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Synthesis and Complexation Studies of Optically Active Aza- and Diazacrown Ethers Containing a Pyrene Fluorophore Unit

Dávid Pál[1], Martin Gede[1], Ildikó Móczár[1], Péter Baranyai[2], Péter Bagi[1], Péter Huszthy[1*]

[1] Department of Organic Chemistry and Technology, Faculty of Chemical Technology and Biotechnology, Budapest University of Technology and Economics, P.O.B. 91, H-1521 Budapest, Hungary
[2] Department of Applied and Nolinear Optics, Institute of Solid State Physics and Optics, Wigner Research Center for Physics, Hungarian Academy of Sciences, P.O.B. 49, H-1525 Budapest, Hungary
[*] Corresponding author, e-mail: huszthy@mail.bme.hu

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Abstract

Novel enantiopure azacrown [(*R*,*R*)-**1** and (*S*,*S*)-**1**] and diazacrown [(*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4**] ethers containing a pyrene fluorophore unit and two phenyl groups at their chiral centers were obtained in multistep syntheses. The action of these chemosensors is based on the photoinduced electron transfer (PET) process, thus they show fluorescence enhancement in the presence of protonated primary amines and amino acid esters. Their recognition abilities toward the enantiomers of 1-phenylethylamine hydrogen perchlorate (PEA), 1-(1-naphthyl) ethylamine hydrogen perchlorate (NEA), phenylglycine methyl ester hydrogen perchlorate (PGME), and phenylalanine methyl ester hydrogen perchlorate (PAME) were examined in acetonitrile using fluorescence spectroscopy.

Keywords

molecular recognition, fluorescence, PET sensor, azacrown ether, chiral crown ether

1 Introduction

Host–guest molecular recognition of organic ammonium ions is important in a variety of processes such as the interaction of molecules bearing ammonium ions with protein receptors [1]. Our current research in molecular recognition focuses on the interactions of fluorescent optically active crown ethers with protonated chiral primary amines and amino acid esters. Discrimination of the enantiomers of biologically active primary amines, amino acids, and amino alcohols including neurotransmitters, vital α-amino acids, and active pharmaceutical ingredients is also of great importance because of the potentially diverse physiological effects of such species [2]. The sensing based on fluorescence is attractive due to the selectivity, high sensitivity and quick response time of fluorescence spectroscopy [3]. Great efforts have been made on the design, synthesis, and use of chiral fluorescent chemosensors [4–19]. The first use of photophysical techniques for elucidation of chiral recognition by crown ethers was reported in 1980 [20]. Since then, other optically active crown ethers containing different fluorophore units have been synthesized to this purpose, and their enantiomeric discrimination abilities toward the enantiomers of primary amines, amino acids, amino alcohols, and their derivatives were investigated [21, 22]. Some of them were tested with both protonated primary amines and amino acid esters [21–26].

Certain free fluorescent sensor molecules have poor fluorescence due to an efficient quenching process (photoinduced electron transfer, PET) in the excited state. Upon complexation with different cationic guests they show fluorescence enhancement, by this providing a very sensitive response to such analytes [27–37]. Using PET type fluorescent chemosensors is advantageous, because their behavior can be predicted; therefore, for example, guest-induced 'off–on' fluorescence is designable [27, 33]. These sensor molecules have a 'fluorophore–spacer–receptor' structure, in which distinct components perform each one of the necessary functions. The fluorophore unit is the site of excitation and emission, and the receptor unit is responsible for guest complexation. The spacer, which is often a short alkylene group, holds the fluorophore and receptor close to, but separate from, each other. Several host molecules

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possessing the modular structure referred above, among them crown ethers too, have been synthesized, and their selectivities for different metal ions or organic cations have been studied [27–37]. Some reported aza- and azathiacrown ethers contain a pyrene fluorophore unit attached by a methylene spacer to the nitrogen atom of the crown ether, which enables PET type fluorescence response in the presence of inorganic cations [38–42]. Optically active azacrown ether-based PET chemosensors having a modular structure and a binaphthyl chiral unit [43] or alkyl groups at their chiral centers [44] were also synthesized. Their enantiomeric recognition abilities toward chiral ammonium salts [43, 44] and potassium mandelate [44] were examined.

Considering these results, we designed and synthesized novel enantiopure azacrown [(*R*,*R*)-**1** and (*S*,*S*)-**1**] and diazacrown [(*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4**] ethers (Fig. 1) having phenyl groups at their stereogenic centers and a pyrene fluorescent signaling unit attached through a methylene bridge to the nitrogen atom of the macrocycles. Studies on the molecular recognition abilities of these fluorescent sensor molecules toward the enantiomers of protonated chiral primary amines and amino acid esters were performed in acetonitrile using fluorescence spectroscopy.

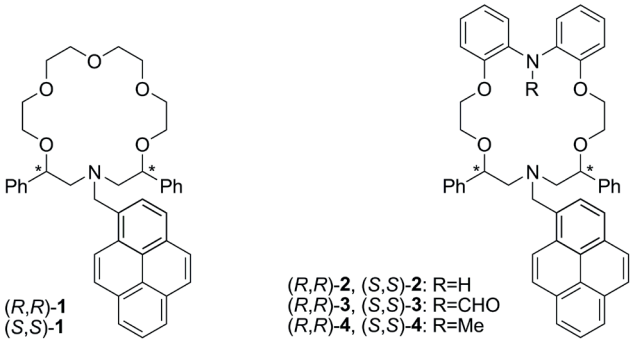


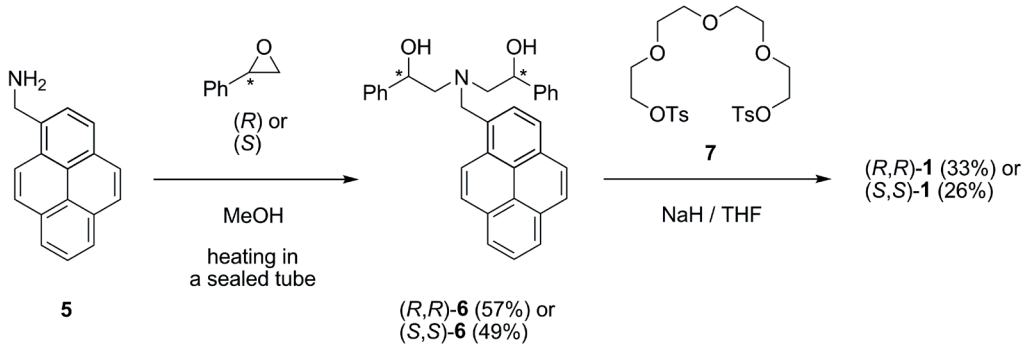
Fig. 1 Schematics of enantiopure aza- and diazacrown ethers containing a pyrene fluorophore unit

2 Results and discussion

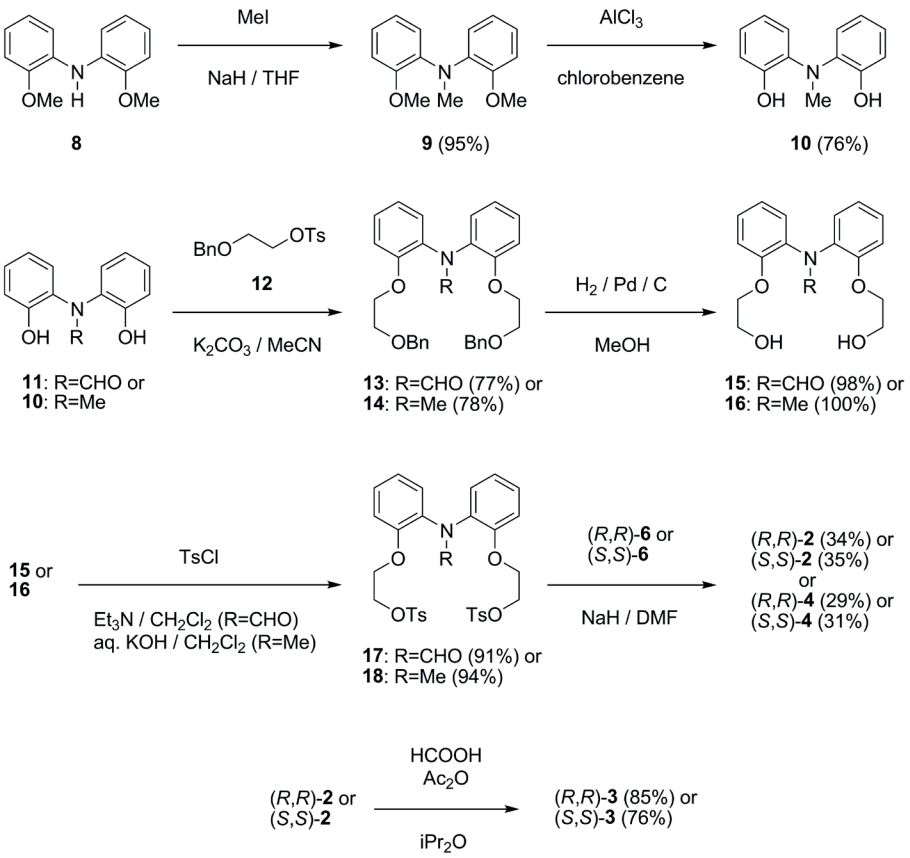
2.1 Synthesis

The synthesis of new azacrown ether derivatives (*R*,*R*)-**1** and (*S*,*S*)-**1** (Fig. 1) was carried out as outlined in Scheme 1. Pyren-1-ylmethanamine (**5**) [45] was heated with (*R*)-phenyloxirane and (*S*)-phenyloxirane in methanol in sealed tubes to give enantiopure aminodiols (*R*,*R*)-**6** and (*S*,*S*)-**6**, respectively. Azacrown ether derivatives (*R*,*R*)-**1** and (*S*,*S*)-**1** were prepared by a macrocyclization reaction starting from aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** and tetraethylene glycol ditosylate (**7**) [46] in THF using sodium hydride as a strong base.

