Tetrahedron 64 (2008) 10107–10115

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis and preliminary studies on novel enantiopure crown ethers containing an alkyl diarylphosphinate or a proton-ionizable diarylphosphinic acid unit☆

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ARTICLE INFO

Article history:
Received 28 April 2008
Received in revised form 16 July 2008
Accepted 31 July 2008
Available online 6 August 2008

ABSTRACT

This paper reports the synthesis, characterization and electronic circular dichroism (ECD) spectroscopic studies of a new type of crown ethers and their achiral analogues containing a tetrahedral phosphorous centre. The synthetic routes to the two chiral phosphinate derivatives [(*R*,*R*)-**10** and (*R*,*R*)-**11**] were similar, starting from the earlier reported ethyl bis(2-hydroxyphenyl)phosphinate and the unreported methyl bis(2-hydroxyphenyl)phosphinate, respectively. The enantiopure crown ether containing phosphinic acid unit (*R*,*R*)-**14** was obtained by hydrolysis of the phosphinates (*R*,*R*)-**10** and (*R*,*R*)-**11**, respectively. ECD spectroscopy was used for investigation of the chiroptical properties as well as complex formation ability of the novel enantiopure ligands. Owing to the presence of the aryl substituents the ECD spectra are rich in bands in the ^1B_b, ^1L_a and ^1L_b regions (190–250 nm and 260–330 nm, respectively). In the case of (*R*,*R*)-**14**, a solvent dependent conformational behaviour was observed due to the strong dimer or aggregate forming ability of the POOH groups. This finding was supported by theoretical calculation of the monomer and the dimer forms. Phosphinates (*R*,*R*)-**10** and (*R*,*R*)-**11** form complexes with α-phenylethylammonium perchlorate (PEA) and α-(1-naphthyl)ethyl ammonium perchlorate (NEA) but do not discriminate between their enantiomers. All three chiral crown ethers bind strongly cations of ionic radii $<\sim 1$ Å.

1. Introduction

Proton-ionizable crown ethers have received a great deal of attention, because at pH values higher than their pK_a, they are mostly ionized to ligand anions, which increase the cation–ligand complex stability with enhancement of selectivity, and avoid the need for a counter anion in cation transport through various membrane systems or in solvent extraction.[1–3] The latter feature is very advantageous especially in the case of practical separations where the transport of hydrophilic aqueous phase anions, such as chloride, nitrate and sulfate should be avoided.[2]

Using proton-ionizable crown ethers as carriers in an aqueous source phase–lipophilic membrane–aqueous receiving phase system the transport is mostly pH dependent, so it can be turned on and off by adjusting the pH.[3] The proton-ionizable crown ether carrier should be lipophilic enough to stay in the organic membrane in both complexed and uncomplexed forms, otherwise it leaks into the aqueous phase and it is not available further as a carrier.[3] Our interest has been focused on proton-ionizable macrocycles in which the acidic unit is part of the macroring, thus after deprotonation the negatively charged heteroatom (usually oxygen or nitrogen) is in the coordination sphere, which surrounds the complexed cation.[4–6]

There has always been a strong demand to prepare proton-ionizable crown compounds, which can dissociate to ligand anions at relatively low pH values. These acidic proton-ionizable macrocycles can also be used to transport some heavy metal cations and organic primary ammonium ions from a source phase of relatively low pH value.[3] More than two decades ago Bradshaw and coworkers prepared the achiral and racemic proton-ionizable ligands **1** and *rac*-**2**, respectively, containing a fairly acidic dialkylhydrogenphosphate unit (see Fig. 1).[7] The lipophilic ionophore *rac*-**2** showed a reasonable transport of alkali and some heavy metal cations in an aqueous source phase–dichloromethane bulk membrane–aqueous receiving phase system.[8]

In connection with our present work it is noteworthy to mention that natural ionophores such as valinomycin, monactin, dinactin, monensin, lasalocid, salinomycin, nigericin, narasin and many others are optically active compounds and their stereostructure

☆ Preliminary results presented at the Second International Symposium on Macrocyclic and Supramolecular Chemistry, Salice Terme, Italy, 24–28 June, 2007.

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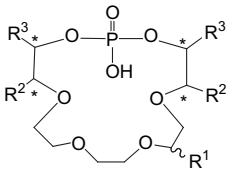
doi:10.1016/j.tet.2008.07.111



1: $R^1=R^2=R^3=H$
rac-**2**: R^1=octyl, $R^2=R^3=H$
(*S*,*S*)-**3**: $R^1=R^2=H$, R^3=Me
(*S*,*S*)-**4**: $R^1=R^3=H$, R^2=Me
(*S*,*S*)-**5**: $R^1=R^2=H$, R^3=octyl
(*S*,*S*)-**6**: $R^1=R^3=H$, R^2=octyl

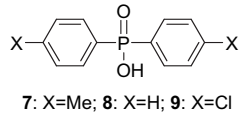
Figure 1. Schematics of the reported proton-ionizable crown ethers containing a dialkylhydrogenphosphate moiety.

plays a crucial role in the selective transport of biologically important metal cations through biomembranes.[9,10] It has been reported that the stereostructure of optically active artificial host molecules also plays an important role in binding, solvent extraction and transport of metal cations.[11–13] Motivated by the latter findings we prepared recently the enantiopure proton-ionizable crown ethers (*S*,*S*)-**3**–(*S*,*S*)-**6** (see Fig. 1) containing a dialkylhydrogenphosphate moiety.[6]

Mastryukova and co-workers reported the pK_a values of some substituted diarylphosphinic acids (**7**–**9** see Fig. 2) determined by potentiometry in three different (7% EtOH–93% H_2O, 50% EtOH–50% H_2O, 80% EtOH–20% H_2O) mixtures of ethanol and water.[14] These values in the order of the above mixtures are pK_a of **7**: 2.47, 3.66, 4.45; pK_a of **8**: 2.32, 3.43, 4.24; pK_a of **9**: 1.86, not given, 3.48.

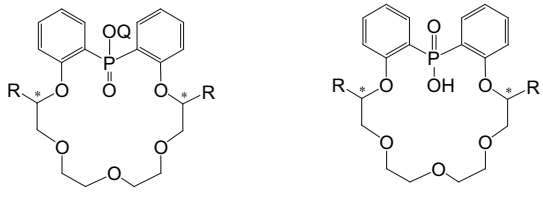
As an extension of our research in order to find crown ether type host molecules possessing enhanced selectivity for both the enantiomers of protonated primary amines and metal cations in binding, solvent extraction, membrane transport and other studies, we prepared novel enantiopure macrocycles (*R*,*R*)-**10**, (*R*,*R*)-**11** and their achiral parent compounds **12**, **13** by hydrolysis of the latter esters (*R*,*R*)-**14** and **15** containing the acidic diarylphosphinic acid moiety (see Fig. 3). Novel proton-ionizable ligands (*R*,*R*)-**14** and **15** seem to have several advantageous features compared to the reported ones **1**–(*S*,*S*)-**6** (see Fig. 1) possessing the dialkylhydrogenphosphate unit. The two aromatic rings make the pseudo-18-crown-6 framework more rigid conferring higher selectivity in the molecular recognition process.[15,16] Ligands (*R*,*R*)-**14** and **15** are more resistant to both acids and bases so their applications can be wider. The aromatic rings of macrocycles (*R*,*R*)-**14** and **15** readily undergo electrophilic substitution and by introducing appropriate substituents into them the acidity of the OH proton, the lipophilicity, the complexation properties and the photophysical behaviour of the latter macrocycles can favourably be altered.

ECD spectroscopy proved to be a simple and powerful tool for monitoring the steric structure, enantiomeric recognition and cation selectivity of chiral pyridino-, phenazino-, acridino-18-crown-6 ethers and other ligands.[17] Preliminary ECD spectroscopic studies on the novel chiral crown compounds (*R*,*R*)-**10**, (*R*,*R*)-**11** and (*R*,*R*)-**14** are also reported here.



