



## Digest paper

## Recent developments of cavitand-recessed type metal catalysts



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## ABSTRACT

Metal catalysis inside cavitand space is an emerging field that achieves chemical reactions that were previously unthinkable in bulk solution and causes selectivities not possible heretofore. As the synthetic ways of making metal centers embedded in the cavitand hollows become more simply developed, the catalytic behaviors are gaining increased attention. This Digest will outline catalytic cavitands that have metal centers definitely positioned in the interior of the hemispherical molecules, with emphasis on reports published in the past few years. Specifically, the following targets and approaches are discussed: resorcin[4]arenes, cyclodextrins, and cyclotrimeratrylenes (hemicryptophanes).

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In 1982, Donald J. Cram who was awarded the Nobel Prize in chemistry in 1987, stated the meaning of term ‘cavitand’ as follows,<sup>1</sup> “We propose the class name *cavitand* for synthetic organic compounds that contain *enforced cavities* large enough to accommodate simple molecules or ions.” Since then, researches regarding to organic cavitand scaffolds have continuously made progress from the supramolecular point of view. Today, there are primarily five classes of the cavitand platforms: calixarenes, resorcinarenes, cyclotrimeratrylenes, cucurbiturils, and cyclodextrins.<sup>2</sup> We chemists have synthetically functionalized these platforms to set up molecular diversity, which enables us to make investigation of multiple chemical areas.<sup>3,4</sup>

As one of those areas, there is a field of organometallic chemistry, chemistry that mainly addresses homogeneous transition metal catalysis. The metal catalysis has, of course, been well developed over the past decades. Nowadays its catalytic protocols are indispensable for modern synthetic organic chemistry, whereas it still awaits full accomplishment from the viewpoint of green chemistry: more selective, more efficient, and more reactive catalysts are strongly desirable.<sup>5</sup> For that reason we have a means in strategies of the mind, to mimic metallo-enzymes. Mother Nature creates enzymes that have incredibly marvelous catalysis and serve as well-organized chemical transformation machines. For example, nitrogenase is a representative metal complex enzyme that catalyzes the reduction of atmospheric nitrogen to ammonia under ambient temperature.<sup>6</sup> Its breathtakingly beautiful function

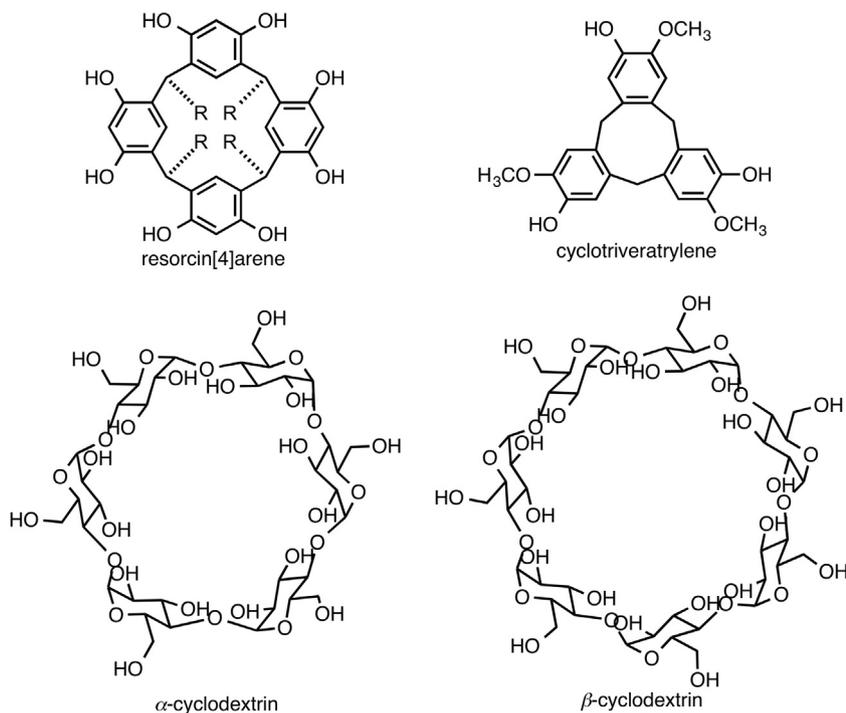
is an excellent teacher for all time: we students should learn and follow the essence of mechanism.

Fortunately for us, enzymes have strong resemblances in two points to supramolecular cavitands.<sup>7</sup> One, enzymes are basically capable of having catalyst centers directed inwardly toward their hydrophobic pockets. Two, the hydrophobic pockets are not tightly sealed so that substrates can readily sample the space, enter and leave. For the first point, cavitands are endowed with gently curved concaves large enough to embrace metal catalyst centers. For the second point, cavitands are originally half open so that guests readily come and go. If these are embodied in the cavitand derivatives as tangible structures, we can provide *definitely cavitand-recessed type metal catalysts* possessing even just a little attribute of metallo-enzymes.

