Synthesis, characterization, and antimicrobial activities of novel double-armed benzo-15-crown-5 and their sodium and potassium complexes

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Abstract

New aldehyde- and halogen- (Cl, Br, I) substituted double-armed benzo-15-crown-5 derivatives are synthesized by the reactions of 4',5'-bis(bromomethyl)benzo-15-crown-5 with 5-chlorosalicylaldehyde, 5-bromosalicylaldehyde, or 5-iodosalicylaldehyde. The sodium and potassium complexes are obtained by reaction of crown ether with sodium perchlorate and potassium iodide, respectively. Novel Schiff base compounds containing three groups of benzo-15-crown-5 are obtained from the condensation of aldehydes with 4'-aminobenzo-15-crown-5. The structures of all compounds are elucidated by elemental analysis, 1H, 13C NMR, IR, and mass spectra. The antifungal and antibacterial effects of the synthesized ligands are evaluated against pathogenic microorganisms and show varying degrees of inhibitory effects against the growth of different pathogenic strains.

Keywords

alkali metal complexes, antimicrobial activity, crown ethers, pathogenic microorganisms, Schiff bases

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Introduction

Crown ethers and their complexes have been the subject of significant interest for more than 50 years. Numerous types of macrocyclic ligands and their complexes have been synthesized, including crown ethers.¹–⁶ Structurally, crown ethers are cyclic structures having a cavity that allows them to form stable complexes with metal ions.⁷–¹¹ In particular, bis-crown ethers have superior selectivity for metal cations. Bis-crown compounds form intramolecular sandwich-type complexes with large metal cations (such as Cs⁺, Sr²⁺, Ti⁴⁺, Ba²⁺).²,³,¹² The flexible linker between both crown ether moieties provides better extraction efficiency, that is, good coordination ability, which increases the selectivity for the cations in solution. There are also examples of substituted crown ethers having different selectivity centers.⁶,¹³–¹⁵ The crown ether center can generate stable complexes with alkali metal and alkaline earth metal cations, while the substituted side center can form transition metal complexes.¹²,¹⁶–²³ Their complexing properties make crown ethers especially interesting and useful compounds in biological research and in chemistry.²⁴–³¹ The ion complex–carrying ability of crown ethers results in them resembling natural ionophores (such as gramicidin). In this context, similar to natural ionophores, their ability to transport ions through lipid membranes by channeling has enabled the use of crown ethers in various biological applications.²⁷ In addition, bis-crown ether Schiff base derivatives and their sodium complexes have been shown to exhibit antibacterial activity against gram-positive and gram-negative bacteria.³²

Numerous examples can be found in the literature with bis-crown ether ligands and complexes, but up to now there have only been a few examples reported of tris-crown ethers.⁴,⁵ This prompted us to synthesize new ionophoric receptors containing more than one crown ether unit in
their structure. Herein, we have designed and synthesized double-armed crown ethers possessing dialdehydes 1–3 (Scheme 1). Schiff base derivatives 4–6 having three benzo-15-crown-5 groups in which two benzo-15-crown-5 moieties are linked via a condensation reaction to the crown ether aldehydes 1–3 using 4′-aminobenzo-15-crown-5 (Scheme 2).

**Results and discussion**

**Syntheses and structural characterizations**

New substituted crown ethers 1–3 were successfully prepared in yields of 60%, 59%, and 73%, respectively. It was observed that the products 1–3 were soluble in solvents such as tetrahydrofuran (THF), acetonitrile, and methanol.

The novel Schiff bases 4–6 were obtained from the condensation reaction of two equivalents of 4′-aminobenzo-15-crown-5 with one equivalent of the aldehyde 1–3.