7: X=Me; **8**: X=H; **9**: X=Cl

Figure 2. Schematics of diarylphosphinic acids.



(*R*,*R*)-**10**: Q=Et, R=Me
(*R*,*R*)-**11**: Q=Me, R=Me
12: Q=Et, R=H
13: Q=Me, R=H

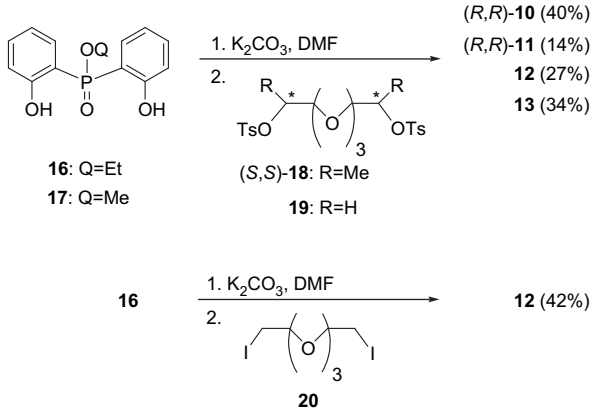
(*R*,*R*)-**14**: R=Me
15: R=H

Figure 3. Schematics of novel enantiopure macrocycles (*R*,*R*)-**10**, (*R*,*R*)-**11**, (*R*,*R*)-**14** and achiral parent compounds **12**, **13**, **15**.

2. Results and discussion

2.1. Synthesis

The enantiopure ligand (*R*,*R*)-**10** (see Scheme 1) was prepared from the reported ethyl bis(2-hydroxyphenyl)phosphinate (**16**)[18] and enantiopure dimethyl-substituted tetraethylene glycol ditosylate (*S*,*S*)-**18**[19,20] at 50 °C in DMF using K_2CO_3 as a base. Our research group showed that the reactions of different phenols with enantiopure secondary tosylates in the presence of K_2CO_3 using several dipolar aprotic solvents can lead to some extent of racemization when carried out at temperatures higher than 50 °C, thus to secure total inversion of configuration, the reaction temperature was always kept at or below 50 °C.[19–21] Enantiopure macrocycle (*R*,*R*)-**11** was prepared in a similar manner as described above for obtaining ligand (*R*,*R*)-**10** using ditosylate (*S*,*S*)-**18** and the unreported methyl bis(2-hydroxyphenyl)phosphinate (**17**, see Scheme 1).



16: Q=Et
17: Q=Me

(*S*,*S*)-**18**: R=Me
19: R=H

(*R*,*R*)-**10** (40%)
(*R*,*R*)-**11** (14%)
12 (27%)
13 (34%)

16

20

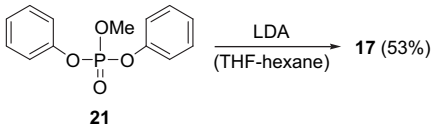
12 (42%)

Scheme 1. Preparation of novel macrocycles containing the diarylphosphinic acid alkyl ester moieties.

The achiral parent compounds **12** and **13** were obtained from phosphinates **16** and **17**, respectively, using the reported tetraethylene glycol ditosylate (**19**)[19] and applying similar reaction conditions as in the case of optically active ligands (*R*,*R*)-**10** and (*R*,*R*)-**11** (see Scheme 1). Ligand **12** was also prepared in a better yield using the reported α,ω-diiodo-oligoether **20**[22] instead of ditosylate **19** (see Scheme 1).

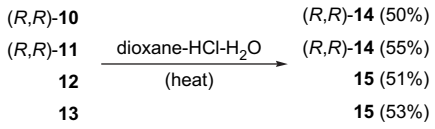
Methyl bis(2-hydroxyphenyl)phosphinate (**17**) was obtained from the reported diphenyl methyl phosphate (**21**)[23] by applying the method described for the preparation of phosphinate **16**[18] with minor modifications (see Scheme 2).

Enantiopure proton-ionizable ligand (*R*,*R*)-**14** containing the diarylphosphinic acid moiety was prepared from the corresponding phosphinic acid esters (*R*,*R*)-**10** and (*R*,*R*)-**11**, respectively, by acidic hydrolysis at elevated temperature using a dioxane–10% aqueous HCl (1:1) mixture (see Scheme 3). The achiral proton-ionizable



Scheme 2. Preparation of methyl bis(2-hydroxyphenyl)phosphinate (**17**).

ligand **15** was obtained from esters **12** and **13**, respectively, applying the same reaction conditions as the ones used in the case of optically active ligand (*R*,*R*)-**14** (see Scheme 3).



Scheme 3. Preparation of novel proton-ionizable crown ethers containing the diarylphosphinic acid moiety.

2.2. Electronic circular dichroism (ECD) spectroscopy

The ECD spectra of chiral crown ethers (*R*,*R*)-**10**, (*R*,*R*)-**11** and (*R*,*R*)-**14** were studied in solvents of different polarity. In acetonitrile (MeCN) the ECD curves of (*R*,*R*)-**10** and (*R*,*R*)-**11** overlap in the 190–330 nm spectral range. The ECD spectrum of (*R*,*R*)-**11** was also measured in 2,2,2-trifluroethanol (TFE), MeOH and 2,2,4-trimethylpentane (isooctane, iOc). Below ~250 nm the spectra of (*R*,*R*)-**11** in all four solvents are marked by two pairs of oppositely signed bands (Fig. 4). Two oppositely signed bands are seen also in the ^1L_b spectral region (see the inset of Fig. 4). The positive band shows a short-wavelength shoulder, which is most separated in iOc and MeCN.

The intensity of the ^1B_b bands below 210 nm is rather high (Table 1). It fulfils the requirement of exciton interaction. The ^1L_a bands also appear with increased intensity. The band positions and intensities of the spectra in iOc, MeCN and MeOH are similar. The less intense ECD bands of (*R*,*R*)-**11** in TFE show a definite blue shift that is likely due to the effect of the strong proton-donating solvent upon the excitation energies and/or conformation. The similarity of the ECD spectra of (*R*,*R*)-**11** in MeCN, MeOH and iOc suggest that the same conformer (*a*) dominates the conformational equilibrium in these solvents and the orientation of the electric transition moment vectors are rather similar. Based on the same sign pattern of the ECD bands observed in TFE and the same negative sign of the ^1B_b exciton couplet, the structure of (*R*,*R*)-**11** in TFE does not differ significantly from conformer *a*. It is an intriguing question whether or not the positive–negative pair of the ^1L_a bands is a consequence of weaker exciton interaction. Remarkably, the sum of the absolute band intensities is the lowest in the spectrum in TFE.

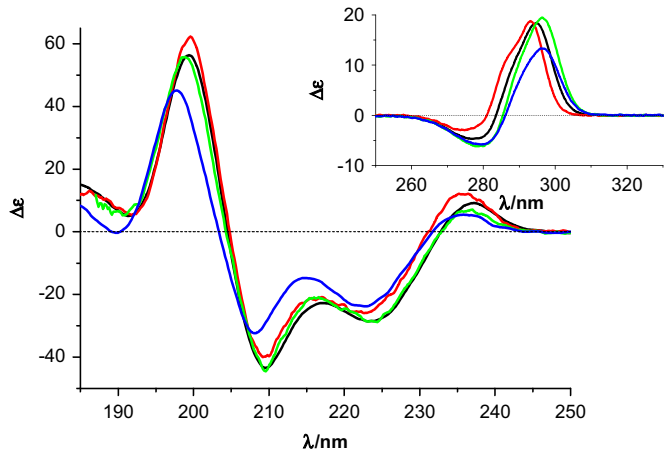


Figure 4. Far-UV ECD spectra of (*R*,*R*)-**11** in MeCN (black), iOc (red), MeOH (green) and TFE (blue). Inset: near-UV ECD spectra in same solvents.