The preparation of diazacrown ethers (*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4** is shown in Scheme 2. Bis(2-methoxyphenyl)amine (**8**) [47] was treated with methyl iodide in THF in the presence of sodium hydride to obtain *N*-methylated amine **9**. Diphenol **10** has already been synthesized, but not fully characterized [48, 49]. For the synthesis of diphenol **10**, selective *O*-demethylation of amine **9** was carried out with anhydrous aluminium chloride in chlorobenzene adopting the procedure [50] described for the synthesis of *N*-formyl analogue **11**. Diphenol derivatives **11** and **10** were reacted with benzyl protected ethylene glycol tosylate (**12**) [51] in acetonitrile using potassium carbonate to furnish formamide derivative **13** and tertiary amine **14**, respectively. Diols **15** and **16** were prepared from *O*-benzyl protected derivatives **13** and **14** by catalytic hydrogenolysis in methanol. Tosylation of diols **15** and **16** in dichloromethane gave ditosylates **17** and **18** in very good yields. Formamide derivative **15** was reacted in the presence of triethylamine as a base, while *N*-methyl derivative **16** was tosylated using aqueous potassium hydroxide. The macrocyclization reactions of ditosylates **17** and **18** with aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** were carried out in DMF in the presence of sodium hydride. The reactions of **17** rendered (*R*,*R*)-**2** and (*S*,*S*)-**2** due to deformylation. Sensor molecules (*R*,*R*)-**4** and (*S*,*S*)-**4** were



Scheme 1 Synthesis of sensor molecules (*R*,*R*)-**1** and (*S*,*S*)-**1**



Scheme 2 Synthesis of sensor molecules (*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4**

prepared from **18**. Formylation of (*R*,*R*)-**2** and (*S*,*S*)-**2** using a mixture of formic acid and acetic anhydride gave (*R*,*R*)-**3** and (*S*,*S*)-**3** successfully.

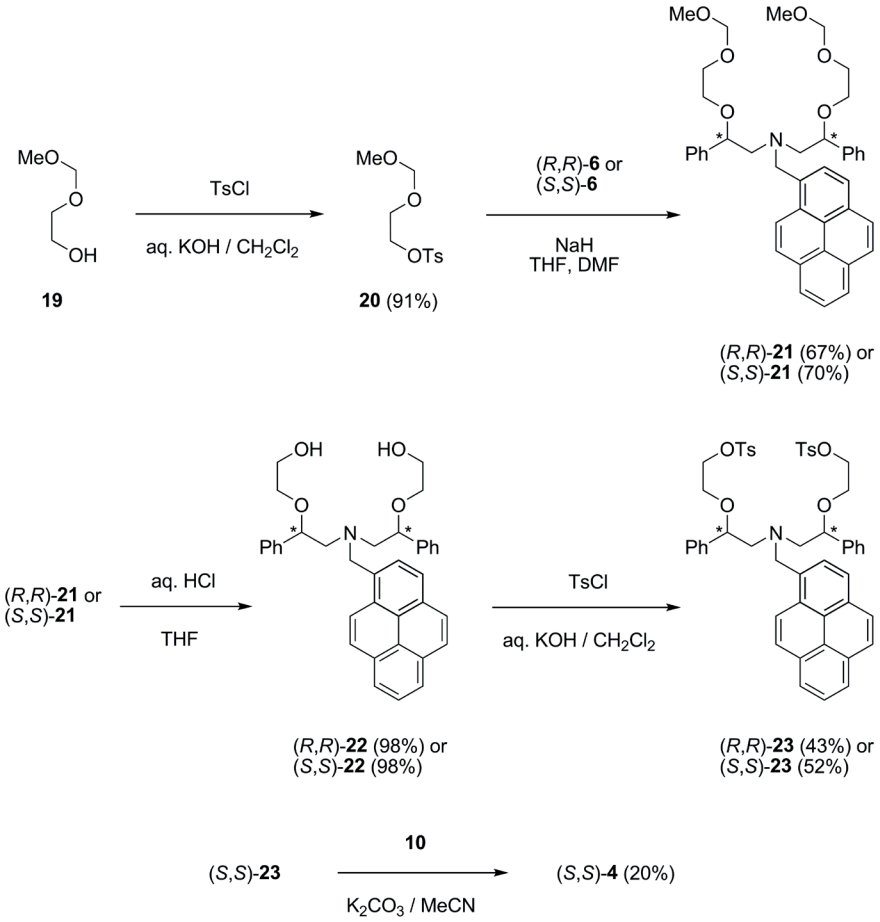
We worked out another route for the synthesis of diazacrown ether (*S*,*S*)-**4** through novel enantiopure precursors (Scheme 3), which can be useful for the preparation of enantioselective fluorescent sensor molecules. Methoxymethyl (MOM)-protected ethylene glycol **19** [52] was tosylated to obtain tosylate **20**. Reaction of the latter with enantiopure aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** was carried out in a mixture of THF and DMF using sodium hydride as a base to give MOM ethers (*R*,*R*)-**21** and (*S*,*S*)-**21**. The removal of the MOM protecting groups of (*R*,*R*)-**21** and (*S*,*S*)-**21** by aqueous hydrochloric acid in THF furnished diols (*R*,*R*)-**22** and (*S*,*S*)-**22**, which were transformed into their ditosylate derivatives (*R*,*R*)-**23** and (*S*,*S*)-**23**. *O*-Alkylation of diphenol derivative **10** with (*S*,*S*)-**23** in acetonitrile using potassium carbonate yielded macrocycle (*S*,*S*)-**4**.

2.2 Complexation studies

Azacrown ethers (*R*,*R*)-**1** and (*S*,*S*)-**1** and diazacrown ethers (*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4** (Fig. 1) have a modular (fluorophore–methylene spacer–receptor) structure, thereby PET type fluorescence response was expected upon complex formation with various chiral primary ammonium salts. It means that the free sensor molecule has strongly reduced fluorescence due to a quenching process (PET) in the excited state directed from the donor nitrogen atom of the crown ether to the acceptor fluorophore unit. Conversely, coordination of a cation decreases the electron donating ability of the nitrogen atom, which induces a significant fluorescence enhancement without spectral shifts.

Crown ethers (*R*,*R*)-**1**–(*R*,*R*)-**4** and (*S*,*S*)-**1**–(*S*,*S*)-**4** have phenyl substituents at their chiral centers. Besides the other aromatic moieties in the receptors, these phenyl substituents can also participate in π–π interactions with the aromatic units and carbonyl groups of the ammonium cation guests or lone pair–π interactions with the carbonyl groups of amino acid esters [53, 54].

The recognition abilities of these ligands toward the enantiomers of 1-phenylethylamine hydrogen perchlorate (PEA), 1-(1-naphthyl)ethylamine hydrogen perchlorate (NEA), phenylglycine methyl ester hydrogen perchlorate (PGME), and phenylalanine methyl ester hydrogen perchlorate (PAME) (Fig. 2) were studied in acetonitrile by UV–vis and fluorescence spectroscopies.



Scheme 3 Synthesis of enantiopure compounds containing a pyrene fluorophore

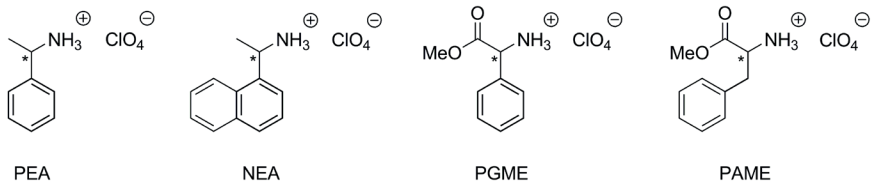


Fig. 2 Schematics of chiral primary ammonium salts used in the enantiomeric recognition studies

The absorption spectra of azacrown ethers (*R*,*R*)-**1** and (*S*,*S*)-**1** showed very small changes upon addition of the chiral primary ammonium salts. During the titrations of diazacrown ethers (*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4** with these chiral guests, small spectral changes could be observed (Fig. 3).

However, the addition of PEA, NEA, PGME, and PAME to sensor molecules (*R*,*R*)-**1**–(*R*,*R*)-**4** and (*S*,*S*)-**1**–(*S*,*S*)-**4** resulted in large fluorescence enhancement (Fig. 4). In all cases, restoration of the pyrene fluorescence with emission bands at 378, 397, and 417 nm could be observed, because complexation of the chiral ammonium guests inhibited the PET quenching directed from the (trialkylamine type) nitrogen to the pyrene unit. Moreover, sensor molecules (*R*,*R*)-**2**, (*S*,*S*)-**2**, (*R*,*R*)-**4**, and (*S*,*S*)-**4** showed decreases in their broad emission band above 450 nm upon complexation (Figs. 4B, D). This band, which was much more pronounced in the cases of ligands (*R*,*R*)-**2** and (*S*,*S*)-**2**, can be attributed to the emission of an intramolecular exciplex formed by the pyrene–diphenylamine interaction.

All the fluorescence spectral changes were evaluated using global nonlinear regression analysis. The titration series of spectra could be fitted satisfactorily for 1:1 complex formation, and the stability constants (Table 1) as well as the degrees of enantiomeric differentiation (Table 2) were calculated.

The results in Table 1 show that macrocycles (*R*,*R*)-**1**–(*R*,*R*)-**4** and (*S*,*S*)-**1**–(*S*,*S*)-**4** form thermodynamically

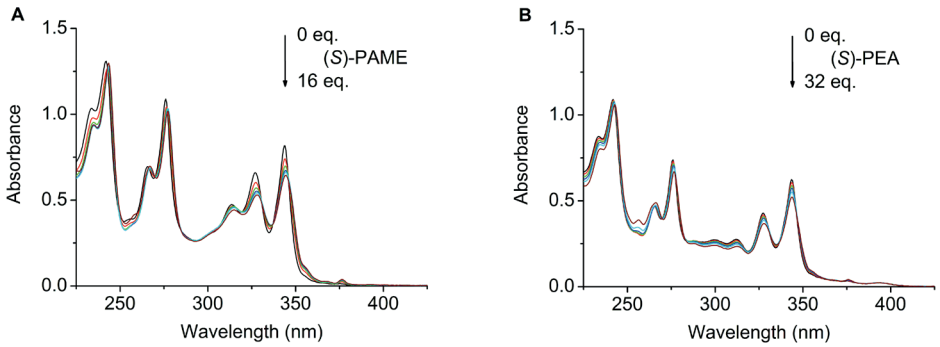


Fig. 3 Series of absorption spectra upon titration of (*S*,*S*)-**2** (20 μM) with (*S*)-PAME (0, 0.5, 1, 2, 4, 16 equiv.) (**A**), (*R*,*R*)-**4** (20 μM) with (*S*)-PEA (0, 1, 4, 8, 16, 32 equiv.) (**B**) in MeCN

