α,ω-Alkanediyldiammonium dications sealed within calix[5]arene capsules with a hydrophobic bayonet-mount fastening

Giovanna Brancatelli,^{*a*} Giuseppe Gattuso,^{*b*} Silvano Geremia,^{*a*} Nadia Manganaro,^{*b*} Anna Notti,^{*b*} Sebastiano Pappalardo,^{*c*} Melchiorre F. Parisi^{*b*} and Ilenia Pisagatti^{*c*}

 ^a Centro di Eccellenza in Biocristallografia, Dipartimento di Scienze Chimiche e Farmaceutiche, Università di Trieste, via L. Giorgieri 1, 34127 Trieste, Italy.
^b Dipartimento di Scienze Chimiche, Università di Messina, viale F. Stagno d'Alcontres 31, 98166 Messina, Italy

^c Dipartimento di Scienze Chimiche, Università di Catania, viale A. Doria 6, 95125 Catania, Italy.

Electronic Supplementary Information

Contents					
1.	Crystal structure determination of $1^{-} \square^{+} H_3 N(CH_2)_n NH_3^{+} \square^{-} (n = 10, 11, 12)$				
1.1	Treatment of the disorder	S2			
	Figure S1	S4			
	Figure S2	S4			
	Table S1	S6			
2.	Calculation of the cavity volume for the capsular assemblies				
	$1^{-} \supset^{+} H_3 N(CH_2)_n NH_3^{+} \subset 1^{-} \text{ and } 2^{-} \supset^{+} H_3 N(CH_2)_n NH_3^{+} \subset 2^{-} (n = 10 - 12)$	S7			
	Table S2	S 8			

1. Crystal structure determination of $1^{-} \square^+ H_3 N(CH_2)_n NH_3^+ \square^-$ (*n* = 10, 11, 12)

Crystals of all the capsular complexes were of small dimensions and data collection was carried out using synchrotron radiation at the X-ray diffraction beam-line of the Elettra Synchrotron, (Trieste, Italy) employing the rotating-crystal method with the cryo-cooling technique. Routinely, the crystal, dipped in Paratone as cryo-protectant, was mounted in a loop and flash frozen to 100 K with liquid nitrogen. Diffraction data for $1 \supset^+ H_3 N(CH_2)_{10} NH_3^+ \subset 1^-$ and $1 \supset^+ H_3 N(CH_2)_{11} NH_3^+ \subset 1^-$ were indexed and integrated using the XDS package,¹ while MOSFLM² was used for $1 \supset^+ H_3 N(CH_2)_{12} NH_3^+ \subset 1^-$. Scaling was carried out with AIMLESS^{3,4} for datasets collected from crystals of $1 \supset^+ H_3 N(CH_2)_{12} NH_3^+ \subset 1^-$, whereas XSCALE⁵ was used for those collected from crystals of $1 \supset^+ H_3 N(CH_2)_{11} NH_3^+ \subset 1^-$. The structures were solved by direct methods using SIR2011.⁶ Non-hydrogen atoms at full occupancy, or with population equal to or higher than 0.5 were anisotropically refined (H atoms at the calculated positions) by full-matrix least-squares methods on F^2 using SHELXL-13.⁷ Crystal data and refinement details are reported in Table S1. A detailed description of the treatment of disorder in each crystallographic model is provided in the following section.

1.1 Treatment of the disorder

$1^{-} \square^{+} H_{3}N(CH_{2})_{10}NH_{3}^{+} \square^{-}$

The structure of capsule $1^{-} \square^{+} H_3 N(CH_2)_{10} NH_3^{+} \square^{-}$ was solved and refined in the non-standard space group *P*can (n° 60). By applying the transformation matrix [0 1 0, 1 0 0, 0 0 -1] to the cell parameters (a = 22.92(1), b = 23.62(1), c = 36.17(2) Å), the **abc** axes can be transformed into the **ba-c** standard settings of the *P*bcn (a = 23.62(1), b = 22.92(1), c = 36.17(2) Å) space group.