The ECD spectrum of crown ether (*R*,*R*)-**14** containing the diarylphosphinic acid unit was measured in MeCN, MeOH, H_2O and TFE [(*R*,*R*)-**14** is not soluble in iOc]. In MeCN the spectrum features one strong asymmetric band below 250 nm (Fig. 5), while two weak bands are present in the ^1L_b spectral region. Contrary to this, five bands appear in MeOH and H_2O above 190 nm. The increased intensity of the negative–positive pair of bands below 210 nm is compatible with exciton interaction between the ^1B_b transitions of the *o*-substituted benzene rings. The ECD spectrum in TFE is dominated by a positive band at 204 nm ($\Delta\varepsilon$=47.8) with a long-wavelength shoulder and a strong negative band at 192 nm ($\Delta\varepsilon$=−23.5). The ^1L_a bands are rather weak in MeOH and H_2O and are almost absent in TFE. Apparently, the spectra measured in protic solvents are strongly influenced by high energy electronic transitions. The ^1L_b region of the spectra in H_2O and MeOH are marked by a relatively strong positive band near 290 nm with a short-wavelength shoulder and a weak negative band below 280 nm (Table 1, Fig. 5, inset). In MeCN the broad negative band is much more intense than the positive one. In TFE only one broad negative band appears.

The sign and position of the negative couplet in the ECD spectra of (*R*,*R*)-**11** in iOc, MeCN and MeOH are the same as those of the negative couplet in the spectra of (*R*,*R*)-**14** in MeOH and H_2O. This is a sign of the dominance of basically the same conformation (*a*) that is a similar relative position of the benzene rings attached to the P-atom. MeCN is a nonprotic solvent that stabilizes another conformation of (*R*,*R*)-**14** (conformer *b*), TFE only changes the position and amplitude of the negative couplet of (*R*,*R*)-**11** while it has a dramatic spectral effect for (*R*,*R*)-**14**. Titration of the MeCN solution of (*R*,*R*)-**14** with H_2O gives rise to a gradual shift of the spectrum from that measured in MeCN to the other one observed in H_2O. The same behaviour is seen in the ^1L_b region upon water titration (Fig. 6). The ECD curves have two isodichroic points at 233 nm and ~203 nm strongly suggesting the presence of two conformers: *a* and *b*.

In summary, ECD measurements indicated the presence of one dominant conformer (*a*) for (*R*,*R*)-**11** and two conformers (*a* and *b*) and a third species observed only in TFE for (*R*,*R*)-**14**. According to ECD spectroscopic studies, enantiomers of α-phenylethylammonium perchlorate (PEA) interact with (*R*,*R*)-**11** at a 1:1 molar ratio but do not result in a significant conformational change. In the presence of (*R*)- or (*S*)-PEA the band positions are practically the same but the amplitudes are smaller than in the spectrum of (*R*,*R*)-**11** (not shown). The two ECD curves do not differ significantly. In short, we cannot speak about enantiomer discrimination.

Enantiomers of α-(1-naphthyl)ethylammonium perchlorate (NEA) interact more strongly with (*R*,*R*)-**11**. According to the sum spectrum, the increased intensity of the band at 223 nm is due to the negative band of (*R*)-NEA. The spectral effect of (*S*)-NEA is less significant: the bands are less intense and similar to the spectra measured in the presence of the enantiomers of PEA. This is a consequence of the positive band of (*S*)-NEA at 222 nm. The sum spectra ($\Delta\varepsilon_{sum}=\Delta\varepsilon_{host}+\Delta\varepsilon_{NEA}$) clearly reflect complexing of NEA but the difference spectra ($\Delta\Delta\varepsilon=\Delta\varepsilon_{exp}-\Delta\varepsilon_{sum}$) are indicative of the lack of enantiomer discrimination (Fig. 7).

The complexing ability and discriminating power of the phosphinic acid (*R*,*R*)-**14** against the deprotonated form of NEA enantiomers were also probed in MeCN. The ECD spectra (not shown) clearly show that (*R*,*R*)-**14** does not bind NEA amines at a 1:1 molar ratio and does not discriminate between the enantiomers. The unique ECD spectrum of the phosphinic acid (*R*,*R*)-**14** in MeCN, the lack of enantiomer discrimination against PEA and NEA, and its negligible affinity for deprotonated NEA as well as the result of

Table 1
ECD data of (*R*,*R*)-**10**, (*R*,*R*)-**11** and (*R*,*R*)-**14**

Crown ether compounds	Solvents	λ_{nm} ($\Delta\varepsilon$)				
(*R*,*R*)-**10**	MeCN		200 (62.3)	210 (−47.2)	224 (−30.8)	237 (8.6)
(*R*,*R*)-**11**	iOc		200 (62.2)	209 (−40.1)	223 (−25.9)	236 (12.1)
	MeCN		199 (56.4)	210 (−43,5)	223 (−28.5)	237 (9.2)
	MeOH		199 (55.8)	210 (−44.5)	224 (−28.8)	237 (7.1)
	TFE		198 (45.1)	208 (−32.4)	223 (−23.8)	236 (5.5)
(*R*,*R*)-**14**	MeCN		196 (−5.4)	209 (37.5)		
	H_2O	193 (−11.7)	200 (32.9)	209 (−32.1)	221 (−17.8)	237 (6.6)
	MeOH	193 (−15.5)	201 (34.6)	210 (−16.9)	225 (−14.6)	237 (6.2)
	TFE	192 (−23.5)	204 (47.8)	213 sh (20.1), 216 sh (15.2)	228 (−1.3)	

Crown ether compounds	Solvents	λ_{nm} ($\Delta\varepsilon$)		
(*R*,*R*)-**11**	iOc	275 (−2.9)	287 sh (11.4)	293 (18.8)
	MeCN	277 (−4.7)	288 sh (9.5)	295 (18.4)
	MeOH	280 (−6.1)	290 sh (10.7)	296 (19.5)
	TFE	279 (−5.8)	290 sh (7.6)	296 (13.3)
(*R*,*R*)-**14**	MeCN	277 (−3.8)	283 (−3.4)	
	H_2O	273 (−2.0)	284 (5.4)	290 (10.3)
	MeOH	275 (−2.1)	283 (2.0)	291 (7.2)
	TFE	279 (−3.5)	282 (−3.5)	

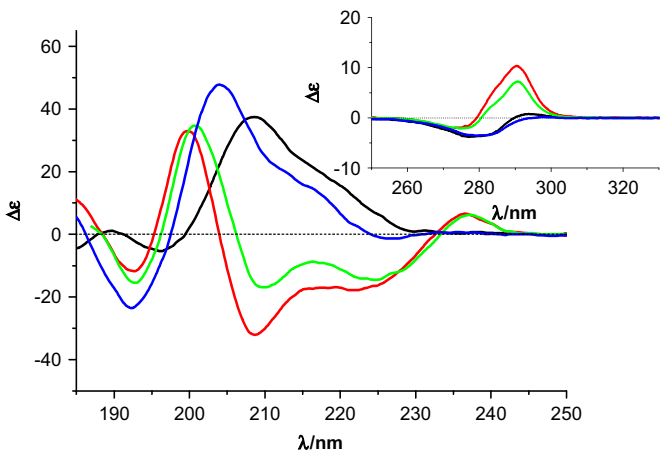


Figure 5. Far-UV ECD spectra of (*R*,*R*)-**14** in MeCN (black), H_2O (red), MeOH (green) and TFE (blue). Inset: near-UV ECD spectra in same solvents.