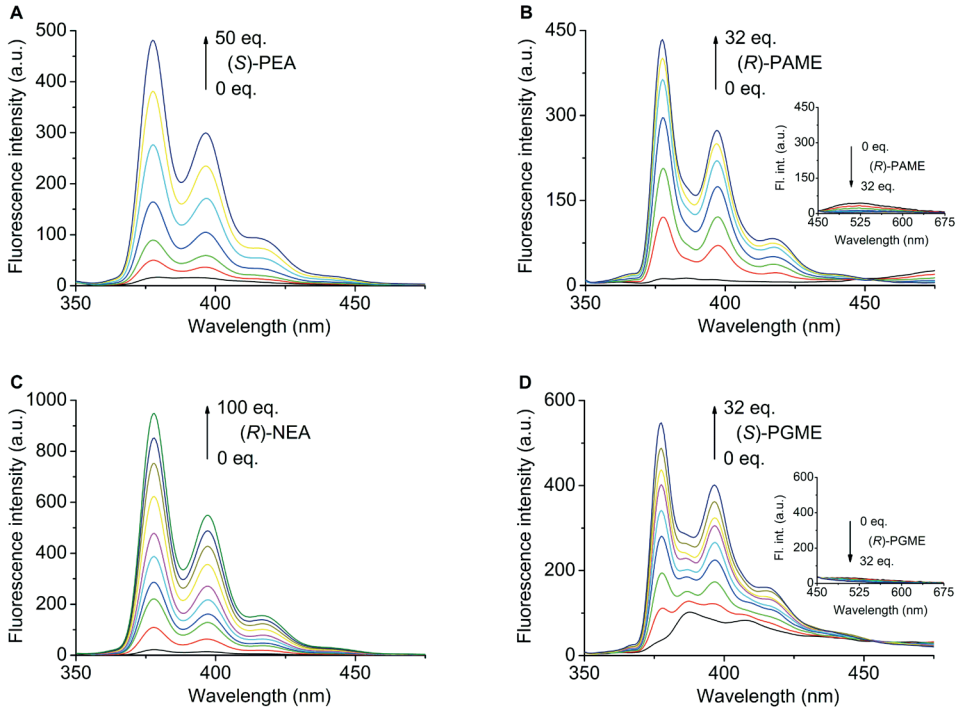


Fig. 4 Series of fluorescence emission spectra upon titration of (*S*,*S*)-**1** (20 μM) with (*S*)-PEA (0, 0.1, 0.4, 1, 4, 8, 50 equiv.) (**A**), (*S*,*S*)-**2** (20 μM) with (*R*)-PAME (0, 0.25, 0.5, 1, 2, 7, 32 equiv.) (**B**), (*S*,*S*)-**3** (20 μM) with (*R*)-NEA (0, 0.1, 0.5, 1, 1.5, 3, 8, 13, 33, 100 equiv.) (**C**), and (*S*,*S*)-**4** (20 μM) with (*S*)-PGME (0, 0.25, 0.5, 0.75, 1, 1.5, 2, 7, 32 equiv.) (**D**) in MeCN, λ_{ex} = 344 nm

stable complexes with chiral primary ammonium cations. The strongest binding of the enantiomers of PEA was observed in the case of azacrown ethers (*R*,*R*)-**1** and (*S*,*S*)-**1** having a more flexible macroring. All the macrocycles formed more stable complexes with NEA than PEA. This can be explained by the presence of the extended aromatic system in the chiral ammonium salt resulting in larger π–π interaction between the host and guest. It can be seen that the stabilities of PGME and PAME complexes are higher than those of PEA and NEA complexes. Diazacrown ethers (*R*,*R*)-**3** and (*S*,*S*)-**3** formed significantly more stable complexes with protonated amino acid esters (PGME and PAME) than with protonated primary amines (PEA and NEA), which make them suitable for selective sensing the former type species (Fig. 5). It can be mentioned that other reported fluorescent optically active crown ethers, which were tested with these two types of guests, did not show such extent of difference in their binding affinities [21–26].

Dibenzo-diazacrown ethers (*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4** have a more rigid system compared to azacrown ethers (*R*,*R*)-**1** and (*S*,*S*)-**1**; therefore, the observation of their enantiomeric discrimination ability toward the enantiomers of the strongly bound primary ammonium

Table 1 Stability constants for complexes of (*R*,*R*)-**1**–(*R*,*R*)-**4** and (*S*,*S*)-**1**–(*S*,*S*)-**4** with the enantiomers of chiral primary ammonium salts in MeCN

	log *K*							
	(*R*,*R*)-**1**	(*S*,*S*)-**1**	(*R*,*R*)-**2**	(*S*,*S*)-**2**	(*R*,*R*)-**3**	(*S*,*S*)-**3**	(*R*,*R*)-**4**	(*S*,*S*)-**4**
(*R*)-PEA	4.86 ± 0.04	4.80 ± 0.03	3.10 ± 0.05	3.12 ± 0.06	3.83 ± 0.05	3.80 ± 0.05	4.07 ± 0.06	4.09 ± 0.04
(*S*)-PEA	4.90 ± 0.04	4.80 ± 0.04	3.18 ± 0.05	3.13 ± 0.07	3.79 ± 0.05	3.82 ± 0.05	4.12 ± 0.05	4.10 ± 0.03
(*R*)-NEA	4.93 ± 0.05	5.07 ± 0.03	3.37 ± 0.06	3.28 ± 0.07	4.01 ± 0.04	4.05 ± 0.04	4.93 ± 0.05	4.73 ± 0.04
(*S*)-NEA	5.01 ± 0.05	5.09 ± 0.04	3.42 ± 0.06	3.36 ± 0.06	4.08 ± 0.04	4.09 ± 0.04	4.85 ± 0.05	4.74 ± 0.04
(*R*)-PGME	6.21 ± 0.16	6.05 ± 0.18	4.90 ± 0.07	4.94 ± 0.11	6.48 ± 0.12	6.48 ± 0.10	5.10 ± 0.04	5.05 ± 0.03
(*S*)-PGME	6.14 ± 0.18	6.17 ± 0.17	4.95 ± 0.09	4.95 ± 0.08	6.43 ± 0.12	6.46 ± 0.10	5.03 ± 0.04	5.02 ± 0.03
(*R*)-PAME	6.25 ± 0.11	6.34 ± 0.13	4.75 ± 0.06	4.91 ± 0.08	6.26 ± 0.10	6.41 ± 0.08	5.05 ± 0.04	5.03 ± 0.04
(*S*)-PAME	6.27 ± 0.10	6.28 ± 0.14	4.86 ± 0.07	4.80 ± 0.08	6.25 ± 0.10	6.51 ± 0.07	5.11 ± 0.02	4.98 ± 0.04

Table 2 Degrees of enantiomeric discrimination of (*R*,*R*)-**1**–(*R*,*R*)-**4** and (*S*,*S*)-**1**–(*S*,*S*)-**4** toward the enantiomers of chiral primary ammonium salts in MeCN

	Δ log *K*[a]							
	(*R*,*R*)-**1**	(*S*,*S*)-**1**	(*R*,*R*)-**2**	(*S*,*S*)-**2**	(*R*,*R*)-**3**	(*S*,*S*)-**3**	(*R*,*R*)-**4**	(*S*,*S*)-**4**
(*R*)-PEA (*S*)-PEA	–0.04	0.00	–0.08	–0.01	0.04	–0.02	–0.05	–0.01
(*R*)-NEA (*S*)-NEA	–0.08	–0.02	–0.05	–0.08	–0.07	–0.04	0.08	–0.01
(*R*)-PGME (*S*)-PGME	0.07	–0.12	–0.05	–0.01	0.05	0.02	0.07	0.03
(*R*)-PAME (*S*)-PAME	–0.02	0.06	–0.11	0.11	0.01	–0.10	–0.06	0.05

[a] $\Delta \log K = \log K_{(R)} - \log K_{(S)}$

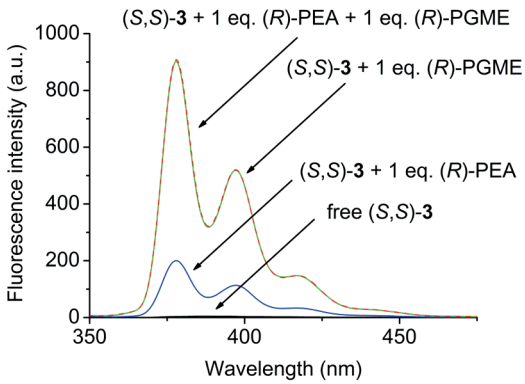


Fig. 5 Fluorescence emission spectra of free (*S*,*S*)-**3** (20 μM), with 1 equiv. of (*R*)-PEA, with 1 equiv. of (*R*)-PGME, and with 1 equiv. of (*R*)-PEA and 1 equiv. of (*R*)-PGME together in MeCN, λ_{ex} = 344 nm

salts was expected. Unfortunately, the sensor molecules revealed practically no enantiomeric recognition ability as the data in Table 2 show.

3 Conclusion

The synthesis and characterization of novel enantiopure fluorescent azacrown [(*R*,*R*)-**1** and (*S*,*S*)-**1**] and diazacrown [(*R*,*R*)-**2**–(*R*,*R*)-**4** and (*S*,*S*)-**2**–(*S*,*S*)-**4**] ethers, and their broadly applicable precursors have been performed. The complex formation of the eight chiral ligands with the enantiomers of PEA, NEA, PGME, and PAME was studied by fluorescence spectroscopy using acetonitrile as a solvent. The sensor molecules exhibited PET type fluorescence response in the presence of these primary ammonium salts as expected. Complexation of the chiral guests was accompanied with large fluorescence enhancement in all cases; however, the macrocycles showed no enantiomeric recognition ability. Diazacrown ethers (*R*,*R*)-**3** and (*S*,*S*)-**3** formed significantly more stable complexes with protonated amino acid esters (PGME and PAME) than with protonated primary amines (PEA and NEA), thus these ligands can be good candidates for selective sensing of guests of the former type.

4 Experimental

4.1 General

All reagents were purchased from Sigma–Aldrich Corporation unless otherwise noted. Compounds **7** [46], **8** [47], **11** [50], and **12** [51] were prepared as reported in the respective literature. All reactions were monitored

by TLC and visualized by UV lamp (254 nm). Silica gel 60 F_{254} (Merck) and aluminium oxide 60 F_{254} neutral type E (Merck) plates were used for TLC. Silica gel 60 PF_{254} (Merck) and aluminium oxide F_{254} type E (Merck) plates were used for preparative TLC. Silica gel 60 (70–230 mesh, Merck) and aluminium oxide (neutral, activated, Brockman I) were used for column chromatography. Ratios of solvents for the eluents are given in volumes (mL/mL). Solvents were dried and purified according to well established methods [55]. Evaporations were carried out under reduced pressure.

