Successive catalytic reactions specific to Pd-based rotaxane complexes as a result of wheel translation along the axle†

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Rotaxane-structure-specific Pd-catalyzed rearrangement of propargyl or allyl urethane groups to oxazolidinone moieties proceeded efficiently. The conversion took place successively by the translation of the wheel along the axle, thus providing a novel macrocyclic catalytic system.

The mechanical axle-wheel linkage that is characteristic of rotaxanes[1] has the potential to be utilized in catalytic systems. Rowan *et al*. have reported polyene epoxidation on the axle catalyzed by a manganese porphyrin-functionalized wheel.[2] In this system, the translation of the wheel along the axle component enabled a catalytic reaction. In addition, we have previously reported asymmetric benzoin condensations catalyzed by thiazolium-functionalized [2]rotaxanes,[3] which induced through-space enantioselective catalysis. Rotaxane catalysts are associated with "macrocyclic catalysts" like λ-exonuclease for DNA duplex formation[4] and with "linear molecular motors,"[5] which are regarded to be one of the major targets of rotaxane chemistry. The unique rotaxane catalysis prompted us to design a novel rotaxane-based catalytic system that exploits the versatility of transition metals using a Pd-containing macrocycle. We believe that such rotaxane catalysts will be applicable in a variety of fruitful systems such as polymer modification, substrate-specific reactions, and linear molecular motors (Fig. 1).[6,7]

Herein, we describe the highly efficient successive catalysis on the axle component of our Pd-based rotaxanes and the application of these complexes to establish an unprecedented "macrocyclic catalyst" system.

The [2]rotaxanates containing propargyl urethane and allyl urethane moieties (**3** and **6**) were prepared according to our reported method with slight modifications (Scheme 1).[7,8]

During the recrystallization process of **3**, we unexpectedly found that the cyclization reaction of the propargyl urethane moiety produced the cyclic derivative **9** only by heating in MeOH. The process formally involves two hydroamination reactions of the urethane N–H to the alkyne group.[9] The structure of **9** was examined by IR, NMR, and MS spectra and finally determined by X-ray single crystal structure analysis (Fig. 2).[10] The X-ray analysis indicated that the newly formed double bond adopted a *syn*-conformation, possibly due to steric constraint from the macrocycle component; this finding was also supported by a CPK model study. The hydroamination of **3** was performed under various conditions and the results are summarized in Table 1. While protic and small-size solvents such as MeOH and H_2O were absolutely indispensable for the reaction (Entries 1, 2, and 5), a prolonged reaction time also worked effectively under base-free conditions. After considerable elaborations, $Mg(OMe)_2$ was found to be the most suitable cocatalyst (Entries 9 and 10) to shorten the reaction time and give **9** in a high yield.

Allyl-urethane-functionalized [2]rotaxanate **6** was *quantitatively* converted to the cyclization product by the same procedure (Scheme 2). The product consisted of two compounds: *syn*–*anti* diastereomers **10** and **11** (1 : 1) with chiral centers at the oxazolidinone moieties. The diastereomers were separated by chromatography and analyzed by ^{1}H NMR (Fig. 3) and structure simulation by DFT calculations (6-31G**, B3LYP).[10]

The much higher conversion of **6** relative to that of **3** is possibly due to not only the high reactivity of the olefin moiety to hydroamination, but also due to the higher stability of the oxazolidinone moiety of **10** and **11** in basic conditions compared with that of the oxazolidone moiety of **9**.

As shown in ^{1}H NMR spectra (Fig. 3), the key signals of the olefinic protons and urethane N–H protons of **6** clearly appeared in toluene-d_8 at 100 °C, while these signals in $CDCl_3$

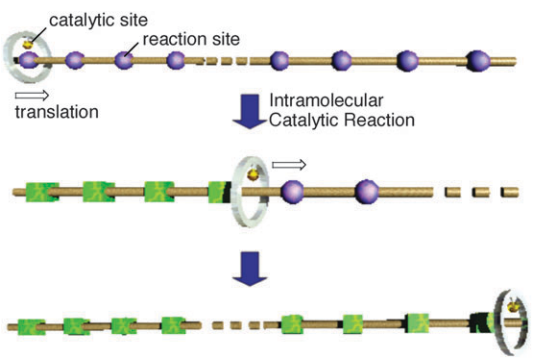

Fig. 1 Design of movable catalyst system.

