An Iterative Synthetic Approach to Nanometre-scale Molecular Ribbons

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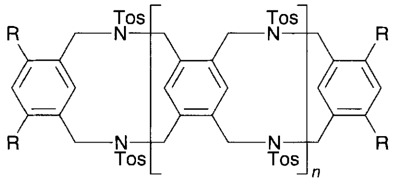
The hitherto longest molecular ribbons (4–6), composed of several [3.3]metacyclophane units, are synthesized using a new iterative synthetic strategy, up to a length of seven fourfold-bridged benzene rings, and it is proved by X-ray crystal structural analyses and ^{1}H NMR spectroscopy that these molecules form meander-type folded *syn* conformations leading to multiple π-staples.

Molecular ribbon-structures were proposed years ago,[1] yet only Stoddart and coworkers have found structure-directed syntheses.[2] Subsequent Diels–Alder reactions led to open-chain and cyclic ribbon structures, which consist of condensed six-membered ring assemblies.[3]

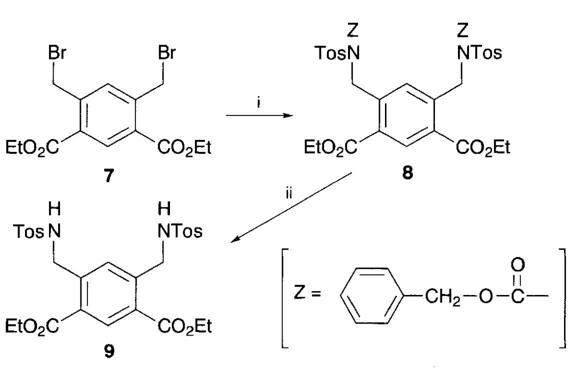
For some years, we have tried to obtain flexible ribbon structures which could be macrocyclized later on account of their four terminal functional groups.[4] So far, we have synthesized only [3.3]metacyclophane structures **1a**–**3a** with a maximum of four benzene ring units.[5]

The usual synthetic methods[5] failed for the preparation of ribbon-type molecules **4a**–**6a** containing more than four benzene rings. The derivatisation of the four terminal ester functions to obtain four terminal aminomethyl groups was not possible in preparative amounts.[5] Therefore, we developed a new iterative† strategy which is reported here. This new strategy for long ribbon molecules starts with **2a** giving the alcohol **2b** after ester reduction. Alcohol **2b** can be transformed with PBr_3 into the cyclisation building block **2c**. This tetrabromo derivative can be reacted with the new key compound **9** developed especially for this strategy (Scheme 1) to yield **4a** in preparative amounts.

Repeated use of this reaction cycle (ester reduction to **4b**, transformation into **4c**, elongation with **9**) results in the successful production of the seven-layered ribbon molecule **6a** (6% overall yield starting from **2a**; Scheme 2). In an analogous manner, we obtained benzeno<6>phane[6] **5a** which contains six benzene rings, starting from **1a** *via* **3a** (10% overall yield starting from **1a**).



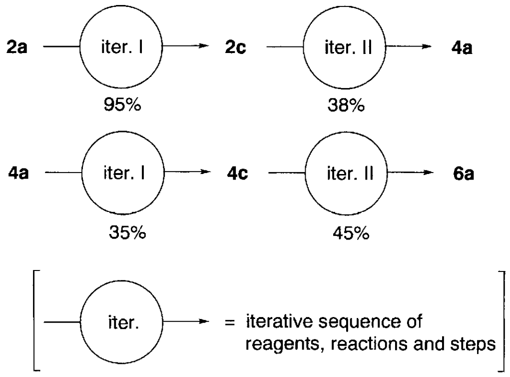
1 $n = 0$ **a** R = CO_2Et
2 $n = 1$ **b** R = CH_2OH
3 $n = 2$ **c** R = CH_2Br



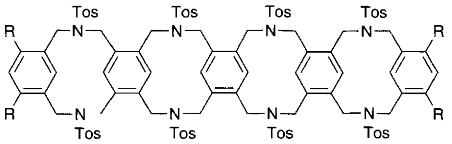
Scheme 1 *Reagents and conditions*: i, TosNHZ, K_2CO_3, DMF, room temp., 3 d, 40%; ii, H_2 (3 bar), Pd/C, $CHCl_3$–MeOH, room temp., 8 h, 98%