Melting points were taken on a Boetius micro-melting point apparatus and are uncorrected. Enantiomeric excess (ee) values were determined by chiral HPLC systems. Chiral separation of (*R*,*R*)-**1** and (*S*,*S*)-**1** enantiomers was carried out on an Agilent 1100 liquid chromatography system. Chromatographic analysis was performed using heptane–iPrOH 93:7 mixture as an eluent in isocratic elution (1.0 mL/min, 25 °C) on a Reprosil Chiral-MIA column (5 µm, 100 × 4.6 mm). Detector wavelength: 242 nm. Retention times: 4.8 min for (*R*,*R*)-**1** and 3.4 min for (*S*,*S*)-**1**. Chiral separation of (*R*,*R*)-**2**, (*S*,*S*)-**2**, (*R*,*R*)-**3**, (*S*,*S*)-**3**, (*R*,*R*)-**4**, and (*S*,*S*)-**4** enantiomers was carried out on a PerkinElmer Series 200 liquid chromatography system. Chromatographic analysis was performed using hexane–EtOH 85:15 mixture as an eluent in isocratic elution (0.8 mL/min, 20 °C) on a Phenomenex Lux® Cellulose-1 column (5 µm, 250 × 4.6 mm). Detector wavelength: 254 nm. Retention times: 11.4 min for (*R*,*R*)-**2**, 10.6 min for (*S*,*S*)-**2**, 15.8 min for (*R*,*R*)-**3**, 14.2 min for (*S*,*S*)-**3**, 7.6 min for (*R*,*R*)-**4**, and 6.9 min for (*S*,*S*)-**4**. Chiral separation of (*R*,*R*)-**6** and (*S*,*S*)-**6** enantiomers was carried out on a VWR-Hitachi LaChrom Elite® liquid chromatography system. Chromatographic analysis was performed using heptane–EtOH mixture as an eluent in gradient elution (5–45 % EtOH, 1.0 mL/min, 40 °C) on a Reprosil Chiral-MIA column (5 µm, 100 × 4.6 mm). Detector wavelength: 235 nm. Retention times: 7.7 min for (*R*,*R*)-**6** and 6.4 min for (*S*,*S*)-**6**. Optical rotations were taken on a Perkin–Elmer 241 polarimeter that was calibrated by measuring the optical rotations of both enantiomers of menthol. Infrared (IR) spectra were recorded on a Bruker Alpha-T FT-IR spectrometer. ^{1}H (500 MHz) and ^{13}C (125 MHz) NMR spectra were obtained on a Bruker DRX-500 Avance spectrometer. ^{1}H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were taken on a Bruker 300 Avance spectrometer. The signals of NH and OH protons in the ^{1}H NMR spectra were helped to identify by shaking the NMR samples with D_2O. Mass spectra (LC-MS) were recorded on an Agilent 1200 Series coupled Agilent 6130 Series Quadrupole spectrometer system in electrospray ionization (ESI) mode using water (1 % NH_4HCO_3) / acetonitrile (8 % water, 1 % NH_4HCO_3) as an eluent in gradient elution (5–100 % acetonitrile, 0.6 mL/min, 40 °C) on a Phenomenex Gemini NX-C18 column (3 µm, 110 Å, 150 × 3.0 mm). Elemental analyses were performed in the Microanalytical Laboratory of the Department of Organic Chemistry, Institute for Chemistry, L. Eötvös University, Budapest, Hungary.

UV–vis spectra were taken on a Unicam UV4-100 spectrophotometer. Quartz cuvettes with path length of 1 cm were used. Fluorescence emission spectra were recorded on a Perkin–Elmer LS 50B luminescent spectrometer and were corrected by the spectrometer software. Quartz cuvettes with path length of 1 cm were used. Enantiomers of PEA, NEA, PGME, and PAME were prepared in our laboratory [56]. The concentrations of sensor molecules were 0.2, 2 or 20 µM during the fluorescence titrations. Stability constants of the complexes were determined by global nonlinear regression analysis using SPECFIT/32™ software.

4.2 General procedure for the synthesis of sensor molecules (*R*,*R*)-1 and (*S*,*S*)-1

A suspension of NaH (51 mg, 1.3 mmol, 60 % dispersion in mineral oil) was stirred vigorously in pure and dry THF (0.5 mL) under Ar for 5 min. To this suspension was added slowly aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** (100 mg, 0.212 mmol) dissolved in pure and dry THF (2 mL). The mixture was stirred at rt for 10 min and at reflux temperature for 4 h. The mixture was cooled down to –60 °C, and tetraethylene glycol ditosylate **7** [46] (138 mg, 0.275 mmol) dissolved in pure and dry THF (3 mL) was added in 5 min. After addition of the ditosylate **7** the reaction mixture was allowed to warm up slowly to rt, and it was stirred at this temperature overnight. The solvent was evaporated, and the residue was dissolved in a mixture of EtOAc (10 mL) and brine (4 mL). The phases were shaken thoroughly and separated. The aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified first by column chromatography on alumina using EtOH–toluene 1:200 mixture as an eluent then by preparative TLC on silica gel using EtOAc–hexane 1:2 mixture as an eluent to give receptor (*R*,*R*)-**1** or (*S*,*S*)-**1** as yellow crystals.

4.2.1 (14*R*,18*R*)-14,18-Diphenyl-16-(pyren-1-ylmethyl)-1,4,7,10,13-pentaoxa-16-azacyclooctadecane [(*R*,*R*)-1]
Yield: 44 mg, 33 %; mp: 45–47 °C; R_f: 0.16 (silica gel TLC, EtOAc–hexane 1:2); ee > 99 %; $[\alpha]_D^{25}$ –23.5 (*c* = 1.00 in acetone); IR (neat) ν_{max} 3369 (br, complexed H_2O), 3077, 3052, 3028, 2862, 1602, 1586, 1491, 1451, 1417, 1348, 1296, 1245, 1097, 1022, 945, 842, 817, 754, 699, 644, 529 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 2.80–2.89 (m, 2H), 2.97 (s, complexed H_2O together with the H_2O content of acetone-d_6, 1H), 3.17–3.28 (m, 2H), 3.42–3.56 (m, 4H), 3.58–3.80 (m, 12H), 4.58 (s, 2H), 4.71–4.79 (m, 2H), 7.14–7.29 (m, 10H), 7.99–8.19 (m, 6H), 8.20–8.26 (m, 2H), 8.46 (d, *J* = 9 Hz, 1H); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 58.12, 61.33, 67.98, 70.48, 70.60, 70.66, 80.88, 124.39, 124.61, 124.75, 124.76, 124.81, 124.90, 125.91, 126.87, 126.88, 126.97, 127.21, 127.50, 128.07, 128.46, 129.88, 130.59, 131.04, 131.38, 133.87, 141.78; MS calcd for $C_{41}H_{43}NO_5$: 629.3, found $(M + H)^+$: 630.3; Anal. calcd for $C_{41}H_{43}NO_5 \cdot 0.5\ H_2O$: C 77.09, H 6.94, N 2.19, found: C 76.70, H 6.93, N 2.14.

4.2.2 (14*S*,18*S*)-14,18-Diphenyl-16-(pyren-1-ylmethyl)-1,4,7,10,13-pentaoxa-16-azacyclooctadecane [(*S*,*S*)-1]
Yield: 35 mg, 26 %; ee > 99 %; $[\alpha]_D^{25}$ +21.1 (*c* = 1.00 in acetone). Spectral data and other physical properties of macrocycle (*S*,*S*)-**1** were the same as those of macrocycle (*R*,*R*)-**1** reported above.

4.3 General procedure for the synthesis of sensor molecules (*R*,*R*)-2 and (*S*,*S*)-2
A suspension of NaH (102 mg, 2.55 mmol, 60 % dispersion in mineral oil) was stirred vigorously in pure and dry DMF (0.5 mL) under Ar for 5 min. To this suspension was added slowly aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** (200 mg, 0.424 mmol) dissolved in pure and dry DMF (2 mL) at –60 °C. The resulting mixture was stirred at 50 °C for 1 h. The mixture was cooled down to –60 °C, and ditosylate **17** (288 mg, 0.460 mmol) dissolved in pure and dry DMF (3.5 mL) was added in 5 min. After addition of the ditosylate **17** the reaction mixture was allowed to warm up slowly to rt, and it was stirred at this temperature overnight. The solvent was evaporated, and the residue was dissolved in a mixture of EtOAc (30 mL) and brine (10 mL). The phases were shaken thoroughly and separated. The aqueous phase was extracted with EtOAc (2 × 30 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on alumina using hexane saturated with acetonitrile as an eluent to give receptor (*R*,*R*)-**2** or (*S*,*S*)-**2** as whitish crystals.

4.3.1 (9*R*,13*R*)-9,13-Diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetra-oxa[7,16]diazacyclooctadecine [(*R*,*R*)-2]
Yield: 105 mg, 34 %; mp: 88–91 °C; R_f: 0.19 (alumina TLC, EtOAc–hexane 1:25); ee > 95 %; $[\alpha]_D^{25}$ –25.5 (*c* = 1.00 in acetone); IR (KBr) ν_{max} 3411 (br, complexed H_2O), 3085, 3056, 3036, 2924, 2866, 2808, 1601, 1588, 1522, 1495, 1452, 1433, 1346, 1285, 1247, 1204, 1156, 1117, 1053, 1041, 1023, 924, 848, 737, 701 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 2.83–2.91 (m, 2H), 2.86 (s, complexed H_2O, 2H), 3.37–3.45 (m, 2H), 3.72–3.83 (m, 4H), 4.19–4.31 (m, 4H), the benzylic type protons give an AB quartet: δ_A 4.52 and δ_B 4.55 (J_{AB} = 14 Hz, 2H), 4.85–4.91 (m, 2H), 6.88 (t, *J* = 8 Hz, 2H), 6.93–7.03 (m, 4H), 7.09 (s, 1H, NH, disappears after shaking the solution with D_2O), 7.12–7.20 (m, 6H), 7.24–7.32 (m, 4H), 7.49 (d, *J* = 8 Hz, 2H), 7.87 (d, *J* = 9 Hz, 1H), 7.95–8.09 (m, 5H), 8.12 (d, *J* = 8 Hz, 1H), 8.20 (d, *J* = 8 Hz, 1H), 8.35 (d, *J* = 9 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 58.30, 61.04, 67.42, 68.65, 81.52, 112.14, 115.09, 120.05, 120.84, 124.34, 124.42, 124.51, 124.63, 124.69, 124.82, 125.79, 126.71, 126.75, 126.90, 127.18, 127.44, 128.03, 128.17, 129.67, 130.46, 130.93, 131.28, 132.93, 133.68, 141.52, 148.41; MS calcd for $C_{49}H_{44}N_2O_4$: 724.3, found $(M + H)^+$: 725.3; Anal. calcd for $C_{49}H_{44}N_2O_4 \cdot H_2O$: C 79.22, H 6.24, N 3.77, found: C 79.11, H 6.31, N 3.73.

