ORGANIC LETTERS

2000
Vol. 2, No. 6
759−762

Toward Daisy Chain Polymers: "Wittig Exchange" of Stoppers in [2]Rotaxane Monomers

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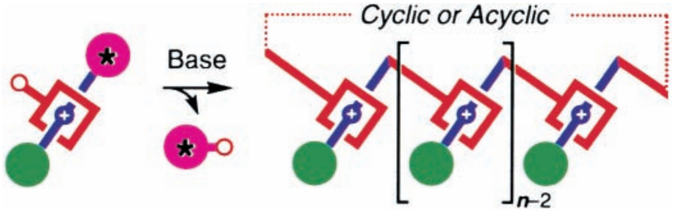
Received December 15, 1999

ABSTRACT



Two ammonium ion/crown ether-based [2]rotaxane monomers—each incorporating (i) a dumbbell-shaped component, possessing an exchangeable benzylic triphenylphosphonium stopper, and (ii) a ring component, bearing an aldehyde function—undergo a sequence of Wittig reactions in which the surrogate triphenylphosphonium stopper is exchanged for a ring component either (i) in *the same* rotaxane molecule to give cyclic daisy chains by an *intramolecular*, chain-terminating reaction or (ii) in *another* rotaxane molecule to give acyclic daisy chains by an *intermolecular* chain-propagating reaction.

The appeal of interlocked molecules[1]—the so-called catenanes and rotaxanes—lies not only in their undoubted aesthetically pleasing forms but also in their potentially unique functions. No longer consigned to the ranks of esoteric chemical curiosities, new generations of these compounds are emerging as prototypical molecular devices.[2] Indeed, their considerable impact in the molecular arena has prompted researchers to extend the concept of the mechanical bond[3] into a macromolecular[4] setting. The most extensively studied examples to date are the polycatenanes[5] and polyrotaxanes.[6] However, within each of these general families, it is possible to formulate many structural variations resulting in a diverse range of polymeric architectures.[7] "Daisy chains" (Figure 1) represent one particular subclass of polyrotaxanes,

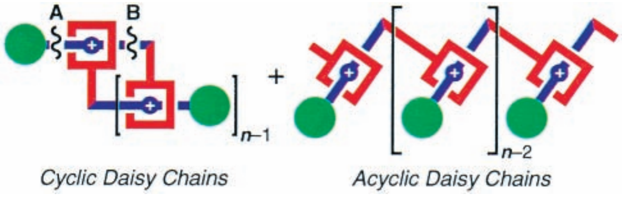


Figure 1. Schematic representations of cyclic and acyclic daisy chain architectures. **A** and **B** represent two conceptually different retrosynthetic disconnections that apply to *both* cyclic and acyclic forms.[8]

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10.1021/ol9913587 CCC: $19.00

distinct from their siblings insofar as they do not possess a continuous covalently bonded backbone.

Retrosynthetic analysis of a daisy chain polyrotaxane reveals two plausible disconnections (**A** and **B** in Figure 1) which correspond conceptually to two different synthetic strategies (Figure 2).

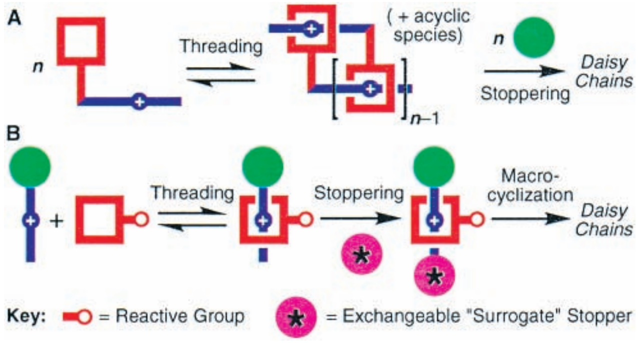


Figure 2. Schematic representations of the two synthetic strategies corresponding to the **A** and **B** disconnections (Figure 1) of daisy chain structures.

