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Porphyrin-based molecular receptors for alkali metal cations: synthesis and chemical modification

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Abstract

A synthetic approach leading to the *meso*-arylporphyrins containing a conformationally mobile polyether fragment on the benzene ring with a terminal pyridine ring has been developed, which opens the possibility for design of new porphyrin-based molecular receptors for detection and selective binding of alkali metal cations.

Porphyrins occupy a unique place among numerous macroheterocyclic compounds, which are able to form self-organized supramolecular ensembles via multisite binding.[1–3] Their properties originate from the unusual geometric and electronic structure of the tetrapyrrole chromophore, which can act as a source of signal reflecting processes occurring in the system under study.[4–6] In recent years, interest in porphyrin derivatives has increased considerably due to their ability to participate in molecular recognition, that is, in a selective binding process in which a receptor interacts effectively only with molecules of a definite type through intermolecular forces.[7–9] In this connection, important results can be obtained by modification of the porphyrin macrocycle with polyether fragments possessing intrinsic binding ability toward different substrates. Combinations of porphyrin and polyether fragments linked together through covalent bonds could give rise to spatially preorganized three-dimensional structures, showing an effective cation-assisted chirality induction.[10,11]

In our investigation, a synthetic approach leading to *meso*-arylporphyrins containing a conformationally mobile complexing polyether fragment on the benzene ring with a terminal pyridine ring has been developed. The results of the studies on the dependence of the spectral parameters of the tetrapyrrole chromophore upon acid–base equilibria and complex formation with alkali metal cations indicate that the porphyrin derivatives can be used to construct molecular devices possessing practically important properties.

The reaction of 2-ethoxycarbonyl-3-butyl-4-methylpyrrole (**1**) with 3-methoxybenzaldehyde (**2**) in ethanol in the presence of HCl gave *meso*-(3-methoxyphenyl)-dipyrrolylmethane (**3**), which was easily converted into *meso*-(3-hydroxyphenyl)-dipyrrolylmethane (**4**) by treatment with BBr_3. The reaction of **4** with polyethylene glycol bis-(4-toluenesulfonates) **5**, **6**, and 3-hydroxypyridine (**7**) in the presence of cesium carbonate in DMF–MeCN resulted in the dipyrrolylmethanes (**8**, **9**) having conformationally mobile polyether fragments with a terminal pyridine group at the *meso*-position. Alkaline hydrolysis and high temperature decarboxylation of the 5,5′-bis(ethoxycarbonyl)-dipyrrolylmethanes **8**, **9** gave the intermediate 5,5′-di-unsubstituted dipyrrolylmethanes, acid-catalyzed condensation of which with 5,5′-diformyl-4,4′-dibutyl-3,3′-dimethyldipyrrolylmethane (**10**) with subsequent oxidation of the reaction mixture using tetrachloro-1,4-quinone resulted in the porphyrin ligands **11**, **12**. The reaction of **11**, **12** with zinc(II) acetate in boiling DMF gave porphyrin metal complexes **13**, **14**. The assumed structures of the dipyrrole and tetrapyrrole compounds **3**, **4**, **8**, **9**, **11**–**14** were consistent

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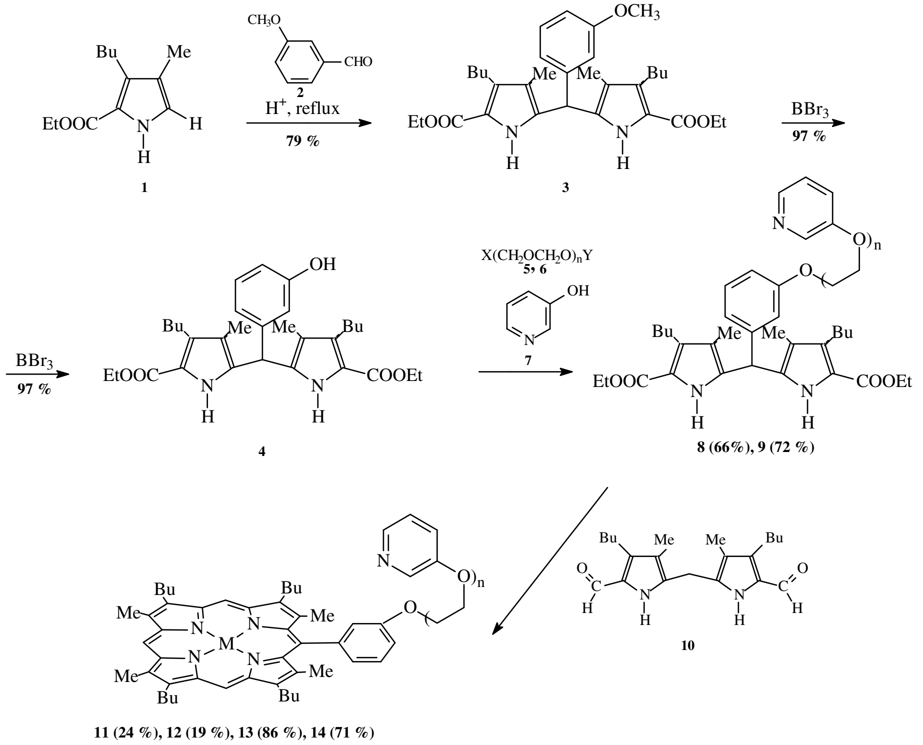
with elemental analysis, electronic absorption, ^1H NMR and mass spectra data.



