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Perhydrotriquinacenic Hosts. 1. Synthesis, Complexation and Transport Properties of Tripodands of C_3 Symmetry.

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Abstract A general strategy for the synthesis of tripodands of C_3 symmetry, which involves the reductive amination of tricyclo[5 2 1 $0^{4,10}$]decane-2,5,8-trione **1**, is described. Preliminary studies show that these tripodands exhibit complexation and transport properties similar to those of previously described podands

Introduction

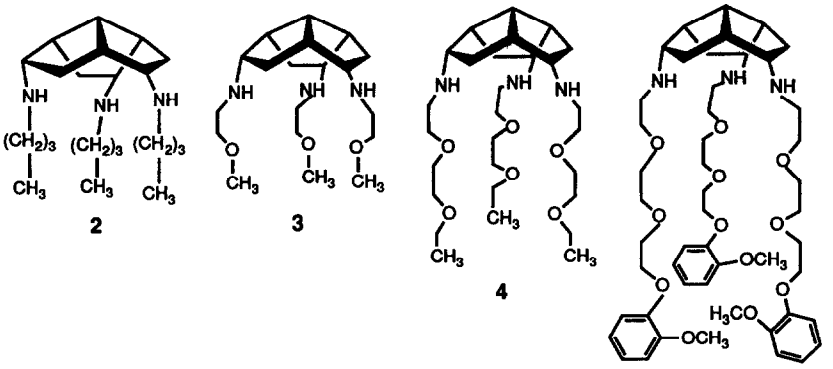
Molecular recognition by means of rationally designed synthetic compounds which may act as receptors or *hosts* of several chemical species is an area of ever-growing importance, which in the last two decades has experienced a rapid expansion [1] A common feature of molecular receptors is the presence of a relatively rigid intramolecular cavity, which together with the adequate positioning of suitable functional groups makes the formation of stable *host-guest* complexes possible

In connection to our work in the field of polyquinane chemistry,[2] we have developed an effective synthesis of *all-cis*-tricyclo[5 2 1 $0^{4,10}$]decane-2,5,8-trione[3] (hereafter referred to as triketone **1**), whose structural characteristics strongly indicate the possibility of its use for the construction of molecular receptors

1

In the first place, the concavity of the perhydrotriquinacene skeleton of **1** suggests that **1** can serve as a concave cap, providing a preorganized cavity around of which rationally designed hosts can be built In the second place, **1** is a chiral molecule of C_3 symmetry, readily accessible in optically active form,[4] this represents an additional bonus since one could obtain chiral hosts derived from **1** suitable for enantioselective molecular recognition [5] In the third place, the triple functionalization in the peripheral rim of triketone **1** represents an adequate feature for the construction of *tripodands*,[6] which on the other hand would maintain the C_3 symmetry

In the present communication, as a first approximation to the preparation of perhydrotriquinacenic hosts, we describe the synthesis of four tripodands (**2-5**) derived from **1** Their complexation and transport properties towards alkali-metal and ammonium cations are also described.

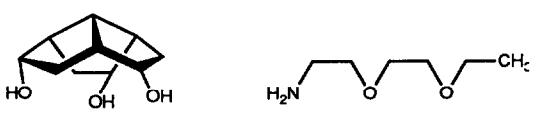


2 3 4 5

Results and Discussion

1. Synthesis.

As a general prerequisite for the preparation of C_3-perhydrotriquinacenic tripodands, it is necessary to exert a rigorous stereochemical control which ensures a *tris-endo* configuration for the built-on chains, in order to preserve both the concavity and the overall C_3 symmetry of the system The only precedent for such a transformation is a previous study from our laboratory on the reduction of **1** to the triol **6**[4], in which we had shown that whereas the reaction of **1** with metal hydrides leads to diastereomeric mixtures of products, catalytic hydrogenation is totally stereoselective and affords the *tris-endo* isomer **6** in 81 % yield