The sodium 1a–3a and potassium complexes 1b and 3b were prepared by reactions of new ligands 1–3 with NaClO4 or KI (Scheme 1). The potassium complex of ligand 2 could not be obtained because the product could not be purified. Although the experiment was repeated several times, the complex was not obtained and the free ligand collapsed. Spectroscopic analyses showed that the stoichiometry of the sodium complexes was 1:1 (Na⁺:benzo-15-crown-5) and that of the potassium complexes was 1:2 (K⁺:benzo-15-crown-5). Sandwich complexes are an expected structural feature for potassium complexes 1b and 3b. Because potassium cation is too large to fit into the benzo-15-crown-5 cavity, in these complexes, K⁺ ion is coordinated by ten 15-crown-5 oxygen atoms. However, Na⁺ ion is smoothly fit into the 15-crown-5 cavity. The solubility of the complexes was very low.

The structures of the solid crown ether ligands 1–6 and complexes 1a–3a, 1b, and 3b are confirmed from their ¹H, ¹³C NMR, IR, and mass spectral data. In all of the new substituted crown ethers 1–3 and Schiff bases 4–6 were investigated for their antimicrobial activity against the pathogenic bacterial strains Bacillus cereus, Listeria monocytogenes, Micrococcus luteus, Staphylococcus aureus, Staphylococcus epidermidis, Salmonella typhi H, Escherichia coli, Enterobacter aerogenes, Sh. dysenteriae type 2, and for their antifungal activity against Candida albicans.

**Fourier-transform infrared spectroscopy spectra**

The Fourier-transform infrared spectroscopy (FTIR) spectra of all the compounds displayed strong stretching bands between 1016 and 1145 cm⁻¹ attributed to the (C–O–C) bond of the crown ether ring. The spectra of the crown aldehydes 1–3 show the broad, strong bands at 1682, 1680, and 1676 cm⁻¹ for the carbonyl group (–C=O) vibration. In the IR spectra of new imine compounds 4–6, the –C=N– stretching vibrations were detected at 1614, 1612, and 1614 cm⁻¹, respectively. The absence of peaks due to the carbonyl groups belonging to compounds 1–3 also supported the successful obtaining imine bond. The (C–O–C) aromatic and aliphatic stretching vibrational modes were detected as broad peaks upon complexation in 1a–3a. The characteristic, wide, and very strong bands observed at 1097, 1068, and 1078 cm⁻¹ provide good evidence of the presence of perchlorate in the sodium complexes 1a–3a.

The IR spectra of potassium complexes 1b and 3b are similar to the ligand spectra, but small shifts were detected on complex formation (see the ‘Experiment’ section).

**¹H and ¹³C NMR spectra**

As expected, the structures of compounds 1–6 and complexes 1a–3a and 1b, 3b in solution are symmetrical (see Figure 1).

In the ¹H NMR spectra of crown ether compounds 1–3 and their complexes 1a–3a and 1b, 3b, characteristic peaks ascribable to the –CHO protons were evident. These proton peaks (–CHO) were observed as singlets at 10.32, 10.12, and 10.26 ppm, respectively. For sodium complexes 1a–3a, these peaks were observed as singlets at 10.21, 10.11, and 10.06 ppm, and for potassium complexes 1b and 3b, at 10.28 and 10.22 ppm, respectively. The benzylic protons (Ph–OCH₂–) for compounds 1–3 were seen as singlets at 5.17, 5.31, and 5.15 ppm, respectively. The crown ether units were evident at 3.41–4.78 ppm with the appropriate integrations. The crown ether proton peaks of sodium complexes 1a–3a in the form of perchlorate salts to a slight shift in comparison with the free ligands. As a result of cation bonding to the crown ether moieties, downfield shifts of the proton peak resonances were observed due to the electron-withdrawing effects of the cation. However, the crown ether proton peaks of the potassium complexes showed slightly upfield shifts. That is unexpected and may be due to the ring current effect resulting from π-stacking in the sandwich complex of the 15-crown-5 moieties upon K⁺ ion binding. A similar situation in a related sandwich structure has been observed and reported. The chemical shifts of the aromatic and crown ether protons in compound 3 and potassium complex 3b are shown in Figure 2. The most significant changes in the spectra were found for the proton signals of the methylene (–OCH₂–CH₂O–) groups of the crown ether moiety.