However, such type of the metallic cavitands has been underdeveloped. Two shortcomings provide chemists a continuing challenge. The first problem is the synthetic difficulty to prepare functionalized cavitands even in laboratory-scale. The second is hardships in the synthesis of metal hybrid cavitands in which inwardly directed functionality acts as a supporting ligand to make a complex with transition metals. 50 years have already passed since supramolecular chemistry began,<sup>8</sup> whereas efforts overcoming these drawbacks have been less successful. Here, major challenges remain.

The purpose of this Digest is to focus on rare complexes that have metal centers *definitely at the cavitand recesses* for catalytic use. For the sake of brevity, we have chosen to focus on the following three cavitands, resorcin[4]arenes, cyclodextrins, and cyclotrimeratrylenes (hemicryptophanes) illustrated in Fig. 1; a

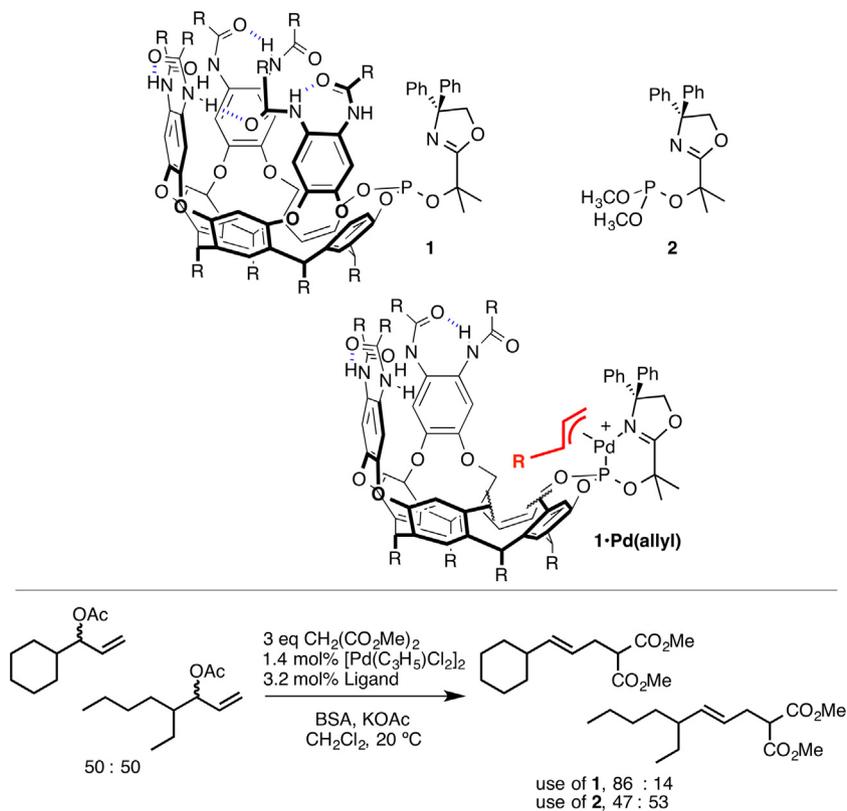
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**Fig. 1.** Three cavitand platforms of resorcin[4]arene,  $\alpha$ - and  $\beta$ -cyclodextrins, and cyclotriveratrylene.

gradual but steady progress in refining these three metallo-catalytic cavitands has been made for the last decade. A full discussion of development around calixarenes, that are flexible compared to other four rigid container frameworks, is best dealt with elsewhere.<sup>9</sup> The chemical reactions catalyzed by cucurbiturils are not in the focus in this Digest, because it is still difficult to definitely put catalytic metal centers in the concave surface.<sup>10,11</sup>

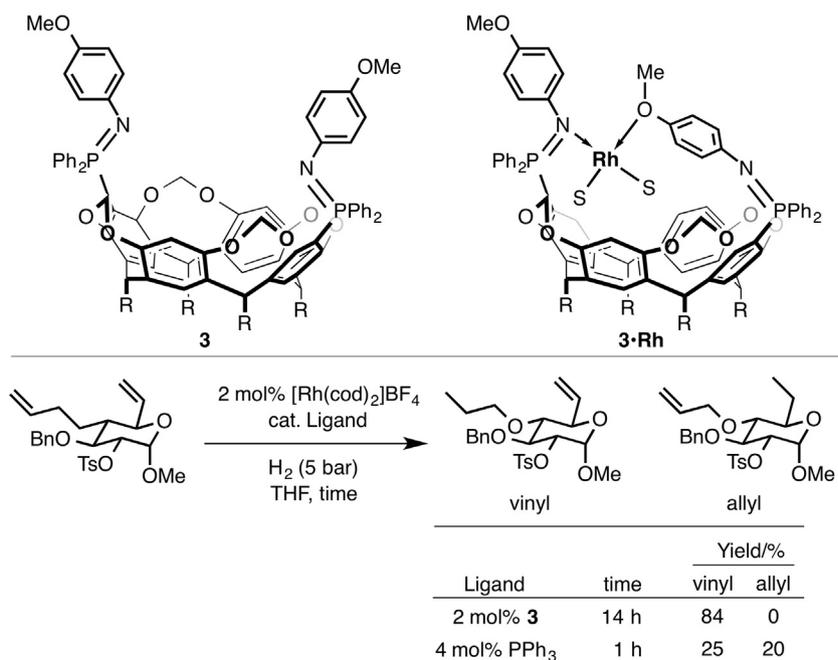
*Resorcin[4]arene-recessed metal catalysts by covalent anchoring.* The resorcin[4]arene scaffold has octanol substructure, which enables us to build up resorcin[4]arene-based cavitands with inwardly directed functional group. We chemists imagine that the 'introvertedly' functional group is up in the interior space toward the tapered end or flanked walls. The reliable method of introvertedly anchoring metal centers to the cavity recess is to



