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Tetraphenylporphyrins Monosubstituted with a Crown Ether in one Phenyl Ring. Synthesis and Characterization

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Summary. The synthesis and spectroscopic characterization of seven new tetraphenyl-porphyrins (**1–7**) derivatized with 12-crown-4, 14-crown-4, 15-crown-5, or 18-crown-6 ether units in *ortho* or *para* position of one of the phenyl rings is described.

Keywords. Porphyrin; Crown ethers; Tetraphenylporphyrins; Tetraphenylporphyrin crown ethers.

In einem Phenylring mit Kronenethern monosubstituierte Tetraphenylporphyrine. Synthese und Charakterisierung

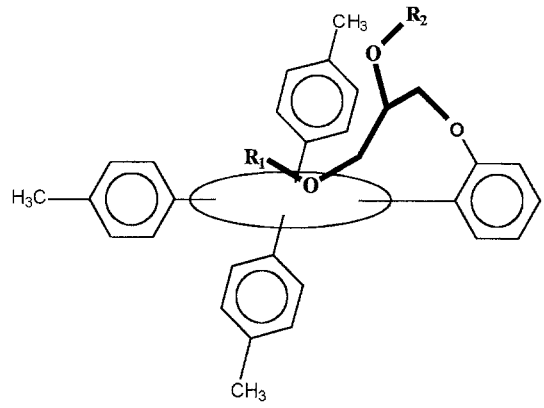
Zusammenfassung. Die Synthese und die spektroskopische Charakterisierung sieben neuer Tetraphenylporphyrine (**1–7**), die mit 12-Krone-4, 14-Krone-4, 15-Krone-5 oder 18-Krone-6 in der *ortho*- oder *para*-Position eines Phenylrings substituiert sind, werden beschrieben.

Introduction

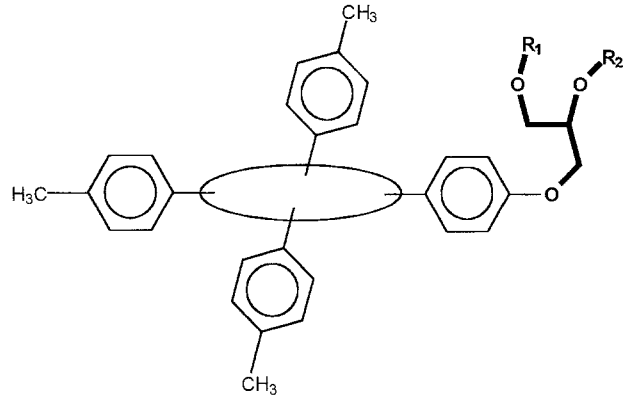
The synthesis of porphyrins derivatized with crown ethers has been studied during the last two decades [1–16]. The main approach was to build porphyrin ligands with a crown ether linked to the porphyrin core itself, thus permitting self-coordination of the inserted metal and/or allowing to bind two different metal ions by means of substrate-specific units.

In continuation of our research on tetraphenylporphyrin glycerol derivatives [17, 18] we now report the synthesis of products formed by etherification of hydroxyphenylporphyrin derivatives and tosyloxymethyl crown ethers (Scheme 1). The presence of crown ethers attached to the *ortho* or *para* positions of one phenyl substituent of the porphyrin (**1**, **2**, **4**, **6** and **3**, **5**, **7**) would allow the investigation of possible interactions between crown ether moieties and the porphyrin core which might differ for *ortho* and *para* derivatives. The adjacent crown ether units of *ortho* derivatives are situated in a manner that the porphyrin core and the crown ether can interact cooperatively with a guest ion.

It is also worth mentioning that attaching the crown ether unit to the *para* position creates a possibility of dealing with porphyrins capable of extended complexation of cations by crown ethers located outside of the porphyrin core.



