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Cyclic di[(*o*-polyethyleneglycoxy)phenyl]amine: new members in the crown ether family

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Abstract

The synthesis of cyclic ethers based on polyethyleneglycol chains grafted on di(*o*-hydroxyphenyl)amine is described. The starting diarylamine is obtained from a melted salt procedure and coupled to the tosylated tri-, tetra- and pentaethyleneglycol. The X-ray crystal structure of the tetraethyleneglycol derivative was determined. For the triethyleneglycol compound, alkylation of the nitrogen atom with 5-bromomethyl-5′-methyl-2,2′-bipyridine (excess or 1 equiv.) led either to the quaternary ammonium salt or to the tertiary amine derivatives, respectively. The latter reacted with $[Re(CO)_5Cl]$ to give the corresponding Re(I) complex in a facial configuration.

During the development of crown ethers, cryptands, podands, coronands, calixcrowns and other lariat ethers, polyethyleneglycol chains has proven to be highly effective for cation complexation and recognition. A current tendency in their use as complexing agent is to graft these chelating chains directly on fluorescent labels[1] or in their close vicinity[2] to obtain photoinduced electron transfer (PET) probes[3] able to modulate their emissive properties in the presence of an adventitious cation.[4]

In this context, aminoaryl derivatives have found some interesting applications as luminophores, but very often the aryl moieties appeared as pendent side arms and more rarely as a building part of the complexing cavity.[5,6] In an effort to produce a family of new complexing agents, we focused our attention on the synthesis of crown ethers based on di(*o*-hydroxyphenyl)amines **1** as a starting synthon (Scheme 1). Cyclization of the crown ring by the hydroxy functions on the one hand and the ability to further functionalize the nitrogen atom on the other hand should lead to new molecules with potentially interesting complexing properties.

The starting material **1**[7] was obtained from *o*-aminophenol in a melted salt procedure under vacuum, in the presence of hydrochloric acid (0.5 equiv.). As previously observed in other experimental conditions,[8] its synthesis is accompanied by the formation of phenoxazine (8%). By treatment with 1.1 equiv. of ditosylated tri-, tetra- and pentaethyleneglycol[9] derivatives in acetonitrile containing Cs_2CO_3 as a base,

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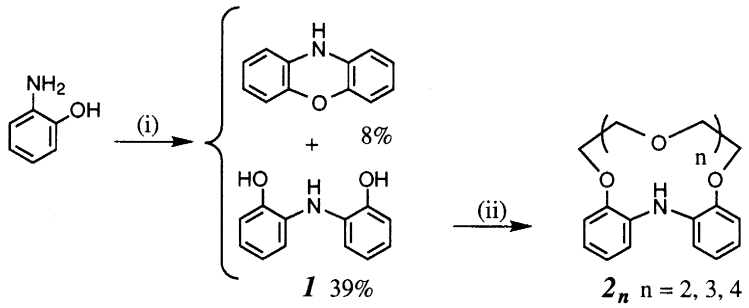


Scheme 1. (i) HCl 0.5 equiv., melted salt, 240°C; (ii) $TsOCH_2(CH_2OCH_2)_nCH_2OTS$, Cs_2CO_3, acetonitrile, 80°C, *n*=2 (68%), *n*=3 (55%), *n*=4 (22%)

the corresponding cyclic diarylamines $\mathbf{2}_n$ (*n*=2, 3 and 4, respectively), were obtained.[10] Recrystallization of $\mathbf{2}_3$ from acetonitrile afforded colorless crystals suitable for X-ray analysis. The structure showed that the cyclic ether crystallized with a water molecule (Fig. 1). One of the aromatic ring (including C1) forms a plane which contains the nitrogen atom with a pronounced delocalization of the aromatic electrons and a marked sp_2 character of the nitrogen atom,[11] as evidenced by the three angles C1–N–C7, C1–N–H and H–N–C7 close to 120° (123, 117 and 118°, respectively). The plane of the second aromatic ring is twisted [ca. 55°] by rotation around the C7–N bond. The rest of the molecule is composed of the tetraethyleneglycol chain joining the oxygen atoms in *ortho* position to the nitrogen atom. When considering the ring formed by the six heteroatoms of the crown, a water molecule is localized at the center of this ring, slightly out of this plane and roughly equidistant with the six heteroatoms [$d_{N–Owater}$=2.901 Å, $d_{Oring–Owater}$=2.902 (O4) to 2.987 Å (O1 and O2)]. The water molecule is held in place by a strong hydrogen bond involving the NH function.

