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Hexafunctionalized Borromeates Using Olefin Cross Metathesis

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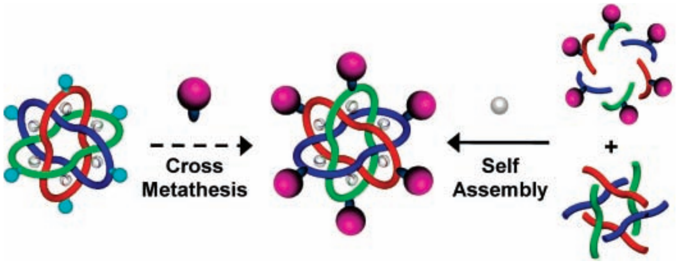
ABSTRACT



Employing well-established template-directed protocols, which depend upon dynamic covalent, coordinative, and noncovalent chemistry for their efficient outputs, we have synthesized, in a convergent manner, Borromeates composed of three identical macrocycles which present, diagonally in pairs, six *exo*-bidentate bipyridyl ligands and six *endo*-diiminopyridyl ligands, each carrying either pentenyloxy or *p*-tolylpentenyloxy substituents on their 4-positions, to six zinc(II) ions.

The molecular construction of the Borromean Ring (BR) topology[1] has been achieved[2] successfully from 18 individual components under dynamic control that characterizes not only the noncovalent but also the coordinative[3] and covalent bonds formed in the molecules. This dynamic covalent chemistry[4] (DCC) assembly process is dependent on the ability of the system to control the placement of 12 organic ligands around six transition metal (zinc) ions in near quantitative yields.

This molecular BR topology[5] provides a unique symmetrical, nanoscale, three-dimensional scaffold onto which particular structural features can be embedded at will. Two orthogonal approaches have been investigated, namely, *pre-assembly modification*, which involves[6] the incorporation of the desired functionality on the incipient tridentate ligand, followed by subsequent assembly of the rings via metal template-directed synthesis,[7] and *post-assembly modification*, which first of all involves the synthesis of Borromeates with pendant reactive groups attached to the incipient tridentate ligand prior to assembly, then modification of the periphery via the introduction of a new functional group. The functional groups that are compatible with pre-assembly modification of the Borromeate core are more or less limited to groups

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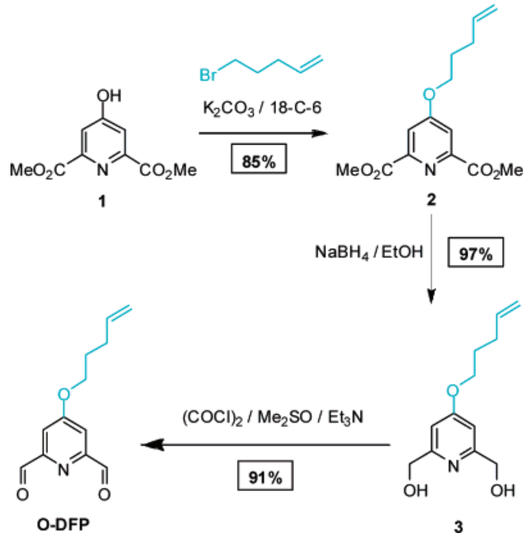
(e.g., olefinic) that do not alter significantly the solubility or interfere with the reactivity of the components.[6] Herein, we show (1) that both pentenyloxy and *p*-tolylpentenyloxy groups can be incorporated into the convergent synthesis of a Borromeate core, and (2) that modification of a hexaolefinic Borromeate using olefin cross metathesis[8] (OXM) as a means of introducing divergently six pendant groups onto the outside of the Borromeate core is inefficient when compared to Borromeates formed in a convergent manner.