1, 2, 4, 6



3, 5, 7

R_1 , R_2 = $-(CH_2CH_2O)_n - CH_2CH_2 -$ n= 2 - 4

or $- CH_2CH_2CH_2OCH_2CH_2OCH_2CH_2CH_2 -$

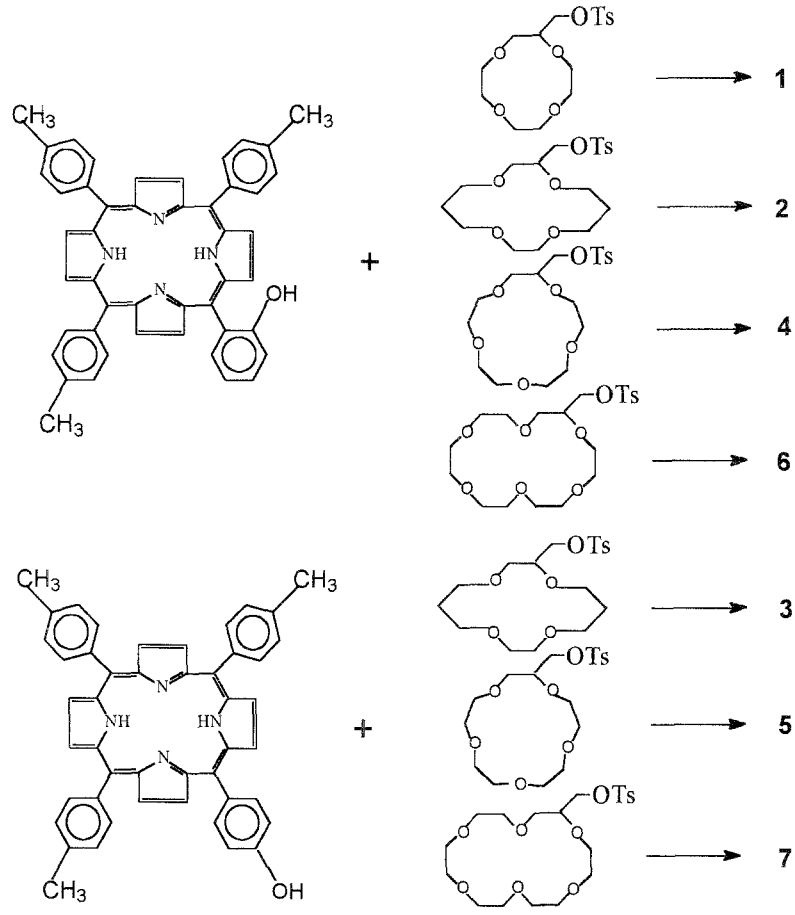
Scheme 1

Results and Discussion

The synthesis of porphyrin crown ethers **1–7** is outlined in Scheme 2.

The porphyrins were synthesized on the basis of the corresponding *meso*-phenyl substituted porphyrins 5-(2-hydroxyphenyl)-10,15,20-tritolylporhyrin and 5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin prepared according to Ref. [25]. Hydroxymethyl crown ethers were obtained as reported in Refs. [19–21]. The tosyloxymethyl derivatives of the crown ethers were synthesized according to the procedure described by *Ouchi et al.* [22] in 60–80% yield. Condensation of the hydroxyphenyl derivatives of porphyrins and tosylated crown ethers proceeded for 30 h in *DMF* in the presence of sodium hydride at 70°C. The raw products were purified 3–4 times by column chromatography on silica gel or/and alumina with different solvent mixtures in yields of 40–60%. Compounds **1–7** were characterized by ^{1}H NMR, MS, and UV/Vis spectra.

The UV/Vis spectra of compounds **1–7** are given in the Experimental. They are typical for *meso*-substituted porphyrins. The *Soret* bands at 421 nm and the other