Route **A** relies initially upon the self-assembly[9] of a self-complementary monomer—designed in such a way that its recognition sites are compelled to interact in an *inter*- rather than *intra*molecular fashion—followed by a "stoppering" reaction to generate the mechanically interlocked daisy chain. Although reports[10] of "uncapped" daisy chains, i.e., pseudopolyrotaxanes,[11] utilizing this noncovalent polymerization protocol are already numerous, there are no instances reported yet in which the post-assembly covalent modification (i.e., stoppering) of these supramolecular edifices has been described. In contrast, route **B** requires the synthesis—via supramolecular assistance[3]—of a [2]rotaxane bearing (i) a reactive surrogate stopper at one end of the dumbbell-shaped component and (ii) an appropriate functional group appended to the ring component.[12] This [2]rotaxane monomer can then be polymerized in a more traditional covalent fashion, affording daisy chain structures. We have recently reported[13] that a [2]rotaxane (**I**)—containing[14] a benzylic triphenylphosphonium group as one of its stoppers—can undergo *stopper exchange* (Figure 3) via a Wittig reaction with a suitably proportioned aldehyde (in this case *p-tert*-butylbenzaldehyde) to afford a new [2]rotaxane (**III**).

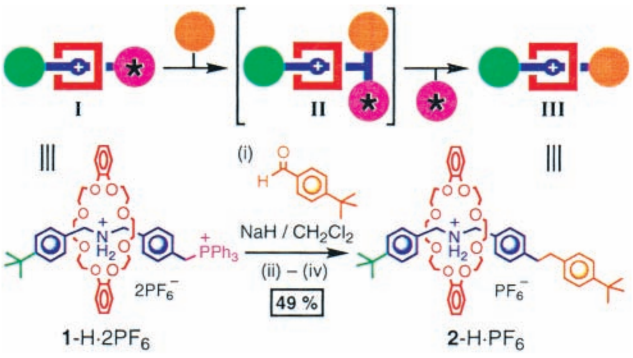
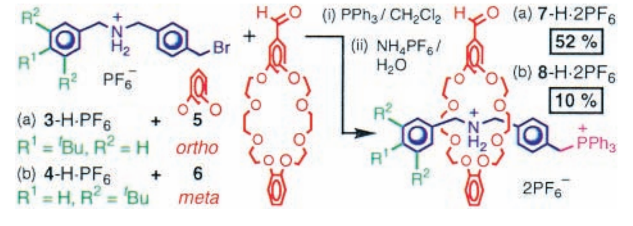


Figure 3. A "reactive" [2]rotaxane **I**—incorporating an exchangeable stopper (*)—is converted, via **II**, into the "inert" [2]rotaxane **III**. The integrity of the mechanical bond is maintained throughout the transformation, i.e., at no point can the ring component escape from the dumbbell-shaped component around which it is trapped. Reagents: (ii) HCl/H_2O; (iii) NH_4PF_6/H_2O; (iv) H_2/PtO_2/THF.

Here, we report (i) the syntheses (Scheme 1) of two [2]-rotaxane monomers—each possessing (a) an exchangeable benzylic triphenylphosphonium stopper and (b) a formyl group appended to one of the aromatic residues of the crown ether component—and (ii) their subsequent uses in daisy chain-forming macrocyclizations.

Scheme 1. Syntheses of the Two [2]Rotaxane Monomers (a) **7**-H·2PF$_6$ and (b) **8**-H·2PF$_6$, Employing Crown Ethers with [24]Crown-8 and [25]Crown-8 Constitutions, Respectively



The [2]rotaxanes **7**-H·2PF$_6$ and **8**-H·2PF$_6$ were prepared[14] by the addition of triphenylphosphine to a CH_2Cl_2 solution

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(8) Cyclic daisy chains are formed whenever chain termination of a propagating acyclic species occurs via intramolecular "backbiting".

