ORGANIC LETTERS

2011
Vol. 13, No. 15
3774–3777

[3]Rotaxane-Based Dinuclear Palladium Catalysts for Ring-closure Mizoroki−Heck Reaction

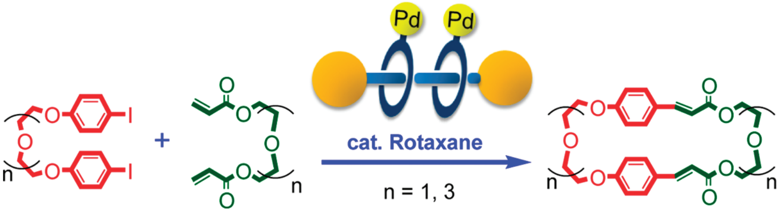
Yuji Suzaki, Kyoichi Shimada, Eriko Chihara, Takashi Saito, Yoshitaka Tsuchido, and Kohtaro Osakada*

Chemical Resources Laboratory R1-3, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503, Japan

kosakada@res.titech.ac.jp

Received March 8, 2011

ABSTRACT



[3]Rotaxane containing two Pd centers in the cyclic compounds catalyzes a Mizoroki−Heck reaction of substrates with two iodophenyl groups with bisacrylate. Formation of the cyclic products is enhanced by the rotaxane catalyst more smoothly than $Pd(OAc)_2$.

Mechanically interlocked molecular systems such as rotaxanes and catenanes have attracted increasing attention due to the unique bonding and structure and a prototype of molecular machines.[1−3] Rotaxane-based molecular shuttles[4,5] are employed as intelligent materials such as molecular devices,[6] solids with functional surface,[7] and topological gels.[8] There have been fewer reports for rotaxanes bearing a reactive site.[9−11] Epoxidation of polybutadiene[9] and asymmetric hydrogenation of enamides[11] were achieved by using rotaxanes containing manganese porphyrin and a Rh complex, as the respective catalysts. Reactions involving transformation of the rotaxane structure were also reported.[12−14] Rotaxanes having multiple reaction sites would provide the catalysts in which individual motion of the component molecules changes the structure and relative position of the active sites. Here we report catalyst with the [3]rotaxane structure containing two cyclic components equipped with a Pd center. The

---

(1) Sauvage, J.−P.; Dietrich-Buchecker, C. In *Molecular Catenanes, Rotaxanes and Knots*; Wiley-VCH: Weinheim, 1999.

(2) (a) Jäger, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930. (b) Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1959. (c) Hubin, T. J.; Busch, D. H. *Coord. Chem. Rev.* **2000**, *200*−*202*, 5. (d) Huang, F.; Gibson, H. W. *Prog. Polym. Sci.* **2005**, *30*, 982. (e) Lehn, J.-M. *Chem. Soc. Rev.* **2007**, *36*, 151. (f) Stoddart, J. F. *Chem. Soc. Rev.* **2009**, *38*, 1802. (g) De Greef, T. F. A.; Smulders, M. M. J.; Wolffs, M.; Schenning, A. P. H. J.; Sijbesma, R. P.; Meijer, E. W. *Chem. Rev.* **2009**, *109*, 5687. (h) Harada, A.; Hashidzume, A.; Yamaguchi, H.; Takashima, Y. *Chem. Rev.* **2009**, *109*, 5974. (i) Niu, Z.; Gibson, H. W. *Chem. Rev.* **2009**, *109*, 6024. (j) Fang, L.; Olson, M. A.; Benítez, D.; Tkatchouk, E.; Goddard, W. A., III; Stoddart, J. F. *Chem. Soc. Rev.* **2010**, *39*, 17. (k) Durola, F.; Sauvage, J.-P.; Wenger, O. S. *Coord. Chem. Rev.* **2010**, *254*, 1748. (l) Hänni, K. D.; Leigh, D. A. *Chem. Soc. Rev.* **2010**, *39*, 1240.

(3) (a) Osakada, K.; Sakano, T.; Horie, M.; Suzaki, Y. *Coord. Chem. Rev.* **2006**, *250*, 1012. (b) Suzaki, Y.; Taira, T.; Osakada, K.; Horie, M. *Dalton Trans.* **2008**, 4823. (c) Suzaki, Y.; Taira, T.; Osakada, K. *J. Mater. Chem.* **2011**, *21*, 931.

(4) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133.

