Communications to the Editor

Precision Molecular Grafting: Exchanging Surrogate Stoppers in [2]Rotaxanes

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Rotaxanes[1] are molecules composed of interlocked parts in the shape of one or more wheels (or beads) that become trapped mechanically on the axle (or rod) of a dumbbell-shaped component. Of late, a number of different synthetic protocols, relying on supramolecular assistance,[2] have been developed[1−3] for making these interlocked molecular compounds efficiently. One of the two kinetically controlled protocols[4] is the so-called threading, followed-by-stoppering one.[5] It can involve the passage of a rivetlike component through a beadlike one to give a 1:1 complex (**I** in Figure 1) or *semirotaxane*[6] that is then transformed into a [2]rotaxane (**II** in Figure 1) by the covalent attachment of a second stopper. Recently, we have reported[7] the template-directed synthesis of the [2]rotaxane **1**-H•2PF$_6$ (Scheme 1) carrying, in addition to an inert *p-tert*-butylphenyl stopper, a potentially reactive benzylic triphenylphosphonium stopper. The supramolecular assistance responsible for the self-assembly of this [2]rotaxane resides mainly in the [N$^+$−H···O] and [C−H···O] hydrogen bonds between the −CH$_2$NH$_2$$^+CH_2$− portion in the middle of the dumbbell-shaped component and the dibenzo[24]-crown-8 (DB24C8) macrocycle encircling it. The availability of **1**-H•2PF$_6$ begs the question − is it possible to replace its potentially reactive stopper by another one, while preserving its interlocked nature, by performing a Wittig reaction on **1**-H•2PF$_6$ with an appropriate aldehyde, i.e., one that is large enough to prevent loss of the DB24C8 macrocycle? Here, we report the successful demonstration of this post-assembly covalent modification of **1**-H•2PF$_6$ by showing how routine Wittig chemistry can be used in a highly predictable and specific manner not only to convert this reactive [2]rotaxane, without any loss of its integrity, into (1) another stable [2]rotaxane, but also to construct from **1**-H•2PF$_6$, with absolute precision (2), a degenerate molecular shuttle[8] and (3) a branched [4]rotaxane.[9] In essence, the reactive stopper in the [2]rotaxane **1**-H•2PF$_6$ acts as a surrogate that can be exchanged (**II** → **III** → **IV** in Figure 1) for a wide range of structural elements.

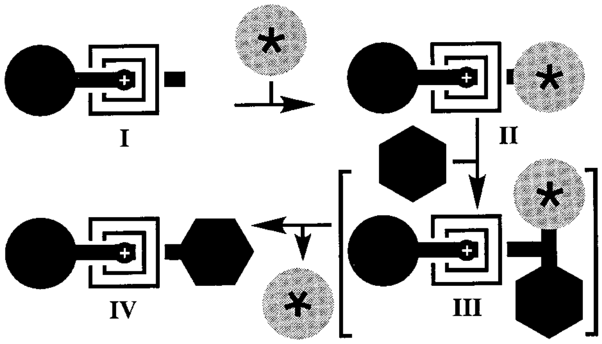
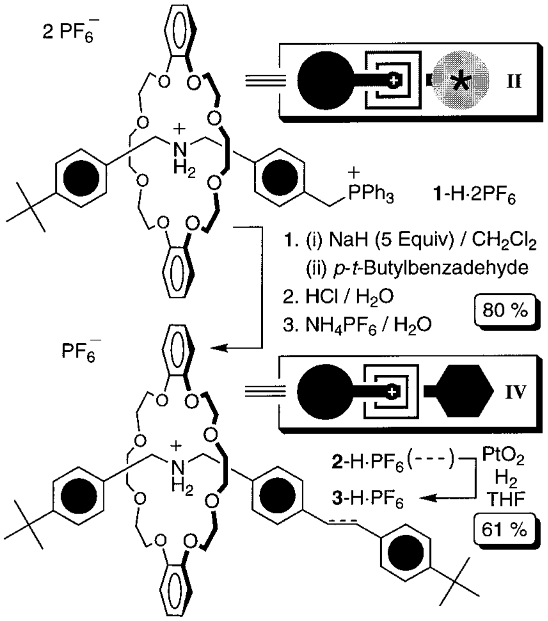


Figure 1. The formation from a semirotaxane **(I)**, with an inert stopper (black moon), of a reactive [2]rotaxane **(II)** with one exchangeable stopper (starred gray moon) and its exchange with a bulky group (black hexagon) to give, via the intermediate **(III)**, another [2]rotaxane **(IV)**.