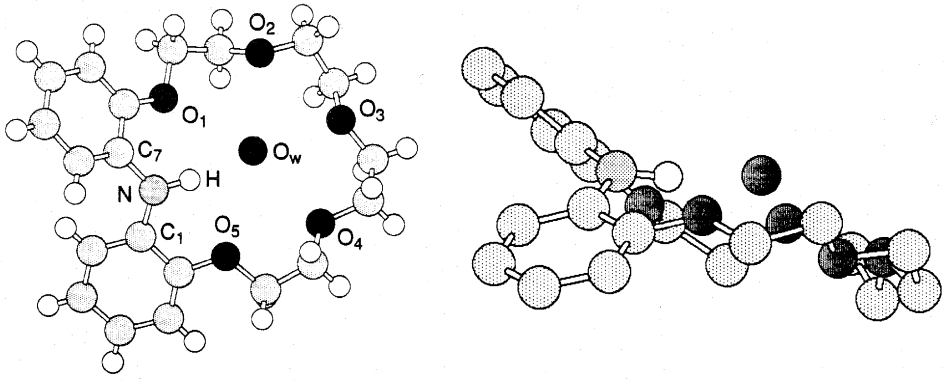
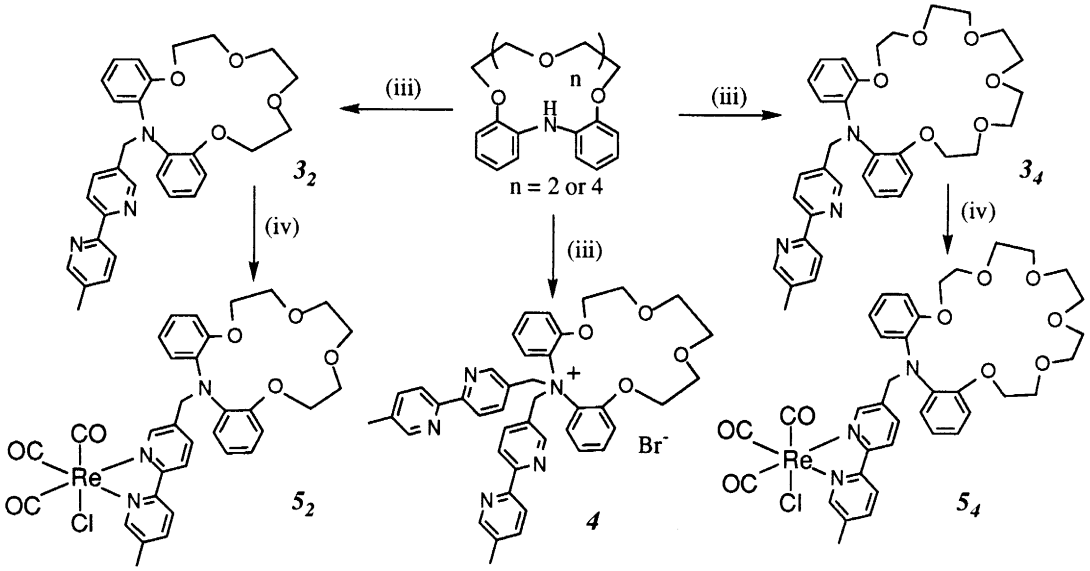


