Synthesis and Structure of New Macrocycles Including Spiro-1,3-Dioxane Units

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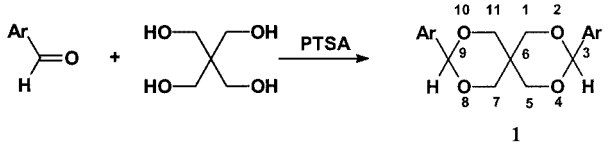
The efficient synthesis of new macrocycles — "monomers" and "dimers" — containing spiro-1,3-dioxane units is reported. The structure of the compounds was determined from high-field NMR spectra, FAB and MALDI$^+$ mass spectrometry investigations. The solid-state molecular structures of three compounds was determined.

Introduction

The synthesis of macrocycles of different sizes and geometries to obtain specific and selective receptors for different cations and molecules is a well-recognized topic in organic chemistry. The macrocyclisation of sugars with specific reagents (e.g. tosylated polyethylene glycols) leads to compounds exhibiting high coordination ability and selectivity for various cations and molecules. Because of their chirality, macrocycles obtained from sugars show enantioselective and enantiospecific supramolecular interactions with chiral guests and they are successfully used in enantiomer discrimination.[1−7]

The advantages of using sugars as substrates in the synthesis of macrocycles are mainly due to the chirality of the molecules and to the presence of anancomeric saturated heterocycles that take part in the coordination processes. In order to obtain different crown ethers with similar properties, the synthesis of macrocycles exhibiting chiral spiro[8−11] or bicyclo[12−17] units with saturated six-membered ring heterocycles was recently developed. NMR and Electrospray (ESI-MS) studies on coronands and cryptands with spiro units revealed the high coordination capacity of these macrocycles and the chemo- and enantioselectivity of this process.[9,10]

Spiro-1,3-dioxanes **1** bearing aromatic groups with an appropriate functionality in the acetal part of the heterocycles are easily prepared by the acetalisation reaction of aromatic aldehydes with pentaerythritol (Scheme 1).[18−20]



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Scheme 1

3,9-Diaryl-2,4,8,10-tetraoxaspiro[5.5]undecane derivatives are chiral and they exhibit the characteristic axial and helical chirality of spiro compounds with six-membered rings.[21−25]

On the other hand, 1,3-dioxane rings are anancomeric; the high *A*-value of aryl groups located at the acetal part of the 1,3-dioxane ring (e.g. A_{Ph} = 13.04 kJ/mol)[26] determines the strong shifting of the conformational equilibria involving the flipping of the 1,3-dioxane rings towards the conformer with both aryl groups in equatorial orientation. Owing to the chirality of the spiro skeleton, these compounds show separable enantiomers and are obtained under the usual conditions of the acetalisation reaction as racemic mixtures (*P* and *M* configurations of the helix, Scheme 2).[27]

In our view, these compounds can be interesting substrates for the synthesis of various sized macrocycles.

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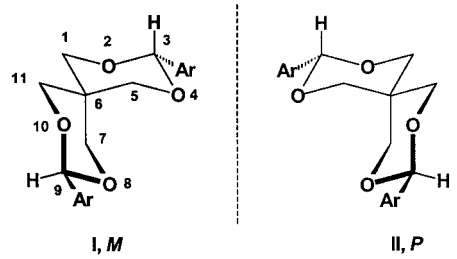


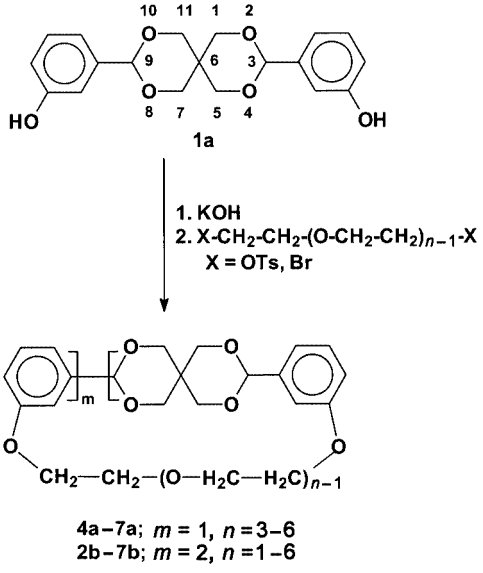
Scheme 2

Results and Discussion

Synthesis of Macrocycles

Spiro 1,3-dioxane **1a** (Ar = *m*-C_6H_4-OH) in reaction with ditosylated (method A) and dibrominated (method B) (poly)ethylene glycol(s) in 2-propanol, using high-dilution conditions was transformed in yields up to 61% into the corresponding macrocycle derivatives **2**−**7** (Scheme 3, Table 1).

The reactions led to the formation of monomeric (**4a**−**7a**, $m = 1$) and dimeric (**2b**−**7b**, $m = 2$) macrocycles. Monomers and dimers were separated by flash chromatography.



Scheme 3

In some fractions collected in the separation of **2**, **3**, and **4**, the FAB and MALDI$^+$ spectra also show the presence of small amounts of trimeric macrocycles.

The ratio of monomers to dimers is mainly correlated with the length of the polyethoxylated chains (Table 1). If the chain is short (one or two ethyleneoxy units, $n = 1, 2$ in Scheme 2) only the dimers (**2b** and **3b**) are obtained, but when the chain is long enough ($n = 4, 5, 6$) the monomers are the major products and the ratio monomer (**a**)/dimer (**b**) varies from 1.5 to 2.1. The highest preference for the formation of monomer is observed in the synthesis of **7**. The ratio of monomeric to dimeric macrocycles is somewhat higher in the reactions performed with ditosylated polyethylene glycols. In the synthesis of **4**, both monomer and dimer are formed, but in this case the dimer is the major product [ratio monomer (**a**)/dimer (**b**) = 0.1 (method A) and 0.4 (method B)].

Yields in the reaction with ditosylated polyethylene glycols are higher (28−61%) than in the reaction with the dibrominated derivatives of polyethylene glycols (5−45%). These differences are smaller when the polyethoxylated chains are long enough ($n = 4-6$) and increase dramatically with the shortness of the chain (Table 1).

Owing to the chirality of the spiro skeleton, monomers are obtained as racemates and dimers are obtained as mixtures of *like* (the spiro units have the same configuration of the helix: *PP*, *MM*) and *unlike* (the spiro units have different configurations of the helix: *MP*) isomers. The racemates of **4a** and **7a** were resolved by HPLC coupled with a Polarimeter Detector using CHIROBIOTIC T (Teicoplanin, **4a**; $t_{R1} = 14.8$ min and $t_{R2} = 16.4$ min, Figure 1) and CHIRACEL OJ (DIACEL, **4a**: $t_{R1} = 54.5$ min and $t_{R2} = 82.9$ min, **7a**; $t_{R1} = 110.3$ min and $t_{R2} = 128.6$ min) columns. Partial resolution ($t_{R1} = 42.1$ min and $t_{R2} = 43.1$ min) of **5a** was observed on a CHIRACEL OD column. The mixture of diastereomers of **4b** were resolved by HPLC using mass spectrometric detection (ESI-MS) and observing the M + Na$^+$ ions ($t_{R1} = 36.3$ min and $t_{R2} = 38.0$ min). The diastereoisomers of **7b** (*like* and *unlike*; a definite assignment was not possible) were satisfactorily separated by flash chromatography, but only one of the isomers (D_1; *like* or *unlike*) could be characterised as a single compound (the best result, after several column separations, for the other isomer was for a ratio $D_2/D_1 = 95:5$). The results of these

Table 1. Results (yields in % of separated compounds) in the synthesis of compounds **2**−**7**

Compound	Method A[a]				Method B[a]			
	monomer (**a**)	dimer (**b**)	global	ratio **a**/**b**	monomer (**a**)	dimer (**b**)	global	ratio **a**/**b**
2	–	28	28	–	–	5	5	–
3	–	48	48	–	–	26	26	–
4	4	33	37	0.1	7	16	23	0.4
5	34	19	53	1.8	27	17	44	1.6
6	32	18	50	1.8	25	17	42	1.5
7	41	20	61	2.1	29	16	45	1.8

[a] A: Reaction with ditosylated polyethylene glycols; B: Reaction with dibrominated polyethylene glycols.