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(10) (a) Hirotsu, K.; Higuchi, T.; Fujita, K.; Ueda, T.; Shinoda, A.; Imoto, T.; Tabushi, I. *J. Org. Chem*. **1982**, *47*, 1143−1144. (b) Zanotti-Gerosa, A.; Solari, E.; Giannini, L.; Chiesi-Villa, A.; Rizzoli, C. *Chem. Commun*. **1996**, 119−120. (c) Mentzafos, D.; Terzis, A.; Coleman, A. W.; de Rango, C. *Carbohydr. Res*. **1996**, *282*, 125−135. (d) Ashton, P. R.; Baxter, I.; Cantrill, S. J.; Fyfe, M. C. T.; Glink, P. T.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1294−1297. (e) Ashton, P. R.; Parsons, I. W.; Raymo, F. M.; Stoddart, J. F.; White, A. J. P.; Williams, D. J.; Wolf, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 1913−1916. (f) Yamaguchi, N.; Nagvekar, D. S.; Gibson, H. W. *Angew. Chem., Int. Ed.* **1998**, *37*, 2361−2364. (g) Mirzoian, A.; Kaifer, A. E. *Chem. Commun*. **1999**, 1603−1604. (h) Bülger, J.; Sommerdijk, N. A. J. M.; Visser, A. J. W. G.; van Hoek, A.; Nolte, R. J. M.; Engbersen, J. F. J.; Reinhoudt, D. N. *J. Am. Chem. Soc*. **1999**, *121*, 28−33. Although in not all of these reports do the authors refer to their systems as "daisy chains" or "pseudopolyrotaxanes", they all describe the noncovalent polymerization of self-complementary monomers.

containing one or the other of the formyl-substituted crown ethers (**5**[10d] or **6**) and the corresponding threadlike benzylic bromide, **3**-H·PF$_6$ or **4**-H·PF$_6$, respectively. The lower yields of the [2]rotaxanes (52% for **7**-H·2PF$_6$ and 10% for **8**-H·2PF$_6$), compared with those observed for the analogous reactions performed with the unsubstituted "parent" crown ethers (80% for DB24C8[14] and 32% for BMP25C8[15]), can be rationalized by the presence of the formyl moiety on the crown ether component. Presumably, this electron-withdrawing group reduces the basicity of the oxygen atoms in the macrorings, thus lowering their affinities for the dibenzylammonium ion-containing threads.[16] In both cases, the lower yields obtained for the crown ethers possessing a BMP25C8 constitution reflect its poorer binding ability[17] for secondary dibenzylammonium ions than that of DB24C8.

X-ray quality single crystals of **7**-H·2PF$_6$ were obtained upon slow evaporation of a CH_2Cl_2 solution that had initially been layered with MeOH. The solid-state structure[18] of the [2]rotaxane **7**-H^{2+} (Figure 4) formed between the formyl-substituted DB24C8 analogue **5** and the dicationic dumbbell is very similar to that of its unsubstituted counterpart.[19] The only major difference is in the torsional relationships between the two phenylene rings and the plane of the $C_{Ph}CH_2NH_2^+$-CH_2C_{Ph} backbone in the dicationic dumbbell component. Here, the *tert*-butylphenyl ring plane lies much closer (28°) to the plane of the backbone than that in the unsubstituted compound where the equivalent inclination is 54°. Stabilization of the [2]rotaxane **7**-H^{2+} is via the usual combination of $[N^+{-}H\cdots O]$ and $[C{-}H\cdots O]$ hydrogen bonding (a−d in Figure 4) and $\pi-\pi$ stacking between one of the phenylene rings in the dication and one of the "catechol" rings of the crown ether (centroid−centroid and mean interplanar separations of 3.78 and 3.47 Å; the rings being inclined by 5°).

