

Oligobisvelcraplex: Self-Assembled Linear Oligomer by Solvophobic π – π Stacking Interaction of Bisvelcrands Based on Resorcin[4]arene

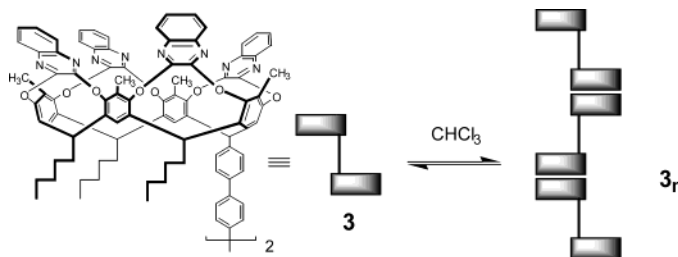
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ABSTRACT



Bisvelcrand **3** based on resorcin[4]arene was obtained by a stepwise route, and the formation of oligobisvelcraplex **3_n** by solvophobic π – π stacking interaction was observed. ¹H NMR spectroscopic studies revealed that $\Delta G^{\ddagger}_{\text{pseudorotation}}$ of oligobisvelcraplex **3_n** is 16.7 kcal mol^{–1} in C₆D₅NO₂ solution. The pulsed field gradient spin–echo (PGSE) NMR experiment and VPO experiment showed that the number of aggregation (*n*) ranges from 7 to 10 in CHCl₃ solution at 298 K. In high concentration, bisvelcrand **3** tends to form gels or fiber.

The self-assembly of low-molecular-weight building blocks into polymeric nanostructures has attracted considerable interests for application in nanotechnology.¹ Multiple interactions between self-organizing building blocks promote the

construction of well-defined supramolecular polymeric structures comparable to covalent polymers. These self-assembled systems are held together by reversible noncovalent forces such as hydrogen bonds,² metal–ion coordination,³ or solvophobic π – π stacking interactions. Among these, the

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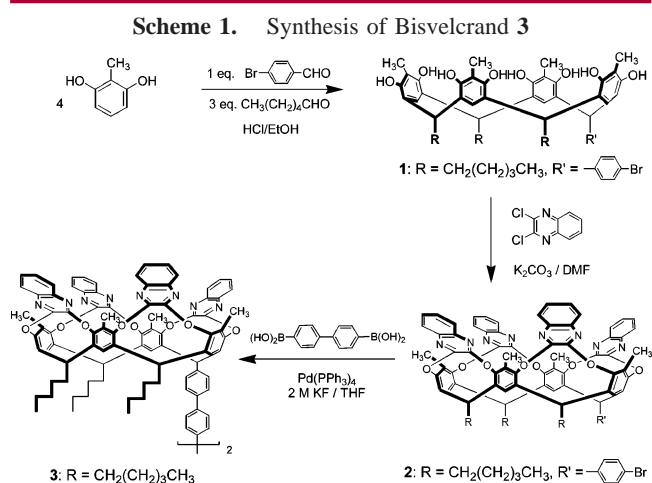
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nanostructural systems formed mainly by π - π stacking interaction are quite limited.⁴

Velcra self-dimerize to velcra by solvophobic π - π interactions of their large common surfaces in which the 2-methyl groups of a velcra insert into the aryl cavity of its partner.⁵ Recently Dalcanale et al. reported a dynamic polyvelcra by solvophobic π - π stacking interaction and metal coordination.⁶ When two velcra were covalently linked through their feet, an unprecedented polyvelcra only by π - π stacking interaction could be formed. Here we report on the synthesis of bisfunctional velcra **3** and its characteristics as an oligomeric self-assembly.

Hexadecols, which consists of two octols (resorcin[4]arene or methylresorcin[4]arene) connected through a biphenyl foot in a back-to-back fashion, were synthesized by heterogeneous condensation among resorcinol or 2-methylresorcinol, hexanal, and 4,4'-bisformylbiphenyl.⁷ However, when tetramethylhexadecol was condensed with 2,3-dichloroquinoxaline, the corresponding bisvelcra could not be isolated. Therefore, a stepwise route for bisvelcra **3** was developed as shown in Scheme 1. Heterocondensation among 2-methyl resorcinol



and a 3:1 molar ratio of hexanal and 4-bromobenzaldehyde in a solution of EtOH and HCl at 60 °C gave octol **1** in 35% yield. Octol **1** was reacted with 2,3-dichloroquinoxaline in a mixture of K_2CO_3 and DMF at room temperature to afford a velcra **2** in 40% yield. Under the Pd(0)-catalyzed Suzuki coupling reaction between velcra **2** and 4,4'-biphenyldiboric acid in a mixture of THF and an aqueous KF solution (2 M),⁸ bisvelcra **3** was obtained in 45% yield. Velcra **2** and **3** were characterized by ^1H NMR and MALDI-TOF MS spectra and elementary analyses.

