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Modular Synthesis of Bipyridinium Oligomers and Corresponding Donor–Acceptor Oligorotaxanes with Crown Ethers

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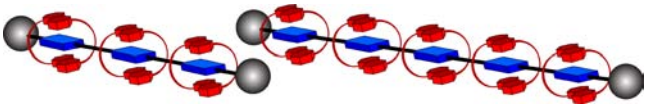
ABSTRACT



Donor–acceptor [4]- and [6]rotaxanes have been prepared from bipyridinium ($BIPY^{2+}$) oligomers and 1,5-dinaphtho[38]crown-10 (DN38C10) by a threading-followed-by-stoppering protocol employing click chemistry. An efficient, straightforward route to the $BIPY^{2+}$ oligomers has been developed that requires little to no chromatographic purification. Unlike most donor–acceptor oligorotaxanes that have been reported to date, 100% of the recognition sites on the dumbbells are occupied by rings.

Mechanically interlocked molecules (MIMs), such as catenanes and rotaxanes,[1] have been the subject of intensive investigations over the past few decades because of their interesting topologies,[2] beauty,[3] potential applications[4] as switches and machines in nanomechanical systems, and their synthetic challenge. The noncovalent bonding interactions involved in the templation[5] of MIMs, which 'live on' in the molecules, provide a handle to control[6] shape, size, isomerism, and intramolecular motion precisely. This control over secondary structure is particularly interesting in the case of polymeric[7] MIMs, where minute structural changes can have dramatic effects on the bulk properties of the corresponding materials.

In particular, we have been interested[8] in MIMs based on donor–acceptor (D–A) interactions between π-electron

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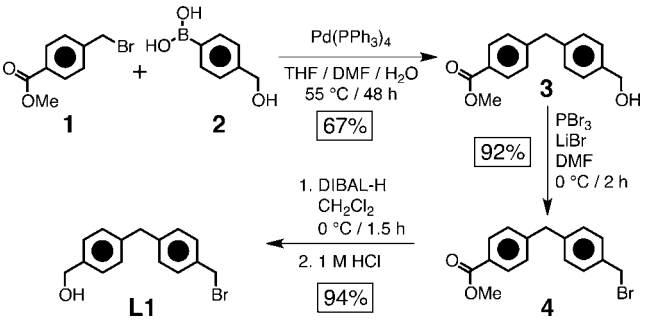
rich donors such as 1,5-dioxynaphthalene (DNP) units and π-electron deficient acceptors such as 4,4′-bipyridinium ($BIPY^{2+}$) units. We have shown[9] previously that oligo- and polyrotaxanes made from DNP oligomers and the $BIPY^{2+}$-based host cyclobis(paraquat-*p*-phenylene)[10] ($CBPQT^{4+}$) tend to form at only ~50% recognition site occupancy because they adopt well-defined folded secondary structures in solution, made possible by interactions between $CBPQT^{4+}$ rings and unencircled 'alongside' DNP units. Here we show that it is possible to create oligorotaxanes with fully occupied recognition sites, and hence a higher density of mechanical bonds, using an inverted recognition system between $BIPY^{2+}$ oligomers and macrocyclic DN38C10. A viable synthetic pathway to fully occupied mechanically interlocked oligomers and polymers can help guide the development of functional materials with novel bulk properties.

The synthesis and purification of a homologous series of well-defined $BIPY^{2+}$ oligomers was a formidable synthetic challenge because they are not amenable to conventional flash column chromatography (FCC) on account of their polycationic backbones. Also, there is little precedence in the literature for synthesizing a series of discrete linear $BIPY^{2+}$ oligomers of arbitrary length rationally. Hence, we sought to develop a modular approach which could be used to generate $BIPY^{2+}$ oligomers with a minimal number of reagents, steps, and purifications. Since benzyl bromides are highly reactive in nucleophilic substitutions, we reasoned that their displacement by pyridine groups would allow us to extend the oligomers in a stepwise manner efficiently. We designed the diphenylmethane-based linker **L1** to connect $BIPY^{2+}$ units together in the oligomerizations, with the expectation that the increased length of the linker (relative to the *p*-xylyl group in $CBPQT^{4+}$) would accelerate reaction rates by further separating the repulsive cationic charges between $BIPY^{2+}$ units while also removing the tendency of the corresponding pseudorotaxanes to form at 50% site occupancy preferentially on account of alongside interactions with the macrocycles.