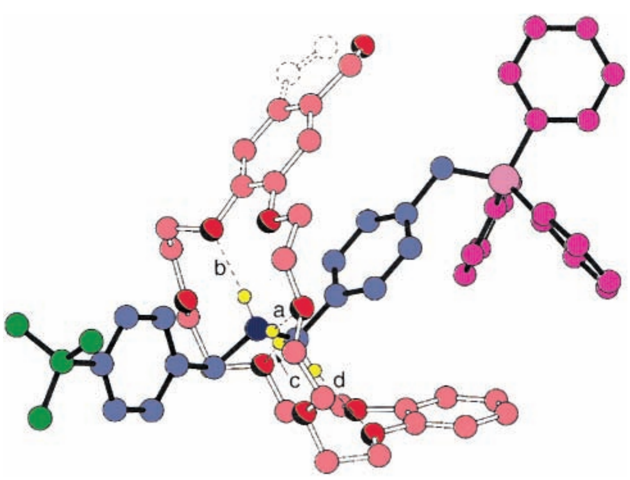
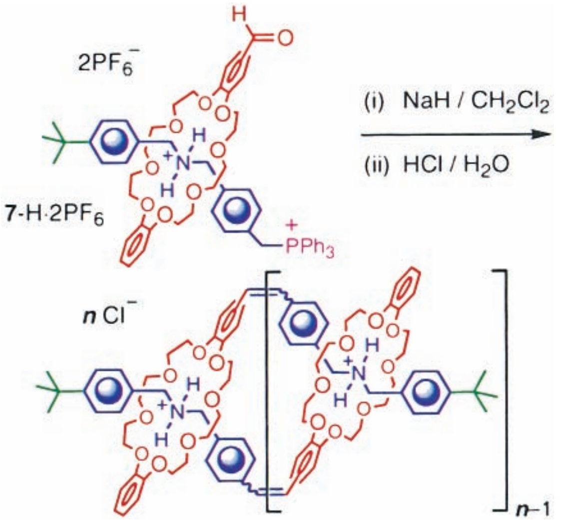


Figure 4. Solid-state structure of the [2]rotaxane **7**-H^{2+}. The hydrogen bond geometries are $[X\cdots O]$, $[H\cdots O]$ (Å), $[X{-}H\cdots O]$ (deg) (a) 3.05, 2.19, 161; (b) 2.95, 2.07, 166; (c) 3.29, 2.36, 162; (d) 3.22, 2.27, 167.

The presence of the formyl groups is accompanied by disorder in the crown ether component, with two slightly sheared orientations of the uppermost "catechol" ring being observed. There is also a small contraction, to 48°, of the cleft angle between the two "catechol" rings. The position of the formyl group is indeterminate; the crystals are racemic[20] and there is evidence for electron density in the regions adjacent to both of the carbon atoms *para* to the OCH_2 substituents on both "catechol" rings. The highest electron density (major occupancy site) is associated with the "full-bonded" position illustrated in Figure 4. The only inter[2]rotaxane interaction of note is a $\pi-\pi$ stacking of the substituted "catechol" ring with its C_i symmetrically related counterpart in another. The centroid−centroid and mean interplanar separations are 3.77 and 3.60 Å, respectively.

Initial experiments designed to investigate the oligomerization of the DB24C8-based [2]rotaxane **7**-H·2PF$_6$ were performed in dilute solution in order to afford smaller oligomers and hence facilitate product identification. Consequently, a 5 mM CH_2Cl_2 solution of this monomer was stirred for 3 d (Scheme 2) in the presence of NaH. Following an acidic workup, characteristic signals arising from the C*H*O and C*H*$_2$P$^+$Ph$_3$ protons were observed in the ^{1}H NMR spectrum, indicating that the reaction was not complete. However, after subjecting this mixture to the same conditions for a further 3 d, ^{1}H NMR spectroscopic analysis revealed no signals for the resonances of either of these two sets of diagnostic protons. This observation—i.e., the lack of any

Scheme 2. Cyclization of the 24C8-Based Monomer **7**-H·2PF$_6$



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(11) The term *pseudopolyrotaxane* was introduced by us in 1994 (see ref 7) to describe polyrotaxanes that lack stoppers. Essentially, pseudopolyrotaxanes are to polyrotaxanes what pseudorotaxanes are to rotaxanes. See: Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1991**, 1677−1679.