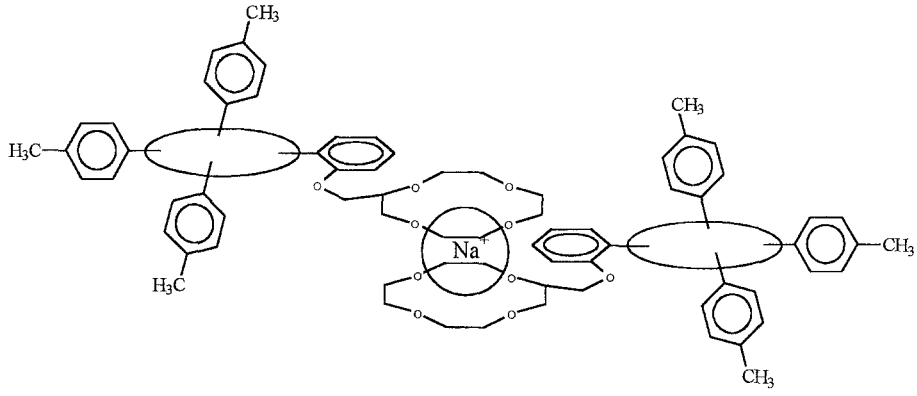


Scheme 2

maxima in the visible region are consistent with a tetraphenylporphyrin spectrum with the positions of bands differing for the individual compounds by no more than 2 nm. The electronic spectra of diprotonated porphyrins **1–7** (with *TFA*) show that both the *Soret* bands and the *Q*-bands are red-shifted. The *Soret* bands of diprotonated porphyrins were observed at 445 nm, thus being red-shifted by *ca.* 20–25 nm compared to neutral compounds. The *Q*-bands of diprotonated *ortho*-derivatives were red-shifted by 10–15 nm, and those of the *para*-derivatives were red-shifted by *ca.* 20 nm compared to the neutral compounds.

In the mass spectra (LSIMS technique), the prominent ions did not correspond to the protonated molecular ion peaks. Under the experimental conditions, crown ether porphyrins do not ionize readily to the protonated molecular ion peaks. The addition of sodium acetate to the matrix solutions resulted in an appearance of $[M + Na]^+$ peaks. This effect suggest that stable complexes (crown ether-Na^+) are formed in the matrix solution. Remarkably, the LSIMS spectrum of **1** gave a peak corresponding to the $[2M + Na]^+$ ion at a relatively high abundance (Scheme 3). In fact, the $[2M + Na]^+$ ion was observed in the FAB mass spectrum of 12-crown-4 after the addition of an equimolar solution of NaCl to the matrix solution [23]. The

stability constants (log K) for the 1:1 and 2:1 complexes of 12-crown-4 and Na^+ are 1.41 and 2.20, respectively [24].



Scheme 3

Chemical shifts in the ^1H NMR spectra of **1–7** are given in the Experimental. The integrated intensity data are in accordance with the proposed structures. The pyrrole β-protons of compounds **3**, **5**, and **7** resonate as singlets at *ca.* 8.85 ppm and as multiplets for the remaining compounds at *ca.* 8.7–8.9 ppm. The central porphyrin protons appeared in the narrow region from −2.76 to −2.79 ppm. Resonances due to the spacer OCH_2-protons occur at *ca* 3.8 ppm and 4.3 ppm for the *ortho* and *para* substituted compounds, respectively. In the ^1H NMR spectra of *ortho* substituted derivatives (**1**, **2**, **4**, and **6**), the signals of the crown ether moiety appear at remarkably high field compared with *para* derivatives. The high-field shifts due to the ring current effect of the porphyrin core demonstrate the conformational features, the crown ether moieties being located above the porphyrin rings.

In summary, we have developed a synthetic route to novel crown ether derivatives of tetraphenylporphyrin in which the functional groups are linked to the porphyrin *via* a flexible spacer so that the adjacent crown ether units can interact cooperatively with a guest ion of the porphyrin core.

Experimental

The proton NMR spectra were recorded with IBM AF-200 and General Electric QE-300 spectrometers; chemical shifts are given in ppm ($CDCl_3$/*TMS*). Electronic spectra were recorded on a Specord UV Vis spectrophotometer (Carl Zeiss-Jena) in CH_2Cl_2 solutions. Mass spectrometry was performed on a LSIMS(+) model AMD 604 (AMD Intectra) spectrometer (NBA matrix). Column chromatography was performed on silica gel 100 (70–230 mesh, Merck). Thin layer chromatography (TLC) was performed using Merck Silica $40F_{254}$ plates precoated with 0.25 mm of silica gel. Unless specified otherwise, starting materials and solvents were reagent grade and used as

received. Methylene chloride was passed through a very short column of basic alumina to remove traces of hydrochloric acid. 5-(4-hydroxyphenyl)- and 5-(2-hydroxyphenyl)10,15,20-tritolylporphyrin were prepared according to Ref. [25]. (Tosyloxy)-methyl-12-crown-4 [26], (tosyloxy)-methyl-14-crown-4 [27], (tosyloxy)-methyl-15-crown-5 [28], and (tosyloxy)-methyl-18-crown-6 [26, 29] were prepared as noted previously. The same tosyl derivatives were prepared in 60–80% yield as described by *Ouchi et al.* [22].

