Bisvelcrands by Metal Coordination : Monomers for Oligovelcraplexes

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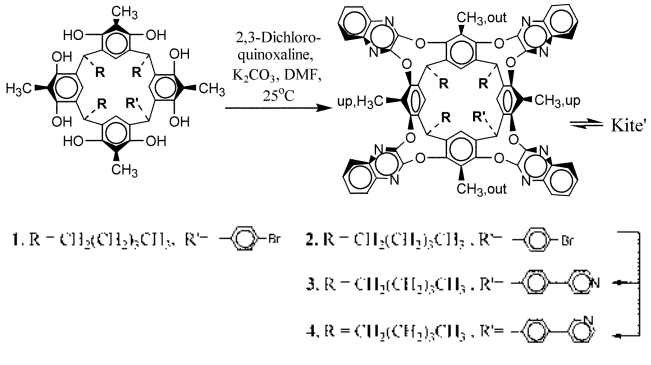
Noble supramolecules that self-assemble by non-covalent interactions, such as hydrogen bonding,[1] metal-ligand,[2] and π-π stacking interactions,[3] have been reported. The efficiency and accuracy of molecular self-assembly to various remarkable suprastructures in biosystems have encouraged many molecular architects to develop *in vitro* self-assembling systems. Cram *et al.* reported solvophobic and entropy-driven self-assembled dimeric systems for which the terms velcrand and velcraplex were coined.[4] Dalcanale *et al.* reported a highly adaptive, dynamic velcrand operating in a multimodal fashion, namely solvophobic π-π stacking interaction of 2-methylresorcin[4]arene-based quinoxaline kite velcrands and metal coordination of pyridyl feet.[5] When two 2-methylresorcin[4]arene-based quinoxaline kite velcrands were bridged in back-to-back fashion by a covalent bond to give a bisvelcrand, the latter then self-assembled to oligovelcraplexes only by solvophobic π-π stacking interactions.[6]

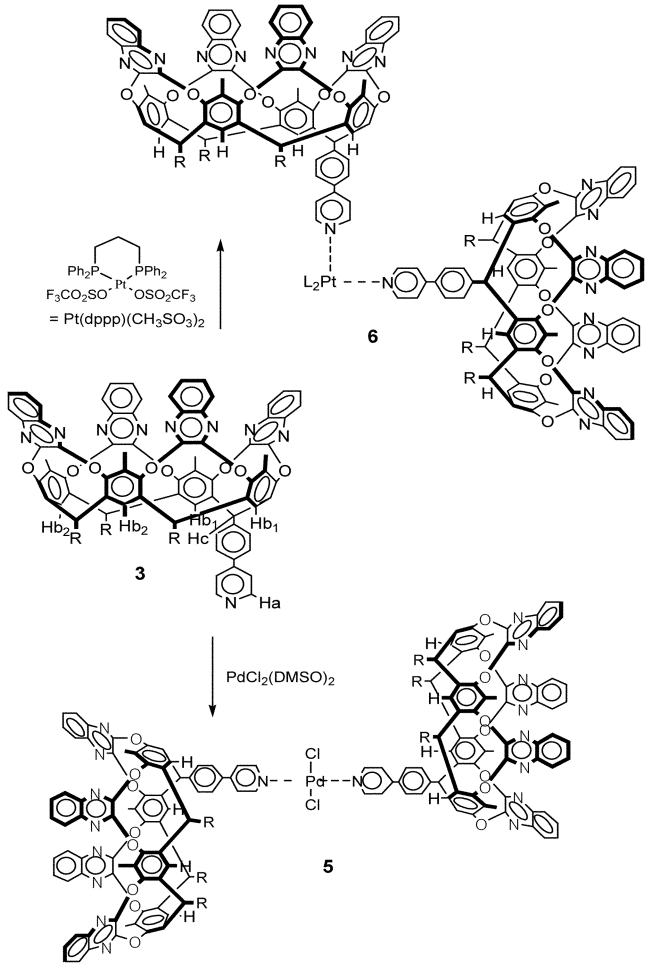
New velcrands **3** and **4** composed of a 2-methylresorcin[4]arene-based quinoxaline kite velcrand unit and a *p*-pyridylphenyl foot, which are quite soluble in non-polar solvents, were synthesized and characterized.[7]

Suzuki coupling reaction between velcrand **2**, which has a *p*-bromophenyl foot, and 4-, or 3-pyridyl boronic acid in a mixture of 2 M KF, EtOH and THF by reflux under argon for 5 days (Scheme 1) gave velcrands **3** and **4** in 32% and 52% yield, respectively. The key intermediate **2** was synthesized in an overall 9% yield by a heterocoupling reaction among 2-methylresorcinol, hexanal, and *p*-bromobenzaldehyde to give octol **1**, followed by bridging of two adjacent hydroxy groups by a quinoxaline unit.[6] Velcrands **3** and **4** were fully characterized by ^{1}H NMR, MALDI-TOF-MS and elemental analyses.