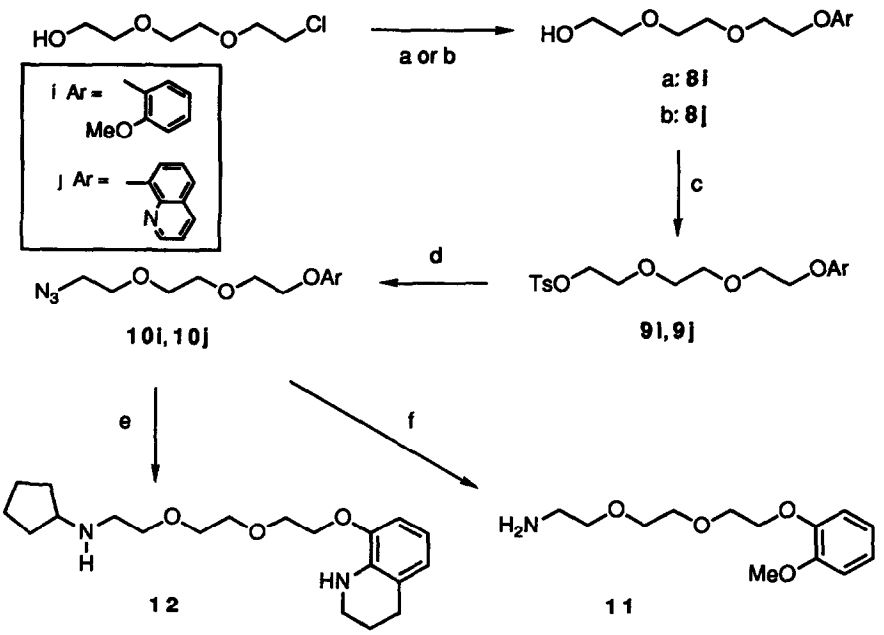


6 7

In the light of these results, the strategy chosen for the preparation of perhydrotriquinacenic podands relies on the reductive amination[7] of triketone **1** under catalytic hydrogenation conditions.

The reductive amination of **1** with *n*-butylamine in EtOH in the presence of 10 % Pd on charcoal gives the triamine **2** in 72 % yield The ^{13}C-NMR spectrum clearly establishes both the diastereomeric purity and the C_3 symmetry of the product, to which we assign the *tris-endo* configuration The reaction with 2-methoxyethylamine in the same conditions leads with a 51 % yield to the tripodand **3**, which has an oxygen atom in the chains This strategy is also effective for the synthesis of podands with longer chains and more donor atoms such as tripodand **4**, which is readily obtained (53 % yield) by reductive amination of **1** with amine **7** This amine is easily prepared through tosylation and subsequent Gabriel reaction of commercially available 3,6-dioxaoctanol [8]

Finally, the use of the method for the assembly of tripodands with aromatic donor end groups (which usually show enhanced complexation properties[9]) is summarized in Scheme 1. Starting from 8-chloro-3,6-dioxaoctanol, chlorine substitution with guaiacol potassium salt, tosylation, azide displacement and catalytic hydrogenation leads to amine **11** Subsequent reductive coupling with **1** affords tripodand **5** with a 55 % yield On the other hand, the analogous compound with 8-quinolyloxy end groups[10] is not easily prepared by this strategy, since the reductive amination of cyclopentanone with azide **10j** gives a compound (**12**) with a hydrogenated pyridine moiety (see Scheme 1) It is important to note that tripodands **3-5** present ^{13}C-NMR spectra corresponding to C_3 symmetry, as described above for **2**



SCHEME I

a) Guaiacol, KOH, nBuOH, 100 % b) 8-Hydroxyquinoline, KOH, nBuOH, 90 %
c) TsCl, pyr, 65 % (9i), 80 % (9j) d) NaN_3, H_2O, $nBu_4N^+I^-$, 76 % (10i), 70 % (10j)
e) Cyclopentanone, H_2, MeOH, Pd-C, 54 % f) H_2, MeOH, Pd-C, 77 %

2. Complexation and transport properties

The complexation ability of the new tripodands 2-5 towards alkali-metal and ammonium cations is evaluated by extraction of aqueous solutions of Li^+, Na^+, K^+, Cs^+ and NH_4^+ picrates with chloroform solutions of the hosts

Association constants (K_a) and complexation free energies ($-\Delta G^o$) in ethanol-free, water-saturated chloroform at 25 °C are conveniently determined by the method of Cram.[11] In our experiments we employ the K_d and ε (acetonitrile, 280 nm) values used by this author, since the initial concentrations of picrate and hosts are identical The position of maximal absorption of the complexed picrate in chloroform, which in all instances appears below 370 nm, shows that the complexes exhibit a 1 1 stoichiometry [12] The K_a and $-\Delta G^o$ obtained for podands 2-5 are shown in Table I It is readily seen that podands 2 and 3 do not show any significant association degree with any of the studied cations, probably due to the lack of electron-donor atoms in the chains On the other hand, podands 4 and 5 present association constants similar (or even larger) to those obtained for previously known podands [6,9,10,13] These podands do not show any sizable selectivity towards a specific cation, it can also be readily seen that the presence of aromatic donor end groups (in podand 5) appears not to be determinant for the complexation process

