ORGANIC
LETTERS

2000
Vol. 2, No. 5
593−595

Rotaxanes via Michael Addition[†]

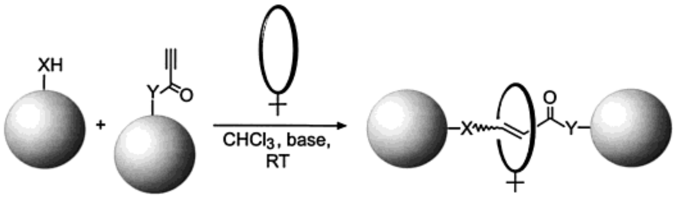
Carin Reuter and Fritz Vögtle*

*Kekulé-Institut für Organische Chemie und Biochemie der Universität Bonn,
Gerhard-Domagk-Strasse 1, 53121 Bonn, Germany*

voegtle@uni-bonn.de

Received December 13, 1999

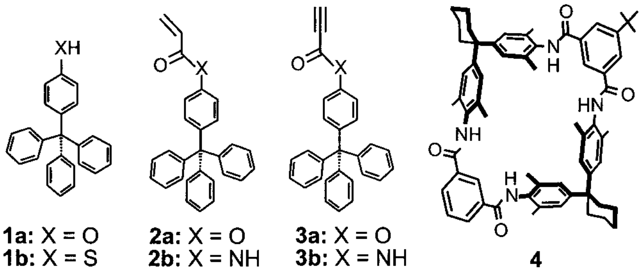
ABSTRACT



The application of a template effect to the classical Michael addition of heteronucleophiles to various Michael acceptor systems leads in good yields to a new trapping synthesis of [2]rotaxanes with conjugated functional groups in their axles.

Rotaxanes and catenanes are molecules that consist of noncovalently interlocked building blocks. They are of current interest as model systems for molecular recognition and as precursors for molecular devices.[1] Efficient rotaxane syntheses make use of template assistance based on a molecular recognition process of the reacting components.[2] Template effects support the preorganization of the reactants by hydrogen bonding, hydrophobic and donor−acceptor interactions, or metal coordination.[3] A recent improvement in rotaxane syntheses was the development of an anion template process which led to generally high yields of [2]- and [3]rotaxanes with ether, ester, and other axles via nucleophilic substitution reactions.[4] This encouraged us to extend this template effect to other essential reactions in organic chemistry. Here we report on the successful application of anion template synthesis to the Michael addition of heteronucleophiles to various Michael acceptors. This allows creation of rotaxanes with conjugated functional groups in their axles.[5]

First we synthesized semiaxles based on acrylic (**2**) and propiolic acid motifs (**3**) (Figure 1). These Michael acceptors were then to be reacted with tritylphenolate (**1a**) or tritylthiophenolate (**1b**) anions in the presence of the tetralactam wheel **4** under basic conditions as shown in Scheme 1.[6] For the



1a: X = O
1b: X = S
2a: X = O
2b: X = NH
3a: X = O
3b: X = NH
4

Figure 1.

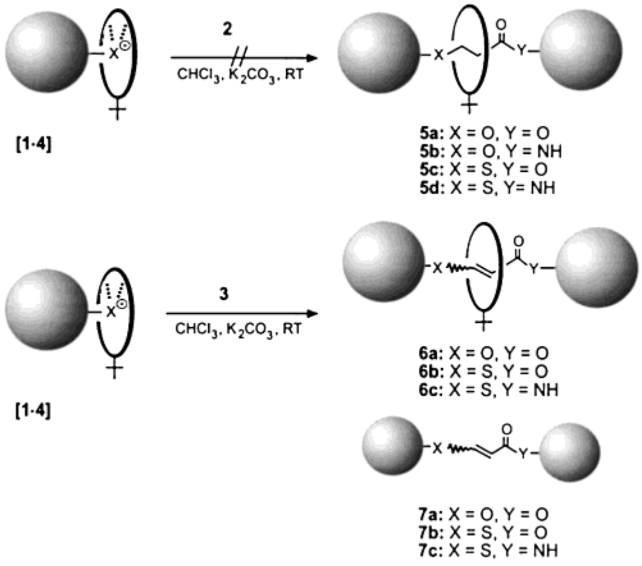
[†] Dedicated to Prof. Dr. Günther Wulff on the occasion of his 65th birthday.