Metal coordinations of velcrand **3** with $Pd(DMSO)_2Cl_2$ and $Pt(dppp)(OTf)_2$ to give bisvelcrands **5** and **6** (Scheme 2),



Scheme 1



Scheme 2

respectively, were followed by ^{1}H NMR spectroscopy in $CDCl_3$ at 25 °C (Fig. 1). Velcrand **3** exists as kite conformers in solution, which is shown by the two sets of Hc peaks in Figure 1 a). When 0.25 eq of metal complex was added, the ^{1}H NMR peaks of H_a, H_b, and H_c (designated in Scheme 2) tend to split into two sets of peaks in a 1 : 1 ratio, indicating the 1 : 1 coexistence of velcrand **3** and bisvelcrand **5** or **6** (partial ^{1}H NMR spectra b and c). However, when 0.50 eq of metal complex was added, only peaks for metal-coordinated bisvelcrand **5** or **6** were apparent (partial spectra d and e).

Table 1 shows the concentration dependence of velcraplex formation for velcrand **3** and bisvelcrand **5** in $CDCl_3$ at 298 K. Only velcraplex or oligobisvelcraplex were observed at or above 0.60 mM for both velcrands, which means the

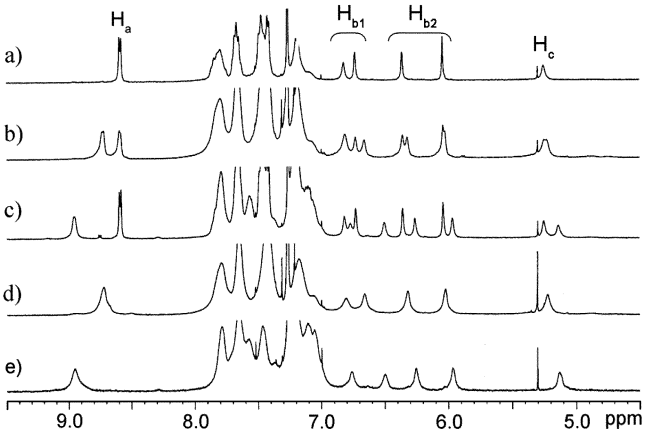


Figure 1. Partial ^{1}H NMR (400 MHz, $CDCl_3$, [**3**] = 2.8 mM). (a) **3** alone; (b) [**3**]/[$Pd(DMSO)_2Cl_2$] = 1 : 0.25; (c) [**3**]/[$Pt(dppp)OTf_2$] = 1 : 0.25; (d) [**3**]/[$Pd(DMSO)_2Cl_2$] 1 : 0.5; and (e) [**3**]/[$Pt(dppp)OTf_2$] = 1 : 0.5.

Table 1. Concentration dependence of the association of velcrands

Concentration ($CDCl_3$, 298 K)	Monomer/Velcraplex	
	Velcrand **3**	Bisvelcrand **5**
0.60 mM	**3**·**3**^{a} only	$\mathbf{5}_n$^{a} only
0.30 mM	1.0 : 3.2	1.0 : 6.0
0.15 mM	1.0 : 2.4	1.0 : 5.2

^{a}The ratios of **3**·**3** or $\mathbf{5}_n$ are the mole ratios of monomers associated.

spectrum in Figure 1 a) and d) or e) are those of velcraplex and oligobisvelcraplex, respectively. At 0.30 mM, the monomer/velcraplex ratio was 1.0 : 3.2 and 1.0 : 6.0 for velcrand **3** and bisvelcrand **5**, respectively. At 0.15 mM, the corresponding ratios were 1.0 : 2.4 and 1.0 : 5.2 for velcrand **3** and bisvelcrand **5**, respectively. These results imply that the monomer percentage of velcrand **3** and bisvelcrand **5** at 0.15 mM is 29% and 16%, respectively, which suggests that bisvelcrand **5** self-assembles better than velcrand **3**.