Table I Guest-Host Molar Fraction (R) [a], Association Constants (K_a)[b] and Complexation Free Energies ($-\Delta G_0$)[c] in Deuterochloroform of Compounds **2**, **3**, **4** and **5** with Alkali-Metal and Ammonium Cations

Host	Cation	Rx10^3	K_ax10^{-3}	$-\Delta G_0$
	Li	0.08	0.25	3 2
	Na	0.08	0.20	3 1
2	K	0 16	0.28	3 3
	Cs	0 16	0.30	3 4
	NH_4	0 16	0 18	3.1
	Li	0 08	0.25	3 2
	Na	0.12	0.31	3 4
3	K	0 16	0.28	3 3
	Cs	0.16	0 30	3.4
	NH_4	0 20	0 22	3 1
	Li	66 03	293.6	7.4
	Na	81 8	325.4	7.5
4	K	53 0	259.2	7 4
	Cs	89 0	240.6	7 3
	NH_4	70 1	234 1	7 3
	Li	57.5	243 6	7 3
	Na	63 5	227.3	7 3
5	K	46 1	218 7	7 3
	Cs	78 4	202.0	7 2
	NH_4	64 3	209 4	7 2

a) See Experimental Section b) In $mol^{-1}L$ c) In kcal mol^{-1}

The transport properties of podands **4** and **5** (which as we have seen present relatively large association constants) through an organic chloroform membrane[14] are shown in Table II for the lithium, sodium, potassium and cesium picrates The results indicate that podands **4** and **5** are carriers of moderate effectivity (by comparison with dibenzo-18-crown-6 **13** used as a reference compound) Although no selectivity towards any specific cation is apparent, one can observe that the transport rate is inversely proportional to the ionic radii of the cations In particular, podand **4** could offer some interest for the transport of lithium cation

Table II Transport Rates[a] of Alkali-Metal Cations By Hosts **4**, **5** and **13** Through an Organic Membrane

	Li	Na	K	Cs
4	4 7	4.2	3.7	2 1
5	2 7	1 9	1 2	1 0
13	1.3	3 7	21 5	10 5

a) In 10^{-8}mol h^{-1}

Experimental

Ultraviolet spectra were obtained with a Perkin-Elmer Lambda 5 spectrometer ^{1}H-NMR (200 MHz) and ^{13}C-NMR (50 MHz) spectra were recorded on a Varian XL-200 instrument Infrared spectra were obtained with a Perkin-Elmer 681 apparatus. Mass spectra were run on a Hewlett-Packard 5988A spectrometer, using both electronic impact and chemical ionization techniques. Elemental analyses were performed with a 1106 Carlo Erba microanalyzer instrument. All chromatographic purifications were performed on silicagel (Merck, 230-400 mesh ASTM), using (except where indicated) hexane-ethyl acetate mixtures of increasing polarity as eluent.

***All-cis,tris-endo*-N,N',N"-*tris*-(*n*-butyl)tricyclo[5.2.1.0^{4,10}]decan-2,5,8-triamine, 2.**

An stirred solution of triketone **1**[3] (0 10 g, 0 56 mmol) and *n*-butylamine (0 12 g, 1.67 mmol) in anhydrous methanol (20 mL) is hydrogenated at room temperature under atmospheric pressure during 24 h, using 10 % Pd-C (0.04 g) as catalyst After filtration through celite and evaporation of the solvents, the crude product is purified by chromatography eluting with a 95 4 1 mixture of CH_2Cl_2/MeOH/aq NH_3 In this way, pure triamine **2** (0 140 g) is obtained in 72 % yield as a colorless oil A sample is distilled (230 °C, 1 mm Hg) to give analytically pure product