5-(2-(1,4,7,10-Tetraoxa-cyclododec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**1**, $C_{56}H_{52}N_4O_5$)

A suspension containing 5-(2-hydroxyphenyl)-10,15,20-tritolylporphyrin (135 mg, 0.2 mmol), (tosyloxy)-methyl-12-crown-4 (100 mg, ~ 0.3 mmol), and sodium hydride (*ca.* 15 mg, *ca.* 0.63 mmol) in 50 ml of anhydrous *DMF* was stirred at 70°C for 30 h. Then the mixture was evaporated to dryness under reduced pressure. The residue was dissolved in a dichloromethane-water mixture. The organic layer was separated, washed twice with water, extracted with 5% hydrochloric acid and then with 5% ammonium hydroxide, and dried over anhydrous $MgSO_4$. The product was purified by chromatography (twice) on a silica gel column using a mixture of dichloromethane and ethyl acetate (1:1, v/v) as eluant (first fraction: unreacted substrate; second fraction: product). The second chromatography on neutral alumina with dichloromethane as eluant afforded 95 mg (55%) of porphyrin **1**. The porphyrin was homogeneous by TLC ($R_F = 0.46$, silica, ethyl acetate).

^{1}H NMR: 8.76–8.84 (m, 8H), 8.15 (m, 1H), 7.70–7.79 (m, 1H), 7.55, 8.07 (dd, 12H, $J = 7.8$ Hz), 7.36–7.45 (m, 1H), 7.24–7.28 (m, 1H), 3.81 (m, 2H), 2.69 (s, 9H), 1.9–2.8 (m, 15H), −2.76 (s, 2H); MS: $m/z = 861$ $(M+H)^+$, 883 $(M+Na)^+$, 1743 $(2M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 421 (103), 519 (3.3), 556 (1.7), 597 (0.9), 653 (1.0) nm.

5-(2-(1,4,8,11-Tetraoxa-cyclotetradec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**2**, $C_{58}H_{56}N_4O_5$)

2 was obtained in the same way as **1** with the substrates 5-(2-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-14-crown-4. The crude product was chromatographed three times on a silica gel column using a mixture of dichloromethane and methanol (10:1, v/v) as eluant. The porphyrin was homogeneous by TLC ($R_F = 0.89$, silica, ethyl acetate).

Yield: 58%; ^{1}H NMR: 8.7–8.93 (m, 8H), 7.53, 8.05 (dd, 12H, $J = 7.8$ Hz), 8.0–8.15 (m, 1H), 7.7–7.9 (m, 1H), 7.35–7.43 (m, 1H), 7.22 (d, 1H), 3.73 (m, 2H), 2.70 (s, 9H), 0.2–2.7 (m, 19H), −2.79 (s, 2H); MS: $m/z = 889$ $(M+H)^+$, 911 $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 422 (60), 520 (4.3), 556 (2.2), 597 (1.5), 654 (1.0) nm.

5-(4-(1,4,8,11-Tetraoxa-cyclotetradec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**3**, $C_{58}H_{56}N_4O_5$)

3 was obtained in the same way as **1** with the substrates 5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-14-crown-4. The crude product was chromatographed three times on an alumina column using dichloromethane as eluant. The porphyrin was homogeneous by TLC ($R_F = 0.82$, silica, ethyl acetate).

Yield: 48%; ^{1}H NMR: 8.85 (s, 8H), 7.54, 8.09 (dd, 12H, $J = 7.8$ Hz), 7.27, 8.08 (dd, 4H, $J = 8.6$ Hz), 3.5–4.4 (m, 17H), 2.70 (s, 9H), 1.86–1.90 (m, 4H), −2.78 (s, 2H); MS: $m/z = 889$ $(M+H)^+$, 911 $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 422 (81), 520 (3.1), 557 (1.7), 597 (0.9), 654 (1.0) nm.

5-(2-(1,4,7,10,13-Pentaoxa-cyclopentadec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**4**, $C_{58}H_{56}N_4O_6$)

4 was obtained in the same way as **1** with the substrates 5-(2-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-15-crown-5. The crude product was chromatographed twice on a silica gel column using dichloromethane and then a mixture of dichloromethane and methanol as eluant. The porphyrin was homogeneous by TLC ($R_F = 0.39$, silica, ethyl acetate-methanol, 1:1, v/v).