4.3.2 (9*S*,13*S*)-9,13-Diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetra-oxa[7,16]diazacyclooctadecine [(*S*,*S*)-2]
Yield: 108 mg, 35 %; ee > 99 %; $[\alpha]_D^{25}$ +25.9 (*c* = 0.99 in acetone). Spectral data and other physical properties of macrocycle (*S*,*S*)-**2** were the same as those of macrocycle (*R*,*R*)-**2** reported above.

4.4 General procedure for the synthesis of sensor molecules (*R*,*R*)-3 and (*S*,*S*)-3
To a stirred solution of (*R*,*R*)-**2** or (*S*,*S*)-**2** (50 mg, 0.069 mmol) in iPr_2O (2 mL) was added a mixture of HCOOH (0.30 mL, 0.37 g, 8.0 mmol) and Ac_2O (0.68 mL, 0.73 g, 7.2 mmol) dropwise. The reaction mixture was stirred at boiling temperature for 2 h and then it was allowed to cool down to rt. The volatile components were

removed, and the residue was dissolved in a mixture of 25 % aqueous Me_4NHCO_3 solution (5 mL) and EtOAc (10 mL) at 0 °C. The phases were shaken thoroughly and separated. The aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by preparative TLC on silica gel using EtOAc–hexane 1:3 mixture as an eluent to give receptor (*R*,*R*)-**3** or (*S*,*S*)-**3** as whitish crystals.

4.4.1 (9*R*,13*R*)-9,13-Diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetraoxa[7,16]diaza-cyclooctadecine-22-carbaldehyde [(*R*,*R*)-3]

Yield: 44 mg, 85 %; mp: 96–97 °C; R_f: 0.33 (silica gel TLC, EtOAc–hexane 1:3); ee > 99 %; $[\alpha]_D^{25}$ –118.5 (*c* = 0.64 in acetone); IR (KBr) ν_{max} 3085, 3060, 3032, 2926, 2869, 2809, 1688, 1596, 1499, 1451, 1332, 1272, 1244, 1103, 1045, 1021, 945, 917, 849, 751, 702 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 2.64–2.73 (m, 2H), 3.11–3.26 (m, 2H), 3.63–3.93 (m, 6H), 3.95–4.03 (m, 1H), 4.14–4.23 (m, 1H), the benzylic type protons give an AB quartet: δ_A 4.28 and δ_B 4.58 (J_{AB} = 13 Hz, 2H), 4.78–4.88 (m, 2H), 6.84 (d, *J* = 8 Hz, 1H), 6.92–7.01 (m, 2H), 7.03–7.34 (m, 15H), 7.92 (t, *J* = 8 Hz, 1H), 7.99–8.11 (m, 6H), 8.18 (d, *J* = 8 Hz, 1H), 8.53 (s, 1H), 8.61 (d, *J* = 9 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 55.48, 60.46, 63.84, 68.48, 68.55, 69.41, 70.02, 81.16, 81.69, 115.23, 115.29, 121.25, 121.82, 125.23, 125.36, 125.55, 125.61, 125.66, 125.98, 126.73, 127.46 (very high, probably two ^{13}C signals together), 127.61, 127.76, 127.90, 128.06, 128.30, 128.49, 128.86, 129.01, 129.08, 129.41, 129.71 (broad, probably two ^{13}C signals together), 130.71, 130.80, 131.57, 131.86, 132.10, 132.44, 134.38, 142.54, 142.65, 154.62, 155.43, 162.92; MS calcd for $C_{50}H_{44}N_2O_5$: 752.3, found $(M + H)^+$: 753.3; Anal. calcd for $C_{50}H_{44}N_2O_5$: C 79.76, H 5.89, N 3.72, found: C 79.44, H 5.83, N 3.47.

4.4.2 (9*S*,13*S*)-9,13-Diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetraoxa[7,16]diaza-cyclooctadecine-22-carbaldehyde [(*S*,*S*)-3]

Yield: 39 mg, 76 %; mp: 95–96 °C; ee > 99 %; $[\alpha]_D^{25}$ +117.1 (*c* = 0.62 in acetone). Spectral data and other physical properties of macrocycle (*S*,*S*)-**3** were the same as those of macrocycle (*R*,*R*)-**3** reported above.

4.5 Procedures for the synthesis of sensor molecules (*R*,*R*)-4 and (*S*,*S*)-4

4.5.1 Procedure for the synthesis of sensor molecules (*R*,*R*)-4 and (*S*,*S*)-4 starting from ditosylate 18 and aminodiol (*R*,*R*)-6 or (*S*,*S*)-6

To a suspension of NaH (51 mg, 1.3 mmol, 60 % dispersion in mineral oil) in pure and dry DMF (0.5 mL) was added slowly aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** (100 mg, 0.212 mmol) dissolved in pure and dry DMF (2 mL) at –60 °C under Ar. The resulting mixture was stirred at 50 °C for 1 h. The mixture was cooled down to –60 °C, and ditosylate **18** (136 mg, 0.223 mmol) dissolved in pure and dry DMF (2 mL) was added in 5 min. After addition of the ditosylate **18** the reaction mixture was allowed to warm up slowly to rt, and it was stirred at this temperature overnight. The solvent was evaporated, and the residue was dissolved in a mixture of Et_2O (20 mL) and water (8 mL). The phases were shaken thoroughly and separated. The aqueous phase was extracted with Et_2O (2 × 20 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on alumina using EtOAc–hexane 1:50 mixture as an eluent to give receptor (*R*,*R*)-**4** or (*S*,*S*)-**4** as yellow crystals.

4.5.1.1 (9*R*,13*R*)-22-Methyl-9,13-diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetraoxa[7,16]diaza-cyclooctadecine [(*R*,*R*)-4]

Yield: 45 mg, 29 %; mp: 60–62 °C; R_f: 0.63 (silica gel TLC, EtOAc–toluene 1:3); ee > 98 %; $[\alpha]_D^{25}$ –46.3 (*c* = 1.00 in acetone); IR (neat) ν_{max} 3394 (br, complexed H_2O), 3080, 3050, 3030, 2922, 2861, 2804, 1587, 1498, 1448, 1336, 1253, 1107, 1041, 1019, 917, 847, 817, 739, 700, 639, 614 cm^{-1}; ^1H NMR (300 MHz, acetone-d_6) δ 2.10 (s, complexed H_2O, 2H), 2.72–2.83 (m, 2H), 3.12–3.21 (m, 2H), 3.21 (s, 3H), 3.26–3.36 (m, 2H), 3.50–3.60 (m, 2H), 3.92–4.02 (m, 2H), 4.26–4.36 (m, 2H), the benzylic type protons give an AB quartet: δ_A 4.42 and δ_B 4.52 (J_{AB} = 13 Hz, 2H), 4.78–4.88 (m, 2H), 6.86–7.08 (m, 8H), 7.14–7.30 (m, 10H), 7.86–8.24 (m, 8H), 8.42 (d, *J* = 9 Hz, 1H); ^{13}C NMR (75.5 MHz, acetone-d_6) δ 38.53, 59.70, 61.69, 67.74, 69.31, 80.97, 115.47, 121.01, 121.44, 122.88, 124.36, 124.55, 124.72, 124.74, 124.75, 124.92, 125.86, 126.71, 126.79, 126.83, 127.14, 127.48, 128.06, 128.32, 129.79, 130.59,

130.99, 131.33, 133.74, 140.98, 141.68, 152.43; MS calcd for $C_{50}H_{46}N_2O_4$: 738.4, found $(M + H)^+$: 739.4; Anal. calcd for $C_{50}H_{46}N_2O_4 \cdot H_2O$: C 79.34, H 6.39, N 3.70, found: C 78.92, H 6.73, N 3.45.

4.5.1.2 (9*S*,13*S*)-22-Methyl-9,13-diphenyl-11-(pyren-1-ylmethyl)-6,7,10,11,12,13,15,16-octahydro-9*H*,22*H*-dibenzo[*e*,*h*][1,4,10,13]tetraoxa[7,16]diaza-cyclooctadecine [(*S*,*S*)-4]

Yield: 48 mg, 31 %; ee > 99 %; $[\alpha]_D^{29}$ +43.1 (*c* = 0.89 in acetone). Spectral data and other physical properties of macrocycle (*S*,*S*)-**4** were the same as those of macrocycle (*R*,*R*)-**4** reported above.

4.5.2 Procedure for the synthesis of sensor molecule (*S*,*S*)-4 starting from diphenol 10 and ditosylate (*S*,*S*)-23

To a suspension of diphenol derivative **10** (24 mg, 0.11 mmol) and finely powdered anhydrous K_2CO_3 (115 mg, 0.83 mmol) in dry MeCN (2 mL) was added a solution of ditosylate (*S*,*S*)-**23** (90 mg, 0.10 mmol) in dry MeCN (4 mL) under Ar. The resulting mixture was stirred vigorously at 50 °C, and after the reaction was complete, it was allowed to cool to rt. The solvent was evaporated, and the residue was taken up in a mixture of water (20 mL) and Et_2O (25 mL). The phases were shaken well and separated. The aqueous phase was extracted with Et_2O (2 × 25 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed. The crude product was purified by preparative TLC on alumina using EtOAc–hexane 1:20 mixture as an eluent to give receptor (*S*,*S*)-**4** (15 mg, 20 %) as yellow crystals. Macrocycle (*S*,*S*)-**4** had the same physical properties and spectral data as the one prepared above from ditosylate **18** and aminodiol (*S*,*S*)-**6**.