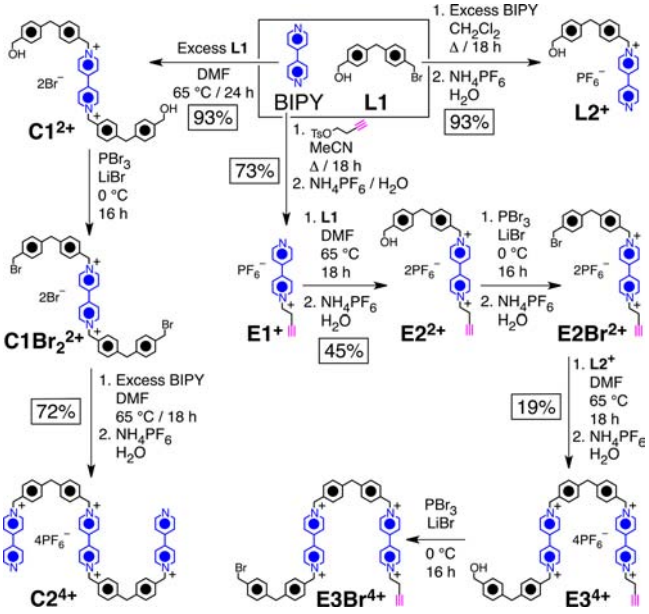
L1 was prepared according to Scheme 1, first by combining benzyl bromide **1** and boronic acid **2** in a Suzuki cross-coupling reaction to form alcohol **3**, followed by bromination of the alcohol with PBr_3 and LiBr in DMF to yield **4** and reduction of the methyl ester with DIBAL in PhMe and CH_2Cl_2.[11] With the exception of the (unoptimized) Suzuki cross-coupling that yielded 67%, these reactions proceeded in excellent (> 90%) yields.

Scheme 1. Synthesis of Diphenylmethane Linker **L1**



We devised a simple modular synthesis of 'center pieces' (denoted with the prefix 'C') and 'end pieces' (denoted by 'E' prefixes) using only linker **L1** and 4,4′-bipyridine (BIPY) as starting materials. All of the building blocks were pieced together (Scheme 2) using only three general transformations: (*a*) nucleophilic substitution by a pyridyl unit, (*b*) bromination of a benzyl alcohol site with PBr_3, and (*c*) counterion exchange to a PF_6 salt by precipitation

Scheme 2. Modular Synthesis of $BIPY^{2+}$ Building Blocks



of the bromide salts from aqueous NH_4PF_6 solution. End piece $\mathbf{E1}^+$ was prepared by reacting an excess of BIPY with 3-butynyl *p*-toluenesulfonate. End piece $\mathbf{E2}^{2+}$ was prepared by subsituting $\mathbf{E1}^+$ at linker **L1**. $\mathbf{E3}^{4+}$ was synthesized by coupling $\mathbf{E2}^{2+}$ with an extended linker $\mathbf{L2}^+$, which was prepared from **L1** and an excess of BIPY. Center piece $\mathbf{C1}^{2+}$ was prepared by reacting BIPY with an excess of **L1**, and then it was extended to $\mathbf{C2}^{4+}$ with a bromination followed by an immediate reaction with excess BIPY. The yields ranged from modest (19%) to excellent (93%), and no chromatography was needed to isolate pure

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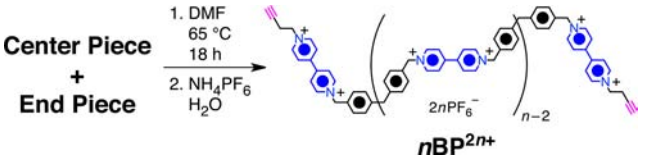
(11) Attempts to reduce **4** with DIBAL in THF returned only starting material, which was likely caused by the more polar THF molecules stabilizing DIBAL to render it a weaker reducing agent. See: Winterfeldt, E. *Synthesis* **1975**, 617–630.