Scheme 1



Reaction (Scheme 1) of **1**-H•2PF$_6$ with *p-tert*-butylbenzaldehyde (*t*-BuC$_6$H$_4$CHO) in the presence of an excess of base NaH in CH$_2$Cl$_2$ afforded **2**-H•PF$_6$ in 80% yield as the expected cis/trans mixture of olefins after reprotonation (1 N HCl) and counterion exchange (NH$_4$PF$_6$/H$_2$O). This isomeric mixture of olefins was hydrogenated using Adams' catalyst (PtO$_2$) to yield the [2]rotaxane **3**-H•PF$_6$. Thus, provided the aldehyde is suf-

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(4) The other kinetically controlled procedure for self-assembling rotaxanes is the so-called clipping one. See: Philp, D.; Stoddart, J. F. *Synlett* **1991**, 445−458.

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(6) The term *semirotaxane* indicates a pseudorotaxane composed of a macrocycle encircling an acyclic component stoppered at only one of its two ends. For an early usage of this term, see: Born, M.; Ritter, H. *Makromol. Chem., Rapid Commun.* **1991**, *12*, 471−476.

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(8) For the first report of a degenerate molecular shuttle, see: Anelli, P.-L.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 5131−5133.

(9) For a more conventional approach to assembling branched rotaxanes, see: Amabilino, D. B.; Asakawa, M.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Belohradsky, M.; Credi, A.; Higuchi, M.; Raymo, F. M.; Shimizu, T.; Stoddart, J. F.; Venturi, M.; Yase, K. *New J. Chem.* **1998**, 959−972.

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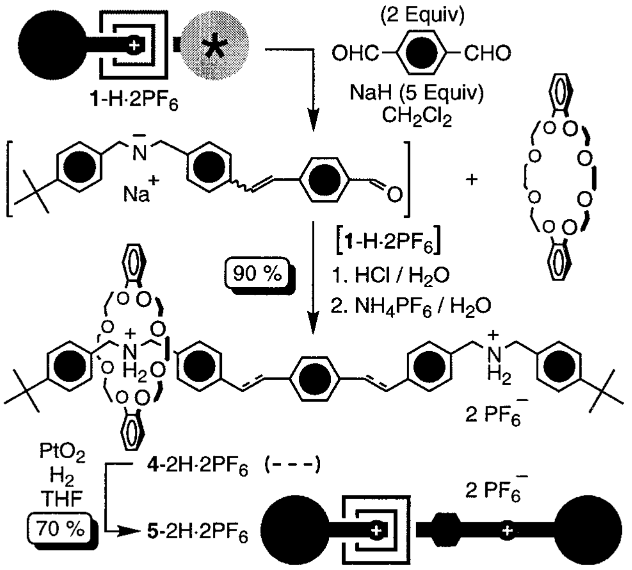
ficiently bulky, the stoppers can be replaced in benzylic triphenylphosphonium-stoppered rotaxanes during Wittig reactions without dethreading of the beads from the dumbbell-shaped components, despite the fact that their NH_2^+ recognition sites are "switched off" by the strong base necessary to generate the ylide intermediate prior to the addition of the bulky aldehyde.