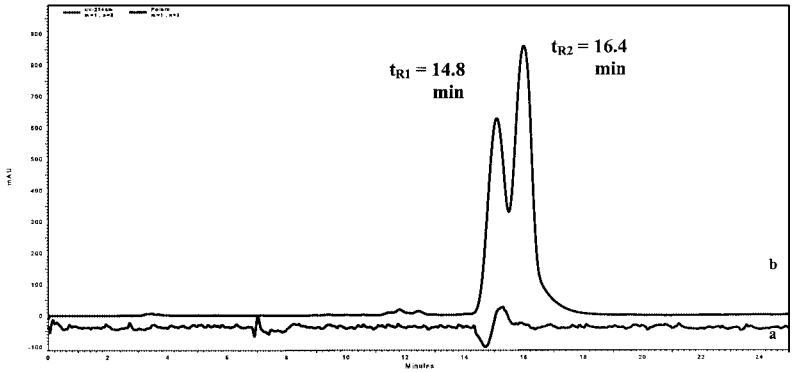


Figure 1. Chromatograms of the resolution of **4a** on a CHIROBIOTIC T column using a chiral detector (polarimeter, **a**) and a standard UV/Vis detector (**b**)

separations show that the *like* and *unlike* isomers of **4b** and **7b** were obtained in a ratio of about 1:1.

In order to investigate the *template* effect of alkali metal cations, compound **5** was synthesised from ditosylated tetraethylene glycol using various metal hydroxides (Table 2). The synthesis of **6** with LiOH and ditosylated pentaethylene glycol proceeded in small yields and with high preference for the monomeric macrocycle (Table 2). In other cases the global yields were not dramatically modified, although synthesis performed with RbOH gave lower yields. In the conditions of this reaction and for this type of substrate no significant template effect was measured.

Comparing the results of these syntheses with data reported in the literature[28−34] for the macrocyclisation of diphenols with ditosylated or dibrominated polyethylene glycols, demonstrates the possibility of using 2-propanol (a more convenient solvent: easier to remove and with higher solubility for the substrate) instead of the usual solvents for this procedure: DMF, 1-butanol, and toluene. The high-dilution technique and the use of a trivial base (KOH) lead to good yields of macrocyclic compounds from both ditosylated and dibrominated polyethylene glycols. On the other hand it also reveals the production of a significant amount of dimeric macrocycles, these being the main products for three of the reported syntheses.

Solid-State Molecular Structures

The solid-state molecular structure was determined for monomers **5a**, **7a**, and the dimer **5b** (Figures 2, 3, and 4). In all the investigated structures the 1,3-dioxane rings exhibit chair conformations and the bond lengths, bond angles, and torsion angles show normal values.[26]

In **5a** the dihedral angles between the best plane of each heterocycle (the plane formed by the exocyclic bonds of the acetal carbon atom) and the plane of the corresponding aromatic ring exhibit values close to 90° ($C^7C^6C^{11}/C^{12}C^{13}C^{14}C^{15}C^{16}C^{17}$ = 85.9° and $C^1C^6C^5/C^{18}C^{19}C^{20}C^{21}C^{22}C^{23}$ = 83.7°) demonstrating the orthogonal orientation of the aromatic substituents. The equatorial aromatic ring in the majority of the investigated molecular structures of 2-aryl-1,3-dioxanes displays a bisectional orientation (the values of the reference dihedral angles close to 0°).[26]

The molecular structure of **7a** reveals that the compound crystallises with the inclusion of a molecule of water. This molecule forms hydrogen bonds with the oxygen atom O^4 of the chain (measured $O^4\cdots H$ distance d = 2.109 Å).

The IR spectrum of the moist compound exhibits two distinct O−H stretch bands at 3498 cm^{-1} and 3598 cm^{-1}.

The structure of **7a** revealed a peculiar orientation of the aromatic rings. The reference dihedral angles between the best plane of each heterocycle and the plane of the corresponding aromatic ring exhibit values ($C^{20}C^{21}C^{22}/C^{26}C^{27}C^{28}C^{29}C^{30}C^{31}$ = 48.8° and $C^{23}C^{21}C^{25}/C^{13}C^{14}C^{15}C^{16}C^{17}C^{18}$ = 59.6°) close to the average of the characteristic values for bisectional (0°) and orthogonal (90°) orientations.

The investigated crystal of **5b** (selected from the mixture of isomers) contains a centrosymmetric molecule (group P 21/c) and represents the *unlike* isomer.

Table 2. Results of the synthesis of macrocycles using different alkali hydroxides

MOH	Monomer (**a**)	Dimer (**b**)	Ratio **a/b**	Yields in macrocyclic compounds
LiOH[a]	17	5	3.4	22
NaOH[b]	31	20	1.5	51
KOH[b]	34	19	1.8	53
RbOH[b]	30	15	2.0	45
CsOH[b]	32	21	1.5	53

[a] Synthesis of **6**. [b] Synthesis of **5**.