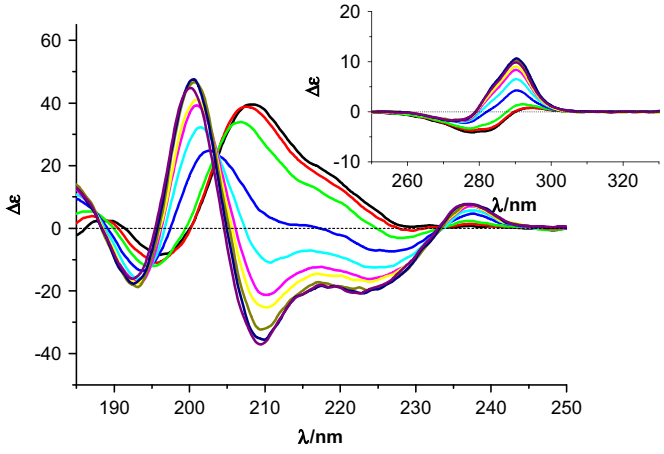


Figure 6. ECD spectroscopy monitored water titration of (*R*,*R*)-**14** starting from 1% v/v H_2O in MeCN to 75% v/v H_2O in MeCN. Inset: near-UV spectra in the same solvent mixture (1% v/v black, 2.5% v/v red, 5% v/v green, 10% v/v blue, 15% v/v pale blue, 20% v/v magenta, 25% v/v yellow, 35% v/v dark yellow, 50% v/v navy, 75% v/v purple).

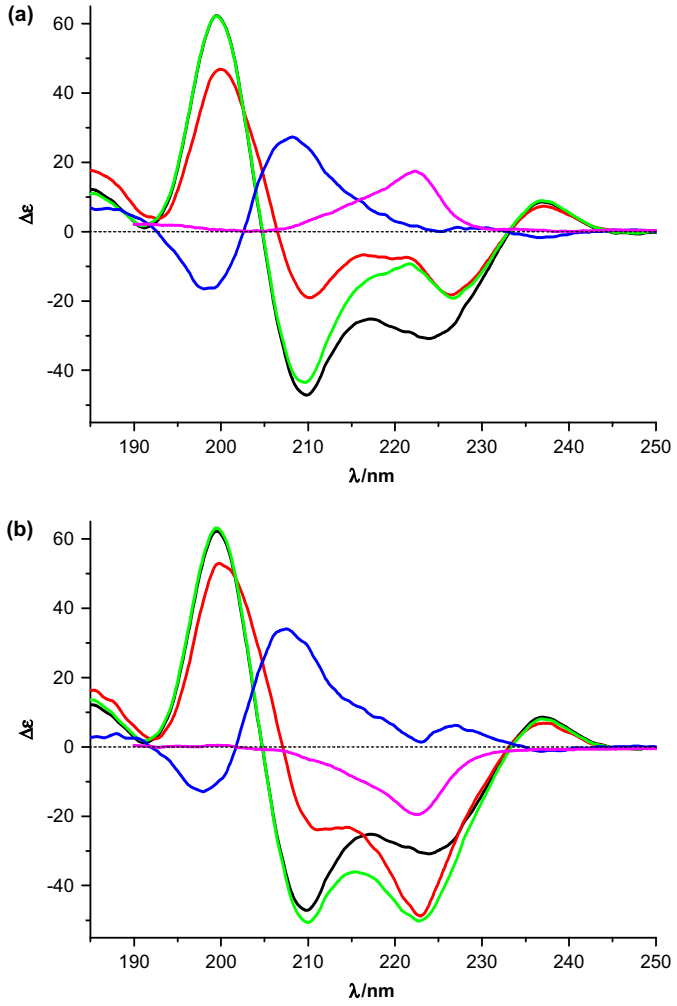


Figure 7. The ECD spectra of (a) (*R*,*R*)-**10** (black), the heterochiral complex with (*S*)-NEA (red) compared to the sum [($\Delta\varepsilon_{sum}=\Delta\varepsilon_{host}+\Delta\varepsilon_{NEA}$), green] and difference [($\Delta\Delta\varepsilon=\Delta\varepsilon_{exp}-\Delta\varepsilon_{sum}$), blue] spectra and the spectrum of (*S*)-NEA (magenta); (b) (*R*,*R*)-**10** (black), the homochiral complex with (*R*)-NEA (red) compared to the sum [($\Delta\varepsilon_{sum}=\Delta\varepsilon_{host}+\Delta\varepsilon_{NEA}$), green] and difference [($\Delta\Delta\varepsilon=\Delta\varepsilon_{exp}-\Delta\varepsilon_{sum}$), blue] spectra and the spectrum of (*R*)-NEA (magenta).

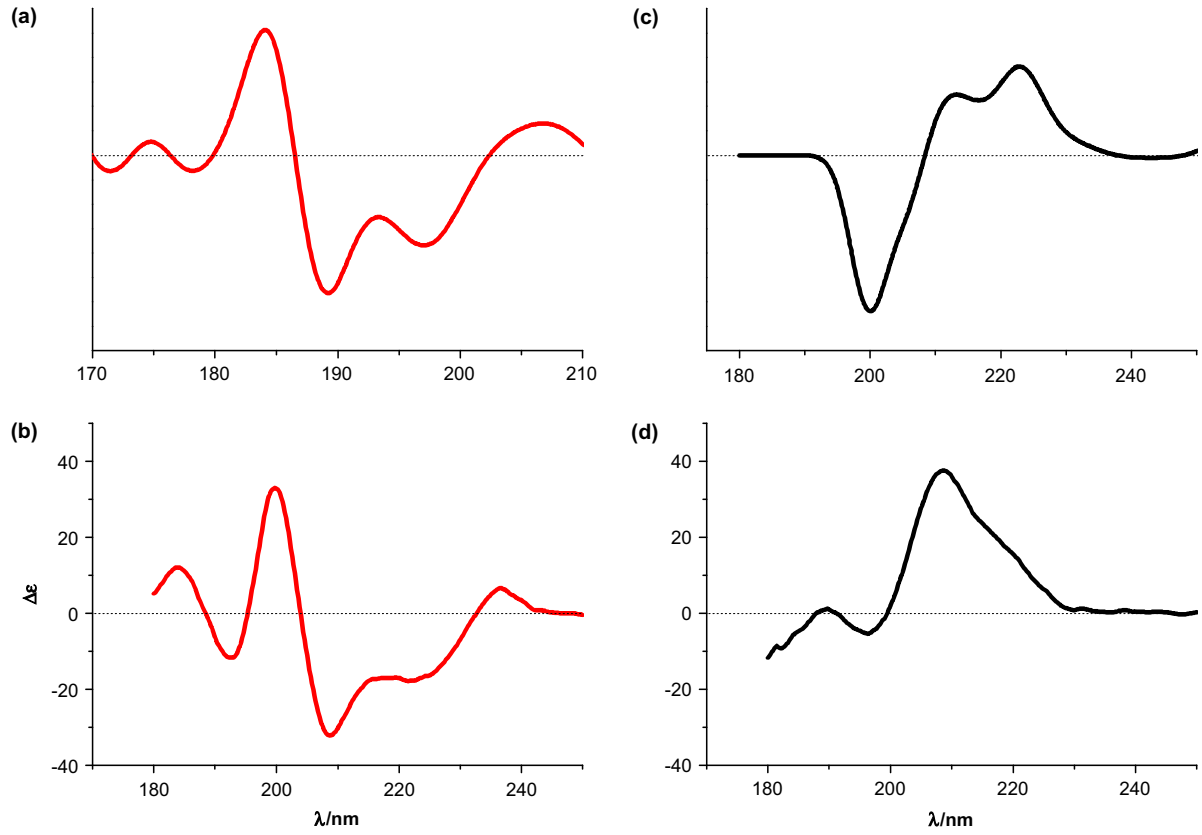


Figure 8. B3LYP/6-311G(d,p) computed ECD spectra of (*R*,*R*)-**14** (a) monomer and (c) dimer compared with experimental results of (*R*,*R*)-**14** (b) in H_2O and (d) in MeCN.

water titration of the MeCN solution of (*R*,*R*)-**14** (Fig. 6) prompted us to consider the possibility of dimerization or aggregation of the crown ether through the POOH groups. Asfin and co-workers described the formation of dimers of simple R_2POOH molecules with a strong H-bond (ΔH=24–50 kcal/mol) in the gas phase, low-temperature argon and N_2 matrices, and crystalline films.[24] Formation of dimers of type R_2POOH phosphinic acids (R=CH_3, CH_2Cl, C_6H_5) was also observed in CCl_4 and CH_2Cl_2 solutions.[25] To support the possible aggregation of the chiral crown ether phosphinic acid (*R*,*R*)-**14**, theoretical calculations were applied. Structure optimization was performed at the B3LYP/6-311+G(d,p) level of theory in the case of both the monomer and the dimer forms of (*R*,*R*)-**14**. For the calculated conformers, time-dependent DFT calculations were carried out to receive the ECD spectrum. The results show similar differences as in the experimental case. The calculated ECD spectrum of (*R*,*R*)-**14** monomer is blue shifted (about 20 nm) but shows the same shape as the measured ECD spectrum. Calculation was repeated for the dimer form. As shown in Figure 8, the calculated ECD spectrum does not agree in details with the one measured in acetonitrile. Nevertheless, the experimental spectrum in acetonitrile does not fit the predicted spectrum of the monomer and therefore suggest dimerization or another form of aggregation.