The ¹H NMR spectra of tritopic Schiff bases 4–6 contain signals for the characteristic azomethine protons (HC=N) at 8.74, 8.73, and 8.68 ppm, respectively. The absence of carbonyl groups belonging to crown ether aldehydes 1–3 also support the formation of obtaining imine bond 4–6. Additional support for the formation of Schiff bases 4–6 was provided (Figure 3), as the addition of second crown ether ring to the compounds 1–3 causes changes in the chemical shift of the methylene group of the crown ether (–OCH₂–CH₂O–) peak.

In ¹³C NMR, the signals of the carbonyl carbons (C-15) in compounds 1–3 were present at 188.0, 188.3, and 187.7 ppm, respectively. However, quite different chemical shifts (126.6, 115.7, and 83.7 ppm) were detected for the C-12 carbons of 1–3. This can be explained by the changing
of the electronegativity from Cl, Br to I. While the electronegativities of the halogens bound to the C-12 carbon make significant changes in the chemical shift of this carbon, the C-15 carbon was less affected by the electronegativities of the halogens and therefore small differences were observed between the chemical shifts. The signals of the four 15-crown-5 carbons (–OCH2CH2O–) and aromatic carbon peaks indicated that compounds 1–3 are symmetric.

Due to the additional crown ring for compounds 4–6, more than four resonances were observed in the crown ether peak region. The absence of carbonyl carbons belonging to crown ether aldehydes 1–3 and the observed imine carbons (–HC=N–) at 156.6, 158.1, and 157.9 ppm support the formation of Schiff bases 4–6.

In the $^{13}$C NMR spectra of the complexes 1a–3a, 1b, and 3b, small chemical shifts observed for all the peaks result from interactions of the 15-crown-5 oxygen atoms with the sodium or potassium cations. The spectra indicate that new complexes had formed.

**Mass spectra**

The mass spectra of the synthesized crown aldehydes 1–3 and Schiff bases 4–6 are given in Table 1. The mass spectra of the all compounds were obtained by the API-ES technique. In these spectra, the ligand plus sodium ([M + Na]$^+$) peaks were observed as molecular ion peaks for all of the substituted crown ethers 1–3 and Schiff bases 4–6. Adduct formation, either with sodium or potassium cations, is frequently observed in mass spectra for crown ethers.\(^{34}\) Actually, the majority of observed ions in the mass spectra of crown ethers are adduct ions or pseudomolecular ions.
(e.g. [M + H]^+ , [M + NH₄]^+ , [M + Na]^+ or [M + K]^+).34–36 The isotope atoms of chlorine and bromine giving rise to M + 2 and M + 4 peaks (compounds 1, 2, 4, and 5). In the mass spectra of 1–3, the dominant peaks at m/z 627 (100%), 717 (100%), and 811 (100%) correspond to [M + Na]^+ (for compounds 1 and 3) and [M + 2 + Na]^+ (for compound 2). The molecular ion peak for the ligand plus sodium ([M + Na]^+) for Schiff bases 4–6 was detected at m/z 1157 (26%), 1245 (26%), and 1341 (71%), respectively.

The mass spectra of the synthesized alkali metal complexes 1a–3a, 1b, and 3b are given in Table 2. Sodium and potassium cations bind to the crown ether cavity by ion dipole interactions. In the mass spectra of the Na^+ complexes 1a–3a, molecular ion peaks corresponding to the ligand plus sodium appeared as expected ([M + Na]^+).

The molecular ion peak [2M + K]^+ of the potassium complexes 1b and 3b were detected at m/z 1247 and 1615. These peaks show that 1:2 (metal / ligand) complexes are formed. In addition [2M + 2 + K] and [2M + 4 + K] peaks confirm the existence of chlorine and bromine in complexes 1b and 3b.

**Antimicrobial activity**

All the newly synthesized compounds 1–6 and different antibiotics were found to be effective to various degrees toward the growth inhibition of different pathogenic strains (Figure 4). The results of the antibacterial screening showed that compound 1 had activity (diameter of zone inhibition: 25 mm) against most strains of the gram-positive and...
gram-negative bacteria (M. luteus, E. aerogenes) tested. Compound 2 showed activity against the strains B. cereus and S. epidermidis (26 and 25 mm).

