Dioxa-[40]decaphyrin(1.0.1.0.0.1.0.1.0.0): An Analogue of Turcasarin with a "Figure-Eight" Structure

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The synthesis and characterization of two different furan containing analogues of turcasarin, namely 46,51-dioxa-2,11,15,20,24,33,37,42-octapropyl-turcasarin (**7a**) and 46,51-dioxa-2,11,24,33-tetrapropyl-15,20,37,42-tetraethyl-16,19,38,41-tetramethyl-turcasarin (**7b**) are described. While **7a** was found to exhibit a "figure eight" structure in solution and in the solid state, **7b** is believed to adopt a different, more symmetric conformation is solution.

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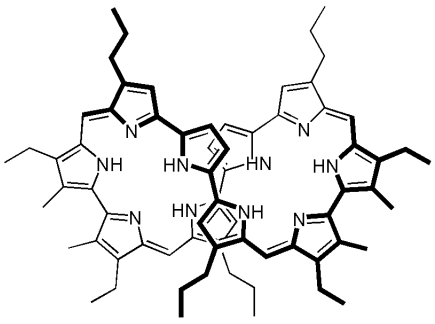
The discovery of [40]decaphyrin(1.0.1.0.0.1.0.1.0.0) (turcasarin, **1**) [1] in 1994 opened the avenue to higher order expanded porphyrins. Prior to its arrival only systems with up to six pyrrolic subunits were known.[2] All these previous systems were flat or at least flat by projection. By contrast, turcasarin was found to adopt a chiral "figure eight" type structure in solution and in the solid state.[1] Subsequently, several other fully conjugated higher order expanded porphyrins were reported. This includes systems such as [32]octaphyrin(1.0.1.0.1.0.1.0) [3], (**2**) [34]octaphyrin(1.1.1.0.1.1.1.0) [4] (**3**) and [36]octaphyrin-(2.1.0.1.2.1.0.1) [4] (**4**) that also adopt "figure eight" structures. Interestingly, the recently reported [32]octaphyrin(1.0.0.0.1.0.0.0), while deviating substantially from planarity, does not show a "figure eight" structure [5]. Presently, even larger expanded porphyrins are known [6,7]. For instance, by condensing tetraethylbipyrrole with 2,6-dichlorobenzaldehyde under conditions of acid catalysis and the presence of Zn^{2+}, Setsune and coworkers obtained a complex mixture that contained, among other products, [48]dodecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0) and [64]hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) [6]. A crystal structure analysis of [48]dodecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0) that was contained in the mixture in up to 6% yield, revealed the presence of a large cavity surrounded by a wall of a "zigzag-tracked π-conjugation system" [6]. By employing a different synthetic strategy, namely the use of a highly reactive bis(azafulvene) species, Setsune also succeeded in preparing expanded porphyrins with up to 24 pyrroles; the largest characterized structurally, [64]hexadecaphyrin-(1.0.1.0.1.0.1.0.1.0.1.0.1.0.1.0) contained 16 pyrroles [7,8]. These systems are of tremendous scientific interest, not only due to their aesthetically appealing structures, but also because of their nonplanar conformations that can render them chiral. In fact, Vogel *et al*. recently reported the successful separation of the two enantiomers of **4** and of some of its metal complexes [9]. In spite of this achievement, the factors that render large fully conjugated expanded porphyrins nonplanar are not completely understood, with, for instance, the balance between conjugation effects and steric factors remaining particularly recondite. The role, if any, that so called heteroatom substitution (replacing one or more pyrroles by furan, thiophene, *etc*.) could play in defining the overall structure and spectroscopic properties of a higher order expanded porphyrin is also of interest. Given the recent attention devoted to the synthesis of medium sized heteroatom-containing expanded porphyrins [10-19], we were keen to address the latter question.

Results and Discussion.

