A Convenient Synthetic Route to Polyether-Tagged Cyclam Ligands and Their Nickel Derivatives

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A specific strategy is described for the synthesis of stable polyethylene oxide tagged tetraazamacrocycles (PEO-cyclam) in five steps (overall yields for **12** and **13** 48% and 22%, respectively). Various attempts via classical pathways demonstrated: (i) the low reactivity of PEO derivatives, and (ii) the necessity of a stabiliser arm between the cyclam and the PEO chain. Nickel complexes have been prepared and characterised by electrochemistry.

Introduction

The attachment of polyethylene oxide (PEO) chains to a molecule has long been known to confer on it the outstanding properties of this family of polymers such as amphiphilic solubility and vectorising ability, nontoxicity, non-antigenicity and biocompatibility.[1] From a biological and biomedical point of view, these properties are of great interest if they are combined with the potential properties of cyclam derivatives such as anti-HIV agents,[2] radioimmunodiagnostic reactants[3] or contrasting agents in medical imagery. In the area of sensors and detectors, the attachment of PEO chains to redox probes, such as metal cyclam complexes, transforms these compounds, in the presence of an electrolyte, into an ionically conductive redox polymer solid or semi-solid phase.[4] The development of "solid state electrochemistry" could allow the electrochemical properties of cyclam derivatives to be explored under these conditions with a view to such applications. Encouraging examples in this area have been obtained with different metal complexes.[5] However, to our knowledge, no example in the case of cyclam derivatives has been reported. This is one of our goals in this domain.

Results and Discussion

We describe herein a specific synthetic strategy which appears to be necessary for the successful tetra- or mono-*N*-alkylation of 1,4,8,11-tetraazacyclotetradecane **(1)** (cyclam) by polyethylene (PEO) chains [$(CH_3)(OCH_2CH_2)_nO-$] (n = 3 or 7 on average). Although general methods for the mono-[6] and tetraalkylation[7] of cyclam are now widely developed, in the present work we show that in the case of PEO as the substituting agent, the preparation of stable derivatives appeared far from straightforward through a classical strategy.

Direct nucleophilic substitution of the tetramine by four equivalents of the activated tosylate PEO derivative led to a complex mixture from which the tetraalkylated derivative was obtained in a poor yield, together with decomposition products.[8] The reaction of the same PEO/tosylate derivative with the phosphoryl triprotected cyclam derivative **2** (cyclam−PO)[6] gave the mono-*N*-substituted derivative **3** in 41% yield (Scheme 1). The nickel(II) complex of this ligand could be obtained by a classical metallation procedure.[9] Cyclic voltammetry in a CH_3CN solution showed that the complex is unstable, and ^{13}C NMR spectroscopy showed an α-N chain cleavage.

Such cleavage of the linking ethylene moiety has already been described.[10] The introduction of a spacing propylene $-(CH_2)_3-$ group between the cyclam probe and the PEO chain is a better mode of stabilisation than the previous one.[11] On this basis the direct synthesis of the tetra PEO substituted cyclam **5** has been realised via the tetra-(hydroxypropyl) derivative **4** (Scheme 2).[12]

However no complexation reaction by nickel(II) was observed under the usual metallation conditions.[9] This is due to the fact that tetra-*N*-alkylation of the cyclam macrocycle considerably decreases the thermodynamic stability of the metal complexes.[13] Moreover the presence of four PEO chains may have a "wrapping" effect around the N_4 coordination site, which is likely to induce a decrease of the kinetics of the metallation. For this reason, although compound **5** might be considered as potentially interesting, the goal was restricted to the mono-*N*-alkylation of cyclam. The direct condensation of the tosylated PEO derivative on the mono-(hydroxypropyl) phosphoryl protected cyclam **7** also failed (Scheme 3).