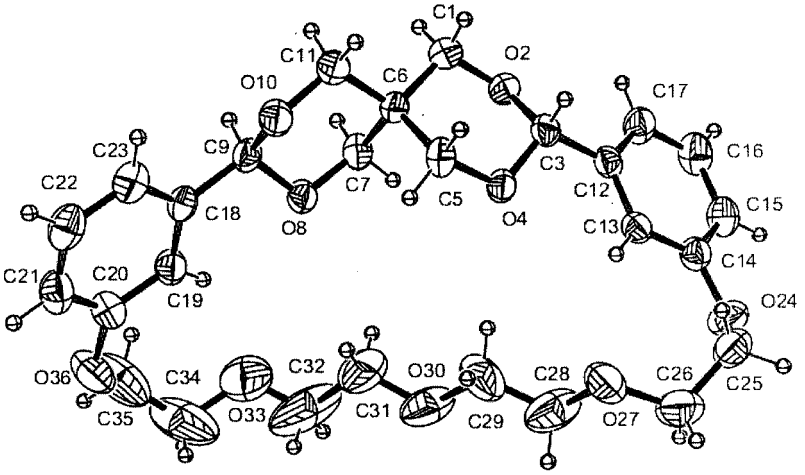


Figure 2. ORTEP diagram for **5a**

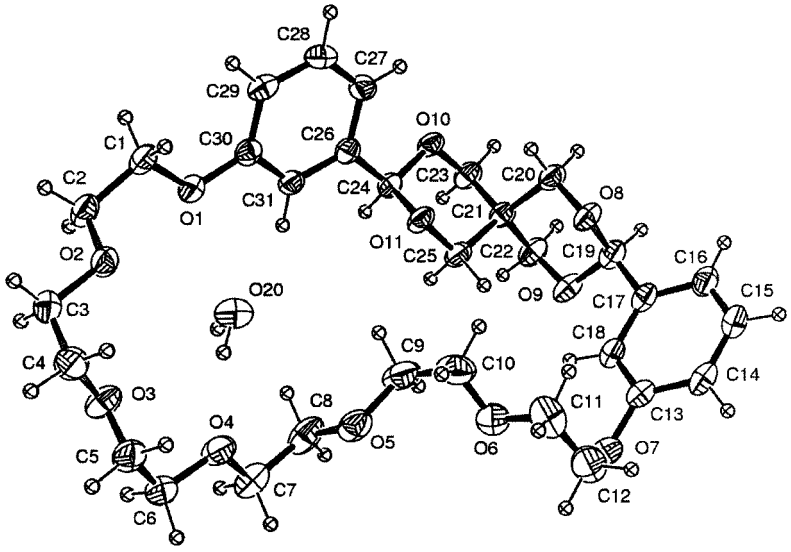


Figure 3. ORTEP diagram for **7a**

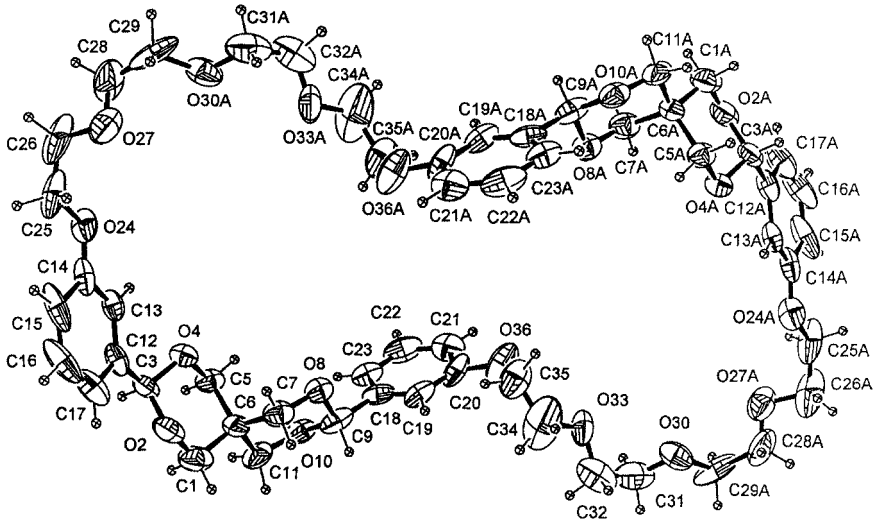


Figure 4. ORTEP diagram for **5b**

Table 3. NMR spectroscopic data (spiranic CH_2 groups) for compounds **2b**−**7b** and **4a**−**7a** (δ ppm; $\Delta\delta_{in\text{-}out}$; C_6D_6 or $CDCl_3$)[a]

Compound	^{1}H						^{13}C		
	e (*in*)	e (*out*)	$\Delta\delta_e$	a (*in*)	a (*out*)	$\Delta\delta_a$	CH_2-*in*	CH_2-*out*	$\Delta\delta_{CH2}$
2b[a]	4.88	3.83	1.05	3.84	3.67	0.17	71.05	70.74	0.31
3b	4.92	3.31	1.61	3.41	3.08	0.33	71.59	70.84	0.75
4a	4.90	3.28	1.62	3.42	3.02	0.40	70.30	70.13	0.27
4b[a]	4.82	3.78	1.04	3.79	3.59	0.20	71.17	70.70	0.47
5a	4.93	3.28	1.65	3.40	2.99	0.41	71.06	70.61	0.45
5b	4.91	3.32	1.59	3.42	2.98	0.44	71.59	70.86	0.73
6a	4.91	3.27	1.64	3.38	2.97	0.41	70.53	70.11	0.42
6b	4.91	3.36	1.55	3.44	3.02	0.42	71.83	70.87	0.96
7a	4.91	3.28	1.63	3.40	2.97	0.43	71.23	70.76	0.47
7b (D_1)	4.92	3.34	1.58	3.46	3.01	0.45	71.58	70.87	0.71

[a] Spectra obtained in $CDCl_3$.

Two of the aromatic rings exhibit orthogonal disposition ($C^7C^6C^{11}/C^{12}C^{13}C^{14}C^{15}C^{16}C^{17}$ = $C^{7A}C^{6A}C^{11A}/C^{12A}C^{13A}$-$C^{14A}C^{15A}C^{16A}C^{17A}$ = 86.9°), while the other two rings display a peculiar orientation ($C^1C^6C^5/C^{18}C^{19}C^{20}C^{21}C^{22}C^{23}$ = $C^{1A}C^{6A}C^{5A}/C^{18A}C^{19A}C^{20A}C^{21A}C^{22A}C^{23A}$ = 40°) intermediate between bisectional and orthogonal rotamers. Two of the aromatic rings ($C^{18}C^{19}C^{20}C^{21}C^{22}C^{23}$ and $C^{18A}C^{19A}$-$C^{20A}C^{21A}C^{22A}C^{23A}$) are parallel. The peculiar shape of the structure of **5b**, showing the collapse of the middle part of the macrocycle, suggests that this compound may be able to coordinate as a ditopic "host" molecule. Generally, the reported di and polytopic "host" molecules exhibit two or more distinct cavities,[35−41] but interesting structures in which two cations are coordinated by the same macrocycle have also been reported.[42,43] The low resolution of **5b** (R = 0.159) is due on the one hand to the poor quality of the crystal and on the other hand to modifications (in the crystal) of the positions of the atoms of the chain even at low temperature (120 K).

Structural Aspects in Solution

The structure of the compounds in solution was investigated by high-field NMR spectroscopy (600 MHz). The NMR spectra of the monomer and of the dimer of the same compound are very similar. The two isomers (*like* and *unlike*) of the same dimer exhibit overlapping signals and could not be discriminated by NMR spectroscopy. The anancomeric behaviour of the spiro skeleton leads to the recording of different signals for protons in the equatorial and axial positions. The chirality of the molecule leads to diastereotopicity of the CH_2 groups of the same six-membered ring heterocycle. One of these groups lies over the other 1,3-dioxane ring of the spirane (methylene "inside" group; positions 5 and 7, Scheme 2) and the signals of these protons (especially the equatorial ones) are strongly deshielded (Table 3). The other CH_2 group is oriented in the opposite direction (methylene "outside" group; positions 1 and 11, Scheme 2) and the protons of these positions exhibit normal δ values.[44−46] The chemical shift differences between the equatorial diastereotopic protons is very high (Table 3), with values up to 1.65 ppm, while for the diastereotopic axial protons this difference is considerably lower (values up to 0.45 ppm).

In ^{13}C NMR spectra the difference in chemical shifts between the CH_2-*in* and CH_2-*out* groups varies from 0.27 ppm to 0.96 ppm.

The spectra of the *like* and *unlike* isomers of **7b** are very close and despite some differences [e.g. the acetalic protons show one singlet in the case of one of the isomers (denoted D_2): δ = 5.220 ppm and two singlets (δ = 5.211; 5.215 ppm) for the other (denoted D_1)] a firm assignment was not possible.

Conclusion

Synthesis of a systematic series of monomeric and dimeric macrocycles including spiro-1,3-dioxane units was carried out in good yields by the high-dilution method. The solid-state molecular structures reveal peculiar dispositions of the aromatic rings. The structure of **7a** shows the coordination of one molecule of water and important interactions between this molecule and the oxygen atoms of the macrocycle. The NMR spectra reveal the anancomeric structure of the spirane skeleton and significant differences of chemical shifts, due to the magnetic anisotropy of the aromatic rings and to the different chemical environments of some homomorphic groups as a result of the chirality of the spiro skeleton.