Olefin metathesis has been developed into a powerful synthetic tool for carbon−carbon bond-forming transformations, important in the fields of synthetic chemistry spanning from natural products[9] to commercial polymeric materials.[10] Since the discovery of functional group tolerant and highly active catalysts by Grubbs,[11] the design of new systems has focused on optimizing products for specific applications.[12] Given the wide applicability and reasonable selectivity of ruthenium-catalyzed olefin metathesis, we envisage that it can be used to attach virtually any olefinic substrate to a pre-assembled olefin-functionalized Borromeate core. In this manner, we can functionalize the 2,6-diformylpyridine (**DFP**) building block with a terminal olefin at its 4-position (**O-DFP**) without affecting the solubility or reactivity of the initially employed[2] unsubstituted **DFP** precursor. Since the olefinic functionality is completely inert during the self-assembly process, it does not interfere with the DCC.[3]

Scheme 1. Synthesis of the **O-DFP** Building Block



The synthesis of the **O-DFP** building block was achieved as outlined in Scheme 1, starting with the alkylation of dimethylchelidamate (**1**) with 5-bromo-1-pentene to afford **2** in 85% yield. Subsequent reduction of **2** with sodium borohydride yielded (97%) the corresponding diol **3**, which was conveniently oxidized to the **O-DFP** building block in 91% yield, employing Swern conditions.[13] See Supporting Information.

The hexaolefinic Borromeate **BRO₆**•12TFA (TFA = trifluoroacetate) was assembled utilizing the diaminobipyridine (**DAB**) component, along with **O-DFP** building block employing the self-assembly conditions developed previously.[2] The reaction was followed (Figure 1) by ^{1}H NMR spectroscopy.

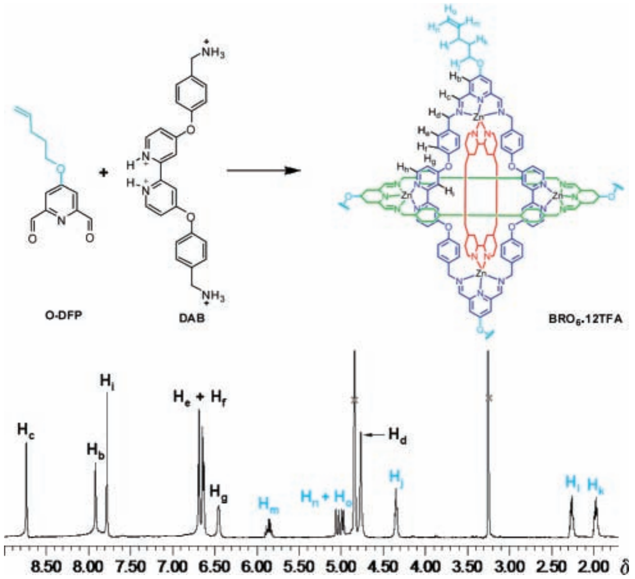


Figure 1. Partial ^{1}H NMR spectrum (600 MHz) recorded in CD_3OD of **BRO₆**•12TFA.

The target **BRO₆**•12TFA was obtained in 85% yield and was fully characterized by ^{1}H NMR spectroscopy and mass spectrometry. The ^{1}H NMR spectra (600 MHz, CD_3OD) reveal the appearance of a new resonance at $\delta = 8.8$ ppm for the imine protons that corresponds to the formation of 12 imine bonds. All of the resonances observed were in agreement with those reported[2,6,14] previously for other Borromeates. High-resolution electrospray ionization mass spectrometry (HR-ESI MS) revealed peaks at *m*/*z* 1632.9560

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for [**BRO$_6$**•12TFA$-$3TFA]$^{3+}$, 1196.7330 for [**BRO$_6$**•12TFA$-$4TFA]$^{4+}$, and 934.6344 for [**BRO$_6$**•12TFA$-$5TFA]$^{5+}$.