A high degree of association between the repeating units is a prerequisite for forming a high degree of self-assembly.

(3) Self-assembled polymeric structures using metal-coordination: (a) Biradha, K.; Fujita, M. *Angew. Chem., Int. Ed.* **2002**, *41*, 3392. (b) Noveron, J. C.; Lah, M. S.; Del Sesto, R. E.; Arif, A. M.; Miller, J. S.; Stang, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 6613. (c) Michelsen, U.; Hunter, C. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 764. (d) Velten, U.; Lahn, B.; Rehahn, M. *Macromol. Chem. Phys.* **2003**, *198*, 2789. (e) Andress, P. R.; Schubert, U. S. *Adv. Mater.* **2004**, *16*, 1043.

The stability of oligovelcra by **3** could be assumed from that of velcra **2**, which has the same aromatic surface as that of bisvelcra **3**. Since the exchange rate between monomeric and dimeric species of velcra **2** is slow on the NMR time scale, the association constant (K_a) of velcra **2** was determined to be $4.9 \times 10^4 \text{ M}^{-1}$ in CDCl_3 at 298 K by the single-point method,⁵ which gave free energy ($-\Delta G^\circ$) of 6.4 kcal/mol (Table 1). As the polarity of the solvent

Table 1. Association Constants (K_a) and Free Energies ($-\Delta G^\circ$) for Dimerization^a of the Velcra **2** in Various Solvents at 25 °C

solvent	$K_a [\text{M}^{-1}]/10^4$	$-\Delta G^\circ [\text{kcal mol}^{-1}]$
CDCl_3	4.9	6.4
5% CD_3OD^b	9.5	6.8
10% CD_3OD^b	176.0	8.5
20% CD_3OD^b	dimer	dimer

^a See ref 5. The initial concentration was 10 mM. ^b In CDCl_3 solution.

increases, the dimerization constants of **2** increase due to the enhanced solvophobic driving forces. In over 20% CD_3OD in CDCl_3 , velcra **2** existed exclusively as velcra. The MALDI-TOF spectrum of velcra **2** showed a velcra peak of 5% intensity.

The X-ray crystal structure of velcra **2** shows its velcra structure as shown in Figure 1.⁹ Even though the feet are disordered, the π - π stacking of aromatic surfaces are intact to those of velcra.⁵

The ^1H NMR spectrum of bisvelcra **3** in CDCl_3 (3.54 mM) at 298 K showed two kinds of methyl peaks (δ 3.17 for out, δ 2.33 for up) and three kinds of methine peaks (δ 3.47, 3.57, 5.14). As this solution is diluted from 3.54 to 0.10 mM, the methyl peaks for monomeric species started to appear at 2.67 (for out methyls) and 2.53 (for up methyls)

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(9) Crystal structure of **2**: $\text{C}_{89}\text{H}_{81}\text{BrN}_8\text{O}_9$, $M = 1486.53$, colorless crystal $0.80 \times 0.50 \times 0.45 \text{ mm}$, monoclinic $\text{C}2/c$, $a = 36.820(3)$, $b = 29.693(3)$, $c = 38.200(3) \text{ Å}$; $\alpha = 90^\circ$, $\beta = 113.646(2)^\circ$, $\gamma = 90^\circ$; $V = 38257(6) \text{ Å}^3$, $Z = 16$, $\rho_{\text{calcd}} = 1.032 \text{ mg/m}^3$ (including solvent), $\mu(\text{Mo K}\alpha, \lambda = 0.71073 \text{ Å}) = 0.482 \text{ mm}^{-1}$, $2\theta_{\text{max}} = 56.64^\circ$; 120 558 measured reflections, 45 568 unique of which 10 057 were observables [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least squares calculations with SHELXTL. The final $R_1 = 0.2233$, $wR_2 = 0.5004$ for 10 057 reflections of $I > 2\sigma(I)$; measurements: Brukers SMART CCD equipped with a graphite crystal incident-beam monochromator.