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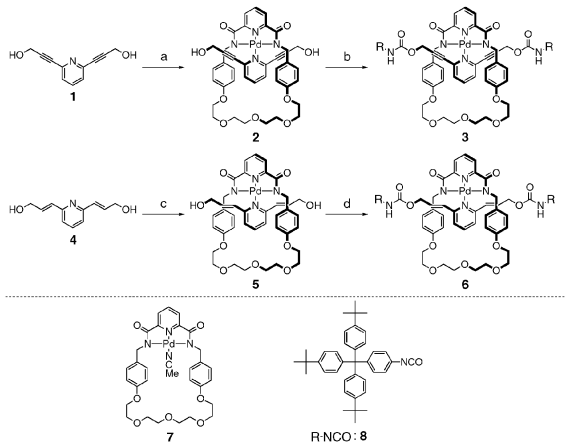


Scheme 1 *Reagents and Conditions*: (a) macrocycle **7** (1.0 equiv.), CH_2Cl_2, RT, 1 h; (b) R-NCO **8** (2.1 equiv.), DBTDL (0.1 equiv.), CH_2Cl_2, RT, 1 h (84%, 2 steps); (c) macrocycle **7** (1.0 equiv.), CH_2Cl_2, RT, 1 h; (d) R-NCO **8** (2.1 equiv.), DBTDL (0.1 equiv.), CH_2Cl_2, RT, 1 h (83%, 2 steps). DBTDL: dibutyltin dilaurate.

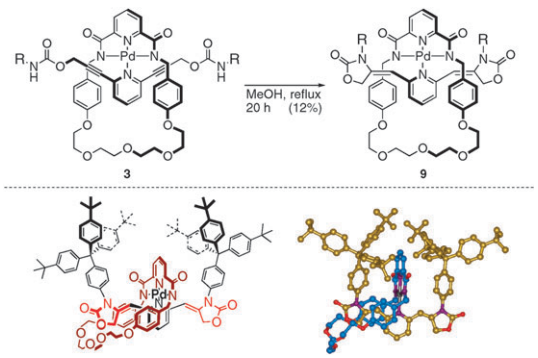
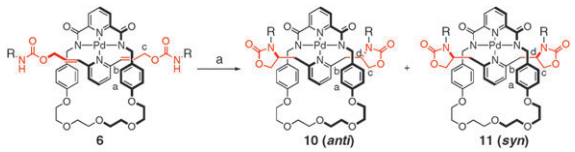


Fig. 2 X-Ray crystal structure of Pd-rotaxanate **9**.

at room temperature disappeared owing to the coalescent rotamers. The olefin and urethane signals of **6** disappeared as methine (signal d) and methylene protons (signal c) of the oxazolidinone moieties appeared. The aromatic proton signals of the wheel component of **10** (signals a and b) were split into two couplets, contrary to the aromatic proton signals of **11**. This is possibly a result of the structural asymmetry of the axle component relative to the wheel component in **10**, as is confirmed by the simulated structures.[10]



Scheme 2 *Reagents and Conditions*: (a) $Mg(OMe)_2$ (0.4 M in MeOH), reflux, 10 min (99%, **10**:**11** = 1 : 1).

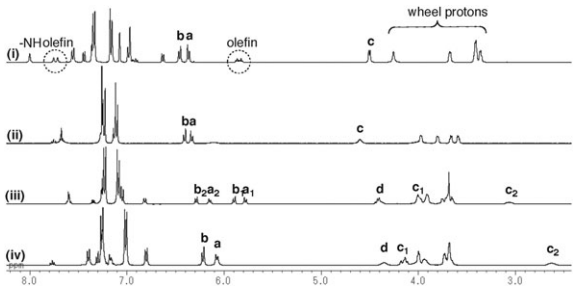


Fig. 3 Partial ^{1}H NMR spectra (400 MHz) of **6** (i) toluene-d_8 at 398 K(ii) $CDCl_3$ at 298 K, **10** (iii) $CDCl_3$ at 298 K, and **11** (iv) $CDCl_3$ at 298 K.

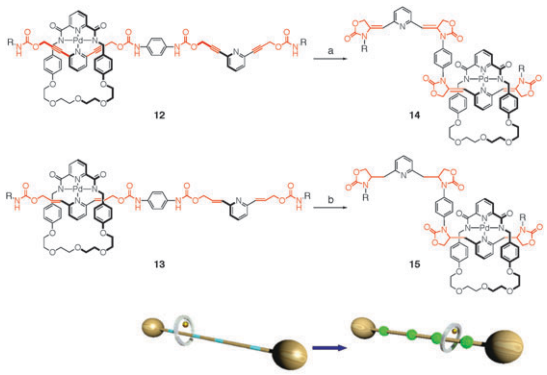
Based on these selective reactions, rotaxanates with two pyridine groups, four reactive points in the axle, and a Pd-containing macrocyclic component were synthesized (**12** and **13**, Scheme 3). Through investigation with variable temperature ^{1}H NMR (VT-NMR), we found that the wheel component of **12** and **13** could alternate between the pyridine stations on the axle, namely the macrocycle transports the Pd metal along the axle.[11] The hydroaminations of **12** and **13** were conducted under similar conditions to those of **3** and **6** (Scheme 3).