This is due to the lack of reactivity of the hydroxylated derivative **7** towards the PEO-Tos, while a longer than normal reaction time led to decomposition by hydrolysis of the tosylated derivative.[14]

All these results emphasise the difficulties associated with the alkylation of cyclam by PEO chains. Previous observations have led us to develop a new general strategy

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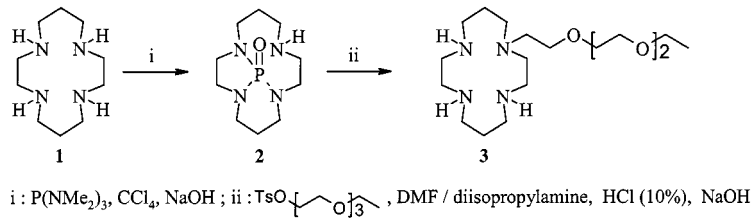
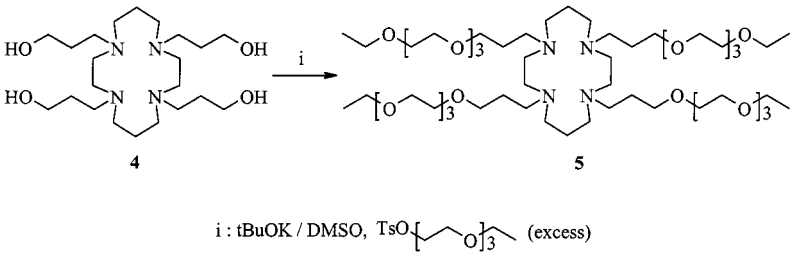
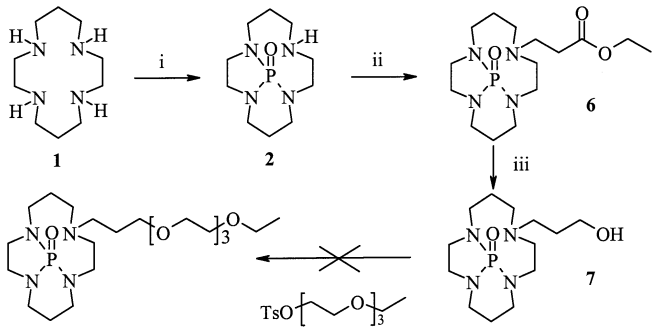


Scheme 1. Direct synthesis of the PEO mono-tagged cyclam **3**

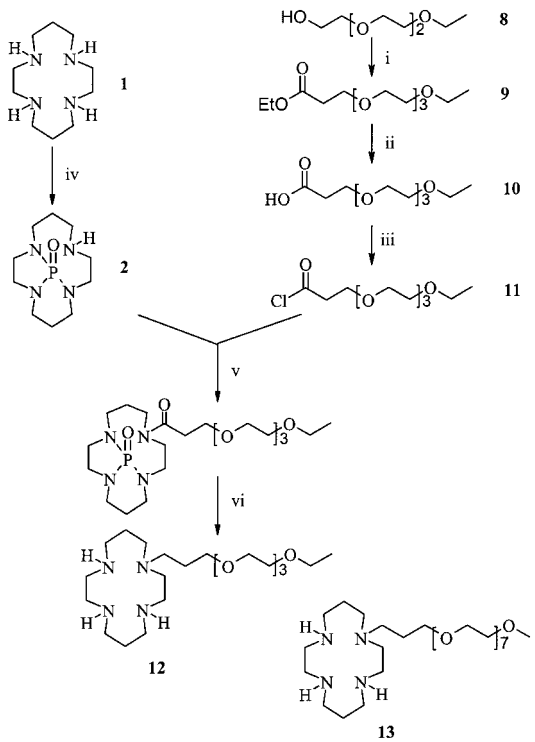


Scheme 2. Synthesis of the tetra-PEO-cyclam **5** with a propyl spacer arm



Scheme 3. Synthetic strategy for PEO mono-tagged cyclam with a propyl spacer arm

centred on the preparation of PEO mono-tagged cyclams. This synthesis is summarised in Scheme 4. The strategy was based on the preliminary modification of the PEO chain itself instead of the cyclam **1**. The introduction of the spacing link into the glycol derivative **8** is realised through a Michael addition with ethyl acrylate. Saponification of the ester derivative **9** was done by treatment with aqueous KOH solution at room temperature to prevent retro-Michael reaction. The carboxylic acid derivative **10** was isolated from hydrochloric acid solution and addition of oxalyl chloride gave rise to the acid chloride intermediate **11**, which is much more reactive than the corresponding tosylate. Reaction of **11** with cyclam−PO in the presence of triethylamine followed by reduction by borane-methylsulfide complex and acid hydrolysis resulted in the formation of **12**. This strategy revealed its efficiency since it also enabled the formation of the equivalent derivative **13** with n = 7 (on average). These compounds were obtained in 48% and 22% yield for **12** and **13**, respectively. They were fully characterised by ^{1}H and ^{13}C NMR spectroscopy, ACPI mass spectrometry and elemental analysis.