Single colorless crystals[15] of **BRO$_6$**•12TFA, suitable for X-ray crystallography,[16] were obtained by vapor diffusion of Et_2O into a methanolic solution of the compound. The solid-state structure revealed (Figure 2a) that all three macrocycles of the hexaolefinic Borromeate adopt chairlike conformations, as in the structure of the parent Borromeates.[2] In the case of the hexaolefinic Borromeate, we expected the rings to adopt S_6 symmetry. However, even though the same chairlike conformations are evident and the rings are pseudo-S_6 with respect to the core, the overall symmetry is reduced to C_i as a consequence of the relative orientations of the olefinic tails. Similar observations have been made[17] in the case of some chiral Borromeates, where the symmetry is also reduced to being C_1. The olefinic tails on two of the macrocycles are pointing in the same direction, whereas, on the third macrocycle, the olefinic tails are pointing in the opposite direction, indicating that there is a center of inversion in the structure (Figure 2a and b). Moreover, beyond the molecule, the packing diagrams (Figure 2c and d) show that these olefinic tails orientate themselves so that they occupy alternating hydrophobic solvent channels throughout the crystal lattice.

For comparative purposes (pre- versus post-assembly), the hexa-*p*-tolylpentenyloxy Borromeate **BRS$_6$**•12TFA was assembled utilizing the **DAB** component, along with **S-DFP** (see Supporting Information) as a building block employing the identical self-assembly conditions used for **BRO$_6$**•12TFA. For each of the precursors (**4**, **5**, and **S-DFP**, see Supporting Information), the *E*-isomer was the major product isolated, resulting from the OXM of 4-methylstyrene with 5-bromo-1-pentene[18] to afford 1-((*E*)-5-bromopent-1-enyl)-4-methylbenzene (**4**), which was in agreement with extensive studies undertaken by Grubbs and co-workers.[18] The target **BRS$_6$**•12TFA (Figure 3) was obtained in 83% yield and was characterized fully by ^1H NMR spectroscopy and mass spectrometry. The ^1H NMR spectra (600 MHz, CD_3OD) revealed the appearance of new resonances at (1) $\delta = 8.7$ ppm for the imine protons and corresponds to the formation of 12 imine bonds, (2) $\delta = 7.18$ and 7.02 ppm for the *p*-tolylpentenyloxy protons and $\delta = 2.19$ ppm for the protons of the aromatic methyl group. The fact that two signals are observed for H_n $\delta = 6.24$ ($J = 14$ Hz) and 5.45 ppm tells us that the *p*-tolylpentenyloxy substituents adopt both *E* and *Z* configurations. HR-ESI MS revealed peaks at *m*/*z* 1813.6404 for [**BRS$_6$**•12TFA$-$3TFA]$^{3+}$ and 1331.9202 for [**BRS$_6$**•12TFA$-$4TFA]$^{4+}$.