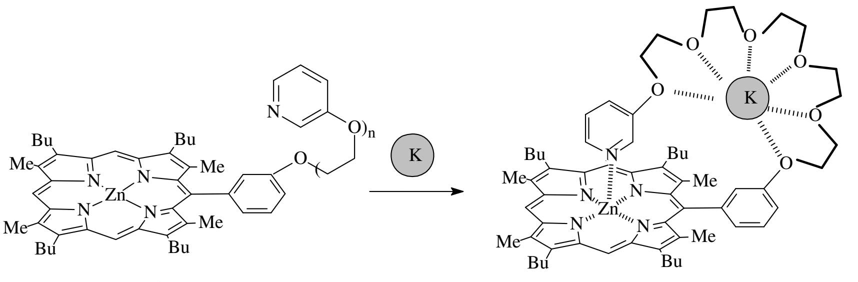
-M = H_2(11, 12), Zn (13,14); n = 4 (8, 11, 13), 5 (9, 12, 14)

The binding ability of porphyrins **13** and **14** toward alkali metal cations (Li^+, Na^+, and K^+) was studied in a 2:1 toluene–methanol mixture. Among the examined compounds, only **14** was able to bind potassium cations with the formation of complex **15** due to the geometric parameters of the polyether cavity. Conformational flexibility of the polyether bridge enables the terminal pyridine ring to approach the tetrapyrrole macrocycle, which is readily detected by the electronic absorption and ^1H NMR spectra. The donor–acceptor interaction between the pyridine nitrogen atom and the zinc cation leads to a red shift of the absorption band (up to 10 nm) in the UV–vis spectra, and shielding of the pyridine fragment by the porphyrin ring current induces upfield shifts of the signals of the protons of the pyridine ring, which reside in the vicinity of the macrocycle.

A study on the complex formation between compound **14** and K^+ by spectrophotometric titration showed that complex **15** has a composition of 1:1. The titration curve is characterized by one step (Fig. 1), which corresponds to an isosbestic point in the electronic absorption spectra (Fig. 2). Upfield shifts of signals of the protons in the pyridine fragment (as compared to pyridine) were observed in the ^1H NMR spectrum of complex **15** ($\Delta\delta = 4.5$ and 1.1 ppm for α-H and β-H, respectively) in the concentration range corresponding to the inflection on the spectrophotometric titration curve.

The stability constant of complex **15** ($K_s = 0.361 \times 10^6\ M^{-1}$) was calculated according to a standard procedure[9] on the basis of spectrophotometric data obtained at two wavelengths (descending and ascending) using formula 1:

$$K_s = \frac{[ZnP\cdot K^+]}{[ZnP][K^+]} = \frac{1}{[K^+]}\left(\frac{\Delta A_{i,\lambda_1}}{\Delta A_{0,\lambda_1}}\,\frac{\Delta A_{0,\lambda_2}}{\Delta A_{i,\lambda_2}}\right). \qquad (1)$$