Scheme 4. Synthesis of PEO mono-tagged cyclams with a propyl spacer arm **12** and **13**

These two ligands, **12** and **13**, were complexed by stoichiometric reaction with $Ni(BF_4)_2$ in methanol. Addition of one equivalent of the metallic cation results in the observation of the maximum of the UV/visible absorption band of the complex (λ = 454 nm). Preliminary electrochemical measurements in CH_3CN, Bu_4NPF_6 revealed essentially irreversible oxidation and reduction processes for both

complexes of Ni^{II} (Table 1). The irreversibility of the systems can be ascribed both to the reactivity of the redox product and to the modification of the coordination of the metal associated with the redox processes, especially in the case of oxidation. Complexes of both ligands **12** and **13** gave the same results: the change in the chain length (from 3 to 7) does not seem to affect to a great extent the electrochemical behaviour. Work is in progress for further characterisation of these and other metal complexes.

As a conclusion, we have shown that classical direct procedures for the alkylation by PEO chains are unsuitable. We have reported an alternative synthetic route leading to stable PEO-tagged cyclam ligands with a stabilising propyl link and their nickel derivatives. This procedure allows one to enlarge the exploitation of the properties of cyclam derivatives in the diverse area that the attachment of PEO chains to this class of molecules promotes.

Experimental Section

General: All ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 300 spectrometer (75.47 MHz for C) or a Bruker AMX3 400 spectrometer (100.62 MHz for C), chemical shifts are given in ppm downfield from external TMS. ^{31}P NMR spectra were recorded on a Bruker AC 300 spectrometer (121.49 MHz), chemical shifts are given in ppm downfield from external 85% H_3PO_4. Mass spectra were measured on a Navigator Finnigan ($APCI^+$). Infrared spectra were obtained on a Perkin−Elmer 1430 spectrophotometer.

All the reactions were run under nitrogen with freshly distilled and dried solvents.

Synthesis of Triethylene Glycol Monoethyl Ether *p*-Tosylate: Tri(ethylene glycol) monoethyl ether (11 mmol) in pyridine (2 mL) was added to an ice-cooled solution of tosyl chloride in pyridine (6 mL). The mixture was allowed to stir at room temperature for two hours. After cooling, concentrated sulfuric acid was added dropwise at 0°C down to pH = 1. The tosylate derivative was extracted with dichloromethane (3 × 20 mL) and isolated as a colourless oil in 97% yield. ^1H NMR ($CDCl_3$): δ = 1.20 (t, J_{HH} = 7.0 Hz, 3 H, CH_3CH_2O), 2.44 (s, 3 H, $CH_3C_6H_4$), 3.51 (q, J_{HH} = 7.0 Hz, 2 H, CH_3CH_2O), 3.55−3.61 (m, 8 H, CH_2O), 3.68 (t, J_{HH} = 4.8 Hz, 2 H, $OCH_2CH_2OSO_2$), 4.15 (t, J_{HH} = 4.8 Hz, 2 H, $OCH_2CH_2OSO_2$), 7.33 (d, J_{HH} = 8.1 Hz, 2 H, *H* arom.), 7.79 (d, J_{HH} = 8.1 Hz, 2 H, *H* arom.). − ^{13}C NMR ($CDCl_3$): δ = 14.9 (CH_3CH_2O), 21.3 ($CH_3C_6H_4$), 66.3, 68. 3, 69.1, 69.5, 70.2, 70.3, 70.4 (CH_2O), 127.7, 129.6, 132.7, 144.6 (*C* arom.)