Table 1. Number of $BIPY^{2+}$ Units, Starting Materials Used, Isolated Yields, Molecular Weights (MWs), and Characteristic Signals Observed in the Mass Spectra of $BIPY^{2+}$ Oligomers



		starting materials				
	no. of $BIPY^2$ (n)	center	end	yield (%)	MW (g mol^{-1})	observed ESI-MS signals[a] (m/z)
$\mathbf{3BP^{6+}}$	3	$\mathbf{C1Br_2^{2+}}$	$\mathbf{E1^{+}}$	56	1833	1687.16 $[M - PF_6]^+$ 771.31 $[M - 2PF_6]^{2+}$
$\mathbf{5BP^{10+}}$	5	$\mathbf{C2^{4+}}$	$\mathbf{E2Br^{2+}}$	72	3114	633.36 $[M - 4PF_6]^{4+}$ 477.79 $[M - 5PF_6]^{5+}$
$\mathbf{7BP^{14+}}$	7	$\mathbf{C2^{4+}}$	$\mathbf{E3Br^{4+}}$	38	4395	1859.41 $[M - 2TFA]^{2+}$ 1202.04 $[M - 3TFA]^{3+}$

[a] $\mathbf{7BP^{14+}}$ was analyzed by MS as the TFA salt after preparative RP-HPLC purification.

compounds, a fact which was verified (Figure S1 in the Supporting Information (SI)) by analytical reversed-phase high performance liquid chromatography (RP-HPLC). The benzyl bromide intermediates were used immediately and without purification because they tended to hydrolyze back to the starting alchohols, especially during RP-HPLC. The lower isolated yields for certain compounds reflect multistep reactions that typically involve bromination (condition *b*) as well as precipitation from aqueous NH_4PF_6 (condition *c*). Condition *c* enhanced the purity of the crude products at the penalty of high yields, which can most likely be attributed to the partial solubility of the PF_6 salts in the solutions from which they were precipitated.

The center and end pieces were transformed into $BIPY^{2+}$ oligomers $\mathbf{3BP^{6+}}$–$\mathbf{7BP^{14+}}$ under Conditions *a* and *c*, as summarized in Table 1 alongside some of the characteristic electrospray ionization (ESI) mass spectrometry (MS) data. Although these reactions also proceed efficiently and do not necessarily require chromatography, high-purity samples were obtained after preparative scale RP-HPLC. Analytical RP-HPLC chromatograms of $\mathbf{3BP^{6+}}$–$\mathbf{7BP^{14+}}$ are shown in Figure 1a–c. In principle, the present methodology could be used to extend the oligomers indefinitely, since linker $\mathbf{L2^{+}}$ can be repeatedly applied to either the center or end pieces to obtain even larger building blocks.

We transformed (Scheme 3) $\mathbf{3BP^{6+}}$ and $\mathbf{5BP^{10+}}$ into the corresponding oligorotaxanes $\mathbf{[4]3BPR^{6+}}$ and $\mathbf{[6]5BPR^{10+}}$, respectively, using the Huisgen[12] Cu(I)-catalyzed azide–alkyne cycloaddition (CuAAC), also known[13] as click chemistry, in a threading-followed-by-stoppering protocol. The $BIPY^{2+}$ oligomers were mixed with an excess of 1,5-dinaphtho[38]crown-10[14] (DN38C10) in $DMF/CHCl_3$