Salmonella typhi H, Sh. dysenteriae type 2 (Sh. dys. type 2), and S. epidermis are pathogenic microorganisms, and these microorganisms are gaining resistance to conventional antibiotics day by day. Therefore, there is a need for new antibiotics effective against these pathogenic microorganisms. Compound 3 showed greater activity against S. typhi H, Sh. dys. type 2, and S. epidermis (30, 20, and 30 mm, 26 and 17 mm, and 30 mm, respectively). Compound 4 showed activity against S. typhi H, Sh. dys. type 2, and S. epidermis (30, 20, and 30 mm).

Table 1. The mass spectral data of crown ether aldehydes 1–3 and Schiff bases 4–6.

| Compound | Calculated Ion; % abundance |
|----------|-----------------------------|
| 1        | [M]+: 604                  |
|          | [M + Na]+: 627; 100        |
|          | [M + Na + H]+: 628; 63     |
|          | [M + 2 + Na]+: 629; 54     |
|          | [M + 4 + Na]+: 631; 11     |
| 2        | [M]+: 692                  |
|          | [M + Na]+: 715; 52         |
|          | [M + Na + H]+: 716; 77     |
|          | [M + 2 + Na]+: 717; 100    |
|          | [M + 4 + Na]+: 719; 54     |
| 3        | [M]+: 788                  |
|          | [M + Na]+: 811; 100        |
|          | [M + Na + H]+: 812; 36     |
| 4        | [M]+: 1134                 |
|          | [M + Na]+: 1157; 26        |
|          | [M + Na + H]+: 1158; 31    |
|          | [M + 2 + Na]+: 1159; 19    |
|          | [M + 4 + Na]+: 1161; 11    |
|          | [C14H19NO5 + Na + 2H]+: 306|
| 5        | [M]+: 1222                 |
|          | [M + Na]+: 1245; 26        |
|          | [M + Na + H]+: 1246; 77    |
|          | [M + 2 + Na]+: 1247; 58    |
|          | [M + 4 + Na]+: 1249; 35    |
|          | [C14H19BrNO5 + CH3CN − H]+: 490; 100 |
| 6        | [M]+: 1318                 |
|          | [M + CH3CN]+: 1359; 81     |
|          | [M + Na]+: 1341; 71        |
|          | [M − C2H4O]+: 1273; 100    |
respectively) than conventional antibiotics such as amoxycillin and sulphamethoxazole. Schiff base 4 showed the most activity against M. luteus, B. cereus, S. epidermis, and E. aerogenes (22, 21, 20, and 25 mm, respectively). Compound 5 showed the most activity against B. cereus and E. aerogenes (22 mm). Compound 6 showed the best activity against M. luteus, S. typhi H, and E. aerogenes (35, 25, and 25 mm, respectively). The change in the electronegativity of halogens did not cause a standard change in the biological activities of the synthesized compounds (1–6).

It is known that C. albicans showing pathogenicity in human fungal infections causes significant morbidity and mortality in immunocompromised patients (AIDS, cancer chemotherapy, organ, or bone transplantation). All the synthesized compounds 1–6 demonstrated effective action against this fungus. In particular, compounds 3 and 4 showed the best inhibitory activity against C. albicans, with inhibition zone values of 40 and 37 mm, respectively.

**Conclusion**

In conclusion, a series of new crown ether compounds containing halogen (Cl, Br, or I), aldehyde, and imine groups have been synthesized. Aldehyde crown ethers 1–3 were synthesized by the reaction of 4′,5′-bis(bromomethyl)benzo-15-crown-5 with substituted salicylaldehyde derivative in the presence of K$_2$CO$_3$. Three crown ether Schiff bases were prepared according to the literature. All the synthesized compounds 1–6 demonstrated effective action against this fungus. In particular, compounds 3 and 4 showed the best inhibitory activity against C. albicans, with inhibition zone values of 40 and 37 mm, respectively.