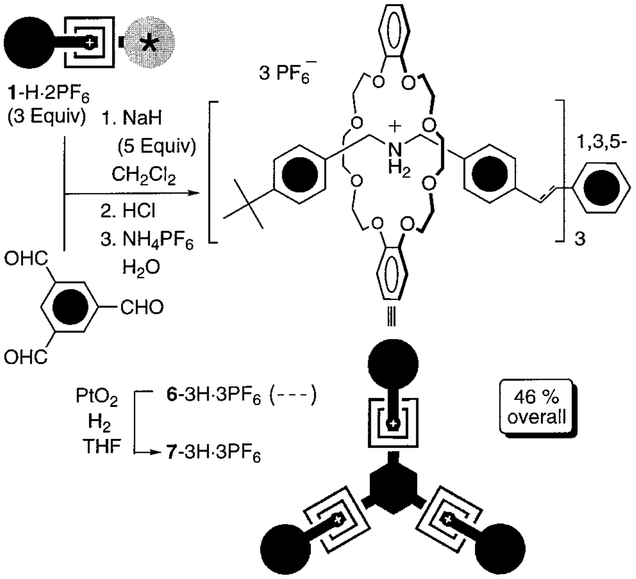
Scheme 2



The synthetic potential of Wittig-style covalent modifications on benzylic triphenylphosphonium-stoppered rotaxanes was demonstrated further (Scheme 2) by reacting (NaH/CH_2Cl_2) **1**-H•2PF$_6$ with terephthaldehyde ($OHCC_6H_4CHO$) which, because it is not large enough to prevent dethreading of DB24C8 after the first Wittig reaction, affords *only* the [2]rotaxane **4**-2H•2PF$_6$ containing one DB24C8 ring shared between its two degenerate recognition sites in 90% yield and *none* of the higher [3]rotaxane carrying two DB24C8 rings, i.e., one located at each site. Hydrogenation of **4**-2H•2PF$_6$ to yield (70%) **5**-2H•2PF$_6$ could also be achieved by using PtO_2 as catalyst. The outcome of this particular sequence of reactions is significant for two reasons. One is that it provides a highly specific way of assembling molecular shuttles and thus affords a precise means of constructing linear molecular motors.[10] The other is that it emphasizes the importance of the particular aldehyde used in this double Wittig reaction. After the first Wittig reaction of **1**-H•2PF$_6$ with $OHCC_6H_4CHO$, the DB24C8 ring dissociates from (Scheme 2) what is effectively a semirotaxane because not only is the NH_2^+ recognition site "switched off", but also the formyl-terminated phenylene ring of the rivet-shaped component is not large enough to prevent dethreading. However, during the second Wittig reaction of this free aldehyde intermediate with another equivalent of **1**-H•2PF$_6$, dethreading is impossible because both termini of the newly created "symmetrical" dumbbell-shaped component are sufficiently large to retain the DB24C8 ring. Thus, this highly specific reaction sequence leads directly and precisely to the degenerate molecular shuttle by (i) starting with a [2]rotaxane molecule with a reactive (exchangeable) stopper, (ii) removing this stopper and, at the same time, "switching off" the recognition site between the ring and rivet components so that they part company, then (iii) using the rivet as an effective stopper in a reaction with a second [2]rotaxane molecule containing the same reactive (exchangeable) stopper, and finally (iv) regenerating both recognition sites on the resulting dumbbell component of a new [2]rotaxane molecule (the degenerate molecular shuttle).

When 1,3,5-triformylbenzene[11] [$C_6H_3(CHO)_3$] is added to a CH_2Cl_2 solution of **1**-H•2PF$_6$ in the presence of an excess of NaH, the "symmetrical" branched [4]rotaxane **6**-3H•3PF$_6$ can subsequently be isolated (Scheme 3) as a mixture of (four) isomers. If it is assumed that the first step is the addition of a single [2]rotaxane to $C_6H_3(CHO)_3$, then the formyl groups on the 3 and 5 positions of the benzene nucleus in the expected first intermediate are presumably large enough to prevent dethreading of the DB24C8 from this intermediate and hence **6**-3H•3PF$_6$ is isolated, rather than the related branched [3]rotaxane lacking one DB24C8 ring. Hydrogenation (H_2/PtO_2) gave the branched [4]rotaxane **7**-3H•3PF$_6$.

Scheme 3



Molecular grafting using routine Wittig chemistry on benzylic triphenylphosphonium-stoppered [2]rotaxanes not only provides novel routes to (switchable) rotaxanes and catenanes and hence to molecular machinery[10] but also opens up new pathways to exotic interlocked macromolecules.[12]

Acknowledgment. We thank the University of California, Los Angeles for its generous support of this research.

Supporting Information Available: Experimental procedures and characterization data for compounds **2**-H•PF$_6$–**7**-3H•3PF$_6$; ^{1}H NMR and mass spectra for **2**-H•PF$_6$, **4**-2H•2PF$_6$, **6**-3H•3PF$_6$; ^{1}H NMR, ^{13}C NMR, and mass spectra for **3**-H•PF$_6$, **5**-2H•2PF$_6$, and **7**-3H•3PF$_6$ (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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