Aggregation of the phosphinic acid-based crown ether (*R*,*R*)-**14** gives an explanation for its unique ECD spectrum in MeCN and the lack of the formation of stable complexes with PEA and NEA perchlorates and amines. In protic solvents (H_2O, MeOH and TFE) the POOH groups are solvated and cannot fix the dimer or aggregate form.

Preliminary ECD studies have shown that both the phosphinates (*R*,*R*)-**10**, (*R*,*R*)-**11** and the phosphinic acid (*R*,*R*)-**14** form complexes with a variety of cations with ionic radii $<\sim 1$ Å (Li^+, Mg^{2+}, Zn^{2+}, Fig. 9). The strong negative ^1B_b couplet of (*R*,*R*)-**10** and (*R*,*R*)-**11** is replaced by a strong positive one in MeCN at $r_{cat}>1$ (r_{cat}=[cation]/[crown ether]). ECD titration with Mg^{2+} ions clearly showed the formation of a 1:1 complex. Phosphinic acid (*R*,*R*)-**14** also binds Li^+, Mg^{2+} and Zn^{2+} ions in MeCN. The comparison of the shape of the ECD spectra of the Mg^{2+} complexes of (*R*,*R*)-**10** and (*R*,*R*)-**14** and the ECD monitored titration of the crown ethers in MeCN indicate the formation of 1:1 complexes with basically the same overall conformation of the macrorings (Fig. 10). It is a question of whether or not the H-bonds between the POOH groups of the phosphinic acids are preserved or replaced by an inward position and participation in cation binding of the POOH groups.

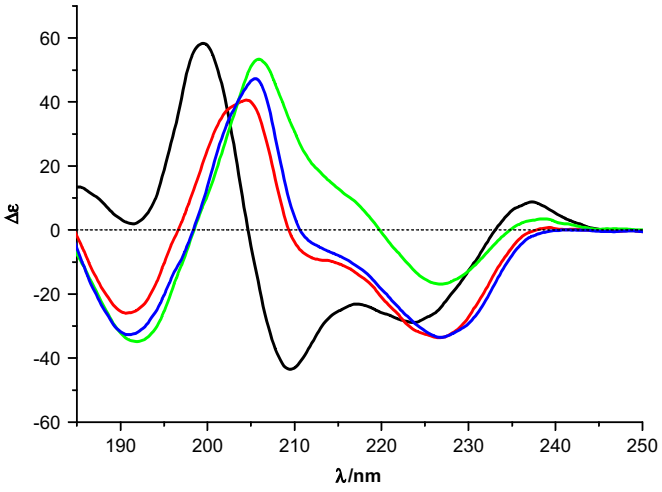


Figure 9. ECD spectra of (*R*,*R*)-**10** (black) and its 1:1 complex (r_{cat}=1) with $Mg(ClO_4)_2$ (red), $Li(ClO_4)$ (green) and $Zn(ClO_4)_2$ (blue).

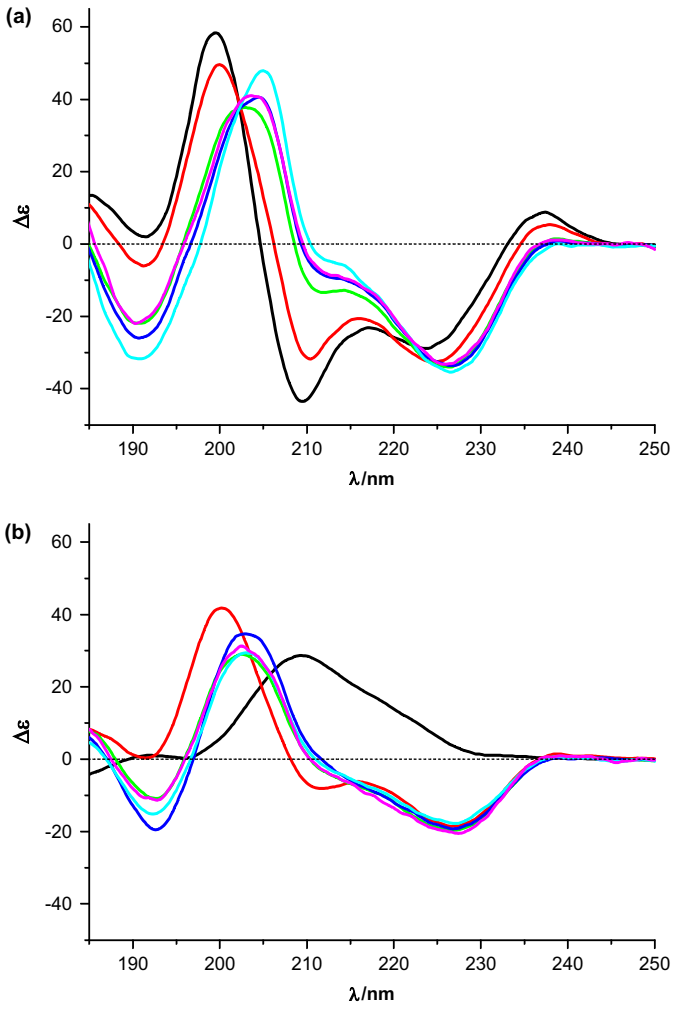


Figure 10. ECD spectra of (a) (*R*,*R*)-**10** (black) and $Mg(ClO_4)_2$ complexes; (b) (*R*,*R*)-**14** (black) and $Mg(ClO_4)_2$ complexes, r_{cat}=0.5 (red), r_{cat}=0.8 (green), r_{cat}=1 (blue), r_{cat}=2 (pale blue), r_{cat}=4 (magenta).

3. Conclusion

The synthesis and characterization of a new type of chiral crown ethers and their achiral analogues containing an alkyl diarylphosphinate moiety or a diarylphosphinic acid unit have been achieved. The ECD spectra of the chiral crown ethers (*R*,*R*)-**10**, (*R*,*R*)-**11** containing an alkyl diarylphosphinate moiety showed strong exciton splitting in the ^1B_b spectral region of the aromatic chromophores. In the case of the proton-ionizable chiral crown ether (*R*,*R*)-**14** containing the phosphinic acid unit the ECD spectrum measured in MeCN suggested dimerization or aggregation. This finding was confirmed by theoretical calculation. Contrary to this, in protic solvents (MeOH, H_2O) the ECD spectra showed exciton interaction of the ^1B_b transitions. The sign and position of the negative ^1B_b couplet of (*R*,*R*)-**11** in iOc, MeCN and MeOH are the same as those of the negative couplet in the spectra of (*R*,*R*)-**14** in MeOH and H_2O. This is a sign of the dominance of basically the same structure (conformer *a*) that is a similar relative position of the benzene rings attached to the P-atom. MeCN is a nonprotic solvent that stabilizes the dimer or aggregate form of (*R*,*R*)-**14** (conformer *b*). According to ECD spectroscopic studies, enantiomers of α-phenylethylammonium perchlorate (PEA) interact with (*R*,*R*)-**11** at a 1:1 molar ratio. However, the two ECD curves do not differ significantly, there is no sign of enantiomer discrimination. Enantiomers of α-(1-naphthyl)ethylammonium perchlorate (NEA) interact more strongly with (*R*,*R*)-**11**. The sum spectra clearly reflect complexing of NEA but the difference spectra are indicative of the lack of enantiomer discrimination. Ligand (*R*,*R*)-**14** does also not discriminate between the enantiomers of NEA and those of the unprotonated NEA, respectively. This can be explained by aggregation of (*R*,*R*)-**14**. Preliminary ECD studies have shown that ligands (*R*,*R*)-**10**, (*R*,*R*)-**11** and (*R*,*R*)-**14** form complexes with a variety of cations with ionic radii $<\sim 1$ Å (e.g., Li^+, Mg^{2+}, Zn^{2+}). The strong negative ^1B_b couplet of (*R*,*R*)-**10** and (*R*,*R*)-**11** is replaced by a strong positive one in MeCN at cation to crown ether molar ratios >1. Our results clearly show the power of ECD spectroscopy in characterizing the conformations of chiral crown ethers and their complexes. Detailed UV and ECD titration experiments are in progress to determine the cation selectivity, stoichiometry and stability of cation complexes of novel ligands (*R*,*R*)-**10**, (*R*,*R*)-**11**, **12**, **13**, (*R*,*R*)-**14** and **15**.