In this paper we report the successful synthesis of a dioxa-analogue of turcasarin and show it also adopts a "figure eight" structure. As implied above, in setting out to



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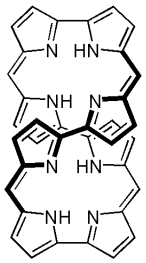

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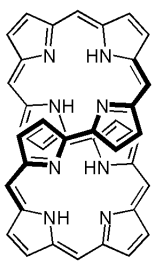

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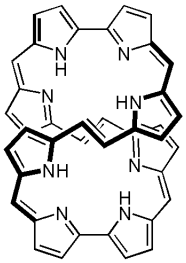

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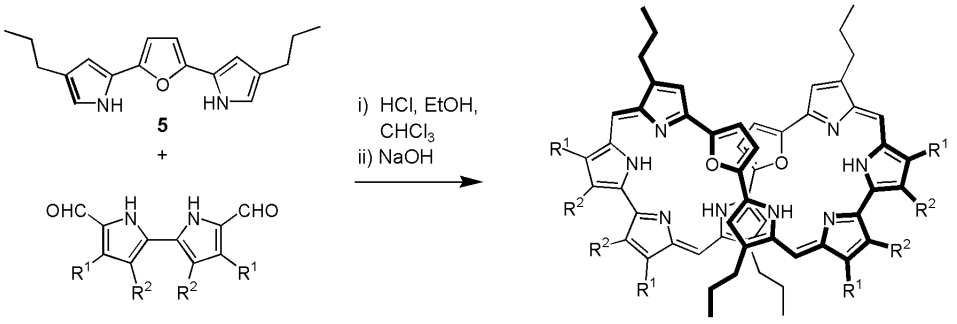
prepare a bis-furan containing turcasarin we were interested in seeing how such a transformation would affect the structure and electronic properties of the macrocycle. Towards this end we prepared the dioxaturcasarin **7a**.

The synthesis of dioxaturcasarin (**7a**) is outlined in Scheme 1. Briefly, acid catalyzed condensation of 2,5-bis(4-propyl-2-pyrrolyl)furan (**5**) [20] with one equivalent of 4,4'-dipropyl-5,5'-diformyl-2,2'-bipyrrole (**6a**) [20] followed by basic workup and column chromatography, gives rise to **7a**, in 31% yield.

as for the two different meso-like C*H* signals. The chemical shift of these latter signals is consistent with what is expected for a non-aromatic species. The alkyl region shows the expected complex splitting pattern based on the presence of four different propyl groups. Of the two possible singlets that might be expected for the two different N*H* signals, only one is observed at room temperature and even then only as an extremely broad signal at 13.25 ppm. When the temperature is gradually lowered to 193 K (see Figure 1), however, this signal turns into a sharp singlet,

Scheme 1



6a (R^1= n-prop, R^2 = H)
6b (R^1= eth, R^2 = me)

7a (R^1= n-prop, R^2 = H), 31 %
7b (R^1= eth, R^2 = me), 28 %

The ^{1}H-NMR and the ^{13}C-NMR spectra of **7a** are consistent with what is expected for a molecule with a "figure eight" structure. As judged from the ^{1}H-NMR spectrum, the macrocycle has an apparent C_2 symmetry, a conclusion that is supported strongly by the number of signals observed in the ^{13}C-NMR spectrum. In the room temperature ^{1}H-NMR spectrum of **7a**, shown in Figure 1, two sets of doublets at 6.65 and 7.20 ppm are seen; these are found to correspond to the two β-protons of the furan subunits, as judged by a COSY analysis. The remaining six singlets in the region between 6.41 and 6.79 ppm, account for the other four magnetically distinct β-pyrrolic protons, as well

while another signal, a singlet, becomes observable at 12.75 ppm. This latter singlet, however, remains broad even at this temperature, potentially indicating a fast exchange between two coexisting tautomers. Interesting also is the change seen in the alkyl region of the spectrum, here the fine splitting pattern seen at room temperature is essentially lost. Comparatively, the spectral change in the region of meso and β-pyrrole protons is rather minor; while the total number of peaks does not change, some of the resolution is lost. Again, the chemical shift of the N*H* protons leads us to assign **7a** as being a non-aromatic species.