Experimental Section

General Remarks: NMR spectra [^{1}H (600 MHz), ^{13}C (150.8 MHz), COSY, APT, HETCOR (HMBC, HSQC), NOESY or ROESY] were recorded at room temp., in C_6D_6 or $CDCl_3$. The liquid chromatographic system consisted of a ThermoQuest P4000 pump, a Rheodyne Model 7125 injector with a 25 μL loop, a ThermoQuest Model 2000 UV/Vis, a JASCO Model OR 1590 chiral detector or a mass spectrometer (ESI-MS, FINNIGAN Navigator) detector and all measurements were run at room temp. Chiral separations were performed using CHIRACEL OJ (DAICEL, 25 cm × 4.6 mm, 10 μm), CHIRACEL OD (25 cm × 4.6 mm, 10 μm), and CHIROBIOTIC T (Teicoplanin, 15 cm × 4.6 mm, 5 μm) columns

and hexane/2-propanol (v_1/v_2 = 80:20) at a flow rate of 1 mL·min^{-1}, hexane/2-propanol (v_1/v_2 = 90:10) at a flow rate of 1 mL·min^{-1}, and ethanol/acetonitrile/water ($v_1/v_2/v_3$ = 10:10:80) at a flow rate of 0.8 mL·min^{-1}, respectively. The separation of diastereoisomers was performed on a C18, Kromasyl (25 cm × 2.1 mm, 5 μm) achiral column, in reversed-phase mode, by changing the methanol/water ratio (v_1/v_2) from 60:40 to 80:20 and using a flow rate of 0.25 mL·min^{-1}. Melting points were measured with a Kleinfeld Apotec melting point apparatus and are uncorrected. Microanalyses (C, H) were performed at the Institute de Recherche en Chimie Organique Fine (IRCOF), Mont Saint-Aignan, France and at the University of Medicine and Pharmaceutics in Cluj-Napoca, Romania. FAB, MALDI$^+$, and CI mass spectra were obtained on a JEOL JMS AX-500 spectrometer.

3,9-Bis(3-hydroxyphenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane (1a): Colourless solid: m.p. 244−246 °C. Yield 60%. The synthesis and NMR analysis of **1a** are already described in the literature.[20]

General Procedure for the Synthesis of 2b−7b and 4a−7a: Spirane **1a** (7.5 mmol) and KOH (15 mmol) were refluxed in 2-propanol (1.9 L) for several hours until a clear solution of the salt of **1a** was obtained. Ditosylated or dibrominated polyethylene glycol (7.5 mmol) dissolved in 2-propanol (0.1 L) [in the case of ditosylated reagents 1,4-dioxane (10 mL) was also used] were added to the solution over 5 days under reflux, using a sensitive push-syringe or peristaltic pump. Reflux of the solvent was continued for one more day, after which the system was brought to room temperature and the solid phase removed by filtration. The 2-propanol was evaporated and the crude product dissolved in CH_2Cl_2 (300 mL), then washed with KOH solution (2%, 2 × 100 mL) and water (2 × 100 mL). After drying with sodium sulfate, the solvent was removed and the crude product separated into its components by flash chromatography or by crystallisation.

2,5,12,16,23,26,33,37,44,47,50,53-Dodecaoxanonacyclo[37.3.2^{11,14}.2^{14,17}.2^{32,35}.2^{35,38}.1^{1,39}.1^{6,10}.1^{18,22}.1^{27,31}]tetrapentaconta-1(54),6,8,10(43),18,20,22(48),27,29,31(49),39,41-dodecaene (2b): Mixture of *like* and *unlike* isomers. Colourless solid: m.p. 278−281 °C. $C_{42}H_{44}O_{12}$, *M* 740.80, (calculated C 68.10 , H 5.99%, found C 67.91 , H 5.87%); crystallised from dichloromethane/methanol (1:1). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.67 (d, *J* = 11.4 Hz, 4 H, 13-H^{ax}, 15-H^{ax}, 34-H^{ax}, 36-H^{ax}), 3.83 (dd, *J* = 11.4, 2.4 Hz, 4 H, 13-H^{eq}, 15-H^{eq}, 34-H^{eq}, 36-H^{eq}), 3.84 (d, *J* = 11.4 Hz, 4 H, 45-H^{ax}, 46-H^{ax}, 51-H^{ax}, 52-H^{ax}), 4.35−4.37 (overlapped peaks, 8 H, 3-CH_2, 4-CH_2, 24-CH_2, 25-CH_2), 4.88 (d, *J* = 11.4 Hz, 4 H, 45-H^{eq}, 46-H^{eq}, 51-H^{eq}, 52-H^{eq}), 5.46 (s, 4 H, 11-H, 17-H, 32-H, 38-H), 6.95 [dt (overlapped ddd), 4 H, *J* = 8.4, 1.2, 7-H, 21-H, 28-H, 42-H], 6.99 (d, *J* = 7.2 Hz, 4 H, 9-H, 19-H, 30-H, 40-H), 7.25 (d, *J* = 7.6 Hz, 4 H, 43-H, 48-H, 49-H, 54-H), 7.29 [t(overlapped dd), 4 H, 8-H, 20-H, 29-H, 41-H] ppm. ^{13}C NMR ($CDCl_3$): δ = 32.83 (C-14, C-35), 66.34 (C-3, C-4, C-24, C-25), 70.74 (C-13, C-15, C-34, C-36), 71.05 (C-45, C-46, C-51, C-52), 101.89 (C-11, C-17, C-32, C-38), 112.17, 112.33 (C-43, C-48, C-49, C-54), 115.68, 115.80 (C-7, C-21, C-28, C-42), 119.46 (C-9, C-19, C-30, C-60), 129.52 (C-8, C-20, C-29, C-41), 139.77 (C-10, C-18, C-31, C-39), 158.89 (C-1, C-6, C-22, C-27) ppm; the assignment is based on H,H COSY, APT, HSQC, and HMBC spectra. FAB−MS (NOBA), *m*/*z* = 741.0 [M + H$^+$], 801.0 (M + Na$^+$ + K$^+$). MALDI, *m*/*z* = 762.9 [M + Na$^+$], 778.9 [M + K$^+$].

2,5,8,15,19,26,29,32,39,43,50,53,56,59-Tetradecaoxanonacyclo[43.3.2^{14,17}.2^{17,20}.2^{38,41}.2^{41,44}.1^{1,45}.1^{9,13}.1^{21,25}.1^{33,37}]hexaconta-1(60),9,11,13(49),21,23,25(54),33,35,37(55),45,47-dodecaene (3b): Mixture of *like* and *unlike* isomers. Colourless solid: m.p. 227−229 °C. $C_{46}H_{52}O_{14}$, *M* 828.91, (calculated C 66.65, H 6.32%, found C 66.55, H 6.35%); crystallised from dichloromethane/methanol (1:1). ^{1}H NMR (600 MHz, C_6D_6): δ = 2.96 (d, *J* = 11.4 Hz, 4 H, 16-H^{ax},18-H^{ax}, 40-H^{ax}, 42-H^{ax}), 3.31 (dd, *J* = 11.4, 2.3 Hz, 4 H, 16-H^{eq}, 18-H^{eq}, 40-H^{eq}, 42-H^{eq}) 3.41 (d, *J* = 11.5 Hz, 4 H, 51-H^{ax}, 52-H^{ax}, 57-H^{ax}, 58-H^{ax}) 3.44−3.45 (overlapped peaks, 8 H, 4-CH_2, 6-CH_2, 28-CH_2, 30-CH_2), 3.76−3.77 (overlapped peaks, 8 H, 3-CH_2, 7-CH_2, 27-CH_2, 31-CH_2), 4.92 (d, *J* = 11.5 Hz, 4 H, 51-H^{eq}, 52-H^{eq}, 57-H^{eq}, 58-H^{eq}), 5.19 (s, 4 H, 14-H, 20-H, 38-H, 44-H), 6.86 (dd, *J* = 8.0, 1.5 Hz, 4 H, 10-H, 24-H, 34-H, 48-H), 7.11 [t (overlapped dd), *J* = 8.0, 4 H, 11-H, 23-H, 35-H, 47-H], 7.18 (d, *J* = 8.0 Hz, 4 H, 12-H, 22-H, 36-H, 46-H) 7.46 (s, 4 H, 49-H, 54-H, 55-H, 60-H) ppm. ^{13}C NMR (C_6D_6): δ = 32.96 (C-17, C-41), 68.38 (C-3, C-7, C-27, C-31), 70.60 (C-4, C-6, C-28, C-30), 70.84 (C-16, C-18, C-40, C-42), 71.59 (C-51, C-52, C-57, C-58), 102.58 (C-14, C-20, C-38, C-44), 113.23 (C-49, C-54, C-55, C-60), 116.57 (C-10, C-24, C-34, C-48), 119.76 (C-11, C-23, C-35, C-47), 129.89 (C-12, C-22, C-36, C-46), 141.14 (C-13, C-21, C-37, C-45), 160.19 (C-1, C-9, C-25, C-33) ppm; the assignment is based on H,H COSY, APT, HSQC, HMBC, and NOESY spectra. FAB−MS (NOBA), *m*/*z* = 829.2 [M$^+$], 889.0 (M + Na$^+$ + K$^+$). MALDI, *m*/*z* = 829.4 [M$^+$], 851.3 [M + Na$^+$], 867.0 [M + K$^+$], 888.5 [M + Na$^+$ + K$^+$].