Using this route the open ribbon structures were lengthened successfully. The molecular ribbons **4a**–**6a** contain heterocyclic twelve-membered [3.3]metacyclophane units and five, six, and seven benzene rings, respectively. They are the longest cyclophane molecules with an all-*meta* connection of their benzene rings.[7]

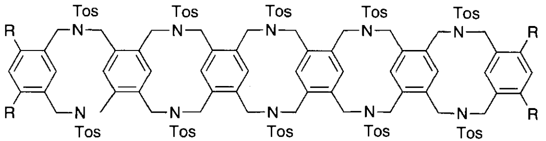
The new ribbon molecules **4a**–**6a** were characterized by MS and NMR spectroscopy.‡ The tetraesters **4a** and **5a** crystallize readily and the results of their single X-ray analyses§ are given schematically in Fig. 1. Compound **6a** is also shown, for which the X-ray analysis has not yet been successfully achieved. As shown, the molecules **4a** and **5a** form staples arranged in such a way that the benzene rings are in approximately parallel planes and the tosyl groups project outwards.



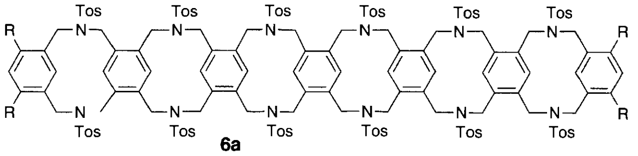
Scheme 2 *Reagents and conditions*: iter. I: i, $LiBH_4$–THF, 6 h, reflux; ii, PBr_3–$CHCl_3$, 48 h, reflux; iter. II: K_2CO_3–DMF, + **9** (2 equiv.), high dilution



4a–c **a** R = CO_2Et
b R = CH_2OH
c R = CH_2Br



5a–c



6a

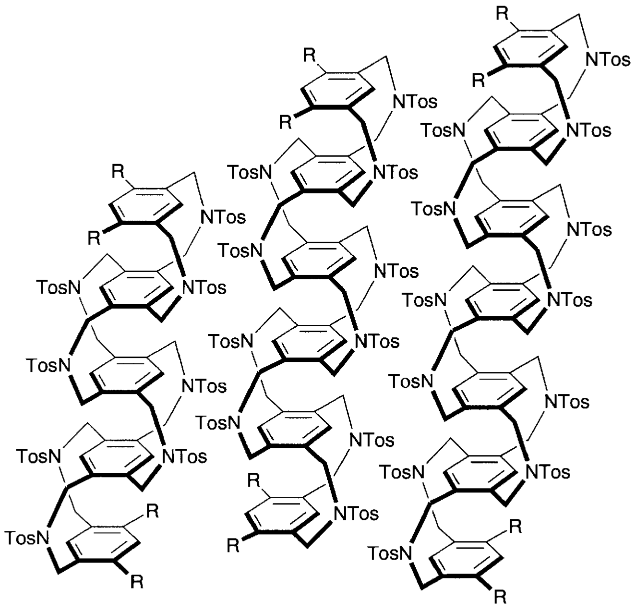
In the all-*syn* conformation the molecules **4a–6a** have lengths of approximately 1.3, 1.7 and 2.0 nm, respectively.¶ As the five- and six-layered molecular ribbons **4a** and **5a** form analogous staples, it can be expected that the seven-layered ribbon **6a** and the higher molecules of this type will also show similar staple structures. This means that a multiple *syn*-staple crystal structure can be predicted in this series.