Fig. 1. Top view (left) and perpendicular view (right) of the $\mathbf{2}_3$ macrocycle. X-Ray data (monoclinic, $P12_1/c1$, *a*=11.841, *b*=12.323, *c*=13.430 Å, β=103.493°, *R*=0.042, R_w=0.065). Hydrogen atoms except for NH have been omitted for the sake of clarity

In the case of $\mathbf{2}_2$, the ability to further functionalize the nitrogen atom was carried out by alkylation with 5-bromomethyl-5′-methyl-2,2′-bipyridine[12] which affords the tertiary amine $\mathbf{3}_2$ in 38% yield (Scheme 2).[13] The quaternized ammonium bromide **4**[14] was prepared when excess of alkylating agent is used. The same alkylation protocol could be used to prepare the crown-ether $\mathbf{3}_4$ (7% yield). Surprisingly, the analogous compound $\mathbf{3}_3$ decomposed during the purification step but no further attempts to identify the resulting compounds have been carried out. One and two dimensional ^{1}H NMR spectroscopy of the ammonium salt **4** shows a set of signals for each bipy unit and a single set for the two aryl rings with three signals for the methylene protons of the chain, indicating the presence of a symmetry plane

passing through the nitrogen atom and transforming one aryl ring into the other. For one of the bipy set, the important deshielding observed for the signals of the methylene bridge and the proton *ortho* to the nitrogen atom of the neighboring pyridine ($\Delta\delta$=1.47 and 1.42 ppm, respectively, comparing to the same signals in $\mathbf{3_2}$) shows these protons to be greatly affected by the ring current of the aryl moieties. Reaction of $\mathbf{3}_n$ with $[Re(CO)_5Cl]$[15] in degassed toluene afforded the corresponding rhenium complex $\mathbf{5}_n$ in 58 and 30% yield after chromatography, respectively, for n=2 and 4.[16] The ^{1}H NMR spectrum of complex $\mathbf{5_2}$ is very complicated, probably as a result of the presence of different conformers at room temperature in $CDCl_3$, as indicated by the three different singlets observed for the methyl of the bipyridine moiety.



Scheme 2. (iii) 5-Methyl-5′-bromomethyl-2,2′-bipyridine (1.1 equiv. for $\mathbf{3_2}$ and $\mathbf{3_4}$, 2.2-fold excess for **4**), K_2CO_3, acetonitrile, 80°C; (iv) $[Re(CO)_5Cl]$ (1.2 equiv.) in toluene at 80°C

In conclusion, we have developed the synthesis of novel diarylamine crown ethers and some of their tertiary amine and quaternary ammonium derivatives. Our efforts are now directed toward the study of the complexing properties of the non-substituted crown ethers as well as of the bipyridine-grafted derivatives. Preliminary results showed that detection of adventitious cations is made possible by the use of steady-state luminescence techniques. Based on this information we surmized that these molecules can work as potential PET sensors. Further understanding of how photoinduced electron transfer processes can be affected upon complexation is carried out using time-resolved fluorescence measurements together with transcient absorption spectroscopy. This set of results will give a clear insight into the mechanism of luminescence amplification. The synthetic methodology, in turn, also provides a new and efficient avenue to cyclic diarylamines.