4.6 Pyren-1-ylmethanamine (5)

Commercially available pyren-1-ylmethanamine hydrochloride (1.00 g, 3.73 mmol) and NaOH (154 mg, 3.85 mmol) were stirred in EtOH (10 mL) at rt under Ar. The solvent was removed, and the residue was dissolved in a mixture of 5 % aqueous NaOH solution (25 mL) and CH_2Cl_2 (50 mL). The phases were shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated to give free amine **5** [45] (845 mg, 98 %) as a white solid.

4.7 General procedure for the synthesis of aminodiols (*R*,*R*)-6 and (*S*,*S*)-6 containing a pyrene unit

Pyren-1-ylmethanamine (**5**, 800 mg, 3.46 mmol) and (*R*)-2-phenyloxirane or (*S*)-2-phenyloxirane (0.99 mL, 1.0 g, 8.6 mmol) were dissolved in dry MeOH (3 mL) and heated in a sealed tube at 80 °C for 4 h. The solvent was evaporated, and the residue was purified by column chromatography on silica gel using EtOAc–hexane 1:4 mixture as an eluent. The product was recrystallized from xylene to give aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** as white crystals.

4.7.1 (1*R*,1'*R*)-2,2'-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethanol) [(*R*,*R*)-6]

Yield: 932 mg, 57 %; mp: 166–167 °C (xylene); R_f: 0.44 (silica gel TLC, EtOAc–hexane 1:2); ee > 99 %; $[\alpha]_D^{25}$ –147.5 (*c* = 1.00 in acetone); IR (KBr) ν_{max} 3582, 3526, 3494, 3079, 3049, 3029, 2947, 2860, 2823, 1602, 1586, 1491, 1453, 1379, 1326, 1312, 1266, 1243, 1194, 1091, 1063, 1024, 894, 851, 763, 753, 702, 634, 554 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 2.83–2.97 (m, 4H), the benzylic type protons give an AB quartet: δ_A 4.44 and δ_B 4.67 (J_{AB} = 13 Hz, 2H), 4.57 (s, 2H, OH, disappears after shaking the solution with D_2O), 4.71–4.76 (m, 2H), 7.14–7.19 (m, 2H), 7.20–7.29 (m, 8H), 8.02 (t, *J* = 8 Hz, 1H), 8.08–8.13 (m, 3H), 8.15–8.26 (m, 4H), 8.70 (d, *J* = 9 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 58.85, 63.45, 70.86, 124.30, 124.50, 124.66, 124.87, 125.06, 125.13, 125.89, 126.05, 126.90, 127.13, 127.29, 127.51, 127.97, 128.68, 130.05, 130.95, 131.02, 131.38, 133.09, 143.71; MS calcd for $C_{33}H_{29}NO_2$: 471.2, found $(M + H)^+$: 472.2; Anal. calcd for $C_{33}H_{29}NO_2$: C 84.05, H 6.20, N 2.97, found: C 83.70, H 6.27, N 2.79.

4.7.2 (1*S*,1'*S*)-2,2'-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethanol) [(*S*,*S*)-6]

Yield: 801 mg, 49 %; ee > 99 %; $[\alpha]_D^{25}$ +148.2 (*c* = 1.00 in acetone). Spectral data and other physical properties of aminodiol (*S*,*S*)-**6** were the same as those of aminodiol (*R*,*R*)-**6** reported above.

4.8 2-Methoxy-*N*-(2-methoxyphenyl)-*N*-methylaniline (9)

A suspension of NaH (6.28 g, 157 mmol, 60 % dispersion in mineral oil) was stirred vigorously in pure and dry THF (20 mL) under Ar for 5 min. To this suspension was slowly added secondary amine **8** [47] (12.0 g, 52.3 mmol) dissolved in pure and dry THF (70 mL) at 0 °C.

The resulting mixture was refluxed for 30 min then a solution of methyl iodide (3.9 mL, 8.9 g, 63 mmol) in pure and dry THF (10 mL) was added dropwise at rt. The reaction mixture was stirred for 2 h at rt. The volatile components were removed, and the residue was dissolved in a mixture of water (300 mL) and Et_2O (300 mL). The phases were shaken well and separated. The aqueous phase was extracted with Et_2O (2 × 300 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on silica gel using EtOAc–hexane 1:20 mixture as an eluent to yield amine **9** (12.1 g, 95 %) as white crystals. Mp: 54–55 °C; R_f: 0.62 (silica gel TLC, EtOAc–hexane 1:4); IR (KBr) ν_{max} 3082, 3069, 3060, 3030, 3003, 2957, 2875, 2850, 2834, 2802, 1585, 1500, 1464, 1455, 1434, 1360, 1332, 1302, 1251, 1181, 1133, 1121, 1101, 1026, 872, 802, 763, 757, 749, 714, 698, 610, 594, 571, 564, 541, 510, 476 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.18 (s, 3H), 3.70 (s, 6H), 6.86 (d, J = 8 Hz, 2H), 6.87 (t, J = 8 Hz, 2H), 6.94 (d, J = 8 Hz, 2H), 7.02 (t, J = 8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 39.98, 55.51, 111.76, 120.72, 121.65, 123.29, 140.32, 152.80; MS calcd for $C_{15}H_{17}NO_2$: 243.1, found $(M + H)^+$: 244.1; Anal. calcd for $C_{15}H_{17}NO_2$: C 74.05, H 7.04, N 5.76, found: C 74.16, H 7.26, N 5.39.

4.9 2,2'-(Methylazanediyl)diphenol (10)

Dimethoxy derivative **9** (9.24 g, 37.9 mmol) was dissolved in chlorobenzene (93 mL) under Ar then anhydrous $AlCl_3$ (20.3 g, 152 mmol) was added, and the resulting mixture was stirred at 90 °C for 7 h. After the reaction was complete, the mixture was allowed to cool to rt, and poured into ice-water (138 mL). Concentrated aqueous HCl solution (12.5 mL) was added, and the resulting mixture was stirred for 30 min. The pH of the mixture was adjusted to 8 with $NaHCO_3$. The precipitate was filtered off, washed with water (150 mL), and dried. The crude product was recrystallized from toluene to give diphenol **10** (6.24 g, 76 %) as white crystals. Mp: 143–145 °C (toluene); R_f: 0.55 (silica gel TLC, EtOAc–toluene 1:5); IR (KBr) ν_{max} 3365, 3335, 3067, 3053, 3034, 2976, 2944, 2881, 2864, 2842, 2797, 2694, 1584, 1509, 1493, 1470, 1452, 1438, 1349, 1285, 1259, 1227, 1192, 1177, 1160, 1109, 1027, 832, 797, 752, 747, 701, 597, 488, 436 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.12 (s, 3H), 5.68 (br s, 2H, OH, disappears after shaking the solution with D_2O), 6.92 (t, J = 8 Hz, 2H), 6.94 (d, J = 8 Hz, 2H), 7.09 (t, J = 8 Hz, 2H), 7.12 (d, J = 8 Hz, 2H); 13C NMR (125 MHz, $CDCl_3$) δ 41.95, 116.06, 121.05, 122.53, 125.93, 137.11, 149.98; MS calcd for $C_{13}H_{13}NO_2$: 215.1, found $(M + H)^+$: 216.1; Anal. calcd for $C_{13}H_{13}NO_2$: C 72.54, H 6.09, N 6.51, found: C 72.19, H 6.23, N 6.23.

4.10 General procedure for the synthesis of precursors 13 and 14 containing benzyl protecting groups

To a solution of formamide derivative **11** [50] (2.29 g, 10.0 mmol) or diphenol **10** (2.15 g, 10.0 mmol) in dry MeCN (66 mL) tosylate **12** [51] (6.74 g, 22.0 mmol) and finely powdered anhydrous K_2CO_3 (11 g, 80 mmol) were added under Ar. The resulting suspension was stirred vigorously, refluxed, and after the reaction was complete, it was allowed to cool to rt. The mixture was filtered, and the precipitate was washed with MeCN (3 × 15 mL). The solvent was evaporated from the combined MeCN solution, and the residue was taken up in a mixture of water (75 mL) and CH_2Cl_2 (150 mL). The phases were shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed. The crude products were purified as described below for each compound.

4.10.1 *N*,*N*-Bis{2-[2-(benzyloxy)ethoxy]phenyl} formamide (13)

Starting from formamide derivative **11** [50]. The crude product was purified first by column chromatography on silica gel using EtOAc–toluene 1:5 mixture as an eluent then by recrystallization from MeOH to yield formamide derivative **13** (3.83 g, 77 %) as pale brown crystals. Mp: 75–76 °C (MeOH); R_f: 0.74 (silica gel TLC, EtOAc–toluene 1:1); IR (KBr) ν_{max} 3083, 3064, 3034, 3023, 3012, 2937, 2926, 2876, 2857, 2848, 2806, 2774, 2753, 1680, 1595, 1503, 1456, 1445, 1356, 1333, 1299, 1284, 1248, 1205, 1100, 1024, 932, 923, 857, 765, 748, 701, 676, 603 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78 (t, J = 5 Hz, 2H), 3.81 (t, J = 5 Hz, 2H), 4.16 (t, J = 5 Hz, 4H), 4.57 (s, 2H), 4.60 (s, 2H), 6.81 (t, J = 8 Hz, 1H), 6.87 (t, J = 8 Hz, 1H), 6.95 (d, J = 8 Hz, 1H), 6.96 (d, J = 8 Hz, 1H), 7.18–7.24 (m, 2H), 7.26–7.42 (m, 12H), 8.44 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 68.17, 68.34, 68.69, 68.83, 73.40, 73.68, 113.19, 113.50, 121.27 (very high, probably two ^{13}C signals together), 127.77, 127.81, 127.84, 127.91, 128.52, 128.60, 128.67, 129.06, 129.26, 129.30, 130.17, 130.94, 138.16, 138.34, 154.38, 154.51, 163.58; MS calcd for $C_{31}H_{31}NO_5$: 497.2, found $(M + H)^+$: 498.2; Anal. calcd for $C_{31}H_{31}NO_5$: C 74.83, H 6.28, N 2.81, found: C 74.56, H 6.31, N 2.96.

