ORGANIC LETTERS

2013
Vol. 15, No. 14
3742–3745

An Amphiphilic Pillar[5]arene as Efficient and Substrate-Selective Phase-Transfer Catalyst

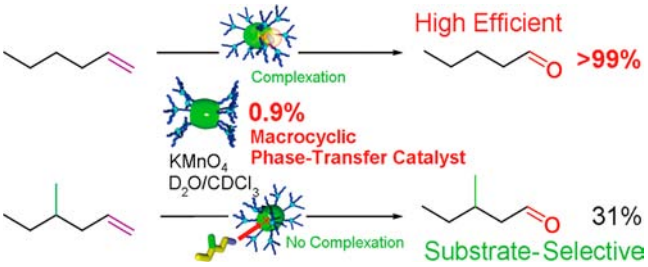
Tomoki Ogoshi,* Naosuke Ueshima, and Tada-aki Yamagishi

Graduate School of Natural Science and Technology, Kanazawa University,
Kakuma-machi, Kanazawa, 920-1192, Japan

ogoshi@se.kanazawa-u.ac.jp

Received June 12, 2013

ABSTRACT



An amphiphilic macrocyclic compound consisting of 10 tetra-alkyl phosphonium bromide groups and a pillar[5]arene core was prepared. This compound was soluble in both aqueous and organic media and acted as a highly efficient and substrate-selective phase-transfer catalyst. In particular, oxidation of the linear alkene1-hexene to 1-pentanal by $KMnO_4$ was >99%, whereas that of the branched alkene 4-methyl-1-hexene was only 31%, under ideal conditions.

Phase transfer catalysts (PTCs) embody the ideals of organic synthesis by providing a simple, cheap, and general protocol for various reactions.[1−4] PTCs allow reactions to proceed through active transport of polar reagents from one phase to another. Amphiphilic small organic molecules such as quaternary ammonium compounds, crown ethers, phosphonium compounds, and pyridinium compounds are generally used as PTCs. Design of new smart PTCs with additional advantages and functions is a new research target.[4] In this letter, we report a new PTC containing a macrocyclic structure (pillar[5]arene) in the core. Pillar[5]arenes[5−9] are new macrocyclic hosts that were first reported by our group[5] and are good hosts for linear guests in organic[7] and aqueous media.[8] Pillar[5]arene has

---

(1) (a) *Phase-Transfer Catalysis: New Chemistry, Catalysts, and Applications*; American Chemical Society: Washington, DC, 1985. (b) Starks, C. M.; Liotta, C. L.; Halpern, M. *Phase-Transfer Catalysis: Fundamentals, Applications and Industrial Perspectives*; Chapman and Hall: New York, 1994. (c) *Phase-Transfer Catalysis: Mechanisms and Syntheses*; Halpern, M. E., Ed.; American Chemical Society: Washington, DC, 1997. (d) Makosza, M.; Fedorynski, M. In *Interfacial Catalysis*; Volkov, A. G., Ed.; Marcel Dekker: New York, 2003; pp 150−201. (e) Chen, L. L.; Yan, Z. *Org. Lett.* **2012**, *14*, 784–787. (f) Denmark, S. E.; Weintraub, R. C.; Gould, N. D. *J. Am. Chem. Soc.* **2012**, *134*, 13415–13429.

(2) (a) Eller, L. R.; Stępień, M.; Fowler, C. J.; Lee, J. T.; Sessler, J. L.; Moyer, B. A. *J. Am. Chem. Soc.* **2007**, *129*, 11020–11021. (b) Shin, J. A.; Lim, Y. G.; Lee, K. H. *J. Org. Chem.* **2012**, *77*, 4117–4122. (c) Sala, G. D.; Nardone, B.; Riccardis, F. D.; Izzo, I. *Org. Biomol. Chem.* **2013**, *11*, 726–731. (d) Hooley, R. J.; Biros, S. M.; Rebek, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 3517–3519.

(3) (a) Lee, D. G.; Chang, V. S. *J. Org. Chem.* **1978**, *43*, 1532–1536. (b) Starks, C. M. *J. Am. Chem. Soc.* **1971**, *93*, 195–199.

(4) (a) Hashimoto, T.; Maruoka, K. *Chem. Rev.* **2007**, *107*, 5656–5682. (b) Maruoka, K.; Ooi, T. *Chem. Rev.* **2003**, *103*, 3013–3028.

