{24}$ 1826.9.

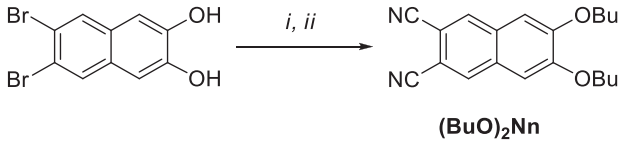
Reaction of ***(BuO)$_2$Pn*** *with PentOLi.* **(BuO)$_2$Pn** (82 mg, 0.3 mmol) was suspended in 2 mL of 0.8 M solution of PentOLi in PentOH. The mixture was degassed, refluxed under argon for 3 h and quenched with 100 μL AcOH. After cooling the product was precipitated with 50 mL of 50 % aqueous EtOH, the solid was filtered, washed with EtOH and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 40→20 % hexane. Yield of mixture of phthalocyanines 56 mg (yield *ca*. 68 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for octabutoxyphthalocyanine): found 1090.5 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{64}H_{82}N_8O_8$ 1090.6; found 1104.5 $[M\text{-}BuO+PentO]^+$ ($I_{rel.}$=7 a.u.), calculated for $C_{65}H_{84}N_8O_8$ 1104.6.

Reaction of ***(BuO)$_2$Nn*** *with PentOLi.* **(BuO)$_2$Nn** (97 mg, 0.3 mmol) was suspended in 2 mL of 0.8 M solution of PentOLi in PentOH. The mixture was degassed, refluxed under argon for 3 h and quenched with 100 μL AcOH. After cooling the product was precipitated with 50 mL of 50 % aqueous EtOH, the solid was filtered, washed with EtOH and purified by column chromatography on neutral alumina, elution with the $CHCl_3$ + 0→2 % MeOH. Yield 77 mg (79 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for octabutoxynaphthalocyanine): found 1290.7 $[M]^+$ (I_{rel}=100 a.u.), calculated for $C_{80}H_{90}N_8O_8$ 1290.7.

*Reaction of **(15C5)Pn** with Mg in PentOH.* **(15C5)Pn** (636 mg, 2 mmol) and magnesium turnings (96 mg, 4 mmol) were suspended in 15 ml of dry PentOH, the mixture was degassed and refluxed under argon for 15 h at 150 °C (oil bath). Then the temperature was lowered to 130 °C and 30 mL of glacial AcOH was added. The mixture was refluxed for 20 min until the *Q*-band of magnesium tetra-15-crown-5-phthalocyaninate at 678 nm disappeared in the UV-Vis spectrum of the reaction mixture and the characteristic *Q*-bands of tetra-15-crown-5-phthalocyanine appeared at 701 and 662 nm. Then the reaction mixture was cooled to RT and poured into 200 mL of the mixture of EtOAc and hexane (1:1 vol.). The formed precipitate was filtered; the brown-orange filtrate was discarded. The solid was washed with EtOAc until the washings were colorless, dissolved in chloroform and chromatographed on neutral alumina using $CHCl_3$ + 0→4 vol.% MeOH. Evaporation of fractions afforded 418 mg of tetra-15-crown-5-phthalocyanine as a dark-green solid (yield – 66 %). MALDI-TOF MS of reaction mixture, *m/z* (M stands for tetra-15-crown-5-phthalocyanine): found 1274.6 $[M]^+$ ($I_{rel.}$=100 a.u.), calculated for $C_{64}H_{74}N_8O_{20}$ 1274.5.

Results and Discussion

Starting phthalonitriles **(15C5)Pn**[33] and **(Bu)$_2$Pn**[34] as well as naphthalonitrile **(15C5)Nn**[18] were synthesized using previously reported procedures. BuO-substituted naphthalonitrile **(BuO)$_2$Nn** was firstly synthesized using alkylation of 2,3-dibromo-6,7-dihydroxynaphthalene with



Scheme 1. Synthesis of (BuO)$_2$Pn. *i:* *n*-BuBr, K_2CO_3, DMF, 90 °C, Ar, yield – 75 %. *ii:* $Zn(CN)_2$, $Pd_2(dba)_3$, dppf, DMAA, 120 °C, Ar, yield – 95 %.

n-BuBr and subsequent Pd-catalyzed cyanation (Scheme 1) similarly to the previously reported procedures.[35–37]

Cyclotetramerization of dinitriles was followed by MALDI-TOF mass-spectrometry to identify the products of S_N2_{Ar}-reaction. In the case of crown-opening reactions together with the target molecular ions [M], the additional peaks in mass-spectra with [M+*n*·88] *m/z* appeared, corresponding to formal insertion of pentanol molecules into the rings (Figure 1a). In the case of butoxy-substituted dinitriles substitution of BuO with PentO-group resulted in appearance of signals with [M+14] *m/z* (Figure 1b).