[1] (a) Rotaxanes are molecules that consist of one or more wheels and penetrating axles; these are mechanically bound together and sterically prevented from dethreading by bulky stopper groups at both ends of the axles. Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1967**, *89*, 5723−5724. (b) For reviews of molecular engineering, see: Balzani, V.; Gómez-López, M.; Stoddart, J. F. *Acc. Chem. Res.* **1998**, *31*, 405−414. (c) Bissell, R. A.; Córdova, E.; Stoddart, J. F.; Tolley, M. S.; Venturi, M.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1997**, *3*, 152−170.

[2] For reviews, see: (a) Schill, G. *Catenanes, Rotaxanes, and Knots*; Academic Press: New York, 1971. (b) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2825. (c) Gibson, H. W. In *Large Ring Molecules*; Semlyen, J. A., Ed.; Wiley: Chichester, 1996; pp 191−262. (d) Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930−944. (e) Sauvage, J. P., Dietrich-Buchecker, C. O., Eds. *Molecular Catenanes, Rotaxanes and Knots*; VCH-Wiley: Weinheim, 1999.

[3] (a) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469−475. (b) Hoss, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1995**, *33*, 375−384. (c) Diederich, F.; Stang, P. J. *Templated Organic Synthesis*; Wiley-VCH: Weinheim, 1999. (d) Gerbeleu, N. V.; Arion, V. B.; Burgess, J.; *Template Synthesis of Macrocyclic Compounds*; VCH-Wiley: Weinheim, 1999. (e) Hubin, T. J.; Kolchinski, A. G.; Vance, A. L.; Busch, D. H. In *Advances in Supramolecular Chemistry*, Vol. 5; JAI Press Inc.: 1999.

10.1021/ol990350u CCC: $19.00



Scheme 1. Synthesis of [2]Rotaxanes via Michael Addition

formation of the crucial supramolecular nucleophiles[7] [**1·4**], nonpolar solvents such as dichloromethane or chloroform, high concentrations, and room temperature are favorable. According to NMR experiments, molecular recognition through hydrogen bonds is almost quantitative under these conditions.[4a]

For comparison we first performed the addition of the stoppers to the semiaxles in the absence of the wheel **4**. Neither of the stoppers **1** yielded the corresponding free axle with the acrylic acid derivatives **2**. However, the phenolate **1a** formed **7a** with the more electrophilic propiolate **3a** in 41% yield. Phenolate **1a** did not react with the less reactive propiolamide **3b**. *p*-Thiophenolate **1b**, which is the stronger nucleophile, was added to both propiolic acid derivatives to give 24% and 53% yields, respectively (Table 1). The same chemical selectivities were observed in the presence of the wheel **4** leading to the rotaxanes **6**, but with somewhat reduced yields (13−35%). Again, no reaction was observed with the acrylic acid derivatives **2** nor did **1a** react with **3b**.

Table 1. (*E/Z*) Isomer Ratio in Percent of the Free Axles **7** and the [2]Rotaxanes **6**

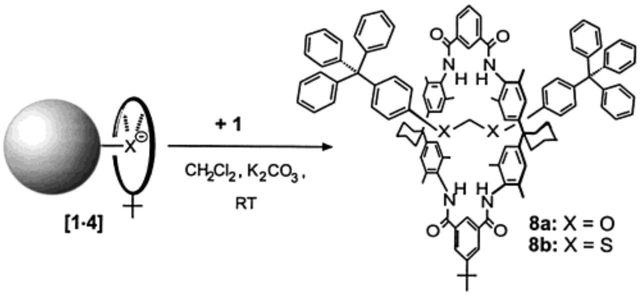
Michael adduct	yield [%]	(*E*/*Z*) ratio [%]
7a	41	63:37
7b	24	29:71
7c	53	0:100
6a	13	66:34
6b	19	22:78
6c	35	0:100