(12) Alternatively, rather than employing an exchangeable stopper, a stopper bearing a reactive functional group may be used. For an example, see: Werts, M. P. L.; van den Boogaard, M.; Hadziioannou, G.; Tsivgoulis, G. M. *Chem. Commun.* **1999**, 623−624.

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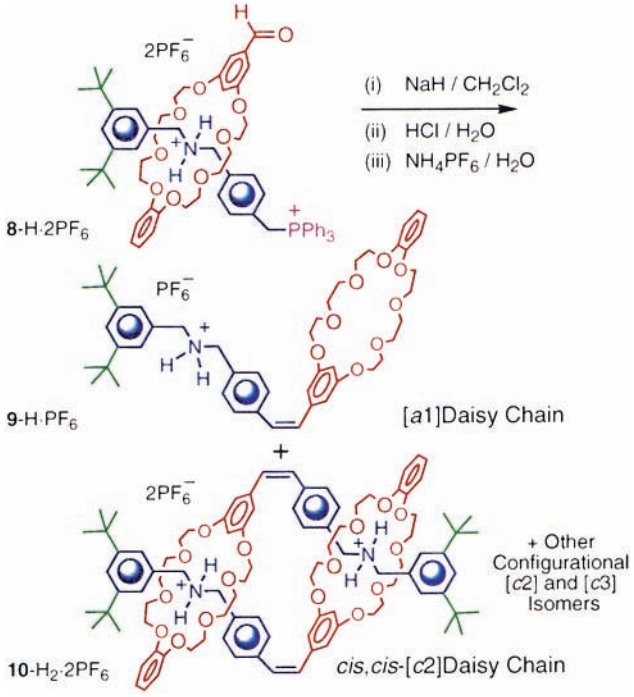
(14) Rowan, S. J.; Cantrill, S. J.; Stoddart, J. F. *Org. Lett.* **1999**, *1*, 129−132.

(15) Rowan, S. J.; Stoddart, J. F. Unpublished results.

end groups—suggested the formation of cyclic rather than linear daisy chains and was corroborated when the FAB-MS analysis revealed only the presence of cyclic monomers ($n = 1$) and dimers ($n = 2$), [*c*1]- and [*c*2]daisy chains, respectively.

Interestingly, the cyclic dimeric daisy chain can exist in numerous isomeric forms as a consequence of (i) the possibility of generating *cis* or *trans* olefins in the Wittig reaction in addition to (ii) the racemic nature of the starting material.[21] Unfortunately, however, these subtle stereochemical differences result in a mixture of inseparable compounds. To simplify the situation, further studies have been conducted with the achiral BMP25C8-based [2]rotaxane **8**-H•2PF$_6$. Once again, the Wittig macrocyclization of this monomer (Scheme 3) was conducted at 5 mM, following exactly the same protocol as that described previously for **7**-H•2PF$_6$. Following protonation (1 N HCl) and anion exchange (NH$_4$PF$_6$/H$_2$O), the crude reaction products were precipitated from CH$_2$Cl$_2$ solution with Et$_2$O. The white solid was collected (ca. 50% mass recovery) and shown by FAB-MS analysis to contain mainly cyclic dimers and some cyclic trimer—i.e., [*c*2]- and [*c*3]daisy chains—respectively. However, the Et$_2$O-containing fraction was also found to contain daisy chain compounds which were separated by column chromatography into two products. ^{1}H NMR spectroscopic and FAB-MS analyses proved these isolated products to be (i) the isomerically pure [*c*2]daisy chain in which both olefinic bonds are *cis* and (ii) the acyclic[22] [*a*1]daisy chain.

Scheme 3. Cyclization of the 25C8-Based Monomer **8**-H•2PF$_6$



By fashioning [2]rotaxane monomers—in which complementary reactive sites are positioned judiciously in both the dumbbell and ring components—we have demonstrated that the concept of stopper exchange[13] can be exploited for the construction of oligomeric daisy chain compounds. Initially, the Wittig macrocyclizations have been conducted at relatively low concentrations (5 mM) in order to facilitate product characterizations and therefore provide proof of principle. However, now that the paradigm has been establised, investigations of the oligo/polymerization of these [2]rotaxane monomers at much higher concentrations are being pursued in an effort to generate larger daisy chain polyrotaxanes.