4.10.2 2-[2-(Benzyloxy)ethoxy]-*N*-{2-[2-(benzyloxy) ethoxy]phenyl}-*N*-methylaniline (14)

Starting from diphenol **10**. The crude product was purified by column chromatography on silica gel using EtOAc–hexane 1:10 mixture as an eluent to yield tertiary amine **14** (3.77 g, 78 %) as a pale yellow oil. R_f: 0.32 (silica gel TLC, EtOAc–hexane 1:5); IR (neat) ν_{max} 3078, 3060, 3028, 2925, 2859, 2808, 1587, 1496, 1448, 1357, 1252, 1238, 1103, 1040, 1027, 928, 914, 863, 733, 696, 606, 459 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.27 (s, 3H), 3.50 (t, J = 5 Hz, 4H), 4.04 (t, J = 5 Hz, 4H), 4.46 (s, 4H), 6.85–6.92 (m, 4H), 6.94–7.01 (m, 4H), 7.28–7.36 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 39.97, 68.05, 68.78, 73.25, 114.30, 121.47, 121.73, 122.89, 127.60, 127.72, 128.36, 138.32, 140.68, 151.86; MS calcd for $C_{31}H_{33}NO_4$: 483.2, found $(M + H)^+$: 484.2; Anal. calcd for $C_{31}H_{33}NO_4$: C 76.99, H 6.88, N 2.90, found: C 76.81, H 7.17, N 2.85.

4.11 General procedure for the synthesis of diols 15 and 16

Formamide derivative **13** (4.98 g, 10.0 mmol) or tertiary amine **14** (4.84 g, 10.0 mmol) containing benzyl protecting groups was hydrogenated in MeOH (200 mL) in the presence of Pd/C catalyst (500 mg, 10 % palladium on charcoal, activated). After the reaction was complete, the catalyst was filtered off and the volatile components were evaporated to yield diol **15** (3.11 g, 98 %) or **16** (3.03 g, 100 %) as white solids. Smaller amounts were recrystallized from toluene for analytical studies.

4.11.1 *N*,*N*-Bis[2-(2-hydroxyethoxy)phenyl]formamide(15)

Starting from formamide derivative **13**. Mp: 137 °C (toluene); R_f: 0.13 (silica gel TLC, EtOAc–toluene 2:1); IR (KBr) ν_{max} 3392 (br, OH), 3074, 3045, 3028, 2941, 2873, 2782, 1685, 1594, 1500, 1479, 1449, 1342, 1282, 1233, 1077, 1049, 1032, 920, 755, 673 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.04 (br s, 2H, OH, disappears after shaking the solution with D_2O), 3.70 (t, J = 4 Hz, 2H), 3.80 (t, J = 4 Hz, 2H), 3.96 (t, J = 4 Hz, 2H), 4.24 (t, J = 4 Hz, 2H), 6.90–6.95 (m, 2H), 6.98–7.03 (m, 2H), 7.04–7.08 (m, 1H), 7.22–7.32 (m, 3H), 8.42 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 60.80, 60.97, 70.08, 71.09, 113.30, 113.80, 121.30, 121.45, 127.87, 128.12, 128.69, 129.07, 129.12, 130.33, 153.29, 153.62, 162.60; MS calcd for $C_{17}H_{19}NO_5$: 317.1, found $(M + H)^+$: 318.1; Anal. calcd for $C_{17}H_{19}NO_5$: C 64.34, H 6.04, N 4.41, found: C 64.16, H 6.04, N 4.12.

4.11.2 2,2'-{[(Methylazanediyl)bis(2,1-phenylene)] bis(oxy)}bis(ethan-1-ol) (16)

Starting from tertiary amine **14**. Mp: 85–86 °C (toluene); R_f: 0.28 (silica gel TLC, EtOAc–hexane 2:1); IR (KBr) ν_{max} 3442, 3384 (br, OH), 3069, 3025, 3006, 2974, 2944, 2931, 2862, 1588, 1500, 1452, 1366, 1340, 1258, 1243, 1084, 1046, 921, 762, 754, 747, 614 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.23 (s, 3H), 3.69 (t, J = 4 Hz, 4H), 4.08 (t, J = 4 Hz, 4H), 4.29 (br s, 2H, OH, disappears after shaking the solution with D_2O), 6.89–7.03 (m, 6H), 7.04–7.12 (m, 2H); 13C NMR (75.5 MHz, $CDCl_3$) δ 40.66, 61.03, 72.10, 115.21, 122.01, 122.08, 124.38, 141.36, 151.88; MS calcd for $C_{17}H_{21}NO_4$: 303.2, found $(M + H)^+$: 304.2; Anal. calcd for $C_{17}H_{21}NO_4$: C 67.31, H 6.98, N 4.62, found: C 67.60, H 7.33, N 4.44.

4.12 {[(Formylazanediyl)bis(2,1-phenylene)]bis(oxy)} bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) (17)

To a solution of diol **15** (1.58 g, 4.99 mmol) in CH_2Cl_2 (32 mL) was added tosyl chloride (2.38 g, 12.5 mmol) followed by Et_3N (8.7 mL, 60 mmol) under Ar, and the resulting mixture was stirred at rt for 21 h. After the reaction was complete, CH_2Cl_2 (120 mL) and water (80 mL) were added to the reaction mixture. The phases were shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic phase was shaken successively with 5 % aqueous HCl solution (160 mL) and water (2 × 80 mL) then dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated. The crude product was purified by recrystallization from CH_2Cl_2–MeOH mixture to give ditosylate **17** (2.85 g, 91 %) as white crystals. Mp: 175 °C (CH_2Cl_2–MeOH); R_f: 0.58 (silica gel TLC, EtOAc–toluene 1:3); IR (KBr) ν_{max} 3080, 3069, 3031, 2961, 2887, 2801, 2774, 1677, 1595, 1505, 1454, 1376, 1360, 1332, 1282, 1190, 1175, 1124, 1097, 1069, 1031, 941, 932, 918, 819, 783, 756, 663, 572, 553, 504, 497, 432 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.41 (s, 3H), 2.43 (s, 3H), 4.09–4.16 (m, 2H), 4.17–4.23 (m, 2H), 4.24–4.34 (m, 4H), 6.80–7.04 (m, 4H), 7.18–7.38 (m, 8H), 7.76 (d, J = 8 Hz, 2H), 7.79 (d, J = 8 Hz, 2H), 8.24 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.78, 21.82, 66.29, 66.47, 67.86, 68.35, 113.28, 113.53, 121.91, 122.07, 128.12, 128.15, 128.92, 129.07, 129.10, 129.23, 129.95, 130.08, 130.22, 130.72, 132.81, 132.99, 145.15, 145.26, 153.47, 153.65, 163.02; MS calcd for $C_{31}H_{31}NO_9S_2$: 625.1, found $(M + H)^+$: 626.1; Anal. calcd

for $C_{31}H_{31}NO_9S_2$: C 59.51, H 4.99, N 2.24, found: C 59.46, H 4.90, N 2.09.

4.13 {[(Methylazanediyl)bis(2,1-phenylene)]bis(oxy)} bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) (18)

To a solution of diol **16** (1.00 g, 3.29 mmol) in CH_2Cl_2 (10 mL) was added tosyl chloride (1.57 g, 8.24 mmol). The mixture was stirred vigorously and cold 40 % aqueous KOH solution (11 mL) was added to it at 0 °C. The resulting emulsion was stirred at rt for 23 h then water (100 mL) and CH_2Cl_2 (100 mL) were added to it. The phases were shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated. The crude product was purified by recrystallization from CH_2Cl_2–MeOH mixture to give ditosylate **18** (1.89 g, 94 %) as white crystals. Mp: 129–130 °C (CH_2Cl_2–MeOH); R_f: 0.22 (silica gel TLC, EtOAc–hexane 1:3); IR (KBr) ν_{max} 3080, 3072, 3042, 3022, 2981, 2957, 2944, 2921, 2875, 2794, 1598, 1583, 1502, 1449, 1403, 1372, 1355, 1251, 1178, 1020, 947, 925, 815, 782, 754, 664, 571, 552 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 6H), 3.13 (s, 3H), 3.94–4.08 (m, 8H), 6.73 (d, J = 8 Hz, 2H), 6.84–6.96 (m, 6H), 7.30 (d, J = 7 Hz, 4H), 7.75 (d, J = 7 Hz, 4H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.65, 39.76, 66.29, 68.35, 115.06, 121.75, 122.20, 123.05, 127.95, 129.85, 132.99, 140.74, 144.85, 151.05; MS calcd for $C_{31}H_{33}NO_8S_2$: 611.2, found $(M + H)^+$: 612.2; Anal. calcd for $C_{31}H_{33}NO_8S_2$: C 60.87, H 5.44, N 2.29, found: C 60.53, H 5.56, N 2.10.

4.14 2-(Methoxymethoxy)ethyl 4-methylbenzenesulfonate (20)

To a vigorously stirred mixture of ethylene glycol derivative **19** [52] (1.63 g, 15.4 mmol) containing a MOM protecting group, CH_2Cl_2 (12 mL), and cold 40 % aqueous KOH solution (17 mL) a solution of tosyl chloride (3.81 g, 20.0 mmol) in CH_2Cl_2 (12 mL) was added dropwise at 0 °C. The resulting reaction mixture was stirred at rt for 1 day then washed into a separatory funnel with CH_2Cl_2 (175 mL) and water (75 mL). The resulting mixture was shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 150 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on silica gel using EtOAc–hexane 1:6 mixture as an eluent to give tosylate **20** (3.65 g, 91 %) as a colorless oil. R_f: 0.18 (silica gel TLC, EtOAc–hexane 1:2); IR (neat) ν_{max} 2948, 2888, 2825, 1598, 1496, 1451, 1399, 1354, 1307, 1291, 1242, 1213, 1189, 1174, 1153, 1120, 1096, 1051, 1007, 913, 815, 773, 706, 691, 661, 575, 552, 501 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3H), 3.32 (s, 3H), 3.72 (t, J = 5 Hz, 2H), 4.20 (t, J = 5 Hz, 2H), 4.57 (s, 2H), 7.36 (d, J = 8 Hz, 2H), 7.81 (d, J = 8 Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.62, 55.31, 65.09, 69.18, 96.46, 127.94, 129.82, 133.03, 144.85; MS calcd for $C_{11}H_{16}O_5S$: 260.1, found $(M + NH_4)^+$: 278.1; Anal. calcd for $C_{11}H_{16}O_5S$: C 50.76, H 6.20, found: C 50.71, H 5.88.