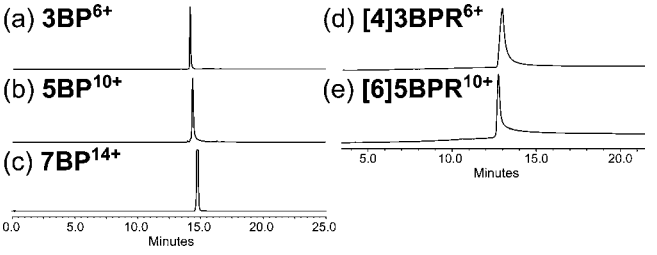


Figure 1. RP-HPLC chromatograms (H_2O–MeCN, 0.1% v/v TFA, λ = 254 nm) of the $BIPY^{2+}$ oligomers (a) $\mathbf{3BP^{6+}}$, (b) $\mathbf{5BP^{10+}}$, and (c) $\mathbf{7BP^{14+}}$ (0–60% MeCN in 20 min) and oligorotaxanes (d) $\mathbf{[4]3BP^{6+}}$ and (e) $\mathbf{[6]5BP^{10+}}$ (80–100% MeCN in 20 min).

to form the corresponding pseudorotaxanes, a situation which was confirmed visually by the red color that appeared because of a charge transfer absorption band from DNP and $BIPY^{2+}$ D–A interactions. Addition of the stopper precursor $\mathbf{StN_3}$ and catalytic amounts of the TBTA ligand and $Cu(MeCN)_4PF_6$ yielded the target oligorotaxanes via triazole formation. The ESI-MS data of the crude reaction suggest that we obtain a statistical mixture of multicomponent rotaxanes, resulting in modest yields (7–11%) for the fully occupied targets. However, the oligorotaxanes with 100% site occupancy ($\mathbf{[4]3BPR^{6+}}$ and $\mathbf{[6]5BPR^{10+}}$) were easily separated by FCC because they elute much more quickly on SiO_2 in 1% NH_4PF_6/Me_2CO than their smaller counterparts (which had a tendency to coelute) with exposed $BIPY^{2+}$ sites. No [8]rotaxane could be isolated from the statistical mixture when we attempted the same protocol on $\mathbf{7BP^{14+}}$, exposing the limits of the threading-followed-by-stoppering approach with regard to polyrotaxane synthesis. A kinetically controlled stoppering approach is unlikely to yield well-defined polyrotaxanes with low polydispersities in the absence of positive cooperativity[15] to drive reactions away from statistical distributions.

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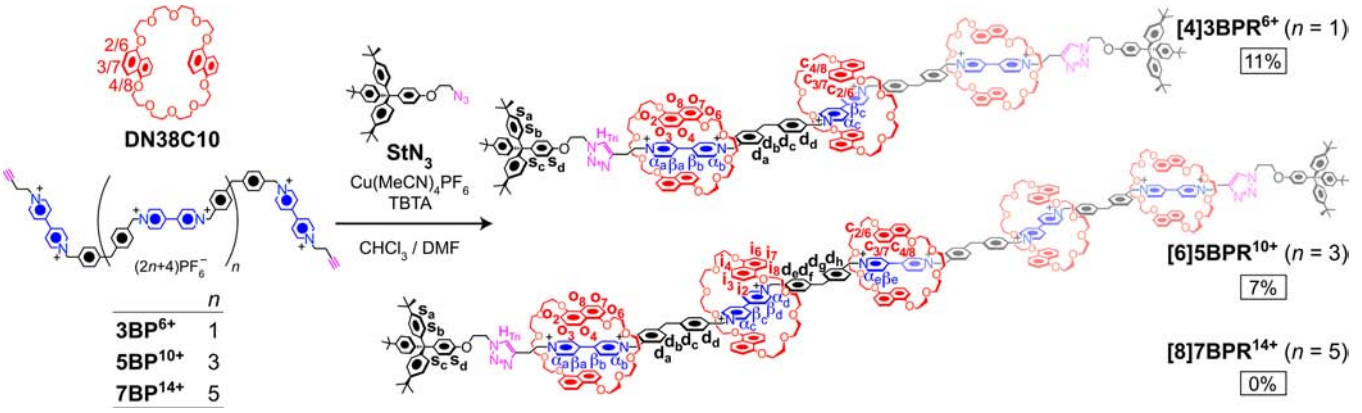
Scheme 3. Synthesis of Donor–Acceptor Oligorotaxanes in which $BIPY^{2+}$ Recognition Sites are Fully Occupied by DN38C10 Rings Using Click Chemistry