Yield: 42%; ^{1}H NMR: 8.73–8.84 (m, 8H), 8.28 (d, 1H, $J = 7.4$ Hz), 7.95–8.1 (m, 6H), 7.68 (t, 1H, $J = 7.8$ Hz), 7.51 (d, 6H), 7.42 (t, 1H, $J = 7.4$ Hz), 7.06 (d, 1H, $J = 7.8$ Hz), 3.7 (m, 2H), 2.68 (s, 9H), 0.6–2.5 (m, 19H), −2.7 (s, 2H); MS: $m/z = 927$ $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 421 (93), 520 (4.3), 556 (2.1), 597 (1.3), 653 (1.0) nm.

5-(4-(1,4,7,10,13-Pentaoxa-cyclopentadec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**5**, $C_{58}H_{56}N_4O_6$)

5 was obtained in the same way as **1** with the substrates 5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-15-crown-5. The crude product was chromatographed twice on a silica gel column using dichloromethane and then a mixture of dichloromethane and methanol as eluant. The porphyrin was homogeneous by TLC ($R_F = 0.17$, silica, ethyl acetate-methanol, 1:1, v/v).

Yield: 50%; ^{1}H NMR: 8.86 (s, 8H), 7.54, 8.09 (dd, 12H, $J = 7.9$ Hz), 7.28, 8.10 (dd, 4H, $J = 8.6$ Hz), 4.32 (t, 2H), 3.6–4.4 (m, 19H), 2.69 (s, 9H), −2.77 (s, 2H); MS: $m/z = 905$ $(M+H)^+$, 927 $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 422 (65), 521 (2.5), 558 (1.4), 598 (0.8), 654 (1.0) nm.

5-(2-(1,4,7,10,13,16-Hexaoxa-cyclooctadec-2-ylmethyloxy)-phenyl)-10,15, 20-tritolylporphyrin (**6**, $C_{60}H_{60}N_4O_7$)

6 was obtained in the same way as **1** with the substrates 5-(2-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-18-crown-6. The crude product was chromatographed first on a silica gel column using dichloromethane and subsequently ethyl acetate as eluants then on alumina with dichloromethane and afterwards with mixture of dichloromethane and ethyl acetate (5:1, v/v). The porphyrin was homogeneous by TLC ($R_F = 0.25$, silica, ethyl acetate-methanol, 1:1, v/v).

Yield: 46%; ^{1}H NMR: 8.78–8.85 (m, 8H), 7.53, 8.07 (dd, 12H, $J = 7.6$ Hz), 8.05–8.18 (m, 1H), 7.4–7.8 (m, 2H), 7.2–7.4 (m, 1H), 3.9 (d, 2H), 2.29 (s, 9H), 1.9–3.0 (m, 23H), −2.77 (s, 2H); MS: $m/z = 949$ $(M+H)^+$, 971 $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 421 (66), 521 (2.4), 557 (1.1), 598 (0.8), 654 (1.0) nm.

5-(4-(1,4,7,10,13,16-Hexaoxa-cyclooctadec-2-ylmethyloxy)-phenyl)-10,15,20-tritolylporphyrin (**7**, $C_{60}H_{60}N_4O_7$)

7 was obtained in the same way as **1** with the substrates 5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin and (tosyloxy)-methyl-18-crown-6. The crude product was chromatographed on a silica gel column using dichloromethane and then ethyl acetate as eluants. The porphyrin was homogeneous by TLC ($R_F = 0.15$, silica, ethyl acetate-methanol, 1:1, v/v).

Yield: 56%; ^{1}H NMR: 8.85 (s, 8H), 7.54, 8.09 (dd, 12H, $J = 7.8$ Hz), 7.28, 8.10 (dd, 4H, $J = 8.6$ Hz), 4.34 (d, 2H), 3.7–4.2 (m, 23H), 2.69 (s, 9H), −2.77 (s, 2H); MS: $m/z = 949$ $(M+H)^+$, 971 $(M+Na)^+$; UV (CH_2Cl_2): λ_{max} (rel.int.) = 422 (75), 520 (2.1), 556 (1.2), 597 (0.8), 654 (1.0) nm.

Acknowledgments

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