(5) Ogoshi, T.; Kanai, S.; Fujinami, S.; Yamagishi, T.; Nakamoto, Y. *J. Am. Chem. Soc.* **2008**, *130*, 5022–5023.

(6) Reviews: (a) Ogoshi, T. *J. Incl. Phenom. Macrocycl. Chem.* **2012**, *72*, 247–262. (b) Ogoshi, T.; Yamagishi, T. *Bull. Chem. Soc. Jpn.* **2013**, *86*, 312–332. (c) Ogoshi, T.; Yamagishi, T. *Eur. J. Org. Chem.* **2013**, 2961–2975. (d) Cragg, P. J.; Sharma, K. *Chem. Soc. Rev.* **2012**, *41*, 597–607. (e) Xue, M.; Yang, Y.; Chi, X.; Zhang, Z.; Huang, F. *Acc. Chem. Res.* **2012**, *45*, 1294–1308.

(7) (a) Ogoshi, T.; Demachi, K.; Kitajima, K.; Yamagishi, T. *Chem. Commun.* **2011**, *47*, 10290–10292. (b) Zhang, Z.; Luo, Y.; Chen, J.; Dong, S.; Yu, Y.; Ma, Z.; Huang, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1397–1401. (c) Li, C.; Xu, Q.; Li, J.; Yao, F.; Jia, X. *Org. Biomol. Chem.* **2010**, *8*, 1568–1576. (d) Shu, X.; Fan, J.; Li, J.; Wang, X.; Chen, W.; Jia, X.; Li, C. *Org. Biomol. Chem.* **2012**, *10*, 3393–3397. (e) Strutt, N. L.; Forgan, R. S.; Spruell, J. M.; Botros, Y. Y.; Stoddart, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 5668–5671.

(8) (a) Ogoshi, T.; Hashizume, M.; Yamagishi, T.; Nakamoto, Y. *Chem. Commun.* **2010**, 3708–3710. (b) Hu, X. B.; Chen, L.; Si, W.; Yu, Y.; Hou, J. L. *Chem. Commun.* **2011**, *47*, 4694–4696. (c) Ma, Y.; Ji, X.; Xiang, F.; Chi, X.; Han, C.; He, J.; Abliz, Z.; Chen, W.; Huang, F. *Chem. Commun.* **2011**, *47*, 12340–12342. (d) Yao, Y.; Xue, M.; Chi, X.; Ma, Y.; He, J.; Abliz, Z.; Huang, F. *Chem. Commun.* **2012**, *48*, 6505–6507.

10.1021/ol4016546

10 reactive sites at its rims, and introduction of functional groups on these rims affects the physical properties of the pillar[5]arene because these groups cover the core.[9] In this study, we prepared a pillar[5]arene derivative containing 10 phosphonium cations **1** (Figure 1). Thanks to the phosphonium cations, **1** was soluble in a wide variety of solvents. Here, we report the very efficient PTC properties and substrate selectivity of **1** based on the host−guest chemistry of pillar[5]arene.

The new amphiphilic pillar[5]arene **1** was obtained as a white solid in 95% yield by reacting **2**[10] with excess tributylphosphine. **1** was soluble in a wide variety of solvents including water, alcohols, acetone, tetrahydrofuran, chloroform, acetonitrile, DMF, and DMSO and insoluble in hexane and diethyl ether. Based on this amphiphilicity, we investigated the oxidation of alkenes by $KMnO_4$ in a two-phase chloroform−water solvent system using **1** as a PTC. First, we investigated host−guest complexation of **1** with alkene substrates such as the linear alkene 1-hexene and branched alkene 4-methyl-1-hexene, in $CDCl_3$ by ^1H NMR. As the concentration of **1** increased, upfield shifts of the peaks for the methylene for 1-hexene (Figure 1, proton Ha) were observed (Figure 2a),[11] which suggests complexation occurs between **1** and 1-hexene. The driving force of the complexation is the CH−π interaction, which is also observed in the host−guest complexes between hydrocarbons and pillar[5]arenes.[7] The stoichiometry of the complex determined from a Job plot (Figure S3) was 1:1, and the association constant K for the binding of 1-hexene into the cavity of **1** was calculated as $65 \pm 16\ M^{-1}$ using nonlinear curve fitting analysis (Figure S4). By contrast, no peak shifts of 4-methyl-1-hexene were observed even with excess **1** (Figure 2b), which indicates that the branched alkene 4-methyl-1-hexane did not interact with **1**. The compact linear shape of 1-hexene is favorable for complexation, but the branched shape of 4-methyl-1-hexene is not. This is because the cavity of pillar[5]arene is very narrow (~5 Å) and has a well-defined cylindrical architecture.[5] The same size-selective host−guest system has been reported in hydrocarbon recognition using pillar[5]arenes.[7]