The oligorotaxanes were characterized by analytical RP-HPLC, ESI-MS (Figures S2 and S6 in the SI), and ^{1}H NMR spectroscopy. The significant hydrophobicity imparted to the oligomers by the rings and stoppers renders them reluctant to elute even in nearly 100% MeCN during RP-HPLC, as indicated by the broad traces in Figure 1d–e. The assignments of the aromatic signals in the ^{1}H NMR spectra (Figure 2b–c) of **[4]3BPR^{6+}** and **[6]5BPR^{10+}** were assisted by multidimensional ^{1}H NMR analysis (Sections 4 and 5 of the SI). All $BIPY^{2+}$ and DNP protons resonate at lower frequencies than their uncomplexed counterparts (Figure 2a and 2d) as a result of shielding from the local magnetic fields induced by aromatic ring currents in the D–A stacks that underpin π–π recognition between DN38C10 and $BIPY^{2+}$ units. The spectra also reveal that 'pirouetting' motions of the DNP units (rotations about the central C–C bond) occur rapidly on the NMR time scale in CD_3CN at 293 K, giving the rotaxanes an averaged D_{2h} symmetry, a conclusion that can be drawn from the number of observed $BIPY^{2+}$ and DNP signals. For example, DNP protons in the outermost rings (labeled with 'o' prefixes) give rise to single resonances for pairs of otherwise heterotopic protons (2/6, 3/7, 4/8) because they undergo rapid site exchange through pirouetting. Likewise, the C_2 symmetry of DNP is not imposed on the terminal $BIPY^{2+}$ units, since they express only two α and β signals.

In summary, we have developed a straightforward synthetic route to linear $BIPY^{2+}$ oligomers of arbitrary length (in principle) and employed them in the kinetically controlled synthesis of two donor–acceptor oligorotaxanes with fully occupied recognition sites.

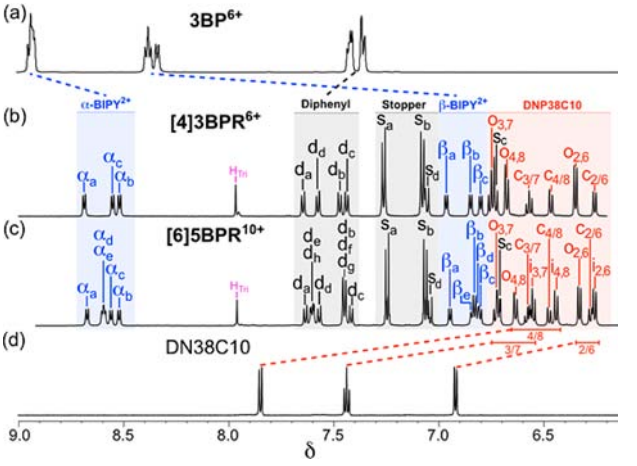


Figure 2. Partial ^{1}H NMR spectra (600 MHz, 293 K, CD_3CN) of (a) **3BP^{6+}**, (b) **[4]3BPR^{6+}**, and (c) **[6]5BPR^{10+}** as their PF_6 salts and (d) DN38C10. See Scheme 3 for proton labels.

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Supporting Information Available. Materials and methods, synthetic procedures, spectroscopic characterization of new compounds, analytical RP-HPLC traces. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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