The crystal structure of the $1^{-} D^{+}H_3N(CH_2)_{10}NH_3^{+} C1^{-}$ capsular complex showed two disordered orientations for one *tert*-butyl group at the upper rim, that were refined at 0.8/0.2 of partial occupancy.

^{1.} W. Kabsch, Acta Crystallogr., 2010, D66, 125-132.

^{2.} G. G. Battye, L. Kontogiannis, O. Johnson, H. R. Powell and A. G. W. Leslie, *Acta Crystallogr.*, 2011, **D67**, 271–281.

^{3.} P. R. Evans, Acta Crystallogr., 2006, D62, 72–82.

M. D. Winn, C. C. Ballard, K. D. Cowtan, E. J. Dodson, P. Emsley, P. R. Evans, R. M. Keegan, E. B. Krissinel, A. G. W. Leslie, A. McCoy, S. J. McNicholas, G. N. Murshudov, N. S. Pannu, E. A. Potterton, H. R. Powell, R. J. Read, A. Vagin and K. S. Wilson, *Acta. Crystallogr.*, 2011, D67, 235–242.

^{5.} W Kabsch, Acta Crystallogr, 2010, D66, 133-144.

^{6.} M. C. Burla, R. Caliandro, M. Camalli, B. Carrozzini, G. L. Cascarano, L. De Caro, C. Giacovazzo, G. Polidori, D. Siliqi and R. Spagna, *J. Appl. Crystallogr.*, 2007, **40**, 609–613.

^{7.} G. M. Sheldrick, Acta Crystallogr., 2008, A64, 112–122.

The cell contained severely disordered solvent molecules with partial occupancy, that were not modelled but taken into account using the SQUEEZE/PLATON⁸ procedure. The residual electron density of 1753 electrons/cell found in the inner space of $1^{-} D^{+}H_3N(CH_2)_{10}NH_3^{+} C1^{-}$ (corresponding to about 23% of the cell volume) was attributed to 35 trifluoroethanol (TFE) solvent molecules. A refinement using reflections modified by the SQUEEZE procedure gave good results and the *R*-factor was reduced from 26.2 to 17.7%.

$1^{-} \square^{+} H_{3}N(CH_{2})_{11}NH_{3}^{+} \square^{-}$

The structure of the $1 \ \mathbb{D}^+H_3N(CH_2)_{11}NH_3^+ \ \mathbb{C}1^-$ capsular complex showed both the guest and the pendant substituents, at the calixarene lower rim, to be severely disordered.

Three of these *tert*-butyloxycarbonylmethyl chains were found to be disordered over two positions and refined at 0.85/0.15, 0.6/0.4, 0.55/0.45 of partial occupancy, respectively. In addition, the carboxylate group was seen disordered over three positions refined at 0.5/0.4/0.1 of partial occupancy. One *tert*-butyl group at the upper rim was also found to be disordered over two positions refined at 0.65/0.35 of partial occupancy. Two orientations of equal population were found for the undecanediammonium guest. In Figure S1 all the orientations of the disordered moieties with lower occupancy are depicted in blue.

Restraints on geometrical parameters for all the disordered fragments were introduced during the refinement cycles, by using the DFIX, DANG and SADI cards, as well as restraints on anisotropic thermal parameters for carbon atoms by using the card SIMU.

The cell contained severely disordered solvent molecules with partial occupancy, which could be modelled. The SQUEEZE/PLATON procedure was used to correct the structure factors of these disordered solvent molecules. The residual electron density of 512 electrons/cell found in the inner space of $1^{-} \Box^{+} H_3 N(CH_2)_{11} N H_3^{+} \subset 1^{-}$ (15% of the cell volume) corresponded to about 10 TFE molecules (1.3 molecules in the asymmetric unit). A refinement using reflections modified by the SQUEEZE⁸ procedure gave good results and the *R*-factor was reduced from 20.7 to 16.5%.