IR ($CHCl_3$) 3150, 2970, 2940, 1470, 1360, 1140 cm^{-1} ^{1}H-NMR ($CDCl_3$) 0 91 (t, J = 7 2 Hz, 9H), 1.04-1 84 (m, 18 H), 2 3-2 8 (m, 7H), 2 59 (t, J = 7 Hz, 6H), 3 08 (p, J = 6 1 Hz, 3H) ^{13}C-NMR ($CDCl_3$) 13 9 (q), 20 5 (t), 30 2 (t), 32 6 (t), 42 9 (d), 48 4 (t), 48 8 (d), 62 1 (d) MS (e i) 349 (M^+), 306, 292, 277, 233, 206, 164, 138, 112 Anal calcd for $C_{22}H_{43}N_3$ C, 75 64, H, 12 18, N, 12 03 % Found C, 75 30, H, 12 18, N, 11 78 %

***All-cis,tris-endo*-N,N',N"-*tris*-(2-methoxyethyl)tricyclo[5.2.1.0^{4,10}]decan-2,5,8-triamine, 3.**

An stirred solution of triketone **1**[3] (0 10 g, 0 56 mmol) and 2-methoxyethylamine (0 13 g, 1 68 mmol) in absolute ethanol (10 mL) is hydrogenated at room temperature under atmospheric pressure during 24 h, using 10 % Pd-C (0 04 g) as catalyst After filtration through celite and evaporation of the solvents, the crude product is purified by chromatography eluting with a 88 10 2 mixture of CH_2Cl_2/MeOH/aq NH_3 In this way, pure triamine **3** (0 075 g) is obtained in 40 % yield as a yellow oil, which can not be purified further by distillation

IR ($CHCl_3$) 3320, 2950, 1460, 1350, 1240, 1200, 1110 cm^{-1} ^{1}H-NMR ($CDCl_3$) 1 20 (m, 3H), 1 8 (m, 3H), 2 0 (m, 3H), 2 4-2 9 (m, 4H), 2 77 (t, J = 5 Hz, 6H), 3 10 (p, J = 6 Hz, 3H), 3 35 (s, 9H), 3 48 (t, J = 5 1 Hz, 6H) ^{13}C-NMR ($CDCl_3$) 30 1 (t), 43 1 (d), 48 2 (t), 48 9 (t), 58 7 (q), 62 1 (d), 72 3 (d) MS (e i) 354 (M-1$^+$), 324 (M-MeOH$^+$), 310, 296, 281, 135, 207, 140, 117, 105, 91, 69, 59

3,6-Dioxaoctylamine, 7

a) To a cold (10 °C) solution of 3,6-dioxaoctanol (3 0 g, 22 mmol) in anhydrous pyridine (3 47 g, 0 44 mol) is added slowly *p*-toluenesulphonyl chloride (5 55 g, 27 mmol) The mixture is stirred overnight at 5 °C and subsequently treated with water (30 mL) and methylene chloride (30 mL). The aqueous phase is further extracted with methylene chloride (15 mL) The combined organic phase is successively washed with aq 1 M hydrochloric acid, aq saturated sodium bicarbonate and water (20 mL each) Evaporation of the solvent affords 3,6-dioxaoctyl *p*-toluenesulfonate (6 6 g, quantitative yield, pure by TLC) as a dense oil

IR (film) 2980, 2880, 1610, 1450, 1360, 1185, 1030 cm^{-1} ^{1}H-NMR ($CDCl_3$) 1 15 (t, J = 6 Hz, 3H), 2 40 (s, 3H), 3 5 (m, 8H), 4 15 (t, J = 5 Hz, 2H), 7 2-7 8 (AA'XX' system, 4H)

b) Without further purification, a solution of 3,6-dioxaoctyl *p*-toluenesulphonate (1 0 g, 3 5 mmol) and potassium phthalimide (0 64 g, 3 5 mmol) in anhydrous xylene (3 mL) is heated at 150 °C for 3 h 2mL of xylene are subsequently distilled *in vacuo* and the residue is heated again at 150 °C during 15 h After cooling at room temperature, acetone (8 mL) is added and the resulting mixture is stirred at reflux for 10 minutes The

precipitate is filtered and thoroughly washed with acetone Evaporation of the filtrates affords N-(3,6-dioxaoctyl)phthalimide (0 8 g) in 87 % yield