2,5,8,11,18,22,29,32-Octaoxapentacyclo[22.3.2^{17,20}.2^{20,23}.1^{1,24}.1^{12,16}]tritriaconta-1(28),12,14,16(33),24,26-hexaene (4a): Colourless solid: m.p. 148−149 °C. $C_{25}H_{30}O_8$, *M* 458.51, (calculated C 65.49, H 6.59%, found C 65.43, H 6.41%); R_f = 0.78 (ethyl acetate/dichloromethane/petroleum ether/ethanol = 30:70:40:4). ^{1}H NMR (600 MHz, C_6D_6) 3.02 (d, *J* = 11.4 Hz, 2 H, 19-H^{ax}, 21-H^{ax}), 3.28 (dd, *J* = 11.4, 2.4 Hz, 2 H, 19-H^{eq}, 21-H^{eq}), 3.42 (d, *J* = 11.4 Hz, 2 H, 30-H^{ax}, 31-H^{ax}), 3.39−3.47 (overlapped peaks, 4 H, 4-CH_2, 9-CH_2), 3.49 (s, 4 H, 6-CH_2, 7-CH_2), 4.08−4.15 (overlapped peaks, 4 H, 3-CH_2, 10-CH_2), 4.90 (dd, *J* = 11.4, 2.4 Hz, 2 H, 30-H^{eq}, 31-H^{eq}), 5.31 (s, 2 H, 17-H, 23-H), 7.03−7.05 (overlapped peaks, 4 H, 13-H, 15-H, 25-H, 27-H), 7.10 (dd, *J* = 8.4, 7.2 Hz, 2 H, 14-H, 26-H), 7.95 (s, 2 H, 28-H, 33-H) ppm. ^{13}C NMR (C_6D_6): δ = 33.80 (C-20), 68.46 (C-3, C-10), 70.13 (C-19, C-21), 70.30 (C-30, C-31), 70.49 (C-4, C-9), 70.73 (C-6, C-7), 101.23 (C-17, C-23), 112.44 (C-28, C-33), 119.32, 119.95 (C-13, C-15, C-25, C-27), 129.86 (C-14, C-26), 141.43 (C-16, C-24), 160.30 (C-1, C-12) ppm; the assignment is based on H,H COSY, APT, and HSQC spectra. FAB−MS (NOBA), *m*/*z* = 460.0 [M$^+$]. MALDI *m*/*z* = 459.1 [M$^+$], 481.0 [M + Na$^+$], 497.0 [M + K$^+$].

2,5,8,11,18,22,29,32,35,38,45,49,56,59,62,65-Hexadecaoxanonacyclo[49.3.2^{17,20}.2^{20,23}.2^{44,47}.2^{47,50}.1^{1,51}.1^{12,16}.1^{24,28}.1^{39,43}]hexahexaconta-1(66),12,14,16(55),24,26,28(60),39,41,43(61),51,53-dodecaene (4b): Mixture of *like* and *unlike* isomers. Colourless solid: m.p. 206−209 °C. $C_{50}H_{60}O_{16}$, *M* 917.01, (calculated C 65.49, H 6.59%, found C 65.39, H 6.54%); R_f = 0.53 (ethyl acetate/dichloromethane/petroleum ether/ethanol = 30:70:40:4). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.59 (d, *J* = 11.5 Hz, 4 H, 19-H^{ax}, 21-H^{ax}, 46-H^{ax}, 48-H^{ax}) 3.75 (s, 8 H, 6-CH_2, 7-CH_2, 33-CH_2, 34-CH_2), 3.78 (d, *J* = 11.5 Hz, 4 H, 19-H^{eq}, 21-H^{eq}, 46-H^{eq}, 48-H^{eq}), 3.79 (d, *J* = 11.1 Hz, 4 H, 57-H^{ax}, 58-H^{ax}, 63-H^{ax}, 64-H^{ax}), 3.85−3.87 (overlapped peaks, 8 H, 4-CH_2, 9-CH_2, 31-CH_2, 36-CH_2), 4.13−4.15 (overlapped peaks, 8 H, 3-CH_2, 10-CH_2, 30-CH_2, 37-CH_2), 4.82 (d, *J* = 11.1 Hz, 4 H, 57-H^{eq}, 58-H^{eq}, 63-H^{eq}, 64-H^{eq}), 5.39, 5.40 (s, 4 H, 17-H, 23-H, 44-H, 50-H), 6.91 (dd, *J* = 7.9, 1.9 Hz, 4 H, 13-H, 27-H, 40-H, 54-H), 7.03 (d, *J* = 7.6 Hz, 4 H, 15-H, 25-H, 42-H, 52-H), 7.10 (s, 4 H, 55-H, 60-H, 61-H, 66-H), 7.26 [t (overlapped dd), 4 H, *J* = 7.9, 7.6 14-H, 26-H, 41-H, 53-H] ppm. ^{13}C NMR ($CDCl_3$): δ = 32.71 (C-20, C-47), 67.73 (C-3, C-10, C-30, C-37),

69.99 (C-4, C-9, C-31, C-36), 70.70 (C-19, C-21, C-46, C-48), 71.17 (C-6, C-7, C-33, C-34, C-57, C-58, C-63, C-64), 102.14 (C-17, C-23, C-44, C-50), 112.11 (C-55, C-60, C-61, C-66), 116.07 (C-13, C-27, C-40, C-54), 118.90 (C-15, C-25, C-42, C-52), 129.55 (C-14, C-26, C-41, C-53), 139.59 (C-16, C-24, C-43, C-51), 159.10 (C-1, C-12, C-28, C-39) ppm; the assignment is based on H,H COSY, APT, HSQC and HMBC spectra. FAB−MS (NOBA), *m*/*z* = 917.4 [M^+], 940.7 [M + Na^+], 978.0 [M + Na^+ + K^+]. MALDI, *m*/*z* = 917.6 [M^+], 939.7 [M + Na^+].