Synthesis of 1-(3,6,9-Trioxaundecanyl)-1,4,8,11-tetraazacyclotetradecane (3): A mixture of cyclam phosphoryl (1 mmol), diisopropylamine (1 mmol) and triethylene glycol monoethyl ether *p*-tosylate (1 mmol) in DMF (10 mL) was heated to 100°C for 4 hours. The solvent was removed under reduced pressure and the residue was dissolved in 4M hydrochloric solution (10 mL) and stirred at room temperature overnight. The acidic solution was washed with dichloromethane (2 × 10 mL) and was made strongly basic with NaOH pellets. The crude product was extracted with dichloromethane (3 × 20 mL) and purified by addition of hydrochloric acid in ethanol solution. The tetrahydrochloride salt precipitated and was washed with ethanol. The white solid was then dissolved in 4M NaOH solution and extracted with dichloromethane to yield **3** as an oil in 41% yield. ^1H NMR ($CDCl_3$): δ = 1.20 (t, J_{HH} = 7.0 Hz, 3 H, CH_3CH_2O), 1.81 (m, 4 H, CH_2CH_2N), 2.52−2.83 (m, 18 H, CH_2N), 3.50−3.71 (m, 12 H, CH_2O). − ^{13}C NMR ($CDCl_3$): δ = 14.8 (CH_3CH_2O), 25.8, 28.1 (CH_2CH_2N), 47.1, 47.5, 48.3, 48.9, 49.4, 50.7, 51.6, 54.1, 54.9 (CH_2N), 66.3, 68.7, 69.5, 70.1, 70.3 (CH_2O).

Synthesis of 1,4,8,11-Tetra-(hydropropyl)-1,4,8,11-tetraazacyclotetradecane (4): A mixture of cyclam (5 mmol), Na_2CO_3 (30 mmol) and 3-bromo-1-propanol (22 mmol) in DMF (20 mL) was heated to 100°C for 12 hours. The solvent was removed under reduced pressure, dichloromethane (10 mL) was added and Na_2CO_3 was eliminated by filtration. The solvent was evaporated and the crude product was recrystallised in acetone. White crystals were isolated in 28% yield. ^1H NMR ($CDCl_3$): δ = 1.74 (m, 12 H, CH_2CH_2N), 2.41−2.53 (m, 24 H, CH_2N), 3.73(t, J_{HH} = 6.2 Hz, 8 H, CH_2OH), 4.91 (s, 4 H, CH_2OH). − ^{13}C NMR ($CDCl_3$): δ = 24.1 (CH_2CH_2N), 28.2 ($NCH_2CH_2CH_2OH$), 49.8, 50.6, 51.1 (CH_2N), 60.7 (CH_2OH).

Synthesis of 1,4,8,11-Tetra-(4,7,10,13-tetroxapentadecanyl)-1,4,8,11-tetraazacyclotetra decane (5): A mixture of tetra(hydroxypropyl)cyclam (1 mmol), *t*BuONa (12 mmol) and triethylene glycolmonoethyl ether *p*-tosylate (11 mmol) in DMSO (15 mL) was stirred at room temperature for 24 hours. The solvent was removed under reduced pressure, acetone (15 mL) was added and, after cooling, the excess of tosylate precipitated. The filtrate was evaporated, the residue was dissolved in 4M NaOH solution and the basic solution was extracted with dichloromethane (3 × 20 mL). The solvent was evaporated and compound **5** was isolated as an oil in 21% yield. ^1H NMR ($CDCl_3$): δ = 1.12 (t, J_{HH} = 7.0 Hz, 12 H, CH_3CH_2O), 1.53 (m, 12 H, CH_2CH_2N), 2.12−2.45 (m, 24 H, CH_2N), 3.36−3.48 (m, 64 H, CH_2O). − ^{13}C NMR ($CDCl_3$): δ = 14.3 (CH_3CH_2O), 26.6, 28.4 (CH_2CH_2N), 50.1, 50.5, 51.1 (CH_2N), 60.1, 65.6, 68.7, 68.8, 69.1, 69.5, 69.6, 70.1 (CH_2O)

Synthesis of *N*-(ethyloxypropionyl)cyclam Phosphoryl (6): Cyclam phosphoryl (1 mmol), ethanol (20 mL) and ethylacrylate (1.2 mmol) were refluxed for 24 hours. The excess ethylacrylate and solvent was evaporated and compound **6** was isolated as an oil in 100% yield. ^{31}P NMR ($CDCl_3$): δ = 26.1. − ^{13}C NMR ($CDCl_3$): δ = 13.9 (CH_3CH_2OCO), 21.9, 25.6 (CH_2CH_2N), 32.1 (CH_2CO_2Et), 40.4, 41.4, 41.6, 44.0 (d, J_{PC} = 15.4 Hz), 45.2 (d, J_{PC} = 11.2 Hz), 48.3, 51.1, 51.6, 52.5 (CH_2N), 60.0 ($CO_2CH_2CH_3$), 172.2 (*C*O).