IR (film) 3200, 3070, 2990, 2940, 2880 cm^{-1} ^{1}H-NMR (CD_3OD) 0.70 (t, J = 6 Hz, 3H), 2 8-3 3 (m, 10 H), 7 3 (br s, 4H)

c) Without further purification, a solution of N-(3,6-dioxaoctyl)phthalimide (0 67 g, 2 5 mmol) and hydrazine hydrate (0 13 mL, 2 5 mmol) in methanol (6 mL) is heated at reflux during 6 h After separation of the phthalimide and evaporation of the solvents the crude product is purified by column chromatography eluting with a 88:10.2 mixture of CH_2Cl_2/MeOH/ aq NH_3 This gives 3,6-dioxaoctylamine (7) (0 212 g) as a colorless oil in 64 % yield

IR ($CHCl_3$) 3400, 2980, 2930, 1870, 1600, 1450, 1360, 1120 cm^{-1} ^{1}H-NMR ($CDCl_3$) 1 22 (t, J = 7 Hz, 3H), 1 78 (s, 2H), 2 89 (t, J = 5 1 Hz, 2H), 3 53 (t, J = 5 3 Hz, 2H), 3 54 (q, J = 7 Hz, 2H), 3 62 (m, 4H) MS (c i , NH_3)$^+$ 154 (M+18), 134 (M+1)

***All-cis,tris-endo*-N,N',N"-*tris*-(3,6-dioxaoctyl)tricyclo[5.2.1.0^{4,10}]decan-2,5,8-triamine, 4**

An stirred solution of triketone **1**[3] (0 15 g, 0 84 mmol) and amine **7** (0 34 g, 2 53 mmol) in anhydrous methanol (30 mL) is hydrogenated at room temperature under atmospheric pressure during 24 h, using 10 % Pd-C (0 06 g) as catalyst After filtration through celite and evaporation of the solvents, the crude product is purified by chromatography eluting with a 88 10.2 mixture of CH_2Cl_2/MeOH/aq NH_3 In this way, pure triamine **4** (0 235 g) is obtained in 53 % yield as a yellow oil, which cannot be purified further by distillation.

IR ($CHCl_3$) 3000, 2950, 2880, 1600, 1500, 1450, 1330, 1250, 1125, 1050, 1030 cm^{-1} ^{1}H-NMR ($CDCl_3$) 1 22 (t, J = 7 1 Hz, 9H), 1 66 (p, J = 6 Hz, 3H), 2 22 (br s, 3 H), 2 47 (p, J = 8 Hz, 3H), 2 75 (m, 1H), 2 79 (t, J = 5 4 Hz, 6 H), 3 08 (p, J = 6 Hz, 3H), 3 4-3 6 (m, 27 H). ^{13}C-NMR ($CDCl_3$) 15 2 (q), 30 1 (t), 43 2 (d), 48 2 (t), 48 9 (d), 62 1 (d), 66 6 (t), 69 8 (t), 70 4 (t), 70 83 (t). MS (c i , NH_3) 530 (M+1), 134

8-(*o*-Methoxyphenoxy)-3,6-dioxaoctanol, 8i

Guaiacol (3 97 g, 32 mmol) and KOH (1 79 g, 32 mmol) are added to boiling *n*-butanol (150 mL) When all solids are dissolved, 8-chloro-3,6-dioxaoctanol (5 0 g, 30 mmol) is added and the resulting mixture is heated at reflux during 20 h The KCl precipitate is filtered off and the solvent eliminated The residue is dissolved in chloroform and the solution successively washed with 1 M aq NaOH and water Elimination of the solvent affords alcohol **8i** (7 1 g) in essentially quantitatively yield as a brown-coloured oil

^{1}H-NMR ($CDCl_3$) 3 9 (s, 3H), 3 5-4 4 (complex signal, 13H), 6 9 (br s, 4H) MS (c i , NH_3) 274 (M+18), 257 (M+1)

8-(*o*-Methoxyphenoxy)-3,6-dioxaoctyl *p*-toluenesulphonate, 9i

To a cooled (0 °C) solution of alcohol **8i** (7 1 g, 28 mmol) in pyridine (5 1 g, 64 mmol) is added slowly *p*-toluenesulphonyl chloride (8 0 g, 38 mmol) The resulting mixture is stirred overnight at 20 °C and poured over a mixture of water and methylene chloride (50 mL each) The aqueous phase is washed with additional methylene chloride and the combined organic phases are successively washed with aq 1 M HCl, aq saturated $NaHCO_3$ and water After elimination of the solvents, the crude product is purified by chromatography In this way, *p*-toluenesulphonate **9i** (7 95 g) is obtained in 65 % yield as a white solid