14, n = 5

15

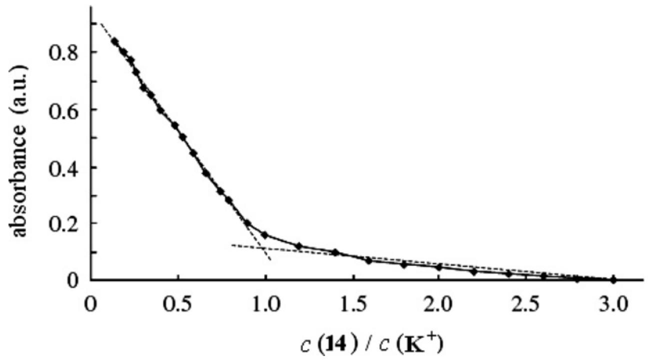


Fig. 1. Spectrophotometric titration curve of **14** with K^+ in toluene–MeOH (2:1) at the ascending wavelength ($\lambda = 415$ nm, c (**14**) $= 5.5 \times 10^{-6}$ M) at 298 K.

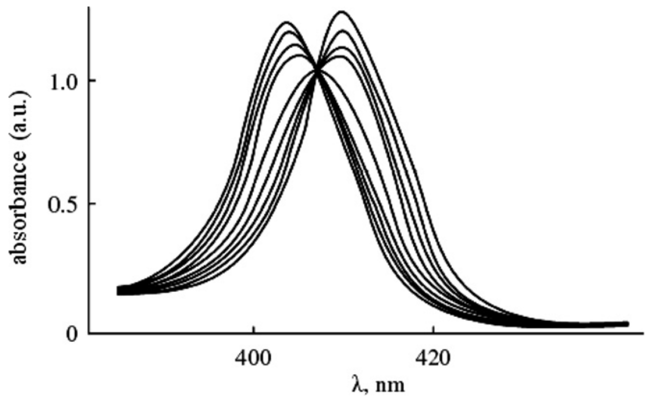


Fig. 2. Changes in the electronic absorption spectra of **14** (Soret band region) upon addition of K^+ from 0 to 10^{-3} M in toluene–MeOH (2:1) at 298 K (c (**14**) $= 5.5 \times 10^{-6}$ M).

Here λ_1 is the descending wavelength, λ_2 is the ascending wavelength, $[K^+]$ is the concentration of K^+ ions, [ZnP] is the concentration of zinc–porphyrin, ΔA_0 is the maximal variation of the absorption at a given wavelength, and ΔA_i is the absorption at a given wavelength and concentration.[9] The error in the determination of K_s was 7–10%. No binding with Li^+ or Na^+ ions was observed.

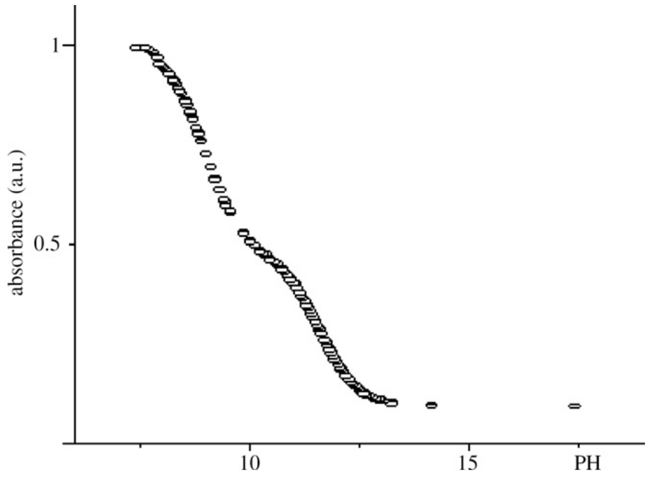


Fig. 3. Spectrophotometric titration curve of **12** with H^+ in the system **12**-$HClO_4$–MeCN at 298 K.