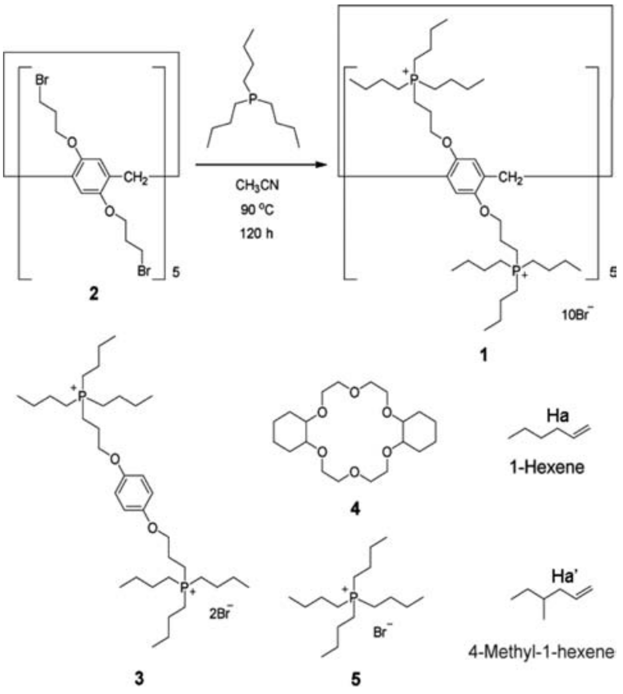


Figure 1. Phase-transfer catalysts: pillar[5]arene modified with 10 tetra-alkylphosphonium bromide groups (**1**), unit model (**3**), dicyclohexano-18-crown-6 (**4**), and tetrabutyl phosphonium bromide (**5**). Substrates: 1-hexene and 4-methyl-1-hexene.

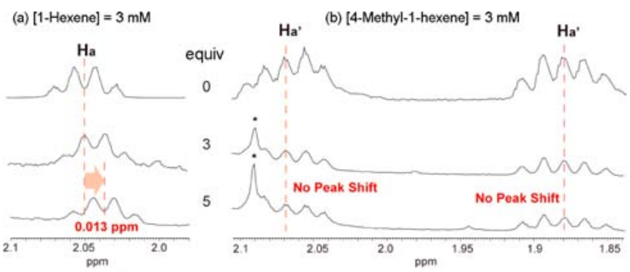


Figure 2. ^1H NMR titrations of (a) 1-hexene (3 mM) and (b) 4-methyl-1-hexene (3 mM) on addition of **1** (0−5 equiv) in $CDCl_3$ at 25 °C. Resonances are labeled in Figure 1. A peak with an asterisk derives from host **1**.

We investigated the oxidation of alkenes in a two-phase $D_2O-CDCl_3$ solvent system using PTCs and the oxidant $KMnO_4$. In the presence of **1**, the chloroform phase (lower phase) quickly became colored (Figure 3a-i), and took on the original deep purple color of the aqueous solution (upper phase). However, phase transfer did not take place in the absence of **1** (Figure 3a-ii). These observations suggest phase transfer of MnO_4^- from the aqueous to chloroform phase. The oxidation reaction of the guest 1-hexene by $KMnO_4$ in the two-phase $D_2O-CDCl_3$ solvent system in the presence of **1** (Figure 3b) was monitored by ^1H NMR. We found the new proton peak from the aldehyde moiety of 1-pentanal along with the proton peaks from remaining substance 1-hexene in the $CDCl_3$ phase, but not in the D_2O phase (Figure S5), which indicates that the oxidation reaction proceeded in the $CDCl_3$ phase, but not in the D_2O phase. The conversions from 1-hexene to 1-pentanal were calculated using the integration ratio of

---

[9] (a) Ogoshi, T.; Shiga, R.; Yamagishi, T. *J. Am. Chem. Soc.* **2012**, *134*, 4577–4580. (b) Ogoshi, T.; Kida, K.; Yamagishi, T. *J. Am. Chem. Soc.* **2012**, *134*, 20146–20150. (c) Ogoshi, T.; Aoki, T.; Shiga, R.; Iizuka, R.; Ueda, S.; Demachi, K.; Yamafuji, D.; Kayama, H.; Yamagishi, T. *J. Am. Chem. Soc.* **2012**, *134*, 20322–20325. (d) Nierengarten, I.; Guerra, S.; Holler, M.; Nierengarten, J. F.; Deschenaux, R. *Chem. Commun.* **2012**, *48*, 8072–8074.