4. Experimental

4.1. General

Infrared spectra were recorded on a Zeiss Specord IR 75 spectrometer. Optical rotations were taken on a Perkin–Elmer 241 polarimeter that was calibrated by measuring the optical rotations of both enantiomers of menthol. ^1H (500 MHz, reference: TMS) NMR spectra were obtained on a Brucker DRX-500 Avance spectrometer. ^{13}C NMR spectra were taken either on a Bruker DRX-500 Avance spectrometer (125.8 MHz, reference: TMS) or on a Brucker 300 Avance spectrometer (75.5 MHz, reference: TMS) and it is indicated in each individual case. ^{13}P (121.5 MHz, reference: H_3PO_4) NMR spectra were recorded on a Brucker 300 Avance spectrometer. Mass spectra were recorded on a ZQ 2000 MS instrument (Waters Corp.) using ESI method. Elemental analyses were performed in the Microanalytical Laboratory of the Department of Organic Chemistry, Institute of Chemistry, L. Eötvös University, Budapest, Hungary. Melting points were taken on a Boetius micro-melting point apparatus and were uncorrected. Starting materials were purchased from Aldrich Chemical Company unless otherwise noted. Silica gel 60 F_{254} (Merck) and aluminium oxide 60 F_{254} neutral type E (Merck) plates were used for TLC. Aluminium oxide (neutral, activated, Brockman I) and silica gel 60 (70–230 mesh, Merck) 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[26] methods. Evaporations were carried out under reduced pressure unless otherwise stated.

Electronic circular dichroism measurements were performed on a Jasco Dichrograph J-810 at room temperature using 0.02 cm quartz cell for measurements between 185 and 250 nm and using 0.1 cm between 250 and 330 nm. The spectra were averaged of five scans. The concentration of crown ethers was 0.5 mM.

Geometry optimizations and the computation of ECD spectra were performed at the B3LYP/6-311+G(d,p) and B3LYP/6-311G(d,p) DFT levels with the Gaussian 03 quantum chemical software package.[27]

4.2. Synthesis

*4.2.1. (6R,16R)-22-Ethoxy-6,16-dimethyl-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one [(R,R)-**10**]*

Ethyl bis(2-hydroyphenyl)phosphinate (**16**) (2.1 g, 7.5 mmol), dimethyl-substituted tertaethylene glycol ditosylate (*S*,*S*)-**18** (4.0 g, 7.5 mmol) and finely powdered anhydrous K_2CO_3 (10.4 g, 75.2 mmol) were mixed with vigorous stirring in dry DMF (84 mL) at rt under Ar. After stirring the reaction mixture at rt for 10 min, the flask was immersed in an oil bath and the temperature of the reaction mixture was raised to 50 °C and kept at this temperature

with vigorous stirring until TLC analysis showed the total consumption of the starting ditosylate (*S*,*S*)-**18** (20 days). The solvent was removed at 40 °C and the residue was taken up in a mixture of ice-water (160 mL) and CH_2Cl_2 (200 mL). The aqueous phase was extracted with CH_2Cl_2 (3×60 mL). The combined organic phase was shaken with water (200 mL), dried over $MgSO_4$, filtered and the solvent was removed. The crude product was purified by chromatography first on aluminium oxide using EtOH–toluene (1:80) mixture as an eluent followed by chromatography on silica gel using MeOH–CH_2Cl_2 (1:40) mixture as an eluent. The white solid was recrystallized from hot hexane to give (*R*,*R*)-**10** (1.41 g, 40%) as white needles. Mp: 111–112 °C (hexane). R_f: 0.25 (aluminium oxide TLC, EtOH–toluene 1:40), R_f: 0.14 (silica gel TLC, MeOH–CH_2Cl_2 1:40); $[\alpha]_D^{25}$ −3.13 (*c* 3.8, CH_2Cl_2); IR (KBr) ν_{max} 3064, 3040, 2976, 2952, 2936, 2912, 2896, 1696, 1592, 1476, 1448, 1380, 1288, 1264, 1244, 1224, 1208, 1144, 1128, 1116, 1080, 1072, 1032, 984, 928, 872, 792, 760, 712, 608, 552 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (d, *J*=7 Hz, 3H), 1.26 (d, *J*=7 Hz, 3H), 1.39 (t, *J*=7 Hz, 3H), 2.76–2.79 (m, 2H), 2.89–2.92 (m, 2H), 2.93–3.06 (m, 2H), 3.29–3.40 (m, 6H), 3.86–3.88 (m, 1H), 4.16–4.18 (m, 1H), 4.51–4.55 (m, 2H), 6.94–7.06 (m, 4H), 7.45–7.54 (m, 2H), 7.91–7.94 (m, 1H), 8.19–8.22 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 16.65 (d, *J*=6.82 Hz, ethyl CH_3), 17.42 and 17.56 (s, diastereotopic CH_3 groups attached to the macroring), 60.18 (d, *J*=5.58 Hz, ethyl CH_2O), 71.08 and 71.12 (s, diastereotopic OCH_2 groups), 71.20 and 71.32 (s, diastereotopic OCH_2 groups), 72.50 and 73.38 (s, diastereotopic OCH_2 groups), 74.52 and 74.58 (s, diastereotopic OCH groups), 112.34 and 113.14 (d, *J*=7.44 and 8.68 Hz, diastereotopic ArC_3), 119.95 (d, *J*=12.41 Hz, ArC_5), 121.10 and 122.67 (d, *J*=134.60 and 150.11 Hz, diastereotropic ArC_1 next to P atom), 132.89 and 136.43 (d, *J*=1.86 and 6.82 Hz, diastereotopic ArC_6), 133.40 and 133.46 (s, diastereotopic ArC_4), 159.32 and 160.19 (d, *J*=3.72 and 5.58 Hz, diastereotopic ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 25.25; MS: 465 $(M+1)^+$. Anal. Calcd for $C_{24}H_{33}O_7P$: C, 62.06; H, 7.16; P, 6.67. Found: C, 62.04; H, 7.20; P, 6.46.