With a view to design sterically preorganized complexing cavities for selective binding of alkali metal cations, we also examined the effect of acid–base equilibria on the spectral parameters of the tetrapyrrole chromophore. Spectrophotometric–potentiometric titration of porphyrin **12** in the system **12**-$HClO_4$–MeCN showed that the process can be represented by equilibria 2 and 3.

$$H_2P + H^+ \overset{K_{b1}}{\rightleftarrows} H_3P^+, \tag{2}$$

$$H_3P + H^+ \overset{K_{b2}}{\rightleftarrows} H_4P^{2+}. \tag{3}$$

The spectrophotometric titration curve of **12** with H^+ is characterized by two steps (Fig. 3), each corresponding to a family of isosbestic points (Fig. 4). At the limiting values

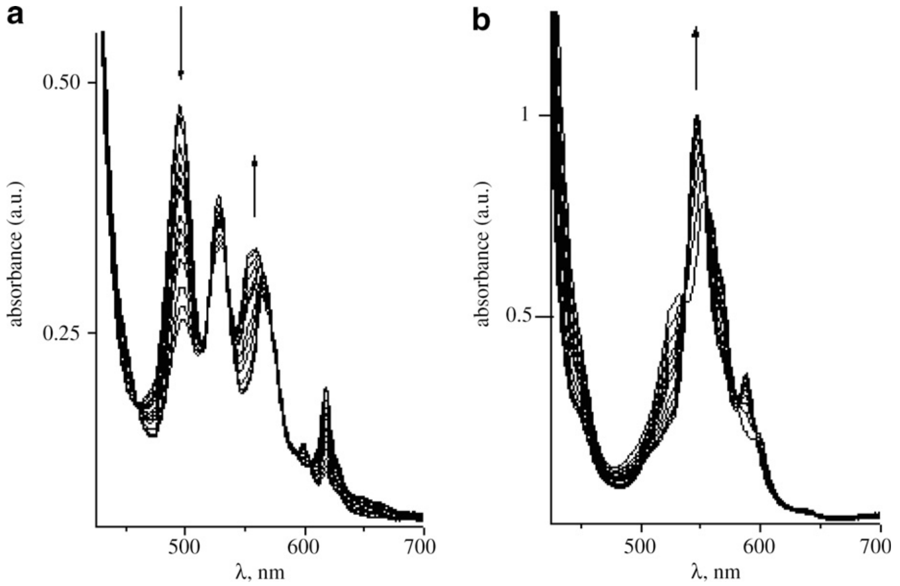


Fig. 4. Changes in the UV–vis spectra of the **12**-$HClO_4$–MeCN system in the region of $HClO_4$ concentration 10^{-14}–10^{-10} M (a) and 10^{-10}–10^{-7} M (b) at 298 K (c (**12**) $= 1.51 \times 10^{-5}$ M).

of the examined acidity range, we observed absorption spectra of individual neutral porphyrin **12** [H_2P, λ_{max}, nm ($\log\varepsilon$): 496 (4.17), 528 (4.01), 565 (3.87), 618 (3.74)] and its mono- [H_3P^+, λ_{max}, nm ($\log\varepsilon$): 499 (3.91), 530 (3.95), 559 (3.95), 599 (3.57), 618 (3.45)] and di- [H_4P^{2+}, λ_{max}, nm ($\log\varepsilon$): 547 (4.45), 588 (3.94)] cations. The equilibrium constants calculated according to a standard procedure[12] were $\log K_{b1} = 11.58 \pm 0.01$ (Eq. 2) and $\log K_{b2} = 8.77 \pm 0.01$ (Eq. 3).

The constants K_{b1} and K_{b2} were calculated, and their accuracy was estimated from two parallel measurements using the SigmaPlot program by fitting the parameters in Eq. 4, which relates absorption to the pH of solutions of dibasic acids:[13]

$$A_c = \frac{A_{H_2P} + 10^{pH} K_{b1} A_{H_3P^+} + 10^{2pH} K_{b1} K_{b2} A_{H_4P^{2+}}}{1 + 10^{pH} K_{b1} + 10^{2pH} K_{b1} K_{b2}}. \qquad (4)$$

Here, A_c is the current absorption of H_2P solution at an analytical wavelength, and A_{H_2P}, $A_{H_4P^{2+}}$, and $A_{H_3P^+}$ are the absorptions of solutions of individual H_2P, H_4P^{2+}, and H_3P^+ species with an analytical concentration (c_0). The titration curve shown in Figure 3 has a stepwise shape since the difference between the first and second protonation constants is about three orders of value.[13]

Due to the binding of K^+ by the $–(OCH_2CH_2)_n–$ complexing site of **12**, the conformation of the polyether chain changes in such a way that the pyridine and tetrapyrrole fragments in the resulting complex **16** become spatially close and the pyridine nitrogen atom interacts with the hydrogen atoms in the coordination site of the protonated tetrapyrrole macrocycle. It should be noted that only H_4P^{2+} generates **16**. Such self-organization seems to be fairly promising from the viewpoint of the design of supramolecular receptors for alkali metal cations. It provides a means for optimization of the geometric parameters of a receptor cavity to match the substrate parameters.