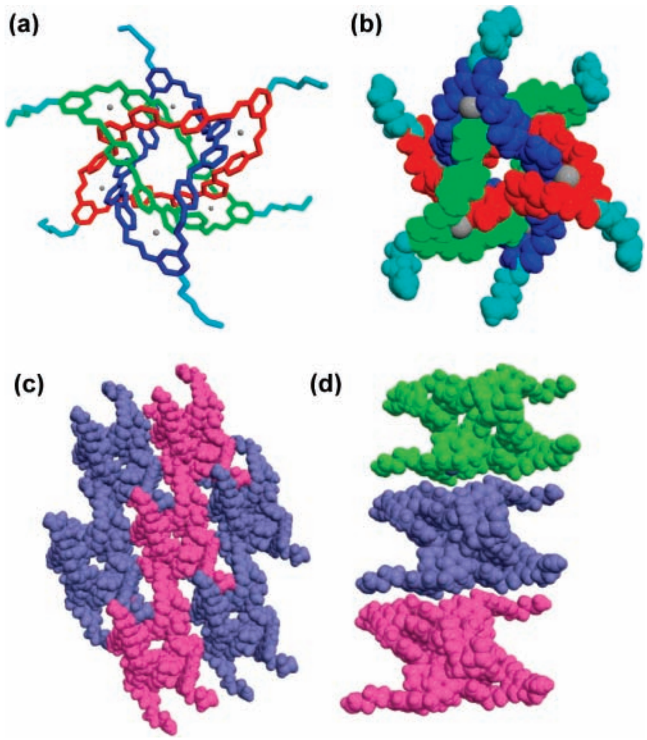

Figure 2. Different structural and superstructural representations of the **BRO$_6$**$^{12+}$ dodecacation(s) in the solid state, as deduced from X-ray crystallography carried out on a single crystal of **BRO$_6$**•12TFA; (a) tubular representation viewed down the S_6 axis, revealing the low symmetry (C_i) resulting from the opposite orientations in two of the terminal olefin tails; (b) space-filling representation of a, showing the cavity with a diameter of 2.08 Å; (c) space-filling representation of the packing of **BRO$_6$**$^{12+}$ dodecacations viewed down the *a*-axis, revealing alternating hydrophobic solvent channels occupied by the olefinic tails; and (d) stack of three **BRO$_6$**$^{12+}$ dodecacations present in superstructural columns that run through the crystal lattice in the *a* direction. The distance within the columns between the centers of repeating **BRO$_6$**$^{12+}$ dodecacations is 18.7 Å.

The hexaolefinic Borromeates were modified in a post-assembly fashion with styrenic substrates employing ruthenium-based catalysts[19] in an attempt to afford exclusively hexasubstituted Borromeates. See Supporting Information. **BRO$_6$**•12TFA was subjected to OXM with 4-methylstyrene in CH_2Cl_2 in the presence of the Grubbs second-generation catalyst[20] employing[18] a large excess (10 equiv per olefin) of the styrenic substrate. HR-ESI MS (Figure 4) was employed to determine the efficacy of the OXM reactions. Reactions of this type would be expected to yield a statistical

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(15) Empirical formula $[(C_{72}H_{62}N_{10}\underline{O}_6)_3(ZnCF_3CO_2)_6]$ $2[Zn(CF_3CO_2)_4]$, $M = 5580.68$, triclinic, space group $P1$; $a = 18.668(7)$, $b = 20.237(8)$, $c = 20.728(8)$ Å; $\alpha = 84.727(6)$, $\beta = 75.374(6)$, $\gamma = 74.548(5)°$, $V = 7301(5)$ Å^3, $Z = 1$, $\rho_c = 1.357$ g cm^{-3}, μ(Mo Kα) $= 0.750$ mm^{-1}, $F(000) = 3034$, $T = 100$ K; colorless platelets, 0.20 × 0.10 × 0.10 mm^3, 69 506 independent observed reflections, F^2 using SHELXTL software package, 1724 parameters, $R1/wR2$ $[I > 2\sigma(I)] = 0.116/0.2943$. A single colorless crystal was attached with oil to a thin glass fiber. Solvent loss was immediately evident as soon as the crystal was removed from the mother liquor, which caused some disorder in embedded solvents. One of the long olefinic chains and a free TFA anion were also disordered, and their geometries were constrained. Beside the disordered atoms and solvent molecules, the rest of the structure was refined anisotropically.

(16) Crystals were analyzed with a Bruker Smart 1000 CCD-based diffractometer. Narrow-frame integration used the Bruker SAINT program system. Crystallographic data (excluding structure factors) for the structure of the hexaolefinic Borromeate reported in this communication have been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication no. CCDC-638763. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EK, U.K. (fax (+44)1223−336-033; e-mail deposit@ccdc.cam.ac.uk).

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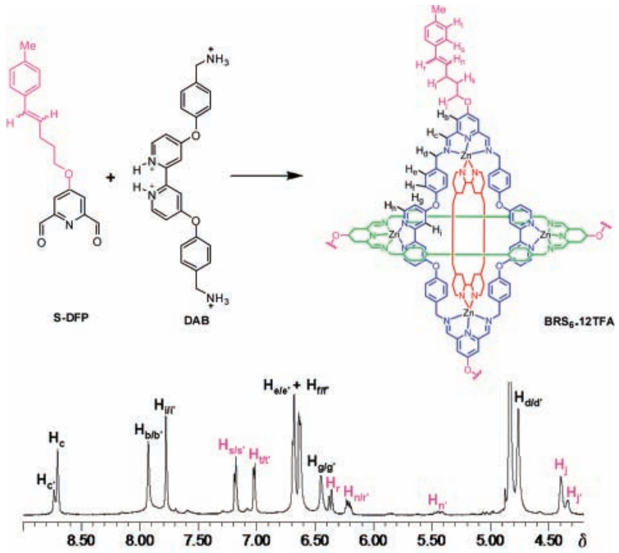