Synthesis of *N*-(3-hydroxypropyl)cyclam Phosphoryl (7): Compound **6** (1 mmol) was dissolved in THF (50 mL). The solution was cooled to 0°C and $LiAlH_4$ (1.2 mmol) was added. The mixture was stirred for two hours at room temperature. The excess $LiAlH_4$ was hydrolysed by addition of water and NaOH (15%). The mixture was filtered and the residue was washed with THF. The filtrate was dried with $MgSO_4$ and the solvent was evaporated. Compound **7** was isolated as an oil in 77% yield. ^{31}P NMR ($CDCl_3$): δ = 26.5. − ^{13}C NMR ($CDCl_3$): δ = 21.9, 26.4, 30.2 (d, J_{PC} = 5.3 Hz, CH_2CH_2N), 41.7, 41.9, 42.5, 44.2 (d, J_{PC} = 11.2 Hz), 46.0 (d, J_{PC} = 15.4 Hz), 51.4, 52.1, 53.3, 52.5 (CH_2N), 61.6 (CH_2OH).

Synthesis of Ethyl 4,7,10,13-Tetroxapentadecanoate (9): Triethylene glycol monoethyl ether **(8)** (5 g, 28 mmol) was dissolved in toluene (50 mL) and dried by azeotropic distillation. After removal of the solvent under reduced pressure, ethanol (5 mL), ethyl acrylate (34 mmol) and a catalytic amount of sodium ethoxide were added. The mixture was refluxed for 48 hours. After cooling, solvent and the excess ethyl acrylate were evaporated to yield the ester as an oil in 94% yield. IR (KBr): ν_{CO} = 1740 cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 1.18 (t, J_{HH} = 7.0 Hz, 3 H, CH_3CH_2O), 1.24 (t, J_{HH} = 7.0 Hz, 3 H, $COOCH_2CH_3$), 2.57 (t, J_{HH} = 6.5 Hz, 2 H, CH_2COO), 3.50 (q, J_{HH} = 7.0 Hz, 2 H, CH_3CH_2O), 3.63 (m, 12 H, CH_2O), 3.73 (t,

J_{HH} = 6.5 Hz, 2 H, OCH_2CH$_2$COO), 4.12 (q, J_{HH} = 7.0 Hz, 2 H, COOCH_2CH$_3$). – ^{13}C NMR ($CDCl_3$): δ = 13.8 (COOCH$_2$*C*H$_3$), 14.7 (*C*H$_3$CH$_2$O), 34.7 (*C*H$_2$COO), 60.0 (COO*C*H$_2$CH$_3$), 61.1, 66.2, 69.4, 69.9, 70.2, 72.2 (*C*H$_2$O), 171.2 (*C*O).

4,7,8,13-Tetroxapentadecanoïc acid (10): Ethyl 4,7,10,13-tetroxapentadecanoate (1.34 g, 4.8 mmol) was allowed to stir at room temperature in 10% aqueous potassium hydroxide solution (10 mL) for 24 hours. The mixture was washed with dichloromethane (2 × 20 mL). The aqueous solution was made strongly acidic by addition of concentrated hydrochloric acid and finally extracted with dichloromethane (3 × 20 mL) to yield the carboxylic acid as an oil in 96% yield. IR (KBr): ν_{CO} = 1735 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 1.18 (t, J_{HH} = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 2.60 (t, J_{HH} = 6.3 Hz, 2 H, C*H*$_2$COOH), 3.54 (q, J_{HH} = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 3.61 (m, 12 H, C*H*$_2$O), 3.72 (t, J_{HH} = 6.3 Hz, 2 H, OC*H*$_2$CH$_2$COOH), 10.32 (s, 1 H, COO*H*). – ^{13}C NMR ($CDCl_3$): δ = 14.7 (*C*H$_3$CH$_2$O), 34.5 (*C*H$_2$COOH), 66.1, 66.2, 69.4, 70.0, 70.1 (*C*H$_2$O), 175.1 (*C*O).