At the first step, we have studied template-free cyclotetramerization of starting dinitriles in refluxing PentOH in the presence of DBU (Figure 2). MALDI-TOF MS analysis of the reactions of **(15C5)Pn** with DBU evidenced of the formation of symmetrical A_4-type tetra-15-crown-5-phthalocyanine as a major product (M=1274.4 *m/z*) and minor amount of the product with M+88 *m/z*, corresponding to the A_3B-type product with one cleaved crown ether ring. Similarly, in the case of **(BuO)$_2$Pn** major signal corresponded to octabutoxyphthalocyanine (M=1090.7 *m/z*) and minor signal with M+14 *m/z* was also observed corresponding to substitution of one BuO- with PentO-group. The side products occurring because of nucleophilic substitution could not be separated by column chromatography on alumina. The isolated yields of phthalocyanines were low, their values were 26 and 10 % based on **(15C5)Pn** and **(BuO)$_2$Pn,** respectively.

To the contrast in the case of naphthalonitriles neither the products of 15C5-cleavage, nor substitution of BuO-groups were observed. Therefore, in principle, template-free condensation of crown- and alkoxy-substituted naphthalocyanines can be performed by cyclotetramerization of corresponding naphthalonitriles in the presence of DBU, however this process is not efficient since it affords target macrocycles in mediocre yields – 31 and 15 %, respectively.

At the next step we have studied cyclotetramerization of dinitriles in refluxing *n*-pentanol in the presence

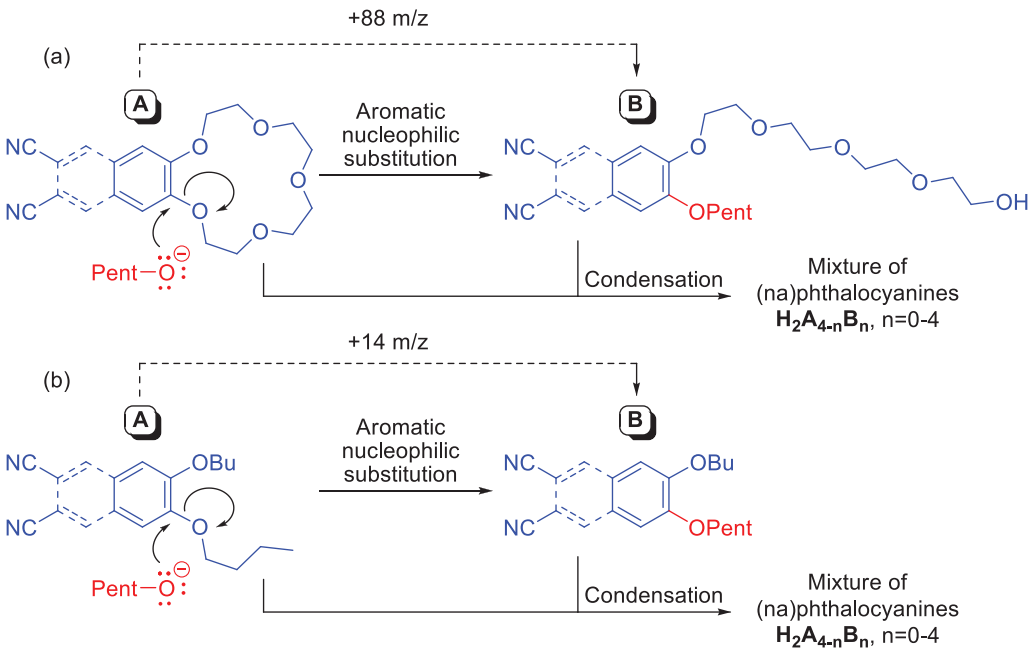


Figure 1. Products of S_N2_{Ar} reactions of crown-substituted dinitriles (a) and butoxy-substituted dinitriles (b) with pentoxide-anion.