The higher yield of rotaxane **6c** as compared to those of **6a** and **6b** might in part result from hydrogen bonding between the amide group of the semiaxle **3b** and the amide groups of the wheel **4** in addition to the host/guest interactions of the wheel **4** and the thiolate **1b**.[8]

In analogy to the base-catalyzed hetero-Michael addition described in the literature,[9] the addition of the oxygen nucleophile **1a** to propiolate **3a** resulted mainly in (*E*)-**7a** while with the sulfur nucleophile **1b** (*Z*)-adducts were preferably formed (Table 1). The isomers could be easily distinguished by the ^{1}H NMR coupling constants of the olefinic protons. Integration of the signals of the free axle **7a** revealed an (*E/Z*) ratio of 63:37 ($^3J_{(E)} = 12.1{-}12.2$ Hz, $^3J_{(Z)} = 8.5{-}8.6$ Hz) whereas **7b** was isolated with an (*E/Z*) ratio of 29:71 ($^3J_{(E)} = 15.1{-}15.2$ Hz, $^3J_{(Z)} = 9.8{-}10.2$ Hz 71−78%). **7c** was formed exclusively as the (*Z*) adduct in the reaction of **1b** with **3b**.[10] In all cases the ratios of the corresponding rotaxanes were very similar to those of the free axles. This means that despite the steric hindrance of the supramolecular nucleophiles [**1·4**], there seems to be no significant control of the (*E*/*Z*) selectivity by the wheel **4**. This is particularly remarkable in the case of the (*Z*)-only addition of [**1b·4**] to **3a**.

Using dichloromethane instead of chloroform as the solvent, we isolated the corresponding acetal[2]rotaxanes **8** bearing a methylene unit in their axles as byproducts with yields of 81% (**8a**) and 23% (**8b**) (Scheme 2).[11]

Scheme 2. Synthesis of the Acetal[2]rotaxanes **8**



The attempted catalytic hydrogenation of **6a** with Pd/C did not lead to the desired [2]rotaxane with an aliphatic axle **5a**. Instead the axle was cleaved into *p*-tritylphenol **1a** and

---

(4) (a) Hübner, G. M.; Gläser, J.; Seel, C.; Vögtle, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 383−386. (b) Reuter, C.; Wienand, W.; Hübner, G. M.; Seel, C.; Vögtle, F. *Chem. Eur. J.* **1999**, *5*, 2692−2697. (c) Schmieder, R.; Hübner, G. M.; Seel, C.; Vögtle, F. *Angew. Chem., Int. Ed.* **1999**, *38*, 3528−3530. (d) Hübner, G. M.; Reuter, C.; Seel, C.; Vögtle, F. *Synthesis* **2000**, 103−108.

(5) For the end-capping of pseudorotaxanes under radical conditions, see: Takata, T.; Kawasaki, H.; Asai, S.; Furusho, Y.; Kihara, N. *Chem. Lett.* **1999**, 223−224.

(6) Because of the low acidity of common CH acids, it was not possible to use carbon nucleophiles; the strong bases needed for their deprotonation also led to a deprotonation of the carbonamide groups of wheel **4**.

(7) For complexes such as [**1·4**] the term supramolecular nucleophiles was coined, see ref 4a. The molecular recognition of the anionic stoppers results from hydrogen bonding with one of the two isophthalamide units of the wheel **4**, whose hydrogens are pointing toward the cycle's center, as shown by X-ray structure analyses: (a) Fischer, C.; Nieger, M.; Mogck, O.; Böhmer, V.; Ungaro, R.; Vögtle, F. *Eur. J. Org. Chem.* **1998**, 155−161. (b) See also: Adams, H.; Carver, F. J.; Hunter, C. A.; Osborne, N. J. A. *Chem. Commun.* **1998**, 2449−2450. (c) Clegg, W.; Gimenez-Saiz, C.; Leigh, D. A.; Murphy, A.; Slawin, A. M. Z.; Teat, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 4124−4129.