The difference Fourier electron density map showed a residual positive peak of 1.3 e/Å^3 very close to the nitrogen atom of the guest (distance to the nitrogen atom: 1.5 Å), located almost at the centre of the calixarene cavity (distance to the oxygen atoms: 2.5-3.3 Å). Given that this type of interactions have

 ⁽a) A. L. Spek, Acta Crystallogr., 2015, C71, 9–18; (b) P. Sluis, v.d.; A. L. Spek, Acta Crystallogr., 1990, A46, 194–201.

been previously observed in the crystal structure of the $1^- \subset K^+$ complex (crystal structure deposited in the CCDC with the code 1056976, Figure S2), this residual peak was tentatively assigned to a K^+ ion with very low occupancy factor (0.1).



Figure S1. a) Side view of the solid-state structure of the $1^{-}_{+}H_3N(CH_2)_{11}NH_3^+ \subset 1^-$ capsular complex. The orientations of the disordered calixarene moieties with lower occupancy are shown in blue, whereas the two orientations of the guest having equal occupancy are depicted in violet and magenta. The sphere in violet, seen inside the calixarene cavity, indicates a K⁺ ion present in the crystal lattice with 0.1 of partial occupancy. b) Section of the electron density map (2Fo – Fc, contour level 0.8 σ) observed for the undecanediammonium guest disordered over two positions.



Figure S2. Crystallographic structure of the $1^{\frown}CK^+$ complex. In the asymmetric unit of the complex two crystallographic independent complexes $1^{\frown}CK^+$ (I and II) were found together with six trifluoroethanol molecules. The key crystallographic data for $1^{\frown}CK^+$ are: triclinic space group *P* 1, FW 3189.76, *a* 12.02(1), *b* 14.68(1), *c* 27.57(2) Å, *a* 77.97(3), *β* 89.64(4), *γ* 84.28(2)°; *V* 4734(6) Å³; *R*₁ 0.1100, *wR*₂ 0.3151, *R*₁(all) 0.1331, *wR*₂(all) 0.3504. K⁺···O_{Phenol} bond distances: 2.641(6) – 3.285(6) Å (I), and 2.650(6) – 3.204(7) Å (II), K⁺···O_{Ester} bond distances: 2.557(7) – 2.904(6) Å (I), 2.551(6) – 3.303(6) Å (II). K⁺···O_{Water} bond distance: 2.51(2) Å (II).

$1^{-} \square^{+} H_{3}N(CH_{2})_{12}NH_{3}^{+} \square^{-}$

In the asymmetric unit of the $1 \ \exists^+H_3N(CH_2)_{12}NH_3^+ \ d^-$ quasi-capsular complex four TFE solvent molecules were detected and refined at 0.80, 0.75, 0.60, and 0.6 of partial occupancy. In the crystallographic model of $1 \ \exists^+H_3N(CH_2)_{12}NH_3^+ \ d^-$ one pendant substituent was found disordered over two positions and refined at 0.65/0.35 of partial occupancy. For the geometrical parameters of this fragment restraints were applied on bond lengths and angles (using the cards DFIX, DANG and SADI). In addition, the thermal parameters of the atoms present in this fragment were restrained to be similar (using the card SIMU).