Synthesis of 4,7,10,13-Tetroxapentadecanoyl Chloride (11): An excess of oxalyl chloride (4 mmol) was added to a solution of 4,7,8,13-tetroxapentadecanoic acid (2 mmol) in dichloromethane (5 mL). The mixture was allowed to stir at room temperature overnight. After removal of the solvent and the excess oxalyl chloride, the product was isolated as an oil and used as such in the next step. IR (KBr): ν_{CO} = 1800 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 1.20 (t, J_{HH} = 7.0 Hz, 3 H, CH_3CH_2O), 3.13 (t, J_{HH} = 5.9 Hz, 2 H, CH_2COCl), 3.52 (q, J_{HH} = 7.0 Hz, 2 H, CH_3CH_2O), 3.65 (m, 12 H, CH_2O), 3.79 (t, J_{HH} = 5.9 Hz, 2 H, OCH_2CH_2COCl). – ^{13}C NMR ($CDCl_3$): δ = 15.1 (CH_3CH_2O), 47.2 (CH_2COCl), 65. 7, 66.4, 69.6, 70.2, 70.3, 70.4, 70.5 (CH_2O), 171.7 (CO).

Synthesis of 1-(4,7,10,13-Tetroxapentadecyl)-1,4,8,11-tetraazacyclotetradecane (12): A solution of cyclam phosphoryl (1 mmol, 245 mg) in THF (25 mL) was cooled to −30°C and a solution of butyllithium (1 mmol) in THF was added. Ten minutes later, 4,7,10,13-tetroxapentadecanoyl chloride in THF (5 mL) was added dropwise. The mixture was warmed up to room temperature and stir for 3 hours. After evaporation to dryness and addition of water (5 mL), the solution was extracted with dichloromethane (3 × 20 mL) to yield the *N*-acylated product as an oil in 98% yield. IR (KBr): ν_{CO} = 1650 cm^{-1}. – ^{31}P NMR ($CDCl_3$): δ = 24.8. – ^{13}C NMR ($CDCl_3$): δ = 14.3 (*C*H$_3$CH$_2$O), 21.0, 25.2 (*C*H$_2$CH$_2$N), 33.7 (*C*H$_2$CON), 40.2, 41.3, 42.2, 43.6 (d, J_{PC} = 10.7 Hz), 44.3 (d, J_{PC} = 15.1 Hz), 47.7, 48.6, 48.9 (*C*H$_2$N), 65.5, 66.6, 68.8, 69.4(2C), 69.5(2C), 69.6 (*C*H$_2$O), 172.3 (*C*O).

The borane dimethylsulfide complex (4 mmol) in THF (8 mL) was added dropwise to a solution of *N*-acylated product (1 mmol) in THF (20 mL). The mixture was refluxed for 48 hours. After cooling, the reaction was quenched by dropwise addition of methanol and the solvents were evaporated. The residue was then refluxed in 4M hydrochloric acid solution (10 mL) overnight. After cooling, the acid solution was washed by dichloromethane (2 × 20 mL), made strongly basic by addition of NaOH pellets and finally extracted with dichloromethane (3 × 20 mL). The crude product was purified by column chromatography on silica gel with an elution mixture ($CHCl_3$/CH_3OH/concentrated NH_4OH, 2:2:1) to yield the cyclam−PEO as a colourless oil in 48% yield. APCIMS $[M + H]^+$ = 419.5. – ^{1}H NMR ($CDCl_3$): δ = 1.13 (t, J_{HH} = 7.0 Hz, 3 H, C*H*$_3$CH$_2$O), 1.64−1.78 (m, C*H*$_2$CH$_2$N), 2.48−2.83 (m, 18 H, C*H*$_2$N), 3.43 (q, J_{HH} = 7.0 Hz, 2 H, CH$_3$C*H*$_2$O), 3.46−3.57 (m, 14 H, C*H*$_2$O), 4.81 (m, 3 H, N*H*). – ^{13}C NMR ($CDCl_3$): δ = 14.1 (*C*H$_3$CH$_2$O), 23.9, 24.3, 25.7 (*C*H$_2$CH$_2$N), 45.6 (2C), 46.8, 47.0, 47.8, 47.9, 49.0, 51.4, 51.6 (*C*H$_2$N), 65.1, 67.9, 68.5, 68.7, 69.2(3C), 69.3 (*C*H$_2$O). – $C_{21}H_{46}N_4O_4 \cdot 3H_2O$ (472.67): calcd. C 53.35, H 11.09, N 11.86; found C 53.77, H 9.75, N 11.19.