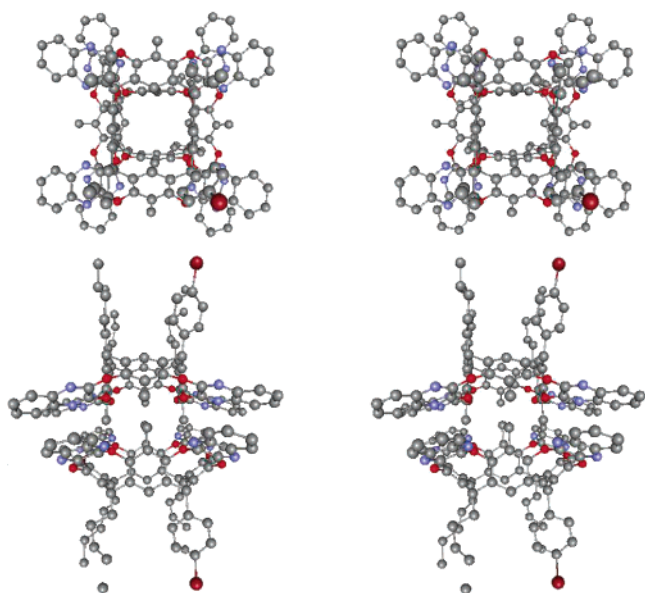


Figure 1. Stereoviews of X-ray crystal structure of velcralex **2**: top-view (upper) and side-view (lower). The feet are disordered. Hydrogens and solvents are omitted for clarity.

ppm. These chemical shifts at high concentration (0.5 ppm downfield shift for out methyl, 0.2 ppm upfield shift for up methyls) prove the oligovelcralex formation of **3** in solution.

The energy barrier for pseudorotation between the so-called kite conformers of oligobisvelcralex **3_n** was observed by ¹H NMR VT experiment.¹⁰ As the temperature was increased from 25 to 100 °C, the chemical shifts of methyls of oligovelcralex **3_n** in C₆D₅NO₂ were observed as shown in Figure 2. As the temperature increases, the two kinds of

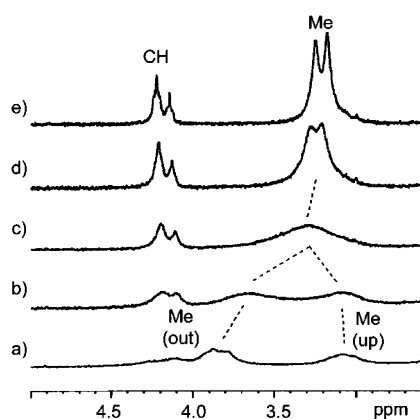


Figure 2. Partial variable-temperature ¹H NMR spectra (400 MHz) of bisvelcralex **3** in C₆D₅NO₂ (3.5 mM) at (a) 25, (b) 60, (c) 75, (d) 90, and (e) 100 °C.

methyl proton peaks (centered at 3.08, 3.88 ppm) broadened and coalesced as a doublet at about 90 °C to provide ΔG^\ddagger of 16.7 kcal mol⁻¹. When velcralex **2** was studied in the same

conditions, ΔG^\ddagger of 15.7 kcal mol⁻¹ was observed. The higher ΔG^\ddagger of oligovelcralex **3** in solution than velcralex **2** also supports that bisvelcralex **3** exists as oligobisvelcralex **3_n** in solution, imposing a larger hindrance to fast equilibrium between kite structures on the ¹H NMR time scale.

The pulsed-field gradient spin-echo (PGSE) NMR technique¹¹ was used to measure the diffusion coefficients of CDCl₃ solution of **2** or **3** at 298 K. As the solution of **2** is concentrated from 0.2 to 4 mM, the diffusion coefficient of **2** decreases from $5.7 \pm 0.2 \times 10^{-10}$ to $4.9 \pm 0.2 \times 10^{-10}$ m² s⁻¹, respectively, which means that the overall average size of **2** increases, supporting the dimerization of **2**. In the case of bisvelcralex **3**, the measured diffusion coefficient shows a noticeable change at concentrations from 0.1 to 0.3 mM as shown in Figure 3. The concentration dependence

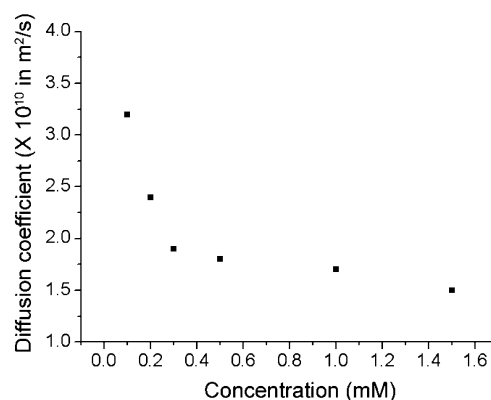


Figure 3. Concentration dependence of diffusion coefficient of polyvelcralex **3** in CDCl₃ at 298 K.

of the diffusion coefficients indicates that bisvelcralex **3** oligomerizes as its concentration increases. And then, from the concentration of 0.4 mM, the diffusion coefficient decreases slightly. The overall volume estimated from the diffusion coefficient at 1.5 mM is approximately 10 times larger than that obtained at 0.1 mM. Such an oligomerization of bisvelcralex **3** was disrupted by adding velcralex **2**. The diffusion coefficient of **3** at 2.0 mM CDCl₃ increased remarkably from $1.4 \pm 0.1 \times 10^{-10}$ m² s⁻¹ to $3.4 \pm 0.1 \times 10^{-10}$ m² s⁻¹ upon addition of 2 equiv of **2**.