-	$1^{-} \Box^{+} H_3 N(CH_2)_{10} N H_3^{+} \subset 1^{-}$	$1^{-} O^{+} H_3 N(CH_2)_{11} N H_3^{+} C 1^{-}$	$1^{-} {\supset}^{+} H_3 N(CH_2)_{12} NH_3^{+} \subset 1^{-}$	
Empirical formula	$2(C_{81} H_{111} O_{15}), C_{10} H_{26} N_2,$	$2(C_{81} H_{111} O_{15}), C_{11} H_{28} N_2,$	$2(C_{81} H_{111} O_{15}), C_{12} H_{30} N_2,$	
Empirical formula	$8.8 (C_2 H_3 F_3 O)$	2.6 (C ₂ H ₃ F ₃ O), 0.2 K	5.5 (C ₂ H ₃ F ₃ O)	
Formula weight	3704.05	3105.66	3403.02	
<i>T</i> (K)	100(2)	100(2)	100(2)	
λ (Å)	0.900	0.800	0.8856	
Crystal system	Orthorhombic	Orthorhombic	Monoclinic	
Space group	Pcan	Pbcn	$P2_1/a$	
Unit cell dimensions (Å, °)	$a = 22.92(1), \alpha = 90$	a = 22.509(1), a = 90	a = 22.59(1), a = 90	
	$b = 23.62(1), \beta = 90$	$b = 22.972(2), \beta = 90$	$b = 16.93(1), \beta = 92.54(4)$	
	$c = 36.17(2), \gamma = 90$	$c = 35.249(2), \gamma = 90$	$c = 25.77(2), \gamma = 90$	
$V(\text{\AA}^3)$	19581(16)	18226(2)	9846(11)	
Ζ	8	8	4	
$\rho_{(calc)} (g/mm^3)$	1.256	1.132	1.148	
$\mu (\mathrm{mm}^{-1})$	0.085	0.068	0.148	
F(000)	7889	6635	3650	
Resolution range (Å)	36.08-1.15	50.00-0.88	25.80-0.91	
Reflections collected	39363	67897	29484	
Independent reflections	7517	13881	13054	
Data / restraints /	7517 / 81 / 936	12628 / 226 / 1126	12638 / 74 / 1170	
parameters	/51//01//50	12020 / 220 / 1120		
GooF	1.026	0.974	1.037	
$R_1, wR_2 [I \ge 2\sigma(I)]$	0.1118, 0.2035	0.1251, 0.3275	0.1187, 0.3095	
R_1 , wR_2 (all data)	0.1537, 0.2162	0.1579, 0.3592	0.1462, 0.3476	
CCDC code number	1037220	1039436	1038992	

Table S1. Crystal data and structure refinement for $\mathbf{1}^{\neg} H_3 N(CH_2)_{10} NH_3^+ \subset \mathbf{1}^-$, $\mathbf{1}^{\neg} H_3 N(CH_2)_{11} NH_3^+ \subset \mathbf{1}^-$ and $\mathbf{1}^{\neg} H_3 N(CH_2)_{12} NH_3^+ \subset \mathbf{1}^-$.

2. Calculation of the cavity volume for the capsular assemblies $1^{-} \supset^{+} H_3 N(CH_2)_n NH_3^{+} \subset 1^{-}$ and $2^{-} \supset^{+} H_3 N(CH_2)_n NH_3^{+} \subset 2^{-}$ (n = 10-12).

Preliminary calculations of the cavity volume on the new capsular complexes $1^{-}H_3N(CH_2)_nNH_3^+ \subset 1^{-}$ were carried out with the default setting parameters of the VOIDOO software,⁹ following the same procedure as for the previously reported capsular complexes $2^{-}H_3N(CH_2)_nNH_3^+ \subset 2^{-}$. Such calculations, however, gave very high packing coefficients for the new structures: 75%, 80% and 70% for $1^{-}H_3N(CH_2)_{10}NH_3^+ \subset 1^{-}$, $1^{-}D^+H_3N(CH_2)_{11}NH_3^+ \subset 1^{-}$ and $1^{-}H_3N(CH_2)_{12}NH_3^+ \subset 1^{-}$, respectively. These suspicious high values, that to the best of our knowledge have never been reported so far even for solid state structures, prompted us to re-analyze the default parameters of the VOIDOO software. New calculations were then performed on both capsular complexes $(1^{-}H_3N(CH_2)_nNH_3^+ \subset 1^{-}$ and 2^{-} $D^+H_3N(CH_2)_nNH_3^+ \subset 2^{-}$), by setting the atomic radii equivalent to those used by Mecozzi and Rebek:¹⁰ aliphatic carbon = 1.70 Å, aromatic carbon = 1.75 Å, oxygen = 1.60 Å, nitrogen = 1.65 Å, aliphatic hydrogen = 1.20 Å, aromatic hydrogen = 1.00 Å.