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5. For example, see: Löhr, H.-G.; Vögtle, F. *Acc. Chem. Res.* **1985**, *18*, 65–72; Bourson, J.; Valeur, B. *J. Phys. Chem.* **1989**, *93*, 3871–3876.
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7. ^{1}H NMR ($CDCl_3$) for **1**: δ 5.42 (s, 2H, OH), 5.51 (s, 1H, NH), 6.80–6.94 (m, 8H, H_{aro}); ^{13}C NMR ($CDCl_3/CD_3OD$, 1/1) δ 114.3, 116.6, 119.4, 120.4, 131.5, 146.6; EI/MS: *m/z*=201.1 (M=201.2 g mol^{-1} for $C_{12}H_{11}NO_2$). Anal. calcd for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.52; N, 6.97. Found: C, 71.34; H, 5.30; N, 6.63.
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10. ^{1}H NMR ($CDCl_3$) for $\mathbf{2_2}$: δ 3.74 (s, 4H, O-CH_2), 3.87–3.91 (m, 4H, O-CH_2), 4.15–4.19 (m, 4H, O-CH_2), 6.75–6.97 (m, 6H, H_{aro}), 7.25 (s, br, 1H, NH), 7.47–7.51 (m, 2H, H_{aro}). ^{13}C NMR ($CDCl_3$) δ 67.9, 69.5, 70.0, 111.7, 114.1, 119.4, 121.1, 133.1, 147.8. EI/MS: *m/z*=315.2 (M=315.4 g mol^{-1} for $C_{18}H_{21}NO_4$). Anal. calcd for $C_{18}H_{21}NO_4$: C, 68.54; H, 6.72; N, 4.44. Found: C, 68.30; H, 6.60; N, 4.11. ^{1}H NMR ($CDCl_3$) for $\boldsymbol{2_3}$: δ 3.75 (s, 8H, O-CH_2), 3.91–3.95 (m, 4H, O-CH_2), 4.16–4.21 (m, 4H, O-CH_2), 6.72 (s, br, 1H, NH), 6.80–6.89 (m, 6H, H_{aro}), 7.37–7.43 (m, 2H, H_{aro}). ^{13}C NMR ($CDCl_3$) δ 68.0, 69.9, 70.9, 71.2, 111.7, 115.8, 112.0, 120.9, 133.0, 148.4. Anal. calcd for $C_{20}H_{25}NO_5$: C, 66.82; H, 7.02; N, 3.90. Found: C, 66.60; H, 6.74; N, 3.62. ^{1}H NMR ($CDCl_3$) for $\boldsymbol{2_4}$: δ 3.68 (s, 4H, O-CH_2), 3.75 (s, 8H, O-CH_2), 3.91–3.98 (m, 4H, O-CH_2), 4.16–4.22 (m, 4H, O-CH_2), 6.67 (s, br, 1H, NH), 6.78–6.95 (m, 6H, H_{aro}), 7.35–7.40 (m, 2H, H_{aro}). ^{13}C NMR ($CDCl_3$) δ 68.6, 70.0, 71.0, 71.2 (2C), 112.2, 116.0, 120.2, 121.2, 133.0, 148.4.
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13. ^{1}H NMR ($CDCl_3$) for $\mathbf{3_2}$: δ 2.37 (s, 3H, CH_3), 3.63–3.71 (m, 4H, O-CH_2), 3.71 (s, 4H, O-CH_2), 4.10–4.16 (m, 4H, O-CH_2), 4.82 (s, 2H, CH_{2bipy}), 6.74–6.98 (m, 8H, H_{aro}), 7.57 (dd, 1H_{bipy}, ^{3}J=8.4 Hz, ^{4}J=2.2 Hz), 8.12–8.22 (m, 3H, H_{bipy}), 8.46 (s, br, 1H_{bipy}), 8.66 (s, br, 1H_{bipy}). ^{13}C NMR ($CDCl_3$) δ 18.4, 53.3, 67.9, 70.1, 70.6, 113.6, 120.6, 120.6, 120.8, 123.3, 123.3, 133.1, 135.5, 137.2, 137.5, 