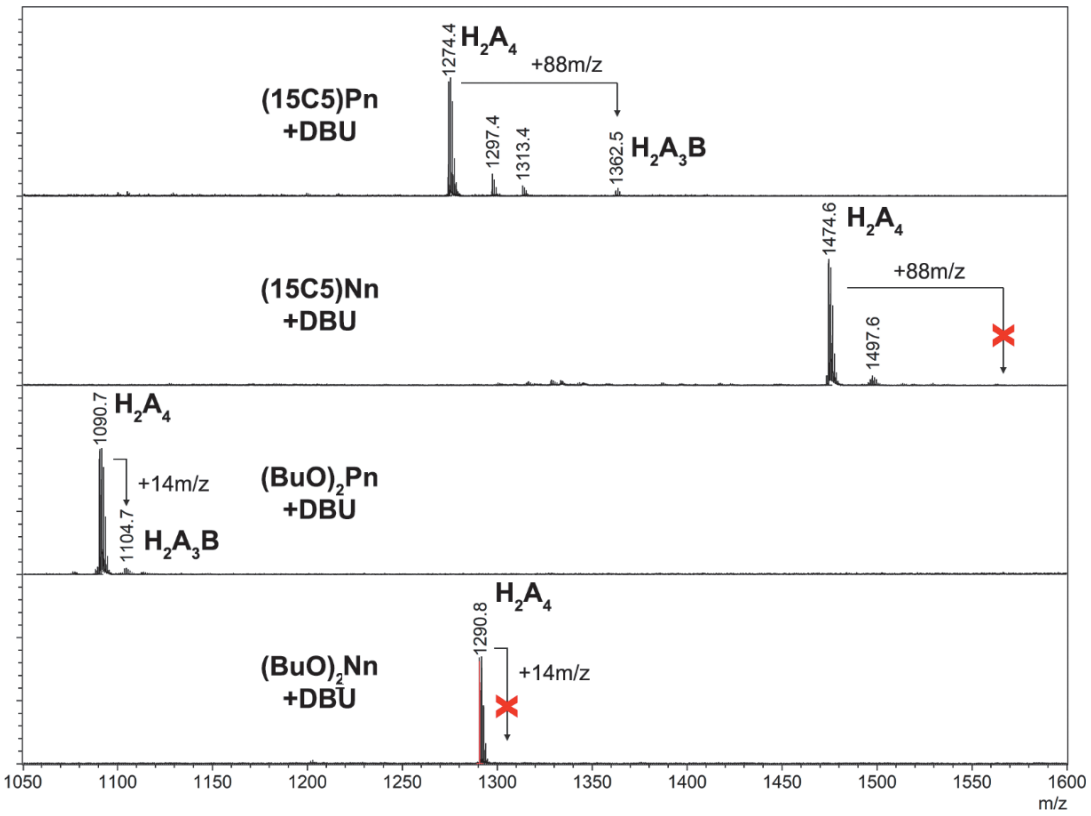


Figure 2. MALDI-TOF mass-spectra of reaction mixtures, formed upon cyclotetramerization of dinitriles in the presence of DBU in refluxing *n*-pentanol. "A" stands for intact isoindoline unit as a part of (na)phthalocyanine, "B" stands for the unit formed because of nucleophilic substitution.

of lithium pentoxide. The resulting lithium complexes were demetalated by addition of AcOH and the composition of reaction mixtures was also analyzed by MALDI TOF mass-spectrometry.

In MALDI-TOF mass-spectrum of the product formed by reaction of both **(15C5)Pn** and **(15C5)Nn** with PentOLi we observed the set of five molecular ions separated by +88 *m/z* units (Figure 3). The mass-spectra of resulting products corresponded to the mixture of different (na)phthalocyanines $H_2A_{4-n}B_n$, n=0–4, where A – units with intact crown ethers and B – units with cleaved rings.