*4.2.2. (6R,16R)-22-Methoxy-6,16-dimethyl-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one [(R,R)-**11**]*

Optically active ligand (*R*,*R*)-**11** was prepared in the same way as described above for its analogue (*R*,*R*)-**10** starting from methyl bis(2-hydroxyphenyl)phosphinate (**17**) (0.50 g, 1.9 mmol), ditosylate (*S*,*S*)-**18** (1.0 g, 1.9 mmol), finely powdered anhydrous K_2CO_3 (2.63 g, 19 mmol) and pure DMF (22 mL). White needles. Yield: 0.12 g (14%). Mp: 127–128 °C (hexane). R_f: 0.25 (aluminium oxide TLC, EtOH–toluene 1:40), R_f: 0.14 (silica gel TLC, MeOH–CH_2Cl_2 1:40); $[\alpha]_D^{25}$ −21.4 (*c* 1.0, CH_2Cl_2); IR (KBr) ν_{max} 3120, 3056, 3040, 2974, 2948, 2910, 2872, 1592, 1480, 1460, 1448, 1376, 1288, 1264, 1248, 1232, 1216, 1144, 1120, 1104, 1028, 960, 884, 792, 768, 568, 552, 516 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (d, *J*=6.5 Hz, 3H), 1.15 (d, *J*=6.5 Hz, 3H), 2.75–2.79 (m, 2H), 2.90–2.96 (m, 2H), 3.01–3.07 (m, 2H), 3.29–3.40 (m, 6H), 3.68 (d, $|^3J|_{P-H(Me)}$=11 Hz, 3H), 4.50–4.57 (m, 2H), 6.95–7.06 (m, 4H), 7.36–7.45 (m, 2H), 7.84–7.87 (m, 1H), 8.11–8.14 (m, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.43 and 17.47 (s, diastereotopic CH_3 groups attached to the macroring), 50.96 (d, *J*=6.20 Hz, OCH_3), 71.07 and 71.12 (s, diastereotopic OCH_2 groups), 71.23 and 71.27 (s, diastereotopic OCH_2 groups), 72.73 and 73.33 (s, diastereotopic OCH_2 groups), 74.49 and 74.54 (s, diastereotopic OCH_2 groups), 112.49 and 113.18 (d, *J*=7.44 and 8.06 Hz, diastereotopic ArC_3), 120.00 and 120.05 (d, *J*=11.79 and 12.41 Hz, diastereotopic ArC_5), 120.34 and 122.34 (d, *J*=134.60 and 150.11 Hz, diastereotopic ArC_1 next to P atom), 133.00 and 133.57 (d, *J*=1.24 and 1.86 Hz, diastereotopic ArC_4), 133.29 and 136.54 (d, *J*=3.72 and 7.44 Hz, diastereotopic ArC_6), 159.34 and 160.17 (d, *J*=3.72 and 5.58 Hz, diastereotopic ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 27.69; MS: 451 $(M+1)^+$. Anal. Calcd for $C_{23}H_{31}O_7P$: C, 61.33; H, 6.94; P, 6.88. Found: C, 61.12; H, 6.74; P, 6.86.

*4.2.3. 22-Ethoxy-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one (**12**)*

*4.2.3.1. Starting from ditosylate **19**.* Achiral ligand **12** was prepared as described above for its optically active analogue (*R*,*R*)-**10** starting from ethyl bis(2-hydrosyphenyl)phosphinate (**16**) (0.50 g, 1.8 mmol), ditosylate **19** (0.19 g, 1.8 mmol), finely powdered anhydrous K_2CO_3 (2.5 g 18 mmol) and pure DMF (21 mL). White prisms. Yield: 0.21 g (27%). Mp: 88–89 °C (isopropyl ether). R_f: 0.20 (aluminium oxide TLC, EtOH-toluene 1:40), R_f: 0.10 (silica gel TLC, MeOH/CH_2Cl_2 1:40); IR (KBr) ν_{max} 3048, 2960, 2880, 1592, 1576, 1544, 1480, 1448, 1352, 1280, 1232, 1212, 1132, 1104, 1040, 944, 760, 544 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, *J*=7 Hz, 3H), 3.20–3.30 (m, 8H), 3.76–3.89 (m, 4H), 4.05–4.17 (m, 6H), 6.98–7.05 (m, 4H), 7.43–7.46 (m, 2H), 7.94–7.99 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 16.48 (d, *J*=6.06 Hz, CH_3), 60.38 (d, *J*=6.06 Hz, ethyl CH_2O), 67.19 (s, OCH_2), 69.87 (s, OCH_2), 70.75 (s, OCH_2), 71.35 (s, OCH_2), 112.08 (d, *J*=7.27 Hz, ArC_3), 120.12 (d, *J*=12.11 Hz, ArC_5), 121.13 (d, *J*=141.69 Hz, ArC_1 next to P atom), 133.07 (s, ArC_4), 134.37 (d, *J*=6.06 Hz, ArC_6), 160.22 (d, *J*=4.84 Hz, ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 27.08; MS: 437 $(M+1)^+$. Anal. Calcd for $C_{22}H_{29}O_7P$: C, 60.54; H, 6.70; P, 7.10. Found: C, 60.54; H, 6.53; P, 6.86.

*4.2.3.2. Starting from α,ω-diiodo-oligoether **20**.* Ligand **12** was also obtained starting from ethyl bis(2-hydrosyphenyl)phosphinate (**16**) (0.50 g, 1.8 mmol), α,ω-diiodo-oligoether **20** (0.75 g, 1.8 mmol), finely powdered anhydrous K_2CO_3 (2.5 g 18 mmol) and pure DMF (21 mL). Yield: 0.33 g (42%). Macrocycle **12** obtained this way was identical in every respect to that prepared by the previous procedure.

*4.2.4. 22-Methoxy-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one (**13**)*

Achiral macrocycle **13** was prepared as described above for its optically active analogue (*R*,*R*)-**10** starting from methyl bis(2-hydrosyphenyl)phosphinate (**17**) (0.50 g, 1.9 mmol), ditosylate **19** (0.95 g, 1.9 mmol), finely powdered anhydrous K_2CO_3 (2.64 g, 19 mmol) and pure DMF (22 mL). White prisms. Yield: 0.27 g (34%). Mp: 117–118 °C (isopropyl ether). R_f: 0.20 (aluminium oxide TLC, EtOH–toluene 1:40), R_f: 0.10 (silica gel TLC, MeOH–CH_2Cl_2 1:40); IR (KBr) ν_{max} 3064, 3040, 2964, 2872, 1592, 1536, 1472, 1460, 1448, 1352, 1292, 1280, 1256, 1248, 1224, 1216, 1208, 1132, 1120, 1104, 1064, 1040, 992, 932, 888, 824, 796, 764, 712, 568, 488, 448 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.22–3.30 (m, 8H), 3.36–3.43 (m, 4H), 3.72–3.74 (m, 3H), 4.09–4.16 (m, 4H), 6.97–7.04 (m, 4H), 7.43–7.46 (m, 2H), 7.89–7.94 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 51.53 (d, *J*=5.58 Hz, OCH_3), 67.56 (s, OCH_2), 70.04 (s, OCH_2), 70.98 (s, OCH_2), 71.54 (s, OCH_2), 112.31 (d, *J*=7.44 Hz, ArC_3), 120.42 (d, *J*=13.65 Hz, ArC_5), 120.72 (d, *J*=141.42 Hz, ArC_1 next to P atom), 133.51 (d, *J*=1.86 Hz, ArC_4), 134.61 (d, *J*=6.82, ArC_6), 160.47 (d, *J*=4.34 Hz, ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 30.07; MS: 423 $(M+1)^+$. Anal. Calcd for $C_{21}H_{27}O_7P$: C, 59.71; H, 6.44; P, 7.33. Found: C, 59.56; H, 6.43; P, 7.06.