**Experiment**

**Reagents and equipments**

The starting materials, tetraethylene glycol dichloride, benzo-15-crown-5, and 4′,5′-bis(bromomethyl)benzo-15-crown-5 were prepared according to the literature. Sodium perchlorate salts. The measurement of melting points was determined on a Gallenkamp melting point apparatus. The IR spectra were recorded using a Shimadzu Infinity model FTIR spectrometer equipped with an attenuated total reflectance (ATR) attachment. The 1H and 13C NMR spectra were recorded with a Varian Mercury, high-performance
Digital FT-NMR (400 MHz) spectrometer (chemical shift values are expressed in ppm, SiMe₄ as an internal standard). Mass spectra were obtained using a Waters 2695 Alliance Micromass ZQ LC/MS spectrometer. The content of carbon, hydrogen, and nitrogen in all compounds was determined on a LECO CHNS-932 elemental analyzer.

**Detection of antimicrobial activity**

*Staphylococcus aureus* ATCC25923, *Staphylococcus epidermis* ATCC12228, *Micrococcus luteus* ATCC9341, *Bacillus cereus* RSKK-863, *Listeria monocytogenes* 4b ATCC19115, *Salmonella typhi* H NCTC901.8394, Entero bacter aerogenes sp., *Escherichia coli* ATCC1280, *Sh. dysenteriae* type 2 and *C. albicans* Y-1200-NIH was used a fungal agent. The antimicrobial activities of the synthesized compounds 1–6 were examined by the well-diffusion method against five gram-positive bacteria (*S. aureus*, *S. epidermis*, *M. luteus*, *B. cereus*, *L. monocytogenes* 4b) and four gram-negative bacteria (*S. typhi* *H. E. aerogenes*, *E. coli*, *Sh. dys. type 2*) and yeast (*C. albicans*).³⁷

The synthesized new compounds were dissolved (10³μM) in DMF (DMF was used as a solvent because it had no antimicrobial activity against any of the tested organisms). 1% (v/v) of the 24-h broth culture (pathogenic microorganisms) containing 106 CFU/mL was placed in sterile Petri dishes. Mueller-Hinton Agar (MHA) (15 mL), had no antimicrobial activity against any of the tested compounds. The 6-mm-diameter wells were then carefully punched using a sterile cork borer and allowed to solidify slowly. The 6-mm-diameter wells were then maintained at 45°C, was poured into a Petri dish and allowed to solidify slowly. The 6-mm-diameter wells were then carefully punched using a sterile cork borer and filled fully with the synthesized compounds. The plates were incubated for 24 h at 37°C. At the end of this period, the mean value obtained for the two wells was used to calculate the zone of growth inhibition of each compound. Pathogenic bacterial cultures and yeast were investigated for resistance to five antibiotics (ampicillin, nystatin, kanamycin, sulfamethazole, and amoxycillin) produced by Oxoid Ltd., Basingstoke, UK.

**Synthesis of compounds**

**General method for the preparation of crown ether aldehydes 1–3**

To the corresponding salicylaldehyde (5-chlorosalicylaldehyde, 5-bromosalicylaldehyde, or 5-iodosalicylaldehyde) (3.5 mmol) dissolved in DMF (20 mL), K₂CO₃ (3.5 mmol) was added, and the reaction mixture was left to stir overnight at room temperature. While stirring, a solution of 4′,5′-bis(bromomethyl)benzo-15-crown-5 (1.75 mmol) in DMF (20 mL) was added dropwise and then the reaction mixture was heated for 2 h. A white solid was obtained that was then filtered, washed with methanol and diethyl ether, and dried at room temperature.