Notably, in the case of the reaction of **(15C5)Pn** with PentOLi the H_2B_4 product is dominant in the mass-spectrum, and only trace amount of H_2A_4 is observed, while in the case

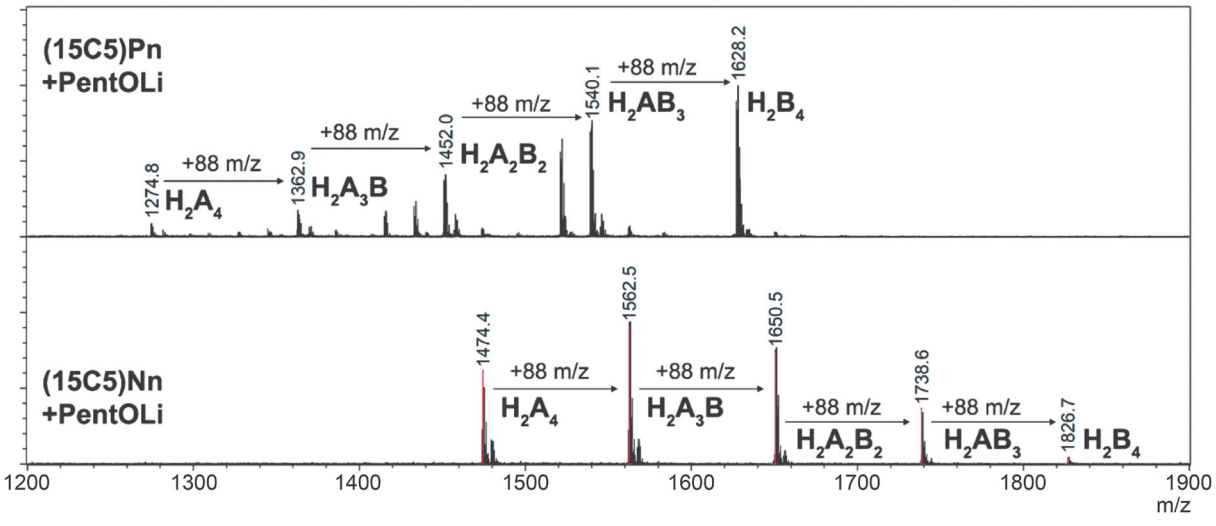


Figure 3. MALDI-TOF mass-spectra of reaction mixtures, formed upon cyclotetramerization of crown-substituted dinitriles in the presence of PentOLi in refluxing *n*-pentanol. "A" stands for intact isoindoline unit as a part of (na)phthalocyanine, "B" stands for the unit formed because of crown ether ring cleavage.

of **(15C5)Nn** all possible products are present in comparable amounts (Figure 3), suggesting that this dinitrile is less reactive in ring-opening reaction. Moreover, in the former case there were observed numerous peaks with *m/z* exceeding the value for tetra-15-crown-5-phthalocyanine. These peaks could not be attributed to any product, suggesting that other unaccounted side processes might occur in this reaction apart from the described ring-opening process.

To determine at which step the crown ether cleavage occurs, we performed the control reaction of tetra-15-crown-5-phthalocyanine with PentOLi in refluxing *n*-pentanol. MALDI-TOF mass spectrum of the isolated phthalocyanine coincided with the starting material, therefore, we confirmed that PentO-anion cleaves crown ether ring in **(15C5)Pn** prior to phthalocyanine formation. Therefore, although PentOLi is inapplicable for the synthesis of crown-phthalocyanines starting from dinitriles, it can be used as a base for generation of lithium crown-phthalocyaninate starting from previously synthesized free base phthalocyanine. In turn, resulting lithium phthalocyaninates can be used for further transmetalation reactions.

MALDI-TOF MS studies of reaction mixtures formed upon interaction of butoxy-substituted dinitriles **$(BuO)_2$Pn** and **$(BuO)_2$Nn** with PentOLi evidenced of much lower susceptibility of these substrates to nucleophilic reactions (Figure 4). In the case of **$(BuO)_2$Pn** only minor amount of H_2A_3B product was observed similarly to the reaction of this phthalonitrile with DBU. Finally, **$(BuO)_2$Nn** formed only the symmetrical octabutoxynaphthalocyanine in excellent yield (79 %)without any traces of the product formed because of substitution of BuO- with PentO-group, suggesting that PentOLi is applicable for the synthesis of alkoxy-substituted naphthalocyanines.

Magnesium alcoholates are well known alternative to AlkOLi reagents. It was previously shown that $Mg(OPent)_2$, which acts both as a base and template, can be successfully used for the synthesis of magnesium tetra-15-crown-5-naphthalocyaninate from **(15C5)Nn** without formation of crown ether cleavage products.[18] We tested this protocol in the present study to synthesize crown-phthalocyanine from **(15C5)Pn** in the presence of magnesium pentoxide. Subsequent demetalation of resulting magnesium tetra-15-crown-5-phthalocyaninate with AcOH yielded target 15-crown-5-phthalocyanine in 66 % yield without any traces of crown ether ring opening side products.