[10] Ogoshi, T.; Ueshima, N.; Yamagishi, T.; Toyota, Y.; Matsumi, N. *Chem. Commun.* **2012**, *48*, 3536–3538.

[11] The peak shifts of the vinyl proton peaks with **1** were not observed. The other methylene peaks were overlapped with **1**; thus the methylene peaks (Figure 1, Ha) were used for investigation of the complexation.

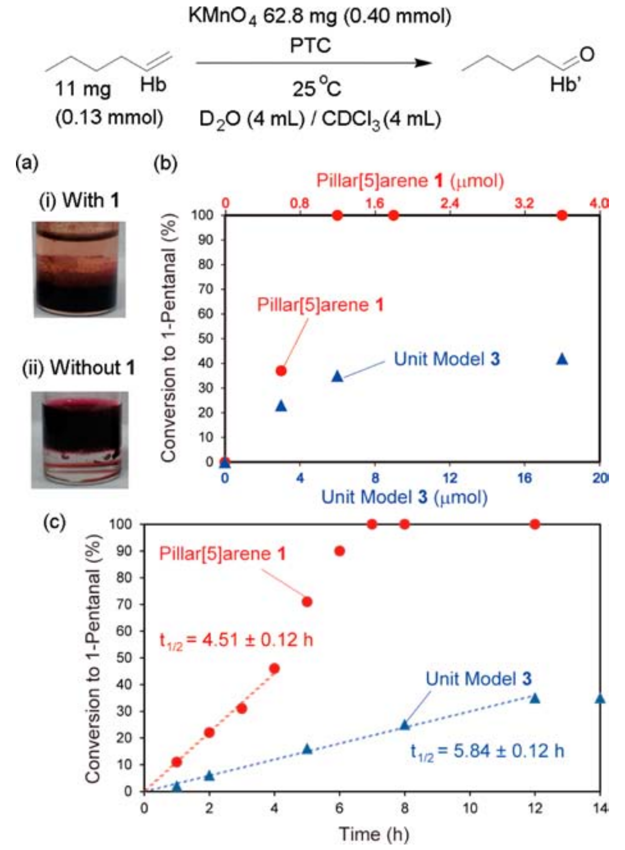


Figure 3. (a) Photographs of $KMnO_4$ in a two-phase D_2O (upper phase)/$CDCl_3$ (bottom phase) solvent system (i) with and (ii) without **1**. (b) Percentage conversion to 1-pentanal versus molar amounts of pillar[5]arene **1** (red circles) and unit model **3** (blue triangles); the reaction time is 12 h. (c) Kinetic studies: percentage conversion to 1-pentanal versus reaction time with pillar[5]arene **1** (1.2 μmol, red circles) and unit model **3** (6 μmol, blue triangles).

the proton peaks between the aldehyde moiety of 1-pentanal (Figure 3, Hb′) and the vinyl moiety of 1-hexene (Figure 3, Hb) in $CDCl_3$. In the absence of PTC, the reaction did not proceed. The percentage converted by the oxidation sharply increased as the amount of **1** increased, and the conversion to 1-pentanal was > 99% with 1.2 μmol of **1** (Figure 3b, red circles, turnover number (TON) = 108.3). By contrast, the conversions were low with a similar amount of the unit model **3** and only reached moderate yields (42%, TON = 3.0) even with a large excess of **3** (Figure 3b, blue triangles).[12] Kinetic studies for the PTC system were also carried out (Figure 3c). Complete oxidation of 1-hexene with **1** required ~7 h ($t_{1/2} = 4.51 \pm 0.12$ h). The turnover frequency (TOF) was calculated to be 15.5 h^{-1}. By contrast, the oxidation with **3** required ~12 h to reach equilibrium ($t_{1/2} = 5.84 \pm 0.12$ h). The TOF was calculated to be 0.25 h^{-1}. These data indicate that **1** has better PTC properties compared to unit model **3**.