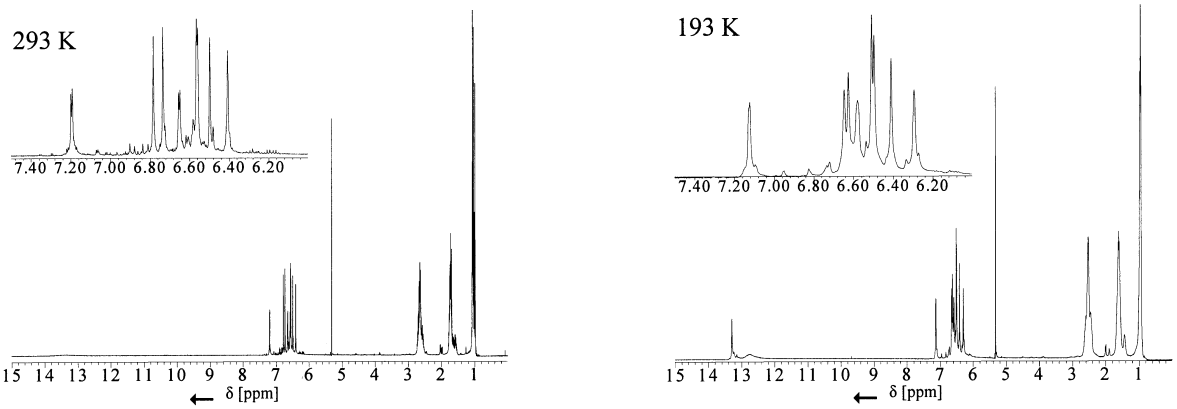


Figure 1. ^{1}H-NMR spectra (CD_2Cl_2) of **7a** at 293 K and 193 K, respectively.

Definite proof for the existence of a "figure eight" motif in the case of dioxaturcasarin **7a** came from a single-crystal X-ray structural analysis of the free base form of **7a**. The resultant structure, shown in Figure 2, is noteworthy for being very similar to that of **1**•4HCl despite the fact that it involves the free base form of dioxaturcasarin (**7a**) as compared to the tetra-HCl salt of turcasarin (**1**•4HCl) [1]. This correspondence is at first blush remarkable, given that two very different stages of protonation are involved. Nonetheless, it underscores the fact that the unique "crossing" motifs seen in both turcasarin and various other higher order expanded porphyrins are intrinsic structural features and not due to ancillary effects such as counter anion binding as was once considered possible [1].

The UV-vis spectrum of the protonated form of dioxaturcasarin **7a**•4HCl (shown in Figure 3), obtained upon bubbling HCl through a solution of the free base, resembles that of the all-aza system (**1**•4HCl) with however some differences. The main difference involves the energy of the transition; the λ_{max} of **7a**•4HCl (λ_{max} = 588 nm, ε = 384000) appears at lower wavelength than the λ_{max} of **1**•4HCl (λ_{max} = 642 nm, ε = 312500). Moreover, **7a**•4HCl exhibits two relatively strong Q-type absorption bands at 681 nm (ε = 104000) and 698 nm (ε = 107000) that are poorly resolved. These bands are missing or are at least much weaker in the case of **1**•4HCl [1,21]. The free-base form of dioxaturcasarin **7a** is characterized by a Soret-type absorption that is both less intense and less red shifted than the fully protonated form (λ_{max} = 548; ε = 125000). It is interesting to note, that the extinction coefficients of **7a**•4HCl are a factor of 1.2 higher than these of **1**•4HCl.