(5) (a) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348. (b) Special issue on molecular machines: *Acc. Chem. Res.* 2001, *34*, 409.

(6) Collier, C. P.; Wong, E. W.; Belohradský, M.; Raymo, F. M.; Stoddart, J. F.; Kuekes, P. J.; Williams, R. S.; Heath, J. R. *Science* **1999**, *285*, 391.

(7) Berná, J.; Leigh, D. A.; Lubomska, M.; Mendoza, S. M.; Pérez, E. M.; Rudolf, P.; Teobaldi, G.; Zerbetto, F. *Nature Mater.* **2005**, *4*, 704.

(8) (a) Okumura, Y.; Ito, K. *Adv. Mater.* **2001**, *13*, 485. (b) Oku, T.; Furusho, Y.; Takata, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 966.

(9) Thordarson, P.; Bijsterveld, E. J. A.; Rowan, A. E.; Nolte, R. J. M. *Nature* **2003**, *424*, 915.

(10) Tachibana, Y.; Kihara, N.; Takata, T. *J. Am. Chem. Soc.* **2004**, *126*, 3438.

(11) Hattori, G.; Hori, T.; Miyake, Y.; Nishibayashi, Y. *J. Am. Chem. Soc.* **2007**, *129*, 12930.

(12) Sato, T.; Takata, T. *Polymer J.* **2009**, *41*, 470.

(13) Cantrill, S. J.; Grubbs, R. H.; Lanari, D.; Leung, K. C.-F.; Nelson, A.; Poulin-Kerstien, K. G.; Smidt, S. P.; Stoddart, J. F.; Tirrell, D. A. *Org. Lett.* **2005**, *7*, 4213.

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

10.1021/ol201357b

catalytic properties for a ring-closing Mizoroki−Heck reaction of difunctionalized substrates are studied in detail.

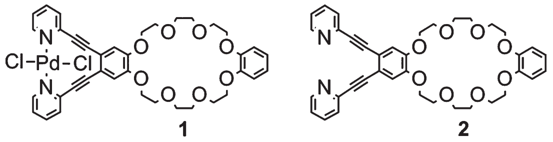


Figure 1. 1,2-Bis(pyridylethynyl)benzene-containing crown ether and its palladium complex.

Figure 1 shows the structure of palladium-containing crown ether, **1**, used in this study. The ligand **2** was prepared by ring-closure Williamson ether synthesis of C_6H_4-1,2-{(O-$CH_2CH_2)_3OTs\}_2$ and C_6H_2-1,2-I_2-4,5-$(OH)_2$, giving diiododibenzo[24]crown-8 (DB24C8−I_2), and by its subsequent Sonogashira reaction with 2-ethynylpyridine.[15,16] Reaction of **2** with $PdCl_2$(cod) (cod = 1,5-cyclooctadiene) at 100 °C yielded Pd complex **1** in 92%.[15,17] Figure 2 shows the structure of **1** obtained from X-ray crystallography. The Pd center of **1** adopts a square planar coordination, and the two Cl ligands are located at *trans* positions. The ^{1}H NMR signal of H6-pyridyl hydrogen of **1** (δ 8.86, in $CDCl_3$) was observed at lower magnetic field position than that of **2** (δ 8.62).

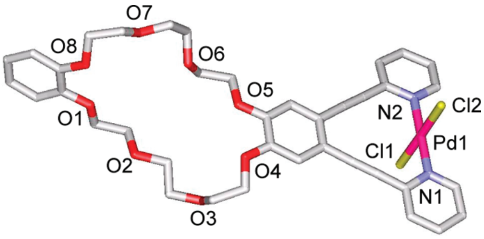


Figure 2. Structure of **1** obtained by X-ray crystallography. Hydrogen atoms and incorporated solvent molecule (*N*-methylpyrrolidone, NMP) were omitted.