Additionally, the following parameters were changed from their default settings:

Primary grid spacing:	0.1
Maximum number of volume-refinement cycles:	30
Grid for plot files:	0.1

A virtual probe with a radius of 1.4 Å was employed for $1 \supset^+ H_3 N(CH_2)_{10} NH_3^+ \subset 1^-$, $1^- \supset^+ H_3 N(CH_2)_{11} NH_3^+ \subset 1^-$, $2 \supset^+ H_3 N(CH_2)_{10} NH_3^+ \subset 2^-$ and $2 \supset^+ H_3 N(CH_2)_{11} NH_3^+ \subset 2^-$, whereas a probe with a lager radius (1.7 Å) was necessary to define the two-host cavity of the *quasi*-capsular aggregates $1 \supset^+ H_3 N(CH_2)_{12} NH_3^+ \subset 1^-$ and $2 \supset^+ H_3 N(CH_2)_{12} NH_3^+ \subset 2^-$, the 1.4 Å probe being smaller than the gap present between the two calixarene upper rims. For a comparison of the internal volumes of the capsular cavities and the corresponding packing coefficients of the six complexes with the two probes see Table S2.

Volumes of the three alkanedyldiammonium guests (V_G) were calculated with the same software.

^{9.} G. J. Kleywegt and T. A. Jones, Acta Crystallogr., 1994, D50, 178–185.

^{10.} S. Mecozzi and J. Rebek, Jr, Chem. Eur. J., 1998, 4, 1016–1022.

Table S2. Estimate of the guest volume (V_G), internal volume of the capsular cavity (V_C) and packing coefficient (PC) of complexes $1^{-} T^{+}H_3N(CH_2)_nNH_3^{+} C1^{-}$ and $2^{-} T^{+}H_3N(CH_2)_nNH_3^{+} C2^{-}$ (n = 10-12).^{*a,b*}

	$V_{\rm G}({\rm \AA}^3)$	$V_{\rm C}({\rm \AA}^3)^a$	PC $(\%)^a$	$V_{\rm C}({\rm \AA}^3)^b$	$PC(\%)^b$
$1^{-} \mathbb{i}^{+} \mathrm{H}_{3} \mathrm{N}(\mathrm{C} \mathrm{H}_{2})_{10} \mathrm{N} \mathrm{H}_{3}^{+} \mathbb{i}^{-}$	195.3	299.4	65.2	279.9	69.8
$1^{-} \mathbf{\Box}^{+} \mathbf{H}_{3} \mathbf{N}(\mathbf{C} \mathbf{H}_{2})_{11} \mathbf{N} \mathbf{H}_{3}^{+} \mathbf{\Box} 1^{-}$	211.3	307.3	68.8	278.7	75.8
$1^{-}\!$	224.9	_	_	368.4	61.0
$2^{-} \square^{+} \mathrm{H}_{3} \mathrm{N}(\mathrm{C}\mathrm{H}_{2})_{10} \mathrm{N}\mathrm{H}_{3}^{+} \square 2^{-}$	196.5	297.2	66.1	267.3	73.5
$2^{-} \square^{+} \mathrm{H}_{3} \mathrm{N}(\mathrm{CH}_{2})_{11} \mathrm{NH}_{3}^{+} \square 2^{-}$	209.3	338.0	61.9	301.9	69.3
$2^{-} \mathbb{i}^{+} \mathrm{H}_{3} \mathrm{N}(\mathrm{CH}_{2})_{12} \mathrm{NH}_{3}^{+} \mathbb{i}^{-} 2^{-}$	223.0	_	_	358.3	62.2

^{*a*}Values refer to calculations carried out with the 1.4 Å probe; ^{*b*}values refer to calculations carried out with the 1.7 Å probe.

Data in Table S2 indicate that the internal volumes of the capsular cavities assessed with a 1.7 Å radius probe –instead of a 1.4 Å one– are on average 6–10% smaller and, as a result, the corresponding packing coefficients are consistently higher. Accordingly, in the case of the *quasi*-capsular complexes $1^{-} \square^{+} H_3 N(CH_2)_{12} N H_3^{+} \square^{-}$ and $2^{-} \square^{+} H_3 N(CH_2)_{12} N H_3^{+} \square^{-}$ —where use of the larger 1.7 Å probe was mandatory to avoid the exit of the rolling probe from the internal cavity– the values of the packing coefficients are likely to be overestimated by about 6–10%.