138.7, 141.7, 148.6, 149.6, 150.3, 152.7. ^{1}H NMR ($CDCl_3$) for $\mathbf{3_4}$: 2.36 (s, 3H), 3.48–3.72 (m, 16H), 4.05–4.12 (m, 4H), 5.02 (s, 2H), 6.70–6.97 (m, 8H), 7.57 (dd, 1H, ^{3}J=8 Hz, ^{4}J=2 Hz), 8.02 (dd, 1H, ^{3}J=8 Hz, ^{4}J=2 Hz), 8.21 (dd, 2H, ^{3}J=8 Hz, ^{4}J=2 Hz), 8.45 (s, 1H, br), 8.78 (s, 1H, br). ^{13}C NMR ($CDCl_3$): 18.4, 52.6, 68.3, 69.7, 70.8, 70.9, 71.1, 113.7, 120.2, 120.4, 120.5, 121.3, 123.3, 123.7, 133.1, 135.9, 137.1, 137.5, 138.3, 149.1, 149.6, 152.5, 153.7.
14. ^{1}H NMR ($CDCl_3$) for **4**: δ 2.39 (s, 3H, CH_{3bipy}), 2.42 (s, 3H, CH_{3bipy}), 3.60 (s, 4H, O-CH_2), 3.60–3.64 (m, 4H, O-CH_2), 3.99–4.03 (m, 4H, O-CH_2), 5.25 (s, 2H, CH_{2bipy}), 6.38 (s, 2H, CH_{2bipy}), 6.75–6.88 (m, 4H_{aro}+1H_{bipy}), 6.97–7.12 (m, 4H_{aro}), 7.54–7.63 (m, 3H_{bipy}), 7.81 (d, 1H_{bipy}, ^{4}J=1.9 Hz), 7.99 (d, 1H_{bipy}, ^{3}J=8.2 Hz), 8.11 (d, 1H_{bipy}, ^{3}J=8.2 Hz), 8.26 (d, 1H_{bipy}, ^{3}J=8.0 Hz), 8.49 (m, 2H_{bipy}), 9.21 (dd, 1H_{bipy}, ^{3}J=8.3 Hz, ^{4}J=1.6 Hz), 9.89 (s, br, 1H_{bipy}). ^{13}C NMR ($CDCl_3$) δ 18.5, 18.7, 53.3, 59.1, 65.8, 67.7, 68.1, 111.7, 111.8, 120.7, 120.8, 121.1, 124.2, 124.5, 126.0, 129.4, 130.7, 134.1, 135.4, 136.4, 136.6, 137.7, 138.8, 142.7, 147.1, 147.7, 147.9, 149.7, 150.1, 150.2, 152.4, 152.4, 156.3. FAB/MS *m/z*=680 [M−Br]$^+$. Anal. calcd for $C_{42}H_{42}BrN_5O_4$: C, 66.30; H, 5.58; N, 9.21. Found: C, 66.19; H, 5.31; N, 8.91.
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16. FAB/MS for $\mathbf{5_2}$: *m/z*=803.2 (M$^{+\cdot}$), 768.2 ([M−Cl]$^+$), 315.1 ([Re(CO)$_3$Cl]$^{+\cdot}$). IR (KBr Pellet, cm^{-1}): 2952, 2852 (ν_{CH2}), 2021, 1905 (ν_{CO}), 1637, 1616 ($\nu_{C=C}$, $\nu_{C=N}$). ^{1}H NMR ($CDCl_3$) for $\mathbf{5_4}$: 2.45 (s, 3H), 3.62–3.80 (m, 16H), 4.12–4.24 (m, 4H), 5.34 (s, 2H), 6.70–6.98 (m, 6H), 7.33–7.41 (m, 2H), 7.67 (d, br, 1H, ^{3}J=8 Hz), 7.96 (d, br, 2H, ^{3}J=8 Hz), 8.42 (d, br, 1H, ^{3}J=8 Hz), 8.80 (s, br, 1H), 9.33 (s, br, 1H). ^{13}C NMR ($CDCl_3$): 18.5, 51.6, 67.7, 69.7, 70.6, 70.7, 70.8, 112.6, 121.4, 121.7, 122.1, 123.9, 126.5, 137.1, 137.3, 139.2, 140.1, 142.0, 152.7, 153.0, 153.1, 153.8, 154.0, 197.3, 197.7 (br).]$^{+\cdot}$). IR (KBr Pellet, cm^{-1}): 2919, 2870 (ν_{CH2}), 2015, 1904, 1887 (ν_{CO}), 1605 ($\nu_{C=C}$, $\nu_{C=N}$). FAB/MS: *m/z*=891 (M$^{+\cdot}$), 856 ([M−Cl]$^+$).