Scheme 1 summarizes the synthesis of a [3]rotaxane bearing **1** as the macrocyclic component. Homometathesis reaction of $[FcCH_2NH_2CH_2C_6H_4\text{-}4\text{-}OCH_2CH_2CH{=}CH_2]PF_6$ (**3**, Fc = $Fe(C_5H_4)(C_5H_5)$) catalyzed by (H_2I-Mes)$(PCy_3)Cl_2RuCHPh$ (H_2IMes = *N*,*N*-bis(mesityl)-4,5-dihydroimidazol-2-ylidene) in the presence of **1** produced dicationic [3]rotaxane **4** in 62% isolated yield.[18−21] The ^{1}H NMR spectrum of **4** contains the NCH_2 hydrogen signal at δ 4.38 and 4.43.[22] The lower magnetic field position of the signal than that of **3** (δ 4.02, 4.04) is attributed to the hydrogen bonds between NCH_2 hydrogen and oxygen atoms of the crown ether. The broadened vinylene hydrogen signal of **4** (δ 5.38) suggests the presence of *trans* and *cis* isomers of the vinylene groups of the axle component of [3]rotaxane.[23]

Scheme 1. Synthesis of [3]Rotaxane, **4**

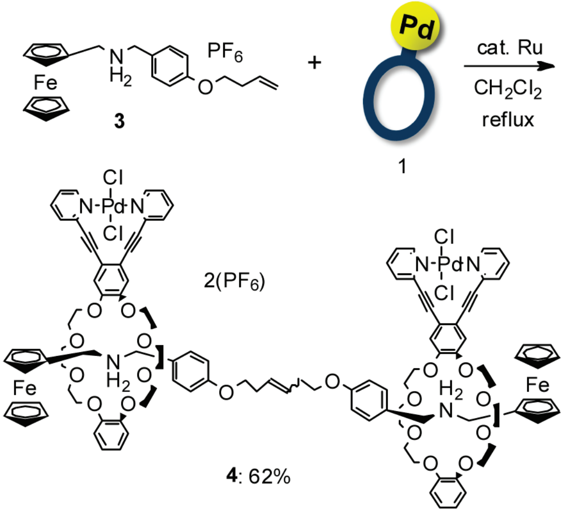
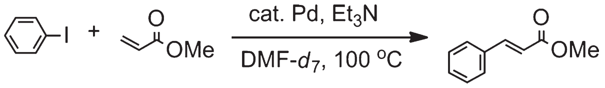


Table 1. Mizoroki−Heck Reaction of Iodobenzene with Methyl Acrylate Using **1** and **4** as the Catalyst[a]



run	catalyst, mol %	yield after 72 h (%)[b]	k_{obsd} /s^{-1}[c]
1	**1**, 1.0	72	2.3×10^{-4}
2	**4**, 0.5	68	3.6×10^{-4}

[a] Reaction conditions: $[PhI]_0$ = [methyl acrylate]$_0$ = 5.0 mM, $[Et_3N]$ = 40 mM, DMF-d_7 solvent. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by the plots assuming the first-order kinetics.

Table 1 summarizes the results of the catalytic Mizoroki-Heck reactions of iodobenzene with methyl acrylate in DMF-d_7. It was conducted to test the catalytic ability of the Pd complexes.[24−26] Both the reactions catalyzed by **1** and by **4** yielded methyl cinnamate. Time profiles of the

---

(15) Hu, Y.-Z.; Chamchoumis, C.; Grebowicz, J. S.; Thummel, R. P. *Inorg. Chem.* **2002**, *41*, 2296.

(16) (a) Mori, A.; Mohamed Ahmed, M. S.; Sekiguchi, A.; Masui, K.; Koike, T. *Chem. Lett.* **2002**, 756. (b) Mohamed Ahmed, M. S.; Sekiguchi, A.; Masui, K.; Mori, A. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 160.

(17) Bosch, E.; Barnes, C. L. *Inorg. Chem.* **2001**, *40*, 3097.

(18) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18.

(19) Coumans, R. G. E.; Elemans, J. A. A. W.; Thordarson, P.; Nolte, R. J. M.; Rowan, A. E. *Angew. Chem., Int. Ed.* **2003**, *42*, 650.

(20) Hannam, J. S.; Kidd, T. J.; Leigh, D. A.; Wilson, A. J. *Org. Lett.* **2003**, *5*, 1907.

(21) (a) Suzaki, Y.; Osakada, K. *Chem. Lett.* **2006**, *35*, 374. (b) Suzaki, Y.; Osakada, K. *Dalton Trans.* **2007**, 2376. (c) Suzaki, Y.; Chihara, E.; Takagi, A.; Osakada, K. *Dalton Trans.* **2009**, 9881.

(22) Ashton, P. R.; Campbell, P. J.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tasker, P. A.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1865.

(23) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360.

(24) (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320.

(25) Oestreich, M. *The Mizoroki-Heck Reaction*; Wiley: Weinheim, 2009.