2,2′-[2,3,5,6,8,9,11,12-octahydrop-1,4,7,10,13-benzopentaaxyacyclododecine-15,16-diylbis(methyleneoxy)]bis(5-bromobenzaldehyde) J: M.p.: 123°C; IR (KBr) cm⁻¹: 2914 (C–H)⼄ replaced, 1682 (C=O), 1595 (C=C), 1273–1215 (C–O)⼄, 1128, 1066 (C–C)⼄; H NMR (400 MHz, CDCl₃): δ = 3.75–4.15 (8H, m, –OCH₂CH₂O–), 5.15 (2H, s, Ph–CH₂O–), 6.97 (1H, d, J = 8.8 Hz, H-14), 7.00 (1H, s, H-6), 7.46 (1H, dd, J = 8.8 Hz, J = 2.7 Hz, H-13), 7.77 (1H, d, J = 2.7 Hz, H-11), 10.32 (1H, s, –CHO); ¹³C NMR (400 MHz, CDCl₃): δ = 68.8 (C-8), 69.2, 69.4, 70.4, 71.0 (C-1-4), 114.5 (C-6), 115.3 (C-12), 120.8 (C-10), 126.6 (C-12), 126.7 (C-7), 127.0 (C-11), 135.5 (C-13), 149.4 (C-5), 159.0 (C-9), 187.9 (C-15); Anal. calcd for C₃₀H₂₉Br₂O₉: C, 51.89; H, 4.35; found: C, 51.52; H, 4.10.

General method for the preparation of sodium complexes 1a–3a

To a stirred solution of crown ether aldehydes (1–3) (0.16 mmol) in methanol (15 mL) was added NaClO₄ (0.16 mmol) and the reaction mixture was heated for 2 h. A white solid was obtained that was then filtered, washed with methanol and diethyl ether, and dried at room temperature. 2,2′-[2,3,5,6,8,9,11,12-octahydrop-1,4,7,10,13-benzopentaaxyacyclododecine-15,16-diylbis(methyleneoxy)]bis(5-iodobenzaldehyde) 2: M.p.: 151°C; IR (KBr) cm⁻¹: 2937 (C–H)aliph, 1680 (C=O), 1589 (C=C), 1273–1234 (C–O–C)arom, 1349 (C–O–C)aliph; H NMR (400 MHz, DMSO-d₆): δ = 3.61–4.09 (8H, m, –OCH₂CH₂O–), 5.31 (2H, s, Ph–CH₂O–), 7.32 (1H, s, H-6), 7.37 (1H, d, J = 8.9 Hz, H-14), 7.71 (1H, d, J = 2.8 Hz, H-11), 7.79 (1H, dd, J = 8.9 Hz, J = 2.8 Hz, H-13), 10.12 (1H, s, CHO); ¹³C NMR (400 MHz, DMSO-d₆): δ = 68.7 (C-8), 69.0, 69.1, 70.0, 70.7 (C-1-4), 113.0 (C-6), 115.7 (C-12), 117.2 (C-14), 126.4 (C-10), 127.6 (C-7), 130.7 (C-13), 138.7 (C-11), 148.6 (C-5), 160.0 (C-9), 188.3 (C-15); Anal. calcd for C₃₀H₂₉Cl₂O₉: C, 59.51; H, 4.99; found: C, 59.28; H, 5.02.