2,5,8,11,14,21,25,32,35-Nonaoxapentacyclo[25.3.2^{20,23}.2^{23,26}.1^{1,27}.1^{15,19}]hexatriaconta-1(31),15,17,19(36),27,29-hexaene (5a): Colourless solid: m.p. 127−128 °C. $C_{27}H_{34}O_9$, *M* 502.56, (calculated C 64.53, H 6.82%, found C 64.39, H 6.73%); R_f = 0.57 (ethyl acetate/dichloromethane/pentane/ethanol = 30:70:30:5). ^{1}H NMR (600 MHz, C_6D_6): δ = 2.99 (d, *J* = 11.3 Hz, 2 H, 22-H^{ax}, 24-H^{ax}), 3.28 (dd, *J* = 11.3, 2.7 Hz, 2 H, 22-H^{eq}, 24-H^{eq}), 3.38−3.41 (overlapped peaks, 4 H, 7-CH_2, 9-CH_2], 3.40 (d, *J* = 11.3 Hz, 2 H, 33-H^{ax}, 34-H^{ax}) 3.43 [td (overlapped ddd), 4 H, *J* = 5.5, 1.6, 4-CH_2, 12-CH_2], 3.52 [td (overlapped ddd), 4 H, *J* = 5.5, 1.4, 6-CH_2, 10-CH_2], 4.00 [td (overlapped ddd), 4 H, *J* = 5.5, 1.6, 3-CH_2, 13-CH_2], 4.93 (dd, *J* = 11.5, 2.7 Hz, 2 H, 33-H^{eq}, 34-H^{eq}), 5.24 (s, 2 H, 20-H, 26-H), 6.97 (ddd, *J* = 7.8, 2.6, 1.4 Hz, 2 H, 16-H, 30-H), 7.06 [dt (overlapped ddd), 2 H, *J* = 7.8, 1.4, 18-H, 28-H], 7.10 [t (overlapped dd), 2 H, *J* = 7.8, 17-H, 29-H], 7.80 (dd, *J* = 2.6, 1.4 Hz, 2 H, 31-H, 36-H) ppm. ^{13}C NMR (C_6D_6): δ = 33.31 (C-23), 68.80 (C-3, C-13), 70.61 (C-33, C-34), 70.76 (C-4, C-12), 71.06 (C-22, C-24), 71.36 (C-6, C-10), 71.60 (C-7, C-9), 102.13 (C-20, C-26), 112.99 (C-31, C-36), 118.80 (C-16, C-30), 120.10 (C-18, C-28), 129.71 (C-17, C-29), 141.22 (C-19, C-27), 160.54 (C-1, C-15) ppm; the assignment is based on H,H COSY, APT, and HMBC spectra. FAB-MS (NOBA), *m*/*z* = 503.0 [M^+], 524.0 [M + Na^+].

2,5,8,11,14,21,25,32,35,38,41,44,51,55,62,65,68,71-Octadecaoxanonacyclo[55.3.2^{20,23}.2^{23,26}.2^{50,53}.2^{53,56}.1^{1,57}.1^{15,19}.1^{27,31}.1^{45,49}]doheptaconta-1(72),15,17,19(61),27,29,31(66),45,47,49(67),57,59-dodecaene (5b): Mixture of *like* and *unlike* isomers. Colourless solid: m.p. 181−184 °C. $C_{54}H_{68}O_{18}$, *M* 1005.12, (calculated C 64.53, H 6.82%, found C 64.36, H 6.66%); R_f = 0.32 (ethyl acetate/dichloromethane/pentane/ethanol = 30:70:30:5). ^{1}H NMR (600 MHz, C_6D_6): δ = 2.981, 2.986 (d, *J* = 11.4 Hz, 4 H, 22-H^{ax}, 24-H^{ax}, 52-H^{ax}, 54-H^{ax}) 3.317, 3.324 (dd, *J* = 11.4, 2.8 Hz, 4 H, 22-H^{eq}, 24-H^{eq}, 52-H^{eq}, 54-H^{eq}), 3.42 (d, *J* = 11.4 Hz, 4 H, 63-H^{ax} 64-H^{ax}, 69-H^{ax}, 70- H^{ax}), 3.42−3.44 (overlapped peaks, 16 H, 6-CH_2, 7-CH_2, 9-CH_2, 10-CH_2, 36-CH_2, 37-CH_2, 39-CH_2, 40-CH_2), 3.52−3.54 (overlapped peaks, 8 H, 4-CH_2, 12-CH_2, 34-CH_2, 42-CH_2), 3.81−3.83 (overlapped peaks, 8 H, 3-CH_2, 13-CH_2, 33-CH_2, 43-CH_2), 4.911, 4.919 (dd, *J* = 11.4, 2.8 Hz, 4 H, 63-H^{eq}, 64-H^{eq}, 69-H^{eq}, 70-H^{eq}), 5.187, 5.196 (s, 4 H, 20-H, 50-H, 26-H, 56-H), 6.83 (ddd, 4 H, *J* = 8.3, 2.6, 1.4 Hz, 16-H, 30-H, 46-H, 60-H), 7.11 [t (overlapped dd), 4 H, *J* = 8.3, 17-H, 29-H, 47-H, 59-H], 7.23 (m, 4 H, 18-H, 28-H, 48-H, 58-H), 7.37 [dt (overlapped ddd), 4 H, *J* = 2.6, 1.4, 61-H, 66-H, 67-H, 72-H] ppm. ^{13}C NMR: δ = 32.96 (C-23, C-53), 68.35 (C-3, C-13, C-33, C-43), 70.49 (C-4, C-12, C-34, C-42), 70.86 (C-22, C-24, C-52, C-54), 71.59 (C-63, C-64, C-69, C-70), 71.70 (C-6, C-7, C-9, C-10, C-36, C-37, C-39, C-40), 102.57 (C-20, C-26, C-50, C-56), 113.50, 113.53 (C-61, C-66, C-67, C-72), 116.16 (C-18, C-28, C-48, C-58), 119.66 (C-16, C-30, C-46, C-60), 130.01 (C-17, C-29, C-47, C-59), 141.15 (C-19, C-27, C-49, C-57), 160.10 (C-1, C-15, C-31, C-45) ppm; the assignment is based on H,H COSY, APT, and HMBC spectra. FAB−MS (NOBA), *m*/*z* = 1006.0 [M + H^+], 1027.9 [M + Na^+], 1043.9 [M + K^+].

2,5,8,11,14,17,24,28,35,38-Decaoxapentacyclo[28.3.2^{23,26}.2^{26,29}.1^{1,30}.1^{18,22}]nonatriaconta-1(34),18,20,22(39),30,32-hexaene (6a): Colourless solid: m.p. 80−82 °C. $C_{29}H_{38}O_{10}$, *M* 546.61, (calculated C 63.72, H 7.01%, found C 63.59, H 7.13%); R_f = 0.56 (ethyl acetate/dichloromethane/petroleum ether/methanol = 30:70:40:7). ^{1}H NMR (600 MHz, C_6D_6): δ = 2.98 (d, *J* = 11.3 Hz, 2 H, 25-H^{ax}, 27-H^{ax}), 3.28 (dd, *J* = 11.3, 2.7 Hz, 2 H, 25-H^{eq}, 27-H^{eq}), 3.37−3.39 (overlapped peaks, 4 H, 6-CH_2, 13-CH_2), 3.41 (d, *J* = 11.5 Hz, 2 H, 36-H^{ax}, 37-H^{ax}), 3.43−3.45 (overlapped peaks, 4 H, 7-CH_2, 12-CH_2), 3.47−3.49 (overlapped peaks, 4 H, 4-CH_2, 15-CH_2), 3.52 (s, 4 H, 9-CH_2, 10-CH_2), 3.87−3.90 (overlapped peaks, 4 H, 3-CH_2, 16-CH_2), 4.92 (dd, *J* = 11.5, 2.7 Hz, 2 H, 36-H^{eq}, 37-H^{eq}), 5.24 (s, 2 H, 23-H, 29-H), 6.90 (ddd, *J* = 7.8, 2.7, 1.4 Hz, 2 H, 19-H, 33-H), 7.09 [dt (overlapped ddd), 2 H, *J* = 7.6, 1.4, 21-H, 31-H], 7.12 [t (overlapped dd), 2 H, *J* = 7.8, 20-H, 32-H], 7.66 (dd, *J* = 2.7, 1.4 Hz, 2 H, 34-H, 39-H) ppm. ^{13}C NMR (C_6D_6): δ = 32.69 (C-26), 67.64 (C-3, C-16), 70.00 (C-4, C-15), 70.11 (C-25, C-27), 70.53 (C-36, C-37), 70.83 (C-7, C-12), 71.16 (C-9, C-10), 71.21 (C-6, C-13), 101.58 (C-23, C-29), 112.24 (C-34, C-39), 116.80 (C-19, C-33), 119.37 (C-21, C-31), 129.18 (C-20, C-32), 140.68 (C-22, C-30), 159.75 (C-1, C-18) ppm; the assignment is based on H,H COSY, APT, HSQC, HMBC and ROESY spectra. FAB-MS (NOBA), *m*/*z* = 547.0 [M^+], 569.0 [M + Na^+], 584.0 [M + K^+].