*4.2.5. (6R,16R)-22-Hydroxy-6,16-dimethyl-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one [(R,R)-**14**]*

*4.2.5.1. Starting from ethyl ester (R,R)-**10**.* To a vigorously stirred solution of optically active macrocycle containing the ethyl diarylphosphinate moiety [(*R*,*R*)-**10**] (288 mg, 0.62 mmol) in freshly distilled dioxane (18 mL) was added 10% (w/w) aqueous HCl solution (18 mL) at rt. The flask was immersed in an oil bath and the temperature of the reaction mixture was raised to 80 °C and kept at this temperature with vigorous stirring until TLC analysis showed

the total consumption of the starting material (60 h). After the reaction was completed, the volatile components were removed by distillation at 30 °C. The residue was taken up in freshly distilled dioxane (12 mL) and the solvent was removed. The latter procedure was repeated and the crude product was dried over KOH pellets under reduced pressure. The white solid material was recrystallized from boiling water using charcoal to give pure (*R*,*R*)-**14** (136 mg, 50%) as white prisms. Mp: 181–182 °C (water). R_f: 0.26 (silica gel TLC, MeOH–$ClCH_2CH_2Cl$ 1:4); $[\alpha]_D^{25}$ −100.74 (*c* 1.35, CH_2Cl_2); IR (KBr) ν_{max} 3448, 3064, 3048, 2976, 2968, 2936, 2312, 1659, 1592, 1578, 1476, 1460, 1444, 1412, 1380, 1355, 1280, 1244, 1140, 1112, 1092, 1024, 1008, 992, 976, 940, 804, 756, 708, 608, 560, 512 cm^{-1}; ^1H NMR ($CDCl_3$+D_2O) δ 1.17 (d, *J*=6 Hz, 6H), 3.13–3.16 (m, 2H), 3.27–3.31 (m, 2H), 3.34–3.38 (m, 2H), 3.43–3.47 (m, 2H), 3.51–3.54 (m, 2H), 3.58–3.62 (m, 2H), 4.56–4.59 (m, 2H), 6.93–6.96 (m, 4H), 7.40–7.43 (m, 2H), 7.75–7.80 (m, 2H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 17.31 (s, CH_3), 70.97 (s, OCH_2), 71.23 (s, OCH_2), 73.23 (s, OCH_2), 74.36 (s, OCH), 112.66 (d, *J*=7.27 Hz, ArC_3), 120.06 (d, *J*=14.53 Hz, ArC_5), 123.02 (d, *J*=144.11 Hz, ArC_1 next to P atom), 132.99 (s, ArC_4), 134.34 (d, *J*=6.06 Hz, ArC_6), 159.52 (d, *J*=3.63 Hz, ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 13.95; MS: 437 $(M+1)^+$. Anal. Calcd for $C_{22}H_{29}O_7P$: C, 60.54; H, 6.70; P, 7.10. Found: C, 60.43; H, 6.60; P, 7.10.

*4.2.5.2. Starting from methyl ester (R,R)-**11**.* Proton-ionizable macrocycle (*R*,*R*)-**14** was also obtained starting from methyl ester (*R*,*R*)-**11** (279 mg, 0.62 mmol) and following the procedure described above for the acid hydrolysis of ethyl ester (*R*,*R*)-**10**. Yield: 149 mg (55%). Ligand (*R*,*R*)-**14** obtained this way was identical in every respect to that prepared by the previous procedure.

*4.2.6. 22-Hydroxy-6,7,9,10,12,13,15,16-octahydro-22H-22λ⁵-dibenzo[n,q][1,4,7,10,13,16]pentaoxaphosphacyclooctadecin-22-one (**15**)*

*4.2.6.1. Starting from ethyl ester **12**.* Achiral macrocycle **15** was prepared as described above for its optically active analogue (*R*,*R*)-**14** starting from ethyl ester **12** (271 mg, 0.62 mmol). White prisms. Yield: 128 mg (51%). Mp: 170–171 °C (water). R_f: 0.14 (silica gel TLC, MeOH–$ClCH_2CH_2Cl$ 1:4); IR (KBr) ν_{max} 3424, 3136, 3080, 3056, 2960, 2944, 2864, 2048, 1658, 1592, 1576, 1476, 1444, 1352, 1304, 1276, 1264, 1216, 1204, 1144, 1136, 1128, 1112, 1104, 1080, 1032, 968, 942, 800, 760, 704, 552, 516, 496, 480, 436 cm^{-1}; ^1H NMR ($CDCl_3$+D_2O) δ 3.63–3.72 (m, 12H), 4.18–4.22 (m, 4 m), 6.91–7.01 (m, 4H), 7.45–7.49 (m, 2H), 7.59–7.63 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 68.46 (s, OCH_2), 69.43 (s, OCH_2), 70.44 (s, OCH_2), 71.47 (s, OCH_2), 112.23 (d, *J*=6.82 Hz, ArC_3), 121.03 (d, *J*=13.03 Hz, ArC_5), 121.95 (d, *J*=138.32 Hz, ArC_1 next to P atom), 133.56 (d, *J*=1.24 Hz, ArC_4), 134.31 (d, *J*=9.92 Hz, ArC_6), 160.12 (d, *J*=1.86 Hz, ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 27.43; MS: 409 $(M+1)^+$. Anal. Calcd for $C_{20}H_{25}O_7P$: C, 58.82; H, 6.17; P, 7.58. Found: C, 58.74; H, 6.20; P, 7.47.

*4.2.6.2. Starting from methyl ester **13**.* Proton-ionizable macrocycle **15** was also obtained starting from methyl ester **13** (262 mg, 0.62 mmol) and following the procedure described above for the acid hydrolysis of ethyl ester (*R*,*R*)-**10**. Yield: 133 mg (53%). Ligand **15** obtained this way was identical in every respect to that prepared by the previous procedure.

*4.2.7. Methyl bis(2-hydroxyphenyl)phosphinate (**17**)*

To a vigorously stirred solution of freshly distilled pure and dry diisopropylamine (35 mL, 25.3 g, 0.25 mol) in pure and dry THF (78 mL) was added 2.5 M *n*-butyllithium solution in hexanes (100 mL, 0.25 mol) at −75 °C under Ar in 30 min and stirring was continued another 30 min at −75 °C. After the LDA solution was formed, diphenyl methyl phosphate (**21**) (16.53 g, 62.6 mmol) dissolved in pure and dry THF (78 mL) was added in 60 min at −75 °C. The resulting reaction mixture was stirred at −75 °C for another 60 min, then it was allowed to warm up to rt and it was stirred at rt for 4 h. After the reaction was completed, the mixture was added in small portions to a vigorously stirred mixture of CH_2Cl_2 (600 mL), saturated aqueous NH_4Cl solution (470 mL) and ice (200 g). The organic phase was separated and the aqueous one was extracted with CH_2Cl_2 (2×200 mL). The combined organic phase was shaken with water (500 mL), dried over $MgSO_4$, filtered and the solvent was removed. The crude product was first purified by chromatography on silica gel using an acetone–toluene 1:20 mixture as eluent then by recrystallization from toluene to give pure **17** as white prisms. Yield: 8.75 g (53%). Mp: 146–147 °C (toluene). R_f: 0.20 (silica gel TLC, acetone–toluene 1:20); IR (KBr) ν_{max} 3430, 3235, 3064, 2960, 2858, 1616, 1608, 1576, 1464, 1456, 1448, 1412, 1372, 1304, 1240, 1184, 1172, 1140, 1128, 1120, 1100, 1088, 1080, 1072, 1060, 1036, 952, 840, 808, 756, 732, 704, 688, 584, 548, 524, 488 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (d, $|^3J|_{P-H(Me)}$=12 Hz, 3H), 6.94–7.00 (m, 4H), 7.43–7.48 (m, 4H), 9.92 (br s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 52.50 (d, *J*=6.82 Hz, OCH_3), 111.03 (d, *J*=137.70 Hz, ArC_1 next to P atom), 118.63 (d, *J*=9.92 Hz, ArC_3), 120.17 (d, *J*=13.02 Hz, ArC_5), 131.67 (d, *J*=8.07 Hz, ArC_6), 135.66 (d, *J*=2.48 Hz, ArC_4), 162.34 (d, *J*=5.59 Hz, ArC_2 next to O atom); ^{31}P ($CDCl_3$) δ 45.86; MS: 265 $(M+1)^+$. Anal. Calcd for $C_{13}H_{13}O_4P$: C, 59.10; H, 4.96; P, 11.72. Found: C, 59.27; H, 4.79; P, 11.64.

Acknowledgements

This work was supported by the Hungarian Scientific Research Fund (OTKA K62654 to P.H., PD71817 to V.F., PD71910 to T.T. and T49792, NI68466 to M.H.), GVOP-3.2.1-2004-04-0345/3,0 and by the Ministry of Education of Hungary (Postdoctoral Fellowship PAL 11/2003 to T.T.). The HPC Group computer facility, University of Szeged was used for several computations. The authors would like to thank Dr. Elemér Vass for helpful discussion.

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