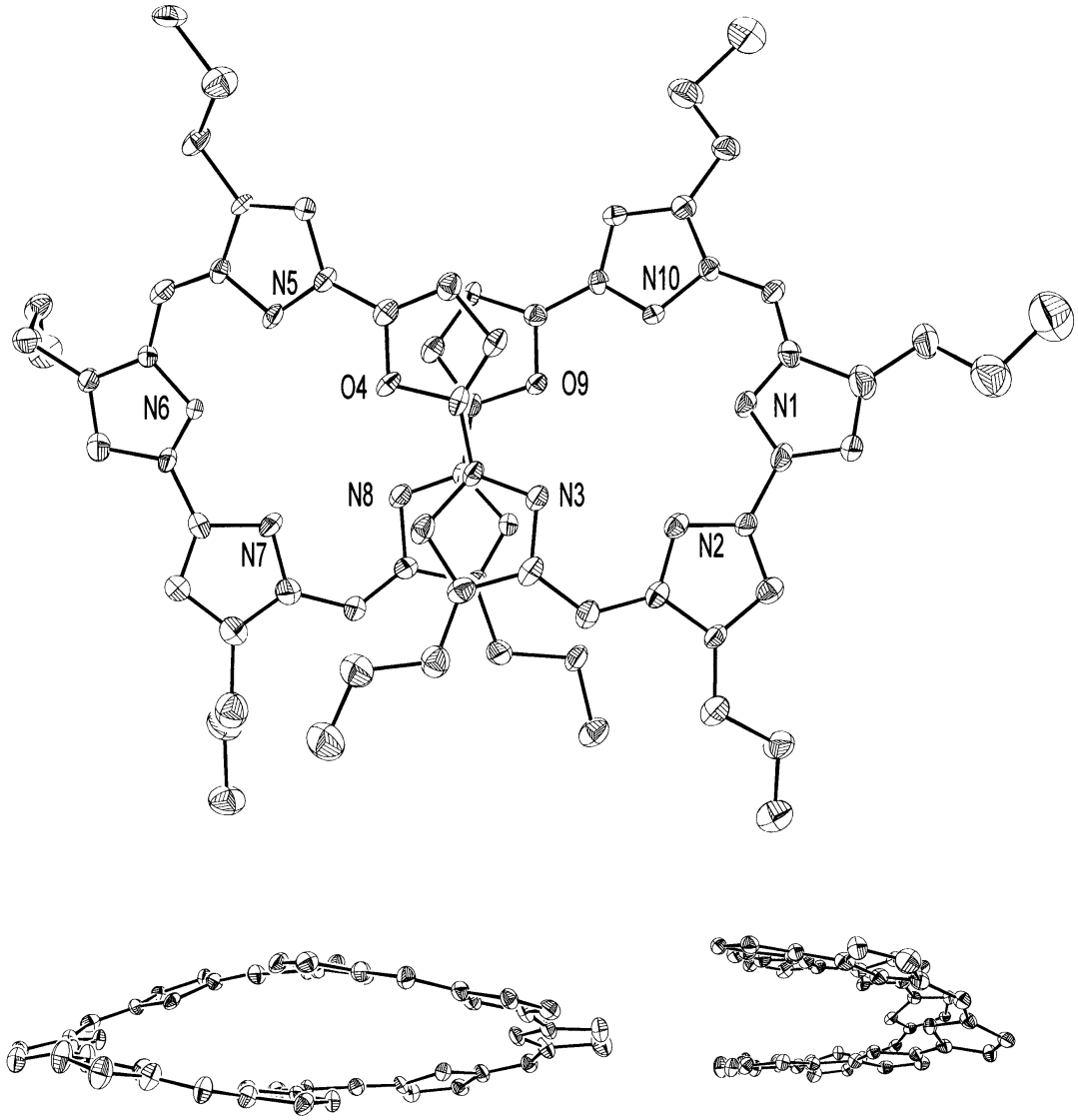


Figure 2. ORTEP views of dioxaturcasarin **7a** showing a partial atom labeling scheme. Hydrogen atoms have been omitted for clarity. Alkyl groups have been omitted in the side views. Thermal ellipsoids are scaled to the 30% probability level.