IR (KBr) 3010, 2960, 2860, 1600, 1500, 1460, 1360, 1255, 1180 cm^{-1} ^{1}H-NMR ($CDCl_3$) 2 40 (s, 3H), 3 5 (s, 3H), 3 5-4 3 (complex signal, 12 H), 6 9 (br s, 4H), 7 2-7 9 (AA'XX' system, 4H) MS (c i , NH_3) 428 (M+18)

1-Azido-8-(*o*-methoxyphenoxy)-3,6-dioxaoctane, 10i

An stirred mixture of *p*-toluenesulphonate **9i** (7 95 g, 19 mmol), sodium azide (2 47 g, 38 mmol), water (10 mL) and tetrabutylammonium bromide (0 5 g) is heated at reflux during 20 h The aqueous phase is extracted with chloroform and the combined organic phases are washed with water. Elimination of the solvents and chromatographic purification gives the azide **10i** (4 7 g) in 76 % yield as a colorless oil.

IR (film): 3080, 2940, 2890, 2110, 1595, 1505, 1450, 1255, 1230, 1180, 1125, 1030, 740 cm^{-1} ^{1}H-NMR ($CDCl_3$)· 3 2-4.4 (complex signal, 12H), 3 85 (s, 3H), 6 9 (br s, 4H) ^{13}C-NMR ($CDCl_3$)· 50 7 (t), 55 9 (q), 68 6 (t), 69 8 (t), 70 0 (t), 70 7 (t), 70 9 (t), 112 1 (d), 114 2 (d), 120 9 (d), 121 5 (d), 148 4 (s), 149 7 (s) MS (c i , NH_3)· 299 (M+18)

8-(*o*-Methoxyphenoxy)-3,6-dioxaoctylamine, 11

An stirred solution of azide **10i** (2 0 g, 7 1 mmol) in dry methanol (40 mL) is hydrogenated at room temperature under atmospheric pressure for 12 h, using 10 % Pd-C as catalyst. Filtration and evaporation of the solvents gives crude material (0 78 g) which is chromatographed eluting with a 88·10 2 CH_2Cl_2/MeOH/aq NH_3 mixture In this way, amine **11** (1 4 g) is obtained in 77 % yield as a colorless oil.

IR (film) 3600-3100, 2940, 2890, 1595, 1510, 1460, 1260, 1230, 1130 cm^{-1} ^{1}H-NMR ($CDCl_3$) 2 5 (br s, 2H), 2 85 (m, 2H), 3 35-4 30 (complex system, 13H), 6 9 (br s, 4H).

***All-cis,tris-endo*-N,N',N"-*tris*-(8-*o*-methoxyphenoxy-3,6-dioxaoctyl)tricyclo-[5.2.1.0^{4,10}]decan-2,5,8-triamine, 5**

An stirred solution of triketone **1**[3] (0 15 g, 0 84 mmol) and amine **11** (0 645 g, 2.53 mmol) in anhydrous methanol (30 mL) is hydrogenated under atmospheric pressure and at room temperature during 3 days, using 10 % Pd-C (0 10 g) as catalyst After filtration through celite and evaporation of the solvents, the crude product (0.775 g) is purified by chromatography eluting with a 88 10 2 mixture of CH_2Cl_2/MeOH/aq NH_3 In this way, pure triamine **5** (0 235 g) is obtained in 55 % yield as a yellow oil, which cannot be purified further by distillation

IR($CHCl_3$) 3070, 2940, 2870, 1595, 1510, 1455, 1350, 1330, 1260, 1230, 1180, 1130 cm^{-1} ^{1}H-NMR ($CDCl_3$) 1 24 (m, 3H), 1 76 (m, 3H), 2 46 (m, 3H), 2 70 (m, 1H), 2 79 (br t, 6H), 2 88-3 18 (complex signal, 6H), 3 54-3 94 (complex system, 24H), 3 84 (s, 9H), 4 18 (t, J = 5 4 Hz, 6H), 6 90 (br s, 12H) ^{13}C-NMR ($CDCl_3$) 29 9 (t), 43 0 (d), 48 1 (t), 48 9 (d), 56 0 (q), 62.1 (d), 68 7 (t), 69 7 (t), 70 3 (t), 70 4 (t), 70 7 (t), 112 2 (d), 114 3 (d), 120 9 (d), 121 6 (d), 148 4 (s), 149 7 (s)