The staple formation shown in Fig. 1 for **6a** can be concluded clearly from the ^1H NMR spectra: as for the shorter ribbons **1a–5a** (solvent $CDCl_3$), characteristic signals for the intraannular protons (inside the twelve-membered rings at δ 5.96, 5.99, 6.05, 6.22, 6.68 and 7.24, respectively) are observed, proving that all the benzene rings of these molecules adopt a *syn* arrangement in solution also. For the arrangement in approximately parallel planes, the favoured *syn* conformation of [3.3]metacyclophanes in general is probably responsible.[6]

A particular advantage of the strategy applied here is the similar solubility properties of the ribbon compounds **1a–6a**, independent of their lengths. This can be attributed to the increasing solubility effect of the *N*-tosyl groups and the four terminal ester groups. This behaviour is expected even for higher homologues of the ribbon molecules. We believe that this knowledge may also be applicable to iterative elongations of other structures (*e.g.* dendrimers) already in the design of the synthesis. We learned to appreciate this effect when we began working with the corresponding thiacycles[4] (*S* instead of *N*-Tos), the already low solubilities of which decreased even further. In addition, the poorer chemical stability of the sulfide bridges excluded further elongation of the ribbon system. The *N*-tosyl ribbon compounds **1a–6a** constitute a much more rewarding progress.

Orientational studies with shorter scale ditosylaza-[3.3]metacyclophanes have already shown that not only can the tosyl groups be removed but also the nitrogen atoms can be extruded to yield the [2.2]metacyclophane hydrocarbon skeleton.[8]

The new open ribbon structures **4a–6a** can now be used to synthesize macrocyclic tubes or belts containing five, six and seven benzene rings. Synthesis according to this method is variable: the breadth of the ribbon can be increased if the benzene rings are replaced by biphenyl units.[9] Further on, we try to obtain [3.3]metacyclophane systems in which the *N*-tosyl groups are replaced by methylene groups.[10]



4a **5a** **6a**

Fig. 1

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Footnotes

† *Iterative*: Starting with a shorter ribbon molecule (*e.g.* **4a**) one proceeds to an analogously substituted homologous structure containing two more benzene rings (*e.g.* **6a**) by the subsequent use of analogous series of reactions and reagents.

‡ All new compounds gave satisfactory spectroscopic or analytical results. Satisfactory elemental analysis have been obtained for the new compounds **4a**, **4c**, **5a**, **8**, **9**.

FAB-MS **4a**: *m/z* (%) 2262.6 (20) $[M + Na]^+$, 2240.7 (75) $[M + H]^+$, 2085.6 (100) $[M + H - Tos]^+$; **5a**: *m/z* (%) 2731.6 (26) $[M + Na]^+$, 2709.5 (74) $[M + H]^+$, 2553.6 (100) $[M + H - Tos]^+$; **6a**: *m/z* (%) 3199.3 (100) $[M + Na]^+$, 3176.6 (35) $[M + H]^+$, 3021.2 (30) $[M + H - Tos]^+$.

§ *Crystal data* for **4a**: $C_{114}H_{118}N_8O_{24}S_8\cdot 4C_2H_5OH$, M = 2425.0, triclinic, space group $P\bar{1}$ (no. 2), colourless crystals, dimensions 0.45 × 0.40 × 0.22 mm, a = 16.814(1), b = 17.198(1), c = 29.223(2) Å, α = 97.62(1), β = 98.78(1), γ = 117.09(1)°, U = 7236(1) Å^3, D_c = 1.11 Mg m^{-3}, Z = 2, μ(Cu-Kα) = 1.68 mm^{-1}, T = 293 K, $F(000)$ = 2564. 18163 Independent reflections were used for the structure solution (direct methods) and refinement (full-matrix least-squares methods on F^2, 1458 parameters), non-hydrogen atoms were refined anisotropically, H-atoms were refined using a riding model. The final R values are $wR2 = 0.432$ $\{R_1 = 0.115$ for 8815, $[I > 2\sigma(I)]\}$. A semiempirical absorption correction on the basis of ψ-scans and an extinction correction were applied.[11] Two of the four ethanol molecules are disordered. Atomic coordinates, bond lengths and angles, and thermal parameters for **4a** have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

For **5a** the structure could be solved but because of the shortage of observed data a reasonable refinement was not possible. Owing to the weak scattering of the crystal only 20% of the reflections were observed $[I > 2\sigma(I)]$ up to $2\theta_{max}$ = 90°.

¶ If the molecules **4a–6a** would accept a stretched hypothetical all-*anti* conformation their lengths would be approximately 2.2, 2.6, and 3.1 nm, respectively [the all-*anti* conformations were determined by force field calculations (MM2)]. These are energetically much less favourable than the all-*syn*-conformations.

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