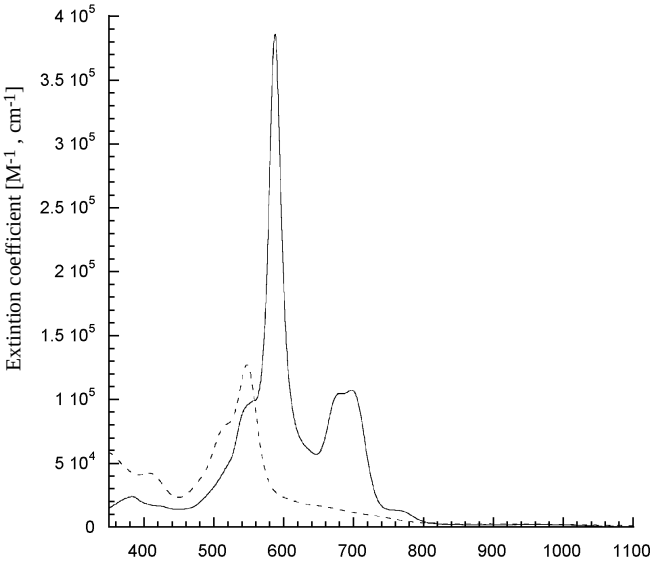


Figure 3. UV-vis spectra of the free base **7a** (--) and tetra-HCl salt **7a**•4HCl (—) of dioxaturcasarin **7a** in CH_2Cl_2.

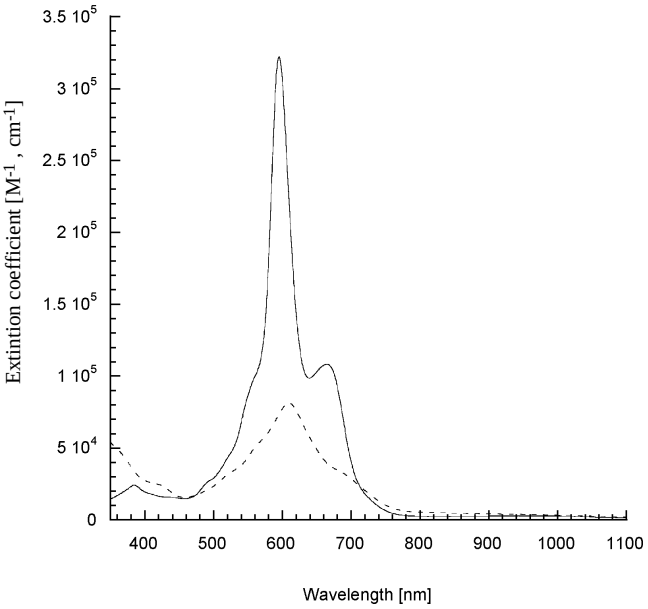


Figure 4. UV-vis spectra of the free base **7b** (--) and tetra-HCl salt **7b**•4HCl (—) of dioxaturcasarin **7b** in CH_2Cl_2.

One explanation for the above spectral discrepancies could be the differing nature of the alkyl substituents of **7a**•4HCl and **1**•4HCl. Such differences were seen to have an important effect in the case of heterosapphyrins [10,11]. Accordingly, **7b** was prepared from **5** [20] and **6b** [10] in 28% yield using a procedure analogous to that used to prepare **7a** (Scheme 1) [22]. This species, in its protonated form (**7b**•4HCl) displays a UV-vis (Figure 4) quite similar to **7a**•4HCl. The main transition seen in the case of **7b**•4HCl (λ_{max} = 596; ε = 322000) is slightly red shifted as compared to **7a**•4HCl. Additionally, the two Q-type absorption bands, seen for **7a**•4HCl, are merged into a single absorption band that is also blue shifted in the case of **7b**•4HCl (λ = 665; ε = 109000). As a result, the UV-vis spectrum of **7b**•4HCl bears a greater resemblance to that of **1**•4HCl than does **7a**•4HCl.