Figure 3. Partial ^{1}H NMR spectra (600 MHz) recorded in CD_3OD of a mixture of isomers of **BRS_6**•12TFA where some of the *p*-tolylpentenyloxy substituents adopt an *E* configuration and others a *Z* configuration. Primed letters relate to this stereoheterogenicity.

distribution[21] of cross-metathesis products. The HR-ESI MS revealed key peaks at *m*/*z* 1022.4319 for [**BRO_1S_5**•12TFA−5TFA]$^{5+}$, 950.3944 for [**BRO_5S_1**•12TFA−5TFA]$^{5+}$, 833.1957 for [**BRO_1S_5**•12TFA−6TFA]$^{6+}$, 788.1723 for [**BRO_4S_2**•12TFA−6TFA]$^{6+}$, and 646.5716 for [**BRO_5S_1**•12TFA−7TFA]$^{7+}$.

From an analysis of HR-ESI MS data obtained, it is evident that the dominant product of the OXM reactions is one that results from five cross metatheses and that there appeared to be no evident peaks that corresponded to unreacted **BRO_6**•12TFA or complete OXM functionalization to afford **BRS_6**•12TFA.[22]

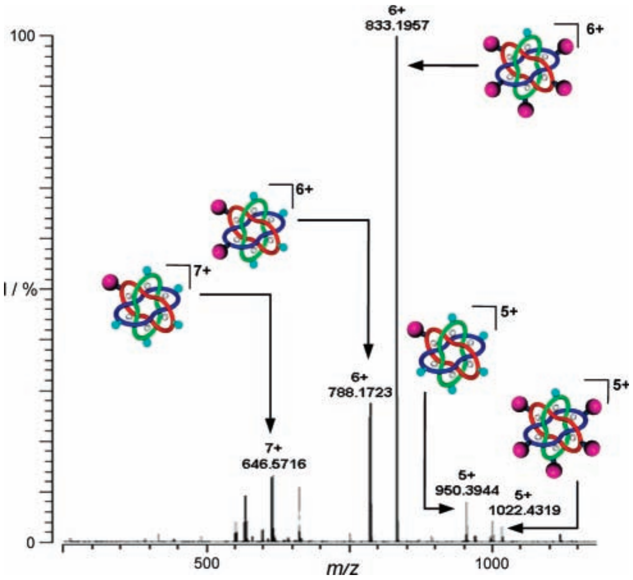

Figure 4. HR-ESI MS of **BRO_6**•12TFA following OXM with 4-methylstyrene employing the Grubbs second-generation catalyst.

The efficient convergent formation of both hexaolefinic and hexa-*p*-tolylpentenyloxy Borromeates has been described. This introduction of a further level of sophistication structure-wise into the metal-containing BRs opens up the ability to create new Borromeates and BR compounds. The making of hexasubstituted Borromeates divergently is still an open challenge, as demonstrated by the application of ruthenium-catalyzed OXM to a pre-assembled hexaolefinic Borromeate core.

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Supporting Information Available: Synthetic procedures for the synthesis of **O-DFP**, **BRO_6**•12TFA, **S-DFP**, **BRS_6**• 12TFA and OXM reactions, mass spectrometric and room temperature ^{1}H and ^{13}C NMR spectroscopic data, as well as the distance and angle measurements associated with all noncovalent and metal bonding interactions present in the **BRO_6**•12TFA. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) **BRO_nS_m** will be used to indicate the number of successful OXM reactions, where **O** = olefin, **S** = styrene, **n** = number of unreacted olefin tethers, and **m** = number of styrene residues.

(22) Given that the product distribution observed in the HR-ESI MS is highly skewed toward lower molecular weight compounds, we believe that, even though we could not positively identify a peak for **BRS_6**, it does not eliminate the real possibility of it being present in a considerable amount in the product mixture.