(8) For the binding of amides by hosts such as **4**, see ref 7b and Seel, C.; Parham, A. H.; Safarowsky, O.; Hübner, G. M.; Vögtle, F. *J. Org. Chem.* **1999**, *64*, 7236−7242.

p-tritylphenyl propionate under the more vigorous reaction conditions (60 °C, 3.5 bar) required. Also, as already observed with other rotaxane systems, the double bond of the rotaxane reacts more slowly as compared to the double bond in the corresponding free axle.[12]

In conclusion, it is possible to use hetero-Michael addition for the trapping syntheses of [2]rotaxanes and to improve and extend the scope of a new synthetic approach to supramolecular systems. In addition to the previously reported substitution reactions of benzyl bromides or carbonyl chlorides with anionic heteronucleophiles, this new template synthesis opens new possibilities for rotaxane syntheses and provides the basis for further developments of hitherto unknown template-controlled formations of rotaxanes, catenanes, and knots.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft. Special thanks are due to Dr. C. Schalley and Dr. C. Seel for advice.

Supporting Information Available: Experimental procedures and full characterization for compounds **2**, **3**, and **5**−**8**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL990350U

---

(9) For the addition of phenolates, see: (a) Winterfeld, E.; Preuss, H. *Chem. Ber*. **1966**, *99*, 450−458. (b) Winterfeld, E.; Krohn, W.; Preuss, H. *Chem. Ber*. **1966**, *99*, 2572−2578. (c) Ciganek, E. *J. Org. Chem.* **1980**, *45*, 1497−1505. (d) Bates; D. J.; Rosenblum, M.; Samuels, S. B. *J. Organomet. Chem.* **1981**, *209*, C55. (e) Vo-Quang, Y.; Marais, D.; Vo-Quang, L.; Le Goffic, F. *Tetrahedron Lett.* **1983**, *24*, 5209−5210. (f) Ferguson, G.; Fisher, K. J.; Ibrahim, B. E.; Ishang, C. Y.; Iskader, G. M.; Katritzki, A. R.; Parvez, M. *J. Chem. Soc., Chem. Commun.* **1983**, 1216−1217. For the addition of thiophenolates, see: (g) Truce, W. E.; Goldhamer, D. L. *J. Am. Chem. Soc.* **1959**, *81*, 5798−5800. (h) Truce, W. E.; Goldhamer, D. L.; Kruse, R. B. *J. Am. Chem. Soc.* **1959**, *81*, 4931−4934. (i) Pfaendler, H. R.; Gosteli, J.; Woodward, R. B. *J. Am. Chem. Soc.* **1979**, *101*, 6306−6310. (j) Wadsworth, D. A.; Detty, M. R. *J. Org. Chem.* **1980**, *45*, 4611−4615. (k) Corbett, D. F. *J. Chem. Soc., Chem. Commun.* **1981**, 803−804. (l) Detty, M. R.; Murray, B. J. *J. Am. Chem. Soc.* **1983**, *105*, 883−890. (m) Detty, M. R.; Murray, B. J.; Smith, D. L.; Zumbulyadis, N. *J. Am. Chem. Soc.* **1983**, *105*, 875−882.

(10) This is similar to the (*Z*)-addition of thioisocyanate to *N*-methylpropiolamide: Crow, W. D.; Leonard, N. J. *J. Org. Chem.* **1965**, *30*, 2660−2665.

(11) **8a**, see ref 4b; **8b**, see Supporting Information.

(12) Parham, A. H.; Windisch, B.; Vögtle, F. *Eur. J. Org. Chem.* **1999**, 1233−1238.