Conclusions

In the present work we demonstrated that the classical methodology of template synthesis in the presence of lithium pentoxide known since 1930's is inapplicable for the synthesis of crown-substituted (na)phthalocyanines because of the nucleophilic ring-opening reaction which proceeds prior to the formation of the tetrapyrrolic macroheterocycles resulting in formation of the inseparable mixture of compounds. To the contrast, crown ether groups in (na)phthalocyanines are stable towards nucleophilic attack of PentO-anion, therefore PentOLi can be safely used for generation of dilitium complexes from free-base (na)phthalocyanines. Application of DBU as a promoter of cyclotetramerization of dinitriles in template-free conditions allows to decrease the amount of side ring-opening products, however it also leads to decrease of (na)phthalocyanines yields.

Under the same conditions acyclic alkoxy-substituted (na)phthalonitriles show much lower tendency to side process of nucleophilic substitution. However, it appears that it is safer to use parent AlkOH/AlkOLi as a pair of solvent and reagent for the synthesis of AlkO-substituted (na) phthalocyanines to avoid formation of mixtures of products with different substitution patterns or to use $Mg(OAlk)_2$ as a convenient templating agent which does not reveal nucleophilicity under the conditions of (na)phthalonitrile macrocyclization.

Acknowledgements. The authors are grateful to Foundation of Russian President for support of young scientists and leading scientific schools (grant MK-141.2017.3) for the studies

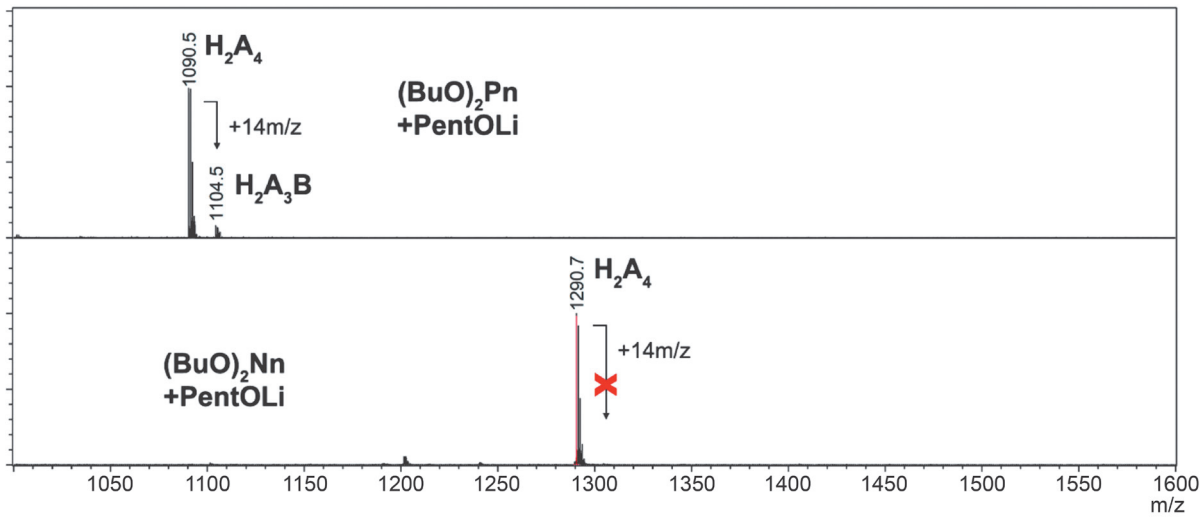


Figure 4. MALDI-TOF mass-spectra of reaction mixtures, formed upon cyclotetramerization of butoxy-substituted dinitriles in the presence of PentOLi in refluxing *n*-pentanol. "A" stands for intact isoindoline unit as a part of (na)phthalocyanine, "B" stands for the unit formed because of nucleophilic substitution of BuO- with PentO-groups.

of reactivity of phthalonitriles and Russian Foundation for Basic Research (grant 18-33-00887-mol_a) for the studies of reactivity of naphthalonitriles.

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Received 10.12.2018
Accepted 12.01.2019