9-(8-Quinolyl)-3,6,9-trioxanonanol, 8j

8-Hydroxyquinolin (4.3 g, 30 mmol) and KOH (1 68 g, 30 mmol) are added to boiling *n*-butanol (150 mL) When all solids are dissolved, 8-chloro-3,6-dioxaoctanol (5 0 g, 30 mmol) is added and the resulting mixture is heated at reflux during 22 h The KCl precipitate is filtered and the solvent eliminated The residue is dissolved in chloroform and the solution successively washed with 1 M aq NaOH and water Elimination of the solvent affords alcohol **8j** (7 5 g) in 90 % yield as a yellowish oil

IR (film) 3600-3100, 2960-2860, 1620, 1600, 1570, 1500, 1380, 1330, 1265, 1100 cm^{-1} ^{1}H-NMR ($CDCl_3$) 3 3-4 5 (m, 13H), 7 0-7 5 (m, 4H), 8 10 (dd, J = 9 Hz, J' = 2 Hz, 1H), 8 90 (dd, J = 9 Hz, J' = 2 Hz, 1H) MS (c i , NH_3) 278 (M+1)

9-(8-Quinolyl)-3,6,9-trioxanonanyl *p*-toluenesulphonate, 9j

To a cooled (0 °C) solution of alcohol **8j** (7 47 g, 27 mmol) in pyridine (4 27 g, 54 mmol) is added slowly *p*-toluenesulphonyl chloride (6 83 g, 32 mmol) The resulting mixture is stirred overnight at 20 °C and poured over a mixture of water and methylene chloride (40 mL each). The aqueous phase is washed with additional methylene chloride and the combined organic phases are successively washed with aq 1 M HCl, aq saturated $NaHCO_3$ and water After elimination of the solvents, the crude product is purified by chromatography, eluting with a 88 10 2 mixture of CH_2Cl_2/MeOH/aq NH_3 In this way, *p*-toluenesulphonate **9j** (9 31 g) is obtained in 80 % yield as a yellow oil

IR(film) 3080, 2930, 2870, 1600, 1570, 1500, 1350, 1310, 1260, 1170, 1110 cm^{-1}. ^1H-NMR ($CDCl_3$) 2 4 (s, 3H), 3 1-4 6 (complex signal, 12H), 7 0-8 2 (complex signal, 9H), 8 9 (m, 1H)

8-(8-Azido-3,6-dioxaoctyloxy)quinoline, 10j

An stirred mixture of *p*-toluenesulphonate **9j** (9.31 g, 22 mmol), sodium azide (2 86 g, 44 mmol), water (10 mL) and tetrabutylammonium bromide (0.5 g) is heated at reflux during 20 h The aqueous phase is extracted with chloroform and the combined organic phases are thoroughly washed with water Elimination of the solvents and chromatographic purification gives the azide **10j** (4 74 g) in a 54 % overall yield from 8-chloro-3,6-dioxaoctanol as a colorless oil

IR (film) 3070, 2940, 2890, 2110, 1620, 1600, 1570, 1500, 1480, 1450, 1380, 1320, 1270, 1110, 830, 800, 760 cm^{-1} ^1H-NMR ($CDCl_3$). 3 3 (t, J = 5 Hz, 2H), 3 7 (m, 6H), 4.1 (t, J = 6 Hz, 2H), 4 5 (t, J = 6 Hz, 2H), 7 0-7 5 (m, 4H), 8 1 (dd, J = 5 Hz, J' = 2 Hz, 1H), 8 92 (dd, J = 5 Hz, J' = 2 Hz, 1H) MS (c.i , NH_3): 303 (M+1).

N-Cyclopentyl-9-(1,2,3,4-tetrahydro-8-quinolyl)-3,6,9-trioxanonanylamine, 12

An stirred solution of cyclopentanone (0 10 g, 1 2 mmol) and azide **10j** (0 359 g, 1 2 mmol) in anhydrous methanol (10 mL) is hydrogenated at room temperature under atmospheric pressure during 24 h, using 10 % Pd-C (0.10 g) as catalyst After filtration through celite and evaporation of the solvents, the crude product is purified by chromatography eluting with a 88 10:2 mixture of CH_2Cl_2/MeOH/aq.NH_3 In this way, amine **12** (0 225 g) is obtained in 54 % yield.