Our results indicate that porphyrins containing polyether moieties can be used for the design of new molecular receptors for alkali metal cations. Such receptors are more advantageous than the traditionally used crown ethers due to the presence of a tetrapyrrole chromophore which makes it possible to apply spectrophotometric methods intrinsic to the chemistry of porphyrins while studying complex formation processes. As a result, the application of tetrapyrrole compounds as selective receptors for extraction and membrane transfer processes and supersensitive switches for data storage could be considerably extended. The selectivity and high sensitivity of porphyrins to low-energy effects provide the possibility for controlling chemical processes involving these compounds.

Zinc(II) 2,8,12,18-tetrabutyl-3,7,13,17-tetramethyl-5-{3-[11-(pyridin-3-yloxy)-3,6,9-trioxaundecyloxy]phenyl}-porphyrin: **13**. To a solution of porphyrin (**13**): (30 mg) in 70 ml of DMF, excess zinc(II) acetate (molar ratio 1:10) was added. The solution was heated for 30 min at the boiling point, cooled, and diluted with an equal volume of water. The residue was filtered, dried, and subjected to chromatography over aluminum oxide using methylene chloride–hexane (1:1) as eluent. A red-brown band was collected and the solvent was evaporated. Recrystallization of the residue from CH_2Cl_2–MeOH (1:1) yielded **15** as purple needles (30.10 mg, 86%), mp 136 °C. Analytical data: R_f 0.63 (Al_2O_3, CH_2Cl_2–C_6H_{14}, 1:2). UV–vis (toluene): λ_{max} in nm, ($\log\varepsilon$): 409.1 (5.03), 539.1 (4.22), 574.1 (3.79). ^1H NMR (300 MHz, $CDCl_3$): 10.03 (s, 2H, *meso*-H), 9.92 (s, 1H, *meso*-H), 7.91 (d, $J = 7.8$ Hz, 1H, 6-H), 7.81 (s, 1H, 2-H), 7.75 (d, $J = 7.8$ Hz, 1H, 4′-H), 7.65 (t, $J = 8.5$ Hz, 1H, 5′-H), 7.53 (t, $J = 8.5$ Hz, 1H, 5-H), 7.49 (m, 2H, 2′-H, 6′-H), 7.29 (m, 1H, 4-H), 3.79 (t, $J = 7.2$ Hz, 8H, $CH_2CH_2CH_2CH_3$), 3.24 (m, 16H, OCH_2CH_2O), 2.39 (m, 8H, $CH_2\mathit{CH_2}CH_2CH_3$), 1.47 (m, 8H, $CH_2CH_2\mathit{CH_2}CH_3$), 1.20 (s, 6H, CH_3), 1.17 (s, 6H, CH_3), 1.05 (t, $J = 7.2$ Hz, 12H, $CH_2CH_2CH_2\mathit{CH_3}$). FAB$^+$ MS: [m/z (rel. intens. %)]: 999.39 (M+1, calcd: 998.41, 71%). Calcd for $C_{59}H_{75}N_5O_5Zn$: C, 70.94; H, 7.51; N, 7.01. Found: C, 70.90; H, 7.49; N, 6.97.

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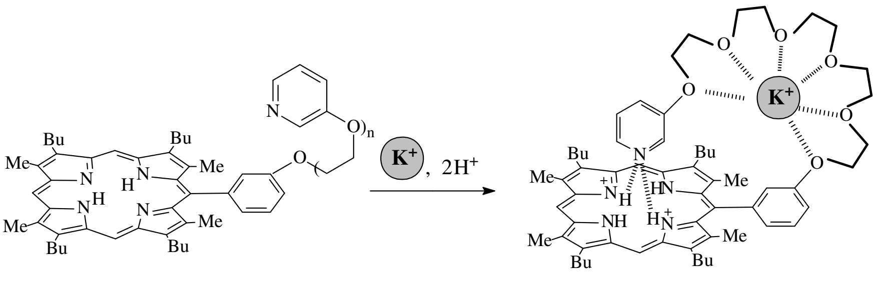
Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.029.



12, n = 5 **16**

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