In spite of the general similarities seen for the protonated forms of **7a** and **7b**, marked differences were seen in the case of the free base systems. Compared to **7a**, **7b** shows only a very broad absorption that is red shifted and much weaker in intensity (for **7b** λ_{max} = 609; ε = 80000 vs. λ_{max} = 548; ε = 125000 for **7a**). This led us to consider whether the more highly substituted species **7b** was adopting a conformation in solution that was different from **7a**. To test this assumption ^{1}H-NMR and ^{13}C-NMR spectral studies were carried out. In fact, the room temperature ^{1}H-NMR spectrum of **7b**, shown in Figure 5, reveals some marked differences as compared to that of **7a**. For instance, in distinct contrast to what is seen in the case of **7a**, a sharp signal is seen at 13.5 ppm that accounts for all four N*H* protons. Additionally, unusual broadening in the spectral region corresponding to the β-pyrrolic and meso-C*H* protons is observed. Instead of the two doublets and four singlets that would be expected for a "figure eight"

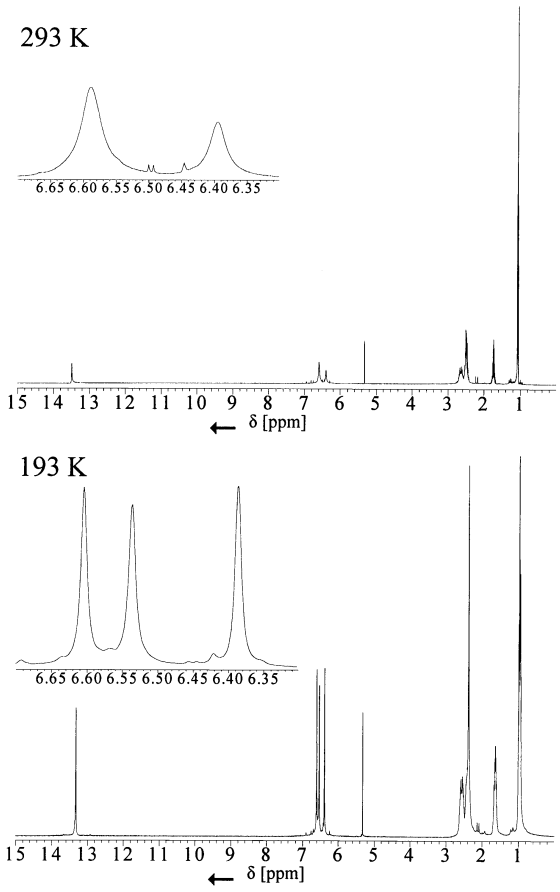


Figure 5. ^{1}H-NMR spectra (CD_2Cl_2) of **7b** at 293 K and 193 K, respectively.

structure, two broad singlets are seen at 6.4 and 6.6 ppm, respectively [23]. When the temperature is lowered to 193 K (see Figure 5), these signals turn into three sharp singlets, which integrate for four protons each. On this basis, it is suggested that **7b**, unlike its analogue **7a**, adopts a net averaged flat structure even at low temperature. An alternative conclusion, which is likewise consistent with the ^{1}H-NMR spectral data is that **7b** becomes "frozen out" at low temperature in the form of a new nonplanar structure of high symmetry. The ^{13}C-NMR spectrum, recorded at 193 K, is likewise consistent with both of these possibilities. Here, in the aromatic region, half the number of signals are seen as compared to **7a** [24].

In conclusion, the two dioxaturcasarin systems reported here provide support for the proposal that heteroatom analogues of large, higher order expanded porphyrins can be readily made and when properly designed will prove quite stable. While the exact factors that lead to the observed higher symmetry of **7b** are not fully understood at present, it nonetheless underscores how subtle differences in structure (**7a** versus **7b**) can influence the overall symmetry of a macrocycle. Further studies of these and other heteroatom systems are in progress.