2,5,8,11,14,17,24,28,35,38,41,44,47,50,57,61,68,71,74,77-Icosaoxanonacyclo[61.3.2^{23,26}.2^{26,29}.2^{56,59}.2^{59,62}.1^{1,63}.1^{18,22}.1^{30,34}.1^{51,55}]octaheptaconta-1(78),18,20,22(67),30,32,34(72),51,53,55(73),63,65-dodecaene (6b): Mixture of *like* and *unlike* isomers. Colourless oil: $C_{58}H_{76}O_{20}$, *M* 1093.23, (calculated C 63.75, H 7.01%, found C 63.60, H 6.94%); R_f = 0.27 (ethyl acetate/dichloromethane/petroleum ether/methanol = 30:70:40:7). ^{1}H NMR (600 MHz, C_6D_6): δ = 3.023 and 3.026 (d, *J* = 11.5 Hz, 2 H, 25-H^{ax}, 27-H^{ax}) and (d, *J* = 11.5 Hz, 2 H, 58-H^{ax}, 60-H^{ax}), 3.358 and 3.360 (dd, *J* = 11.5, 2.7 Hz, 2 H, 25-H^{eq}, 27-H^{eq}) and (dd, *J* = 11.5, 2.7 Hz, 2 H, 58-H^{eq}, 60-H^{eq}), 3.44 (d, *J* = 11.3 Hz, 4 H, 69-H^{ax}, 70-H^{ax}, 75-H^{ax}, 76-H^{ax}), 3.41−3.51 (overlapped peaks, 24 H, 6-CH_2, 7-CH_2, 9-CH_2, 10-CH_2, 12-CH_2, 13-CH_2, 39-CH_2, 40-CH_2, 42-CH_2, 43-CH_2, 45-CH_2, 46-CH_2), 3.52−3.54 (overlapped peaks, 8 H, 4-CH_2, 15-CH_2, 37-CH_2, 48-CH_2), 3.81−3.83 (overlapped peaks, 8 H, 3-CH_2, 16-CH_2, 36-CH_2, 49-CH_2), 4.92 (dd, *J* = 11.3, 2.7 Hz, 4 H, 69-H^{eq}, 70-H^{eq}, 75-H^{eq}, 76-H^{eq}), 5.203 and 5.210 (s, 2 H, 23-H, 56-H) and (s, 2 H, 29-H, 62-H), 6.84 (ddd, 4 H, *J* = 8.0, 2.6, 1.1 Hz, 19-H, 33-H, 52-H, 66-H), 7.11−7.15 (overlapped peaks, 4 H, 20-H, 32-H, 53-H, 65-H), 7.21−7.24 (overlapped peaks, 4 H, 21-H, 31-H, 54-H, 64-H), 7.34−7.36 (overlapped peaks, 4 H, 67-H, 72-H, 73-H, 78-H) ppm. ^{13}C NMR (C_6D_6): δ = 32.98 (C-26, C-59), 68.31 (C-3, C-16, C-36, C-49), 70.47 (C-4, C-15, C-37, C-48), 70.87 (C-25, C-27, C-58, C-60), 71.60 (C-7, C-9, C-10, C-12, C-40, C-42, C-43, C-45), 71.70 (C-6, C-13, C-39, C-46), 71.83 (C-69, C-70, C-75, C-76), 102.59 (C-23, C-29, C-56, C-62), 113.51 (C-67, C-72, C-73, C-78), 116.14 (C-19, C-33, C-52, C-66), 119.67 (C-21, C-31, C-54, C-64), 130.03 (C-20, C-32, C-53, C-65), 141.14 (C-22, C-30, C-55, C-63), 160.07 (C-1, C-18, C-34, C-51) ppm; the assignment is based on H,H COSY, APT, and HMBC spectra. FAB−MS (NOBA), *m*/*z* = 1093.0 [M^+], 1115.0 [M + Na^+], 1131.0 [M + K^+], 1153.8 [M + Na^+ + K^+].

2,5,8,11,14,17,20,27,31,38,41-Undecaoxapentacyclo[31.3.2^{26,29}.2^{29,32}.1^{1,33}.1^{21,25}]dotetraconta-1(37),21,23,25(42),33,35-hexaene (7a): Colourless solid (crystallised with a molecule of water): m.p. 80−82 °C. $C_{31}H_{42}O_{11}\cdot xH_2O$, *M* 608.68, (calculated C 61.17, H 7.29%, found C 60.98, H 7.13%); R_f = 0.31 (ethyl acetate/dichloromethane/petroleum ether/methanol = 30:70:40:5). ^{1}H NMR (600 MHz, C_6D_6): δ = 2.97 (d, *J* = 11.4 Hz, 2 H, 28-H^{ax}, 30-H^{ax}), 3.28 (dd, *J* = 11.4, 2.6 Hz, 2 H, 28-H^{eq}, 30-H^{eq}), 3.38−3.42 (overlapped peaks, 8 H, 6-CH_2, 7-CH_2, 15-CH_2, 16-CH_2), 3.40 (d, *J* =

11.5 Hz, 2 H, 39-H^{ax}, 40-H^{ax}), 3.45 (s, 8 H, 9-CH_2, 10-CH_2, 12-CH_2, 13-CH_2), 3.47−3.52 (overlapped peaks, 4 H, 4-CH_2, 18-CH_2), 3.81−3.85 (overlapped peaks, 4 H, 3-CH_2, 19-CH_2)], 4.91 (dd, J = 11.5, 2.6 Hz, 2 H, 39-H^{eq}, 40-H^{eq}), 5.21 (s, 2 H, 26-H, 32-H), 6.85 (ddd, J = 7.8, 2.6, 1.4 Hz, 2 H, 22-H, 36-H), 7.08 [dt (overlapped ddd), 2 H, J = 7.8, 1.4, 24-H, 34-H], 7.11 [t (overlapped dd), 2 H, J = 7.8, 23-H, 35-H], 7.57 (dd, J = 2.6, 1.4 Hz, 2 H, 37-H, 42-H) ppm. ^{13}C NMR (C_6D_6): δ = 33.12 (C-29), 68.23 (C-3, C-19), 70.46 (C-4, C-18), 70.76 (C-28, C-30), 71.23 (C-39, C-40), 71.53, 71.57, 71.62, 71.66 (C-6, C-7, C-9, C-10, C-12, C-13, C-15, C-16), 102.31 (C-26, C-32), 112.86 (C-37, C-42), 116.73 (C-22, C-36), 119.90 (C-24, C-34), 129.76 (C-23, C-32), 141.20 (C-25, C-33), 160.28 (C-1, C-21) ppm; the assignment is based on H,H COSY, APT, and HMBC spectra. FAB-MS (NOBA), 591.0 [M$^+$], 609.0 [M$^+$ + H_2O], 613.0 [M + Na^+].