Further evidence for the formation of oligobisvelcraplex $\mathbf{6}_n$ by metal coordination was obtained by electrospray ionization mass spectrometry (ESI-MS), wherein the specific molecular ion peaks of tetrameric oligobisvelcraplex $\mathbf{6}_4$ were observed at *m/z* 1716.1 [(**3**-Pd(dppp)OTf_2-**3**)$_4$-8OTf]$^{8+}$ (100 %, calcd. 1716.4), 2338.1 [(**3**-Pd(dppp)OTf_2-**3**)$_4$-6OTf]$^{6+}$ (20%, calcd. 2338.2), and 2835.8 [(**3**-Pd(dppp)OTf_2-**3**)$_4$-5OTf]$^{5+}$ (10%, calcd. 2835.8).

In conclusion, new velcrands **3** and **4** were synthesized and the formation of their metal-coordinated dimer as well as self-assembled oligobisvelcraplexes were studied using the following techniques: comparison of ^{1}H NMR peak shifts; investigation of the concentration dependence of velcraplex formation; and ESI MS. The structures and the degrees of oligomerization of oligovelcraplexes are being studied.

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7. ***para*-Pyridyl Velcrand 3**: To pyridine-4-bronic acid (104.28 mg, 0.85 mmol) and $Pd(PPh_3)_4$ (58 mg, 0.05 mmol) under an argon atmosphere were added argon-saturated THF (50 mL), argon-saturated EtOH (10 mL), and argon-saturated aqueous 2 M KF (30 mL), and velcrand 2 (200 mg, 0.14 mmol). The mixture was stirred at refluxing temperature for 2 days. After cooling to room temperature and evaporation of solvents, the residue was dissolved with CH_2Cl_2. The organic layer was washed with H_2O, and dried over $MgSO_4$. After concentration, the residue was purified by silica gel column chromatography eluted with Hexane : EtOAc (1 : 1) and the concentrate of the best portions was poured into EtOH to give pure 3 as a white solid (64 mg, 32%) : m.p.: > 320 °C (dec.); MALDI-TOF MS ($CHCl_3$): *m/z* 1412.43 (100%) $[M]^+$, 2824.96 (5%) $[3\text{·}3]^+$; Eemental analysis: calcd for $C_{90}H_{72}N_8O_8$·$2H_2O$: C, 74.62; H, 5.64; N, 8.70. found: C, 74.69; H, 5.43; N, 8.36.; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 8.59 (d, 2H, *J* = 4.0 Hz, pyridyl Ha), 7.80 (br-m, 4H, quinoxaline ArH), 7.67 (t, 4H, *J* = 4.0 Hz, quinoxaline ArH), 7.48-7.41 (m, 10H, quinoxaline Ar4H + py-Ar4H, py2H), 7.19 (broad-m, 4H, quinoxaline ArH), 6.82 (s, 1H, ArHc), 6.73 (s, 1H, ArHc), 6.36 (s, 1H, ArHc), 6.04 (s, 1H, ArHc), 5.25 (s, 1H, Hm), 3.61-3.49 (br-m, 3H, methine), 3.19 (br-m, 6H, $ArCH_3$), 2.3 (br-m, 6H, $ArCH_3$), 1.81-1.65 (m, 6H, CH_2), 1.26-0.59 (m, 27H, $(CH_2)_3CH_3$).
***meta*-Pyridyl Velcrand 4**: The same synthetic procedure of *para*-pyridyl velcrands **3** was used, except that pyridine-3-bronic acid was used instead of pyridine-4-bronic acid. After column chromatography, the concentrate of the best portions was poured into EtOH to give pure **4** as a white solid (104 mg, 52%) : m.p.: > 320 °C (dec.); MALDI-TOF MS ($CHCl_3$): *m/z* 1412.43 (75%) $[M]^+$, 2825.64 (5%) $[4\text{·}4]^+$; Elemental analysis: calcd for $C_{90}H_{72}N_8O_8$·$2H_2O$: C, 75.56; H, 5.57; N, 8.81. found: C, 75.54; H, 5.36; N, 8.60; ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ= 8.78 (s, 1H, a to N atom of pyridyl), 8.53 (d, 1H, *J* = 4.0 Hz, a to N atom of pyridyl), 7.85-7.78 (m, 5H, quinoxaline ArH + pyridine H), 7.68-7.65 (m, 5H, quinoxaline ArH + pyridine H), 7.45-7.18 (m, 12H, quinoxaline ArH + feet ArH), 6.83, 6.76, 6.38, 6.06 (s, 4H, ArH), 5.27 (s, 1H, Hm), 3.82-3.50 (m, 3H, methine), 3.21 (m, 6H, $ArCH_3$), 2.34 (m, 6H, $ArCH_3$), 2.12-1.58 (m, 6H, CH_2), 1.10-0.57 (m, 27H, $(CH_2)_3CH_3$).