To determine why **1** has excellent PTC properties, we examined the oxidation of 1-hexene using **1** in the presence of the competitive guest (Table 1).

Table 1. Oxidation Reaction of Alkenes Using PTCs[a]

run	PTC	alkene (0.13 mmol)	conversion (%)[b]
1	–	1-hexene	0
2	**1** (1.2 μmol)	1-hexene	>99
3[c]	**1** (1.2 μmol)	1-hexene	32
4[d]	**1** (1.2 μmol)	1-hexene	7
5	**1** (1.2 μmol)	4-methyl-1-hexene	31
6	**1** (1.2 μmol)	1-hexene + 4-methyl-1-hexene	85[e] + 7[f]
7	**1** (1.2 μmol)	1-heptene	>99
8	**1** (1.2 μmol)	1-octene	14
9	**1** (1.2 μmol)	1-decene	9
10	**3** (6.0 μmol)[g]	1-hexene	35
11[d]	**3** (6.0 μmol)[g]	1-hexene	18
12	**3** (6.0 μmol)[g]	1-heptene	40
13	**3** (6.0 μmol)[g]	1-octene	38
14	**3** (6.0 μmol)[g]	1-decene	30
15	**4** (1.2 μmol)	1-hexene	0
16	**5** (12 μmol)[h]	1-hexene	20

[a] The reactions were carried out with $KMnO_4$ (0.40 mmol) and PTC in a mixture of D_2O (4 mL) and $CDCl_3$ (4 mL) under vigorous stirring at 25 °C for 12 h. [b] Conversion to alkanal. [c] 1,4-Dicyanobutane (0.13 mmol) was added as a competitive guest. [d] A mixture of D_2O (4 mL) and CD_2Cl_2 (4 mL) was used for the reaction. [e] Conversion from 1-hexene to 1-pentanal. [f] Conversion from 4-methyl-1-hexene to 3-methyl-1-pentanal. [g] **1** contains 10 tetrabutylphosponium groups, while unit model **3** contains only 2 of them. Therefore, in order to have an identical concentration of phosponium groups, a 5 times molar amount of **3** over **1** was used. [h] **1** contains 10 tetrabutylphosponium groups, while **5** contains only 1 of them. Therefore, in order to have an identical concentration of phosponium groups, a 10 times molar amount of **5** over **1** was used.

1,4-Dicyanobutane forms very highly stable 1:1 host–guest complexes with pillar[5]arenes. The association constants K of the complexes between 1,4-dicyanobutane and pillar[5]arenes are generally greater than 10^4 M^{-1},[13] while the K of the host–guest complexes between linear hydrocarbons and pillar[5]arenes are very weak (K = 10–100 M^{-1}).[7] The conversion dramatically decreased with the competitive guest 1,4-dicyanobutane (run 3, 1 equiv of 1,4-dicyanobutane to 1-hexene), while the reaction went to completion without 1,4-dicyanobutane (run 2). The association constant K of the 1:1 **1**·1,4-dicyanobutane complex was higher ($K = (1.62 \pm 0.026) \times 10^3$ M^{-1}, Job plot (Figure S6) and determination of K from ^1H NMR) than that of the **1**·1-hexene complex ($K = 65 \pm 16$ M^{-1}). Therefore, 1,4-dicyanobutane acted as a competitive guest and induced dissociation of the **1**·1-hexene complex. The conversion was also extremely low (7%) in a two-phase D_2O/CD_2Cl_2 solvent system using **1** (run 4), which was lower than that in a two-phase $D_2O/CDCl_3$ solvent system using **1** (> 99%, run 2) and in a two-phase D_2O/CD_2Cl_2 solvent system using unit model **3**

---

(12) **1** contains 10 tetrabutylphosponium groups, while unit model **3** contains only 2 of them. Therefore, in order to have an identical concentration of phosponium groups, a 5 times molar amount of **3** over **1** was used.

(13) Shu, X.; Chen, S.; Li, J.; Chen, Z.; Weng, L.; Jia, X.; Li, C. *Chem. Commun.* **2012**, *48*, 2967–2969.