A solution of **12** in MeOH–THF was refluxed for 1 min in the presence of $Mg(OMe)_2$.[12] Repeated purification with preparative HPLC afforded a product in a low yield (16%), which was eventually determined to be isomerized rotaxanate **14**. Similar to the conversion of **3** to **9**, the four propargyl urethane moieties of **12** were all converted to oxazolidone moieties, as is suggested by the spectroscopic and elemental analyses of **14**. Contrary to the conversion of **12** to **14**, treatment of **13** with $Mg(OMe)_2$ for 90 min afforded isomerized rotaxanate **15** in a *quantitative* yield, which proves that the translation of the macrocyclic catalyst enabled a clean successive reaction.

Table 1 Effects of solvents and additives for macrocycle-catalyzed hydroamination reaction of Pd-rotaxanate **3**

Entry	Solvent	Additive (equiv.)	Temp.	Time/h	Yield (%)
1	MeOH	—	Reflux	20	12
2	EtOH	—	Reflux	20	33
3	*i*-PrOH	—	Reflux	27	NR[a]
4	*t*-BuOH	—	Reflux	22	NR[a]
5	MeOH–H_2O (20 : 1)	—	Reflux	20	63
6	THF	Et_3N (2.0)	Reflux	24	Decomp.
7	THF	PPh_3 (2.0)	Reflux	39	NR[a]
8	THF–H_2O (20 : 1)	NaOH[b]	Reflux	1	10
9	MeOH	$Mg(OMe)_2$[c]	Reflux	10 min	48
10	MeOH–H_2O (4 : 1)	$Mg(OMe)_2$[c]	Reflux	10 min	68

[a] No reaction. [b] 0.01 M. [c] 0.4 M.

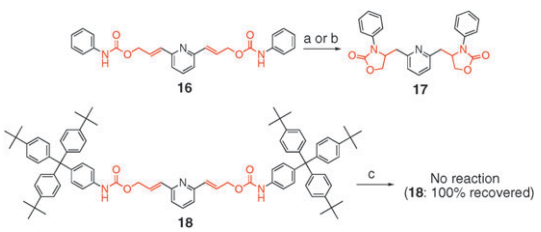


Scheme 3 *Reagents and Conditions*: (a) $Mg(OMe)_2$ (0.4 M in MeOH–THF), reflux, 1 min (16%); (b) $Mg(OMe)_2$ (0.4 M in MeOH–THF), reflux, 90 min (99%).

Thus, products **14** and **15** were formed by *successive catalytic isomerization* caused by the translation of the Pd-carrying wheel along the axle component. VT-NMR analyses revealed that the wheel component of [2]rotaxane **15**, together with the Pd atom, could alternate between pyridine moieties on the axle. On the other hand, the central axle *p*-phenylene bisoxazolidone moiety of **14** was too bulky to allow for translation of the wheel. This is consistent with the low conversion yield of **12**.

From the efficient successive transformation described above, we postulated that native wheel component **7** alone enables the *intermolecular* catalytic reaction where size-selection of the substrate can occur if the rotaxane-like intermediate is formed. To investigate this theory, model reactions were carried out using two substrates that possessed two allyl urethane moieties: simple substrate **16** and end-bulky substrate **18** (Scheme 4). The intermolecular hydroamination of **16** with a stoichiometric amount of **7** in the presence of $Mg(OMe)_2$ smoothly proceeded to give the cyclization compound **17** in a quantitative yield. This reaction required a much greater time than the rotaxane system. The use of a catalytic amount of **7** (20 mol%) also achieved a quantitative yield at 50 °C in the presence of $Mg(OMe)_2$ (0.8 M in MeOH). On the other hand, no reaction occurred when **18** was similarly treated with **7**. These results indicate that Pd-templated macrocyclic catalyst **7** leads to the enzyme-like substrate-specific reaction of **16** to form **17**, in which the penetration of the substrate into the cavity of **7** possibly accelerates the reaction.[13]

Thus, we found that a Pd-based rotaxane skeleton is critical to accelerating the above hydroamination reactions.



Scheme 4 *Reagents and Conditions*: (a) **7** (100 mol% to **16**), $Mg(OMe)_2$ (0.4 M in MeOH), 30 °C, 30 h (99%); (b) **7** (20 mol% to **16**), $Mg(OMe)_2$ (0.8 M in MeOH), 50 °C, 19 h (99%); (c) **7** (100 mol% to **18**), $Mg(OMe)_2$ (0.4 M in MeOH), 30 °C, 30 h (N.R.).

Successive catalytic reactions on the rotaxane axle using this unique system might provide new insights into selective conversion reactions, efficient polymer transformations, and linear molecular motor systems. The scope and limitations of catalytic reactions with Pd-based rotaxanes would be an important focus for future investigations.

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12 The prolonged reaction time resulted in the decrease of yield, due to solvolysis of the oxazolidone moieties of **14**.

13 Treatment of **16** and **18** with an acyclic Pd catalyst with a similar structure to that of **7** but without the tetra(ethyleneoxy) moiety, gave cyclization products (50 °C, 19 h), respectively. This result undoubtedly confirms the essential significance of the macrocyclic catalyst in the size-selective reaction.