Synthesis of Long Chain Cyclam-PEO Derivative (13): Using poly(ethylene glycol) methyl ether (average $M_n \approx 350$) and the same procedure as for **12**, compound **13** was isolated as a colourless oil with 22% yield. APCIMS $[M + H]^+$ = 449.5 to 757.5 mass distribution (average 7 repeat units). – ^{1}H NMR ($CDCl_3$): δ = 1.72−1.92 (m, 6 H, C*H*$_2$CH$_2$N), 2.61−3.02 (m, 18 H, C*H*$_2$N), 3.35 (s, 3 H, C*H*$_3$O), 3.48−3.63 (m, 34 H, C*H*$_2$O), 4.53 (s, 3 H, N*H*). – ^{13}C NMR ($CDCl_3$): δ = 23.5, 24.3, 25.1 (*C*H$_2$CH$_2$N), 45.3, 45.4, 46.6, 47.1, 47.7, 48.0, 48.8, 50.9, 51.7 (*C*H$_2$N), 57.8 (*C*H$_3$O), 67.9, 68.8, 69.3 (2C), 69.4 (9C), 70.7 (2C) (*C*H$_2$O). – $C_{28}H_{60}N_4O_8 \cdot 3H_2O$ (634.85): calcd. C 52.97, H 10.48, N 8.83; found C 52.96, H 9.71, N 8.22.

Synthesis of Nickel Complexes: Cyclam-PEO ligand (0.5 mmol) was dissolved in methanol (5 mL) and a stoichiometric amount of $Ni(BF_4)_2$ was added. The mixture was refluxed for 30 minutes. The solvent was removed under reduced pressure, the oily residue dissolved in dichloromethane (10 mL) and cooled overnight. A small amount of precipitate was removed by filtration and the filtrate was evaporated to dryness to yield the nickel complex as a pale orange solid.

[Ni(12)](BF$_4$)$_2$: UV (CH_3OH, λ_{max}): 454 nm. – $C_{21}H_{46}N_4O_4NiB_2F_8 \cdot 5H_2O$ (741.01): calcd. C 34.03, H 7.61, N 7.56, Ni 7.92; found C 34.23, H, 7.33, N 7.60, Ni, 7.50.

[Ni(13)](BF$_4$)$_2$: UV (CH_3OH, λ_{max}): 461 nm. – $C_{28}H_{60}N_4O_8NiB_2F_8 \cdot 2H_2O$ (849.51): calcd. C 39.58, H 7.59, N 6.60, Ni 6.91; found C 39.73, H 7.11, N 6.34, Ni 6.27.

Table 1. Electrochemical data for Cyclam-PEO complexes[a]

Nickel complexes	[Ni·Cyclam](BF$_4$)$_2$	[Ni·**12**](BF$_4$)$_2$	[Ni·**13**](BF$_4$)$_2$
M^{III}/M^{II}	E'° = 0.64 (80)	Ep_a = 0.98	Ep_a = 0.89
M^{II}/M^{I}	E'° = −1.80 (80)	Ep_c = −1.56	Ep_c = −1.66

[a] Obtained by conventional methods[15] by cyclic voltammetry in CH_3CN + Bu_4NPF_6; Pt electrode; 100 mV·s^{-1}; E'° (V) = 0.5(Ep_a + Ep_c), $\Delta Ep = Ep_a - Ep_c$ (mV), Ep_c or Ep_a (V) = cathodic or anodic peak potential for irreversible systems; potentials *vs* Fc^+/Fc.

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