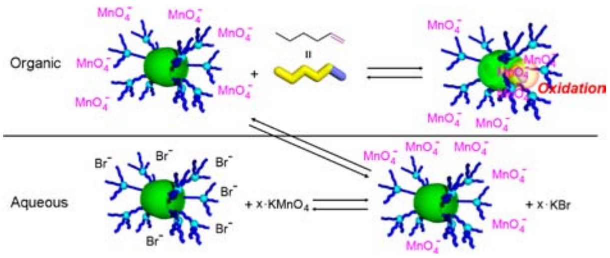


Figure 4. Proposed mechanism of the PTC oxidation reaction based on host–guest complexation.

(18%, run 11). CH_2Cl_2 was included in the cavity of pillar[5]arenes, which was completely characterized by single X-ray crystalline analysis.[14] Thus, the host–guest complexation between **1** and 1-hexene extremely weakened in CD_2Cl_2 because CH_2Cl_2 acts as a competitive guest. The percentage conversion in the oxidation reaction of 4-methyl-1-hexene (run 5) was 31%, which was lower than that of 1-hexene (run 2). This is because branched 4-methyl-1-hexene cannot be included in the pillar[5]arene cavity of **1**, which is confirmed by ^{1}H NMR measurements (Figure 2b). We also carried out the oxidation of the mixture of 1-hexene and 4-metyhl-1-hexene using **1** (run 6). The conversion of 1-hexene to 1-pentanal was 85%, while that of 4-methyl-1-hexene to 3-methyl-1-pentanal was 7%. Thus, the substrate selectivity of **1** based on the conversion was high (~12:1). These results indicate that inclusion of the substrate in the cavity of **1** is important for the oxidation of alkenes.

Figure 4 shows the proposed mechanism of the oxidation reaction using **1** as the PTC. Equilibrium counteranion exchange from bromide to MnO_4^- occurs first. These ion pairs are then transferred across the aqueous–organic interface. In the organic phase, the MnO_4^- anion reacts with 1-hexene. At this stage, 1-hexene within the cavity of **1** is fixed in a close position for efficient oxidation. When 1-heptene was used as a substrate, the oxidation reaction proceeded completely (conversion >99%, run 7). By contrast, the conversion of the oxidation of the long chain alkenes were low (runs 8 (14%) and 9 (9%)). The distance between the C=C bond and the alkylphosphonium bromide groups is very important for the oxidation. The oxidations of the alkenes using **1** are highly substrate selective. On the other hand, the conversions of the alkenes using unit model **3** were 30–40% (runs 10, 12–14), indicating that the substrate selectivity was observed in the pillar[5]arene **1** but not in the unit model **3**. The difference in substrate selectivity between pillar[5]arene **1** and unit model **3** also supports the proposed mechanism of the oxidation reaction.

Crown ether and tetra-alkyl phosphonium bromide are useful PTCs for the oxidation of alkenes. Thus, we compared the conversions with these PTCs in the oxidation reactions under the same conditions. The oxidation reaction using dicyclohexano-18-crown-6 **4** (Figure 1) did not proceed (run 15). With a ten times molar amount of the simple tetrabutyl phosphonium bromide **5** (Figure 1) the conversion was only 20% (run 16), while the oxidation reaction with **1** went to completion (run 2). Therefore, compared to previously reported PTCs, **1** is an excellent PTC for the oxidation of alkenes. Complexation of the substrate with **1** and increasing the local concentration of MnO_4^- around rims increased the efficiency of the oxidation reaction.

In conclusion, the new PTC pillar[5]arene **1** was synthesized and applied with high efficiency and substrate selectivity. Oxidation reactions reached completion even with very small amounts of PTC **1** (amount of substance fraction 0.90%). This is a significant advantage compared with typical PTCs, which generally require an amount of substance fraction 5–100% for oxidation of alkenes.[3] Oxidation of the linear alkenes 1-hexene and 1-heptene completely proceeded, but that of the branched alkene 4-methyl-1-hexene and long chain alkenes did not. Substrate selective PTC properties have not been observed in other PTCs. The host–guest properties of pillar[5]arene contributed to the efficient and substrate-selective PTC properties demonstrated in this study.

Acknowledgment. This work was partly supported by The Japan Securities Scholarship Foundation and Technology (MEXT), Japan and JSPS KAKENHI 23655210 (a Grant-in-Aid for Challenging Exploratory Research).

Supporting Information Available. Experimental section, characterization data, Job plots, and ^{1}H NMR titrations. This material is available free of charge via the Internet at http://pubs.acs.org.

---

(14) Boinski, T.; Szumna, A. *Tetrahedron* **2012**, *68*, 9419–9422.

The authors declare no competing financial interest.