EXPERIMENTAL

46,51-Dioxa-2,11,15,20,24,33,37,42-octapropyl-turcasarin (**7a**).

4,4'-Dipropyl-5,5'-diformyl-2,2'-bipyrrole (**6a**) [20] (77 mg, 0.283 mmol) was dissolved in a mixture of 20 ml of ethanol and 700 ml of $CHCl_3$, followed by the addition of 2,5-bis(4-propyl-2-pyrrolyl)furan (**5**) [20] (80 mg, 0.283 mmol). The resulting solution was stirred under argon for several minutes. Subsequently, HCl gas was bubbled through the reaction mixture for five minutes. The mixture was then stirred under an argon blanket overnight, followed by solvent removal using a rotary evaporator. After redissolving the residue in CH_2Cl_2 (*ca*. 100 ml), the resulting solution was washed with 1 *M* NaOH (1x 20 mL). The CH_2Cl_2 layer was then separated off, dried over anhydrous Na_2SO_4 and concentrated to a small volume on the rotary evaporator before being purified on a pre-basified 2 x 20 cm silica gel column. Here, prebasification was achieved by bubbling ammonia through a CH_2Cl_2-silica gel slurry before packing. The first purple band to elute using CH_2Cl_2 saturated with NH_3 as the eluent was collected und evaporated to dryness. Further chromatographic purification was achieved on a 2 x 20 cm silica gel column, using a 1:1 mixture of hexanes and ethyl acetate as the eluent. The first purple fraction was collected, evaporated to dryness, redissolved in CH_2Cl_2, and washed with 1 M NaOH (2 x 25 ml) and with brine (1 x 25 ml). The organic layer was dried over anhydrous Na_2SO_4 and taken to dryness *in vacuo*. This yielded 45.8 mg (31%) of **7a** in pure form. For **7a**: ^{1}H NMR (500 MHz, CD_2Cl_2, 293 K): δ [ppm] 0.99 - 1.28 (comp, 24H, $CH_2CH_2CH_3$), 1.58 - 1.78 (comp, 16H, $CH_2CH_2CH_2CH_3$), 2.56 - 2.73 (comp, 16H, $CH_2CH_2CH_3$), 6.41 (s, 2H), 6.51 (s, 2H), 6.56 (s, 2H), 6.57 (s, 2H), 6.65 (d, J_{HH} = 4 Hz, 2H, furan*H*), 6.75 (s, 2H), 6.79 (s, 2H), 7.20 (d, J_{HH} = 4 Hz, 2H, furan*H*) 13.25 (br s, 2H, N*H*); ^{13}C NMR (125 MHz, CD_2Cl_2, 293 K): δ [ppm] 14.16, 14.21, 14.50, 22.99, 24.34, 24.45, 24.76, 28.48, 28.62, 28.87, 112.70, 113.01, 114.61, 114.93, 115.44, 116.49, 118.02, 120.14, 137.29, 137.81, 138.31, 140.07, 140.81, 141.26, 146.16, 147.17, 147.58, 147.64, 148.46, 151.83, 152.12, 153.86; HRMS (CI^+) *m/z* calcd. for $C_{68}H_{76}N_8O_2$ (M^+): 1036.6091, found: 1036.6071. UV-vis (CH_2Cl_2) (ε in mol^{-1}•L^{-1}) λ [nm] 408 (ε = 42000), 548 (ε = 125000). This compound was further characterized by X-ray diffraction analysis as described below. For **7a**•4HCl (obtained by bubbling HCl gas through a solution of free base **7a**): UV-vis (CH_2Cl_2) λ [nm] (ε in mol^{-1}•L^{-1}) 385 (ε = 23000), 588 (ε = 384000), 681 (ε = 104000), 698 (ε = 107000); Crystallographic summary for **7a**. Small prisms were grown from CH_2Cl_2/CH_3OH, triclinic, P-1 (No. 2), Z = 2 in a cell of dimensions: a = 17.2027(11), b=18.6199(11), c = 22.9435(14)Å, α = 101.408(1), β = 110.132(1), γ = 106.881(1)°, V = 6229.6(7)Å^3, ρ_{calc} = 1.19 g-cm^{-3}, F(000) = 2376. A total of 36451 reflections were measured, 22895 unique (R_{int} = 0.061), on a Siemens SMART PLATFORM equipped with a CCD area detector using graphite monochromatized Mo Kα radiation (λ = 0.71073Å) at -100 ˚C. The structure was refined on F^2 to an R_W = 0.177, with a conventional R = 0.0945 (5821 reflections with $F_O > 4[\sigma(F_O)]$), and a goodness of fit = 1.34 for 437 refined parameters. There are two molecules of the macrocycle per asymmetric unit. There are two regions of disordered solvent as well.