2,5,8,11,14,17,20,27,31,38,41,44,47,50,53,56,63,67,74,77,80,83-Docosaoxanonacyclo[67.3.2^{26,29}.2^{29,32}.2^{62,65}.2^{65,68}.1^{1,69}.1^{21,25}.1^{33,37}.1^{57,61}]tetraoctaconta-1(84),21,23,25(73),33,35,37(78),57,59,61(79),69,71-dodecaene (7b, D$_1$ isomer): Colourless oil: $C_{62}H_{84}O_{22}$, M 1181.34, (calculated C 63.04, H 7.17%, found C 63.17, H 7.26%); R_f = 0.04 (ethyl acetate/dichloromethane/petroleum ether/methanol = 30:70:40:5; R_f for the D$_2$ isomer 0.11). ^{1}H NMR (600 MHz, C_6D_6): δ = 3.010 (d, J = 11.5 Hz, 2 H, 28-H^{ax}, 30-H^{ax}), 3.011 (d, J = 11.5 Hz, 2 H, 64-H^{ax}, 66-H^{ax}) 3.345 (dd, J = 11.5, 2.6 Hz, 2 H, 28-H^{eq}, 30-H^{eq}), 3.349 (dd, J = 11.5, 2.6 Hz, 2 H, 64-H^{eq}, 66-H^{eq}), 3.44−3.47 (overlapped peaks, 32 H, 6-CH_2, 7-CH_2, 9-CH_2, 10-CH_2, 12-CH_2, 13-CH_2, 15-CH_2, 16-CH_2, 42-CH_2, 43-CH_2, 45-CH_2, 46-CH_2, 48-CH_2, 49-CH_2, 51-CH_2, 52-CH_2), 3.46 (d, J = 11.5 Hz, 4 H, 75-H^{ax}, 76-H^{ax}, 81-H^{ax}, 82-H^{ax}), 3.53−3.55 (overlapped peaks, 8 H, 4-CH_2, 18-CH_2, 40-CH_2, 54-CH_2), 3.82−3.84 (overlapped peaks, 8 H, 3-CH_2, 19-CH_2, 39-CH_2, 55-CH_2), 4.92 (dd, J = 11.5, 2.6 Hz, 4 H, 75-H^{eq}, 76-H^{eq}, 81-H^{eq}, 82-H^{eq}), 5.211 and 5.215 (s, 2 H, 26-H, 62-H) and (s, 2 H, 32-H, 68-H), 6.83−6.85 (overlapped peaks, 4 H, 22-H, 36-H, 58-H, 72-H), 7.13 [t (overlapped dd), 4 H, J = 7.8, 23-H, 35-H, 59-H, 71-H], 7.23 (d, J = 7.2 Hz, 4 H, 24-H, 36-H, 60-H, 70-H), 7.38 (s, 4 H, 73-H, 78-H, 79-H, 84-H) ppm. ^{13}C NMR (C_6D_6): δ = 32.99 (C-29, C-65), 68.31 (C-3, C-19, C-39, C-55), 70.46 (C-4, C-18, C-40, C-54), 70.87 (C-28, C-30, C-64, C-66), 71.58 (C-75, C-76, C-81, C-82), 71.68 (C-6, C-7, C-9, C-10, C-12, C-13, C-15, C-16, C-42, C-43, C-45, C-46, C-48, C-49, C-51, C-52), 102.58, 102.80 (C-26, C-32, C-62, C-68), 113.47 (C-73, C-78, C-79, C-82), 116.14 (C-22, C-36, C-58, C-72), 119.68 (C-24, C-34, C-60, C-70), 130.02 (C-23, C-35, C-59, C-71), 141.15 (C-25, C-33, C-61, C-69), 160.07 (C-1, C-21, C-34, C-57) ppm; the assignment is based on H,H COSY, APT, and HMBC spectra. FAB−MS (NOBA): m/z = 1180.6 [M$^+$], 1202.2 [M + Na^+], 1218.0 [M + K^+], 1239.6 [M + Na^+ + K^+].

X-ray Crystallographic Study: Details are presented in Table 4. Data collection and structure refinement: **5a** and **7a**: The structural (crystallographic) data were collected on an automatic diffractometer CAD4 NONIUS with graphite monochromatized Mo-K_α radiation[47] (λ = 0.71069 Å). The cell parameters were obtained by fitting a set of 25 high-theta reflections. After Lorenz and polarisation corrections,[48] the structure was solved with SIR-97.[49] After anisotropic refinement a Fourier Difference reveals all the hydrogen atoms of the compound. The whole structure was refined with SHELXL-97[50] by the full-matrix least-square on F^2 techniques. Largest difference peak and hole **5a**: 0.445 and −0.354; **7a**: 0.352 and −0.271 e·Å^{-3}. ORTEP view realized with PLATON98[51] and ORTEP-3 for Windows.[52] **5b**: The structural (crystallographic) data were collected on a NONIUS Kappa CCD diffractometer with graphite monochromatized Mo-K_α radiation. The

Table 4. Details of X-ray structure analyses of compounds **5a**, **7a**, and **5b**

Compound	**5a**	**7a**	**5b**
Empirical formula	$C_{27}H_{34}O_9$	$C_{31}H_{44}O_{12}$	$C_{54}H_{68}O_{18}$
Formula mass	502.54	608.68	1052.12
Crystal system	Monoclinic	monoclinic	monoclinic
Space group	$P2_1/n$	$P2_1/c$	$P2_1/c$
Crystal size/mm	0.45 × 0.32 × 0.28	0.33 × 0.33 × 0.14	0.45 × 0.42 × 0.32
Unit cell dimensions:			
a [Å]	12.206(2)	11.335(3)	10.399(4)
b [Å]	14.667(3)	7.911(3)	19.145(12)
c [A]	14.569(3)	29.502(7)	13.434(6)
α [°]	90	90	90
β [°]	91.334(2)	90.380(2)	144.133(3)
γ [°]	90	90	90
V [Å^3]	2607.5(9)	2645.4(1)	2494.7(2)
Z	4	4	4
d [Mg·m^{-3}]	1.280	1.528	1.338
μ [mm^{-1}]	0.096	0.117	0.133
F(000)	1072	1304	1072
T [K]	293	293	120
$2\theta_{max}$ [°]	54	54	60
No. of reflections:			
collected	5707	7115	10686
independent	5464	6820	5504
observed	2580	3408	1979
R_{int}	0.0253	0.0146	0.0650
Parameters	326	395	326
Restrains	0	0	0
R [$I > 2\sigma(I)$]	0.068	0.057	0.159
R_w	0.188	0.145	0.412
GOF	1.040	0.925	1.580

cell parameters were obtained with Denzo and Scalepack[53] with 10 frames (psi rotation: 1° per frame). The structure was solved with SIR-97[48] which reveals all the non-hydrogen atoms of the compounds. After anisotropic refinement, many hydrogen atoms were found with a Fourier Difference. The whole structure was refined with SHELXL-97[49] by the full-matrix least-square on F^2 techniques. Largest difference peak and hole **5b**: 0.885 and −0.435 e·Å^{-3}. ORTEP view realized with PLATON98[50].

CCDC-194713 (**5a**), 194714 (**5b**), and 194715 (**7a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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