4.15 General procedure for the synthesis of precursors (*R*,*R*)-21 and (*S*,*S*)-21 containing MOM protecting groups

A suspension of NaH (510 mg, 12.7 mmol, 60 % dispersion in mineral oil) was stirred vigorously in pure and dry THF (2 mL) under Ar for 5 min. To this suspension was added slowly aminodiol (*R*,*R*)-**6** or (*S*,*S*)-**6** (1.00 g, 2.12 mmol) dissolved in pure and dry DMF (5 mL) at –60 °C. The resulting mixture was stirred at rt for 10 min and at 60 °C for 2 h. The mixture was cooled down to 0 °C, and tosylate **20** (1.32 g, 5.07 mmol) dissolved in pure and dry DMF (2 mL) was added. After addition of the tosylate **20**, the reaction mixture was allowed to warm up to rt, and it was stirred at this temperature overnight. The solvent was evaporated, and the residue was dissolved in a mixture of Et_2O (120 mL) and brine (70 mL). The phases were shaken well and separated. The aqueous phase was extracted with Et_2O (3 × 120 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on silica gel using EtOAc–hexane 1:6 mixture as an eluent. Smaller amounts were purified for analytical studies by preparative TLC on silica gel using EtOAc–hexane 1:3 mixture as an eluent to give diacetal (*R*,*R*)-**21** or (*S*,*S*)-**21** as a yellow oil.

4.15.1 (*R*)-2-[2-(Methoxymethoxy)ethoxy]-*N*-{(*R*)-2-[2-(methoxymethoxy)ethoxy]-2-phenylethyl}-2-phenyl-*N*-(pyren-1-ylmethyl)ethan-1-amine [(*R*,*R*)-21]

Yield: 920 mg, 67 %; R_f: 0.46 (silica gel TLC, EtOAc–hexane 1:2); $[\alpha]_D^{25}$ –9.2 (c = 1.00 in acetone); IR (neat) ν_{max} 3080, 3049, 3029, 2929, 2879, 2820, 1602, 1587, 1492, 1451, 1346,

1311, 1244, 1213, 1152, 1103, 1038, 917, 845, 818, 756, 701, 644, 615 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 2.90–2.96 (m, 2H), 3.06–3.13 (m, 2H), 3.21 (s, 6H), 3.40–3.52 (m, 4H), 3.57–3.65 (m, 4H), the benzylic type protons give an AB quartet: δ_A 4.52 and δ_B 4.76 (J_{AB} = 13 Hz, 2H), 4.53 (s, 4H), 4.54–4.59 (m, 2H), 7.13–7.24 (m, 10H), 8.02 (t, J = 8 Hz, 1H), 8.07–8.14 (m, 4H), 8.17 (d, J = 8 Hz, 1H), 8.21–8.26 (m, 2H), 8.62 (d, J = 9 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 54.21, 58.50, 62.15, 66.83, 68.20, 81.70, 96.18, 124.38, 124.64, 124.78, 124.82, 124.93 (very high, probably two ^{13}C signals together), 125.93, 126.76, 126.79, 126.89, 127.23, 127.52, 128.09, 128.48, 129.95, 130.66, 131.10, 131.40, 134.04, 141.66; MS calcd for $C_{41}H_{45}NO_6$: 647.3, found $(M + H)^+$:648.3; Anal. calcd for $C_{41}H_{45}NO_6$: C 76.02, H 7.00, N 2.16, found: C 75.91, H 7.12, N 2.17.

4.15.2 (*S*)-2-[2-(Methoxymethoxy)ethoxy]-*N*-{(*S*)-2-[2-(methoxymethoxy)ethoxy]-2-phenylethyl}-2-phenyl-*N*-(pyren-1-ylmethyl)ethan-1-amine [(*S*,*S*)-21]

Yield: 962 mg, 70 %; $[\alpha]_D^{25}$ +7.0 (c = 1.00 in acetone). Spectral data and other physical properties of precursor (*S*,*S*)-**21** were the same as those of precursor (*R*,*R*)-**21** reported above.

4.16 General procedure for the synthesis of diols (*R*,*R*)-22 and (*S*,*S*)-22

To a solution of bis(MOM)-protected diol (*R*,*R*)-**21** or (*S*,*S*)-**21** (1.08 g, 1.67 mmol) in THF (8 mL) was added slowly 20 % aqueous HCl solution (50 mL), and the resulting mixture was stirred at 55 °C for 1 h. The solvent was evaporated, and the residue was dissolved in a mixture of saturated aqueous $NaHCO_3$ solution (100 mL) and EtOAc (100 mL). The phases were shaken well and separated. The aqueous phase was extracted with EtOAc (2 × 100 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated to give unprotected diol (*R*,*R*)-**22** or (*S*,*S*)-**22** as white crystals.

4.16.1 2,2'-{[(1*R*,1'*R*)-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethane-2,1-diyl)]bis(oxy)}bis(ethan-1-ol) [(*R*,*R*)-22]

Yield: 917 mg, 98 %; mp: 42–43 °C; R_f: 0.07 (silica gel TLC, EtOAc–hexane 1:2); $[\alpha]_D^{25}$ –48.6 (c = 1.00 in acetone); IR (KBr) ν_{max} 3383 (br, OH), 3083, 3048, 3032, 2923, 2854, 1602, 1586, 1491, 1451, 1417, 1380, 1346, 1313, 1260, 1199, 1096, 1054, 1021, 964, 929, 888, 842, 817, 754, 699, 643, 615 cm^{-1}; ^1H NMR (500 MHz, acetone-d_6) δ 2.82–2.88 (m, 2H), 3.15–3.23 (m, 2H), 3.40–3.48 (m, 4H), 3.62–3.75 (m, 4H), 3.97 (br s, 2H, OH, disappears after shaking the solution with D_2O), the benzylic type protons give an AB quartet: δ_A 4.60 and δ_B 4.64 (J_{AB} = 13 Hz, 2H), 4.66–4.72 (m, 2H), 7.18–7.30 (m, 10H), 8.06 (t, J = 8 Hz, 1H), 8.10–8.17 (m, 4H), 8.20 (d, J = 8 Hz, 1H), 8.24–8.31 (m, 2H), 8.66 (d, J = 9 Hz, 1H); ^{13}C NMR (125 MHz, acetone-d_6) δ 58.41, 61.25, 62.30, 70.50, 80.82, 124.38, 124.61, 124.78 (high, probably two ^{13}C signals together), 124.86, 124.96, 125.94, 126.75, 126.91, 126.95, 127.27, 127.49, 128.12, 128.62, 130.00, 130.70, 131.05, 131.37, 133.51, 141.62; MS calcd for $C_{37}H_{37}NO_4$: 559.3, found $(M + H)^+$: 560.3; Anal. calcd for $C_{37}H_{37}NO_4$: C 79.40, H 6.66, N 2.50, found: C 79.09, H 6.54, N 2.28.

4.16.2 2,2'-{[(1*S*,1'*S*)-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethane-2,1-diyl)]bis(oxy)}bis(ethan-1-ol) [(*S*,*S*)-22]

Yield: 912 mg, 98 %; $[\alpha]_D^{25}$ +50.4 (c = 1.00 in acetone). Spectral data and other physical properties of diol (*S*,*S*)-**22** were the same as those of diol (*R*,*R*)-**22** reported above.

4.17 General procedure for the synthesis of ditosylates (*R*,*R*)-23 and (*S*,*S*)-23

Diol (*R*,*R*)-**22** or (*S*,*S*)-**22** (866 mg, 1.55 mmol) was stirred vigorously in a mixture of CH_2Cl_2 (15 mL) and cold 40 % aqueous KOH solution (20 mL) at 0 °C, and a solution of tosyl chloride (885 mg, 4.63 mmol) in CH_2Cl_2 (5 mL) was added dropwise to it. The resulting reaction mixture was stirred at rt for 1 day then washed into a separatory funnel with CH_2Cl_2 (100 mL) and water (80 mL). The resulting mixture was shaken well and separated. The aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude product was purified by column chromatography on silica gel using EtOAc–hexane 1:4 mixture as an eluent to give ditosylate (*R*,*R*)-**23** or (*S*,*S*)-**23** as white crystals.

4.17.1 {[(1*R*,1'*R*)-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethane-2,1-diyl)]bis(oxy)}bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) [(*R*,*R*)-23]

Yield: 577 mg, 43 %; mp: 60–62 °C; R_f: 0.48 (silica gel TLC, EtOAc–hexane 1:2); $[\alpha]_D^{25}$ –27.4 (c = 1.11 in acetone); IR (KBr) ν_{max} 3433 (br, complexed H_2O), 3082, 3051, 3032, 2952, 2922, 2874, 1597, 1494, 1454, 1357, 1189, 1176, 1120, 1097, 1033, 1012, 921, 852, 816, 760, 702, 680, 664,

554 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.67 (br s, complexed H_2O, 2H), 2.26 (s, 6H), 2.79–2.87 (m, 2H), 2.95–3.03 (m, 2H), 3.36–3.43 (m, 4H), 4.03–4.13 (m, 4H), 4.23–4.29 (m, 2H), the benzylic type protons give an AB quartet: δ_A 4.29 and δ_B 4.58 (J_{AB} = 13 Hz, 2H), 6.94–7.01 (m, 4H), 7.10 (d, J = 8 Hz, 4H), 7.13–7.18 (m, 6H), 7.65 (d, J = 8 Hz, 4H), 7.89 (d, J = 8 Hz, 1H), 7.96 (d, J = 9 Hz, 1H), 8.01 (t, J = 8 Hz, 1H), 8.04–8.09 (m, 3H), 8.15–8.20 (m, 2H), 8.37 (d, J = 9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.60, 59.26, 62.57, 66.40, 69.46, 82.37, 124.45, 124.62, 124.86, 124.93, 124.98, 125.10, 125.92, 126.85, 126.98, 127.10, 127.62, 127.72, 127.95, 128.25, 128.39, 129.79, 129.96, 130.76, 131.07, 131.41, 133.07, 133.52, 140.47, 144.70; MS calcd for $C_{51}H_{49}NO_8S_2$: 867.3, found $(M + H)^+$: 868.3; Anal. calcd for $C_{51}H_{49}NO_8S_2 \cdot H_2O$: C 69.13, H 5.80, N 1.58, found: C 68.89, H 6.08, N 1.56.

4.17.2 {[(1*S*,1'*S*)-[(Pyren-1-ylmethyl)azanediyl]bis(1-phenylethane-2,1-diyl)]bis(oxy)}bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) [(*S*,*S*)-23]

Yield: 698 mg, 52 %; $[\alpha]_D^{25}$ +24.1 (c = 1.00 in acetone). Spectral data and other physical properties of ditosylate (*S*,*S*)-**23** were the same as those of ditosylate (*R*,*R*)-**23** reported above.

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