46,51-Dioxa-2,11,24,33-tetrapropyl-15,20,37,42-tetraethyl-16,19,38,41-tetramethyl-turcasarin (**7b**).

This compound was prepared from 2,5-bis(4-propyl-2-pyrrolyl)furan (**5**) [20] (80 mg, 0.283 mmol) and 3,3'-Dimethyl-4,4'-diethyl-5,5'-diformyl-2,2'-bipyrrole (**6b**) [10] (77 mg, 0.283 mmol) in a manner analogous to that described above. However, in this case, the crude product was purified on a 4 x 20 silica gel column, using CH_2Cl_2 – methanol (99:1; v/v) as the eluent. The amount of methanol in the eluting solvent mixture was gradually raised to 8%, leading to the elution of a yellow [22] and a blue band. The blue fraction was collected, evaporated to dryness, redissolved in CH_2Cl_2, and washed with 1 *M* NaOH (2 x 25 ml) and with brine (1 x 25 ml). The organic layer was dried over anhydrous Na_2SO_4 with the solvent then being removed *in vacuo*. Further purification was achieved *via* recrystallization from CH_2Cl_2/methanol. This yielded 41.2 mg (28%) of **7b** in pure form. For **7b**: ^{1}H NMR (500 MHz, CD_2Cl_2, 193 K): δ [ppm] 0.93 - 1.00 (comp, 24H, $CH_2CH_2CH_3$ and CH_2CH_3), 1.61 - 1.68 (m, 8H, $CH_2CH_2CH_2CH_3$), 2.38 – 2.61 (comp, 28H, $CH_2CH_2CH_3$, CH_2CH_3 and CH_3), 6.39 (s, 4H), 6.54 (s, 4H), 6.61 (s, 4H), 13.3 (s, 4H, N*H*); ^{13}C NMR (125 MHz, CD_2Cl_2, 193 K): δ [ppm] 11.46, 13.63, 15.66, 16.82, 23.85, 27.50, 110.07, 112.57, 113.53, 128.23, 139.30, 140.33, 140.62, 141.02, 142.28, 147.47, 148.08; HRMS (CI^+) *m/z* calcd. for $C_{68}H_{76}N_8O_2$ (M^+): 1036.6091, found: 1036.6095; UV-vis (CH_2Cl_2) (ε in mol^{-1}•L^{-1}) λ [nm] 609 (ε = 80000). For **7a**•4HCl (obtained by bubbling HCl gas through a solution of free base **7a**): UV-vis (CH_2Cl_2) λ [nm] (ε in mol^{-1}•L^{-1}) 596 (ε = 322000), 665 (ε = 109000).

Acknowledgements.

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[22] It is noteworthy that the [1+1] product, 24-monooxa-2,11-dipropyl-15,20-diethyl-16,19-dimethyl-orangarin, was also isolated in 11% yield. Studies of this system are ongoing and will be reported in due course.

[23] Interestingly, line broadening was also observed in the room temperature ^{13}C-NMR spectrum of **7b**.

[24] Unfortunately, the poor solubility of **7a**•4HCl as well as **7b**•4HCl precluded their spectroscopic analysis in dichloromethane solution.