Acknowledgment. We thank UCLA and the Petroleum Research Fund, administered by the American Chemical Society, for generous financial support.

Supporting Information Available: Experimental procedures and characterization data (^{1}H and ^{13}C NMR, FAB-MS) for **7**-H•2PF$_6$, **8**-H•2PF$_6$, **9**-H•PF$_6$, and **10**-H$_2$•2PF$_6$. Crystal data for **7**-H•2PF$_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) Previous results have shown that substitution of the dibenzylammonium ion component with electron-withdrawing groups increases its affinity for DB24C8. Conversely, substitution with electron-donating groups causes a corresponding decrease in the association constants. See: Ashton, P. R.; Fyfe, M. C. T.; Hickingbottom, S. K.; Stoddart. J. F.; White, A. J. P.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2117−2128.

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(18) Crystal data for **7**-H•2PF$_6$: [C$_{62}$H$_{72}$NO$_9$P][PF$_6$]$_2$•0.25H$_2$O, M = 1300.6, triclinic, space group $P\bar{1}$ (No. 2), $a = 10.632(1)$, $b = 14.913(2)$, and $c = 21.145(2)$ Å, $\alpha = 81.83(1)$, $\beta = 82.96(1)$, and $\gamma = 80.73(1)°$, $V = 3258.1(6)$ Å^3, $Z = 2$, $\rho_c = 1.326$ g cm^{-3}, μ(Cu Kα) = 16.1 cm^{-1}, $F(000) = 1357$, $T = 293$ K; clear blocky prisms, 0.50 × 0.40 × 0.40 mm, Siemens P4/RA diffractometer, graphite-monochromated Cu Kα radiation, ω-scans, 9529 independent reflections.

(19) Rowan, S. J.; Stoddart, J. F.; Williams, D. J. Unpublished results.

(20) As a consequence of the reduced symmetry of its components, **7**-H•2PF$_6$ exists in two cycloenantiomeric forms. For the first example of a cycloenantiomeric rotaxane, see: Yamamoto, C.; Okamoto, Y.; Schmidt, T.; Jäger, R.; Vögtle, F. *J. Am. Chem. Soc.* **1997**, *119*, 10547−10548. For a cyclo*diastereoisomeric* [3]rotaxane, see: Schmeider, R.; Hübner, G.; Seel, C.; Vögtle, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3528−3530.

(21) Arbitrarily assigning *R* and *S* descriptors to the two enantiomeric forms of **7**-H•2PF$_6$ highlights the potential for formation of diastereoisomeric cyclic dimers, i.e., it is not only possible to generate the *RR* and *SS* dimers (an enantiomeric pair) but also the “*meso*” achiral *RS* dimer.

(22) By virtue of the very nature of the synthetic strategy, the [*a*1]daisy chain *must* arise from the formation initially of the [*c*1]daisy chain in which the ylide generated in the monomer reacts with the formyl group in the same molecule. Presumably, this [*c*1]daisy chain is then converted into the [*a*1]daisy chain by a process which involves the passage of the *cis*-stilbene unit through the center of the crown ether, as a consequence of its pivoting about the O⋯O axis of the common resorcinol ring. The acyclic nature of this “daisy chain” is supported by its ^{1}H NMR spectroscopic behavior. The resonances arising from the CH$_2$ protons adjacent to the NH$_2^+$ center are highly diagnostic in these systems. When the NH$_2^+$ center is encircled by a crown ether, the signals arising from the flanking CH$_2$ protons appear at δ ~4.3−4.6. In this case, and in others in which the NH$_2^+$ center *is not bound*, the CH$_2$ signal is shifted upfield to a δ value of ~3.7 ppm.