IR (film)· 3400, 2960, 2880, 1610, 1580, 1500, 1340, 1250, 1050 cm^{-1} ^1H-NMR ($CDCl_3$). 1 26-2 0 (complex signal, 10H), 2.6 (br s, 2H), 2 76 (t, J = 6.4 Hz, 2H), 2.79 (t, J = 5 4 Hz, 2H), 3.07 (p, J = 6.9 Hz, 1H), 3 31 (t, J = 5 4 Hz, 2H), 3 65 (m, 6H), 3.83 (t, J = 5 Hz, 2H), 4 12 (t, J = 5 Hz, 2H), 6 57 (m, 3H) ^{13}C-NMR ($CDCl_3$)· 22 1 (t), 24 1 (t), 26 7 (t), 41.5 (t), 47 0 (t), 59 8 (d), 68 0 (t), 68 9 (t), 70 3 (t, 2C), 70 6 (t, 2C), 109 6 (d), 115 6 (d), 121 6 (s), 122 3 (d), 135 2 (s), 145 3 (s) MS (c i , NH_3) 349 (M+1)

Determination of the association constants of tripodands 2, 3, 4, and 5 with alkali-metal and ammonium picrates

Aqueous solutions of concentration 0 015 M (for the Li and Na picrates) and 0 010 M (for the K, Cs and NH_4^+ picrates) are prepared, as well as 0 075 M solutions of each of the podands **2-5** in ethanol-free, water-saturated $CDCl_3$ In separate centrifuge tubes are introduced 0.5 mL of the Li and Na picrates and 1 mL of the remaining three. To each tube are then added 0.2 mL of a given podand solution, the well-stoppered tube is subsequently magnetically stirred during 3 minutes and centrifugated in order to separate the two phases 0 1 mL of the organic phase is extracted via syringe and diluted to 5 mL with anhydrous acetonitrile The absorbance of the resulting solution is then measured at λ = 380 nm using a water blank which has been submitted to the same process than the picrate solution Direct application of the Lambert-Beer law allows the measure of the mmols of picrate extracted by the host, which divided by 0 0075 (the number of mmols of host in the sample) gives the guest host molar ratio, R The process is repeated for each podand Finally, application of the following equation[13] to each R value gives the K_a values shown in Table I

$$K_a = \frac{R}{(1-R)\,K_d\left\{[MX_i]_w - R\frac{V_{chl}}{V_w}[H_i]_{chl}\right\}^2}$$

R = guest / host molar ratio
K_d = dissociation constant of the picrate (see ref 13)
$[MX_i]_w$ = initial concentration of the picrate in the aqueous phase
V_{chl} = chloroform volume used in the extraction
V_w = aqueous solution volume used in the extraction
$[H_i]_{chl}$ = initial host concentration

Transport rate of alkali-metal cations through an organic membrane, using podands 4 and 5

The study of cationic transport through a liquid organic membrane is made on a cilyndric glass cell of 2 cm of internal diameter, 4 cm of external diameter and 8 cm of height, in which the inner and outer cylinders are communicated at the bottom 25 mL of a chloroform $7x10^{-5}$ M solution of podand **4** are introduced in the cell Above this solution, in the outer cylinder, 12 mL of water (aqueous phase I) are disposed In the inner cylinder are introduced 4 mL of an aqueous solution which is 10^{-4} M in one of the metallic picrates and 0.1 M in the corresponding nitrate (aqueous phase II) The organic phase is magnetically stirred at constant rate, taking care to avoid mixing of the phases The measure of the absorbances of the two aqueous phases (at λ = 354 nm) is effected at intervals of 10 minutes. The percent of transported product from aqueous phase II, %II(t), is given by the following expression, $\%II(t) = [(A_0 - A_{tII}) / A_0]x100$, where A_0 is the initial absorbance of phase II and A_{tII} is the measured absorbance of phase II at time t. Applying the expression $\%I(t) = [A_{tI} \times 12 / A_0 \times 4]x100$, where A_{tI} is the measured absorbance of phase I at time t, the percent of transported product to phase I, %I(t), is obtained This process is repeated for podand **5** and for dibenzo-18-crown-6 **13**, for each of the picrates Next, the %I(t) and %II(t) values are plotted towards time It can be seen that during the first 4 hours of transport the points can be fitted with good accuracy to straight lines, whose slopes give the transport rates shown in Table II

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