(26) Mizoroki-Heck reaction of aryl halides and *tert*-butyl acrylate catalyzed by dichloro{bis(pyridylethynylbenzene)}palladium(II) complex: Kawano, T.; Shinomaru, T.; Ueda, I. *Org. Lett.* **2002**, *4*, 2545.

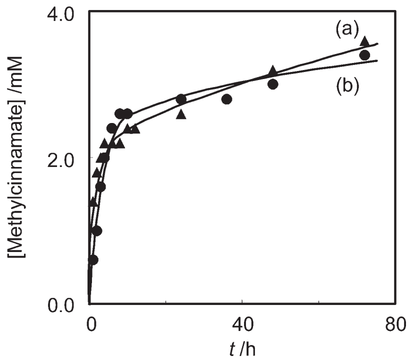
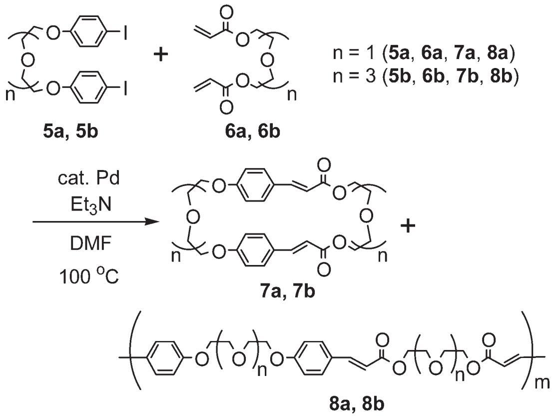


Figure 3. Profile of the reaction of iodobenzene with methyl acrylate catalyzed by (a) **1** (1 mol %) and (b) **4** (0.5 mol %) in DMF-d_7 at 100 °C ($[\text{iodobenzene}]_0$ = $[\text{methylacrylate}]_0$ = 5.0 mM).

reactions are shown in Figure 3. The reaction catalyzed by **1** formed the product in 72% after 72 h, and the first-order rate constant was determined to be $k_{\text{obsd}} = 2.3 \times 10^{-4}\ \text{s}^{-1}$ at 100 °C. The reaction catalyzed by dinuclear rotaxane catalyst **4** proceeds with a larger rate constant ($k_{\text{obsd}} = 3.6 \times 10^{-4}\ \text{s}^{-1}$), and gives the product in 68%.

The Pd complex **4** and $Pd(OAc)_2$ were employed as catalysts for the Mizoroki–Heck reactions of difunctionalized substrates, diethyleneglycol{di(4-iodo-phenyl)} (**5a**) and diethyleneglycol(diacrylate) (**6a**), as well as that of **5b** with **6b**.[27] Rotaxane **4** catalyzes the reaction of **5a** with **6a** ($[\mathbf{5a}]_0 = [\mathbf{6a}]_0 = 5.0$ mM) to yield the cyclic product **7a** (45%) and polymer **8a** (28%) after 48 h, indicating that the 1:1 cyclization reaction and polycondensation occur independently (Table 2, run 1). The reaction catalyzed by $Pd(OAc)_2$ yields **7a** in lower yield (32%, run 2). Similar results are obtained for the reaction of **5b** with **6b**, which yields 40 membered crown ether **7b**. Figure 4 depicts the profile of the reactions. The reaction of **5a** with **6a** catalyzed by rotaxane catalyst **4** takes place much more rapidly than that catalyzed by $Pd(OAc)_2$ (Figure 4a and b), although the difference in the final yield of the product is not large. Formation of the cyclic compound **7b** catalyzed by **4** (Figure 4c) is also much faster than the reaction catalyzed by $Pd(OAc)_2$. These results indicate that the cyclization is enhanced by the rotaxane catalyst efficiently.[28]

Table 2. Ring-closing Mizoroki–Heck Reaction Using Pd Catalyst **4** and $Pd(OAc)_2$[a]



run	substrate	catalyst[b]	yield (%)[c] after 48 h	
			7a, 7b	**8a, 8b**[d]
1	**5a, 6a**	**4**	45%	28%
2	**5a, 6a**	$Pd(OAc)_2$	32%	28%
3	**5b, 6b**	**4**	62%	14%
4	**5b, 6b**	$Pd(OAc)_2$	54%	10%

[a] Reaction conditions: **5a** and **6a** (or **5b** and **6b**) (5.0 mM), Et_3N (20 mmol), DMF solvent, 100 °C. [b] **4** = 1.0 mol %, $Pd(OAc)_2$ = 2.0 mol % (4.0 mol % of PPh_3 was added to $Pd(OAc)_2$). [c] NMR yield. [d] Molecular weights of **8a** and **8b** were determined to be M_n = 1000–2500 by GPC based on polystyrene standards.