The size of oligobisvelcralex **3_n** in CHCl₃ at 40 °C was also observed by vapor pressure osmometry (VPO).¹² As the stoichiometric concentration of **3** increases from 7 to 20 g/kg (solute/solvent), the mean molecular weight was gradually increased from 5600 to 20 000 Da (2821 Da for **3**) and saturated at 20 000 Da. This implies that bisvelcralex **3** exists as averaged heptameric oligovelcralex **3_n** ($n = 7$) in CHCl₃ at 40 °C.

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When bisvelcrand **3** was dissolved in chloroform or THF under the high concentration, the solution became turbid, showing polymerlike viscoelastic behavior. Since the presence of elongated stacks is a possibility in formation of macroscopic organogels, the minimal gel concentration (wt %) of **3** was determined to be 11 wt % in chloroform and 13 wt % in THF. Although the bisvelcrand **3** generally needs a higher minimal concentration than the typical organogels (<5 wt %), macroscopic gelation seems to be due to the fiber-forming property of bisvelcrand **3** in concentrated solution.

When the more concentrated polybisvelcraplex **3_n** was viewed between crossed polarizers with an optical microscope, it was birefringent and produced the polymeric optical textures. The ability to pull fibrous structures from the polymer is similar to the characteristic of other hydrogen-bonded polymers.² This indicates a high degree of the linear chain extension of polybisvelcraplex **3_n**.

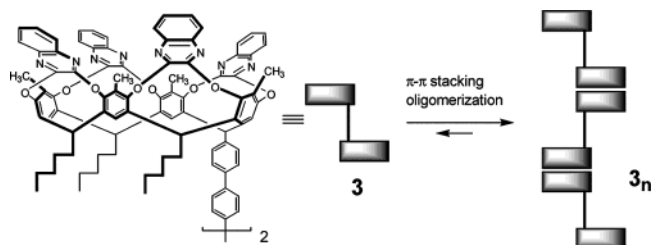
Scanning electron microscopy was used to study the microscopic structure of polybisvelcraplex **3_n**. The electron micrographs of the sample formed by bisvelcrand **3** in CHCl₃ revealed nicely aligned linear strands in a concentration range of 0.03–0.4 mM (Figure 4a).

The diameter of the strands is about 60 nm. Each strand is composed of densely packed small dots whose diameter

corresponds to that of the strands. Under the lower concentration (<0.01 mM), numerous dots were observed. Formation of the polymeric structure depends on the concentration of solute as well as the polarity of solvents.^{1a} In THF, its structure appeared to be different from that in chloroform. Although the structure is not aligned linearly, it shows interesting figures in which long and linear bundles with the diameter of about 110–120 nm are twisted as shown in Figure 4b.

In conclusion, bisvelcrand **3** was obtained by a stepwise route and the unprecedented oligobisvelcraplex **3_n** was observed. Oligobisvelcraplex **3_n** in solution was formed only by solvophobic π – π stacking interaction. In high concentration, bisvelcrand **3** showed a high tendency to form gels or fiber. In solid, the morphology of polybisvelcraplex **3_n** was affected by the solubility and polarity of solvent.

Scheme 2. Illustration of Oligovelcraplex **3_n** Formation of Bisvelcrand **3**



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Supporting Information Available: Experimental procedure of **2**, **3**, and PGSE NMR and crystallographic data (CIF format) of **2**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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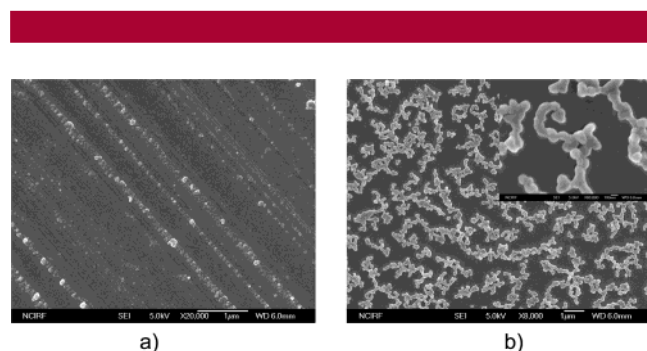


Figure 4. Scanning electron microscopy images of aggregate of polybisvelcraplex **3**; (a) 0.14 mM in chloroform (scale bar = 1 μ m); (b) 0.11 mM in THF, scale bar = 1 μ m (scale bar = 100 nm) (inset: magnified image).