2,2′-[2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaaxyacyclododecine-15,16-diylbis(methyleneoxy)]bis[5-bromobenzaldehyde] 2: M.p.: 151°C; IR (KBr) cm⁻¹: 2937 (C–H)⼄ replaced, 1680 (C=O), 1589 (C=C), 1273–1234 (C–O–C)arom, 1349 (C–O–C)aliph; H NMR (400 MHz, DMSO-d₆): δ = 3.61–4.09 (8H, m, –OCH₂CH₂O–), 5.31 (2H, s, Ph–CH₂O–), 7.32 (1H, s, H-6), 7.37 (1H, d, J = 8.9 Hz, H-14), 7.71 (1H, d, J = 2.8 Hz, H-11), 7.79 (1H, dd, J = 8.9 Hz, J = 2.8 Hz, H-13), 10.12 (1H, s, CHO); ¹³C NMR (400 MHz, DMSO-d₆): δ = 68.7 (C-8), 69.0, 69.1, 70.0, 70.7 (C-1-4), 113.0 (C-6), 115.7 (C-12), 117.2 (C-14), 126.4 (C-10), 127.6 (C-7), 130.7 (C-13), 138.7 (C-11), 148.6 (C-5), 160.0 (C-9), 188.3 (C-15); Anal. calcd for C₃₀H₂₉Br₂O₉: C, 59.51; H, 4.99; found: C, 59.28; H, 5.02.
2.2-[2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaacyclooctadecine-15,16-diybis(methylenoxy)]bis(5-bromobenzaldehyde) potassium complex (2a): M.p.: 194°C; IR (KBr) cm⁻¹: 2968 (C–H aliph), 1680 (C=O), 1589 (C=C), 1273–1215 (C–O–C asym 1145, 1016 (C–O–C sym) 1068 (C=O)). ¹H NMR (400 MHz, DMSO-d₆): δ = 3.59–4.07 (8H, m, –OCH₂CH₂O–), 5.29 (2H, s, Ph–CH₂O–), 7.22 (1H, s, H-6), 7.31 (1H, d, J = 8.9 Hz, H-14), 7.69 (1H, d, J = 2.4 Hz, H-11), 7.76 (1H, dd, J = 8.9 Hz, J = 2.4 Hz, H-13), 10.11 (1H, s, –CHO); ¹³C NMR (400 MHz, DMSO-d₆): δ = 68.3 (C-8), 68.4, 68.6, 69.5, 70.2 (C-1-4), 112.6 (C-6), 115.3 (C-13), 116.7 (C-7), 125.9 (C-10), 127.2 (C-7), 130.2 (C-13), 138.2 (C-11), 148.2 (C-5), 187.5 (C-9); Anal. calc. for C₈₀H₆₀B₈O₂₄K₂: C, 41.35; H, 3.47; found: C, 41.53; H, 3.11.

**General method for the preparation of Schiff bases 4–6**

A solution of the corresponding crown ether aldehyde 1–3 (0.41 mmol) dissolved in ethanol (10 mL) was added and 4′-aminobenz-15-crown-5 (0.82 mmol). The resulting reaction mixture was stirred under reflux for 8 h, then left to stand overnight at room temperature. The crude product was recrystallized from methanol.

N,N′-[2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaacyclooctadecine-15,16-diybis(methylenoxy)[bis(5-chlorobenzaldehyde) potassium complex (3a): M.p.: 220°C; IR (KBr) cm⁻¹: 2958 (C–H aliph), 1687 (C=O), 1585 (C=C), 1276–1234 (C–O–C sym) 1101, 1053 (C–O–C aliph), 1078 (C=O)). ¹H NMR (400 MHz, DMSO-d₆): δ = 3.59–4.06 (8H, m, –OCH₂CH₂O–), 5.27 (2H, s, Ph–CH₂O–), 7.16 (1H, d, J = 8.9 Hz, H-14), 7.21 (1H, s, H-6), 7.84 (1H, d, J = 2.4 Hz, H-11), 7.89 (1H, dd, J = 8.9 Hz, J = 2.4 Hz, H-13), 10.06 (1H, s, –CHO); ¹³C NMR (400 MHz, DMSO-d₆): δ = 68.1 (C-8), 69.0, 69.1, 70.1, 70.5 (C-1-4), 83.6 (C-12), 109.8 (C-10), 114.9 (C-14), 115.1 (C-6), 126.1 (C-7), 137.1 (C-11), 143.2 (C-13), 148.9 (C-5), 159.5 (C-9), 187.5 (C-15); Anal. calc. for C₈₀H₆₀Cl₂B₈O₂₄K₂: C, 59.36; H, 3.32; found: C, 38.96; H, 3.41.
13C NMR (400 MHz, CDCl₃): δ = 68.30 (–OCH₂), 68.53–71.02 (–OCH₂CH₂O–), 84.38, 102.54, 107.20, 114.18, 115.13, 117.28, 127.20, 127.43, 136.10, 136.40, 141.51, 140.74, 145.90, 149.72, 152.43 (Ar-C), 157.90 (HC=N);
Anal. calcd for C₅₈H₆₈I₂O₁₇N₂ (1318.97): C, 52.82; H, 5.20; N, 2.12; found: C, 52.46; H, 5.13; N, 2.33.

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