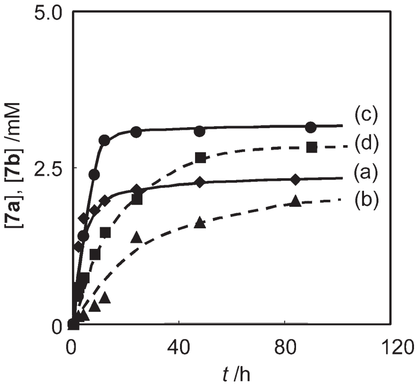


Figure 4. Profile of the reaction of **5a** with **6a** (*n* = 1) catalyzed by (a) **4** (1.0 mol %) and (b) $Pd(OAc)_2$ (2.0 mol %) and the reaction of **5b** with **6b** (*n* = 3) catalyzed by (c) **4** (1.0 mol %) and (d) $Pd(OAc)_2$ (2.0 mol %). The reactions were carried out in DMF-d_7 at 100 °C.

Figure 5 depicts two possible intermediates for the ring closure, giving **7a** (or **7b**). Intermediate **A**, having a single Pd center, causes insertion of a vinyl group at the end of the organic ligand formed by initial Mizoroki–Heck reaction into the Pd–aryl bond. Intermediate **B** can be proposed for the reaction catalyzed by the rotaxane catalyst, and undergoes analogous intramolecular insertion of the terminal vinyl group into the Pd–C bond.

The structure as well as limited flexibility of the ligand is suited for the cyclization rather than the

---

(27) Polycondensation polymerization of **8** and divinylbenzene by Mizoroki–Heck reaction: Suzuki, M.; Lim, J.-C.; Saegusa, T. *Macromolecules* **1990**, *23*, 1574.

(28) A reviewer of this paper kindly suggested that comparison of the results using two rotaxane catalysts with different distance between the two Pd centers would clarify the effects of the rotaxane structure to the catalytic activity and selectivity. We conducted the reaction of the difunctional substrates with different spacer lengths to address these comments. Runs 1 and 3 in Table 2 show different yields of the cyclic product, but a similar tendency is observed also for the reaction catalyzed by $Pd(OAc)_2$ (runs 2 and 4). Thus, comparison of the product yields did not provide useful information on the reaction details in this case.

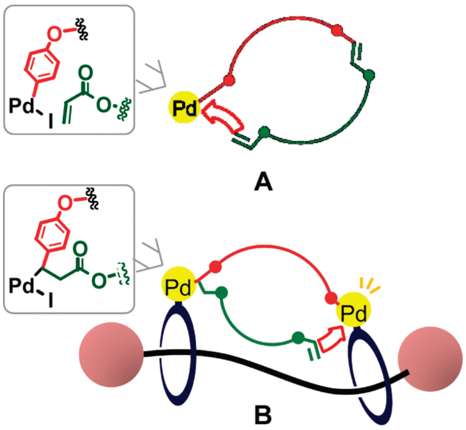


Figure 5. Plausible intermediates for the ring-closure in the reaction of **5a** (**5b**) with **6a** (**6b**).

intermolecular insertion of a new substrate, leading to the polycondensation.

In summary, we have demonstrated that the dinuclear Pd catalysts with [3]rotaxane structures catalyze the Mizoroki-Heck reaction of bifunctional substrates to produce the cyclic product as the major one. Their dinuclear structure supported by the rotaxane template contributes to the ring-closure reaction. Further studies on new reactions catalyzed by the Pd-containing rotaxanes are now underway.

Acknowledgment. We thank the Center for Advanced Materials Analysis, Technical Department, Tokyo Institute of Technology for elemental analysis and for mass measurement. This work was supported by Grant-in-Aid for Scientific Research for Young Scientists (21750058) and for Scientific Research on Innovative Areas "The Coordination Programming" (22108509) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Supporting Information Available. Experimental section and X-ray data for **1**. This material is available free of charge via the Internet at http://pubs.acs.org.