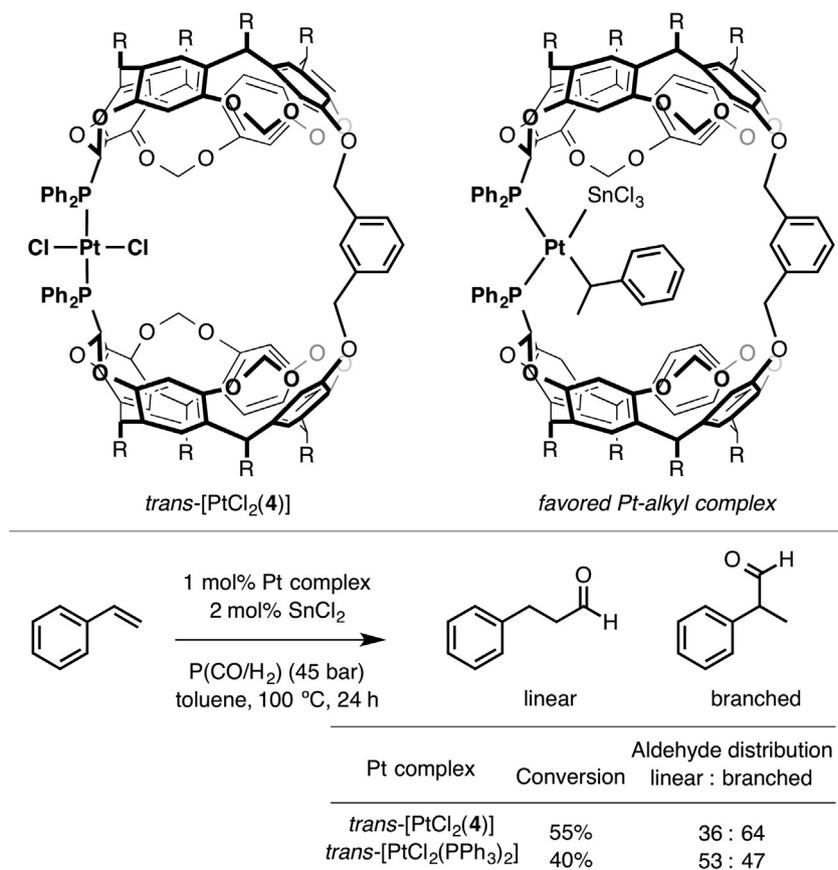
**Fig. 2.** Palladium-catalyzed allylic alkylation reactions were demonstrated through a use of **1** or **2**. (BSA: *N,O*-bis(trimethylsilyl)acetamide).

directly ligate the Lewis base such as P and N atoms in the cavitant and to orient those lone pairs toward the cavity space. The Rebek group in 2002 embodied this idea in use of a resorcin[4]arene skeleton, which was the first use of resorcin[4]arene-based cavity

in transition metal catalysis as a auxiliary unit.<sup>12</sup> They synthesized a bi-dentate ligand **1** that forms a chelate with palladium center directed toward the cavitant hollow (Fig. 2), and investigated the reaction profile in palladium-catalyzed allylic alkylation reactions.



**Fig. 3.** Rhodium-catalyzed competitive hydrogenation of different two terminal olefins in the glucose substrate: the cavitant **3** exclusively catalyzed to reduce the allylic double bond.



**Fig. 4.** Platinum-catalyzed hydroformylation of styrene in the presence of *trans*-[PtCl<sub>2</sub>(**4**)] yielded the branched aldehyde favorably compared to the model complex of *trans*-[PtCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>].

The palladium complex **1-Pd(allyl)** exhibited a substrate specificity that distinguishes between closely related structures: in the presence of a 1:1 mixture of different substrates, **1-Pd(allyl)** preferentially yielded one of two corresponding products. The reason for this effect is that, for example in Fig. 2, the  $\eta^3$ -complex caused by the oxidative addition of Pd to the substrate recognized the cyclohexyl group as a better guest compared to branched-heptyl moiety. On the other hand, the corresponding model **2** that lacks the container space showed no significant difference in the  $\eta^3$ -complex and/or product distribution.

Matt, Sémeril and co-workers have studied effectiveness of catalytic cavitands that are basically functionalized with coordination groups in the upper rim of the resorcin[4]arenes.<sup>13–18</sup> During the course of their study, a bis(iminophosphorane) **3** was synthesized for rhodium-catalyzed hydrogenation reactions of terminal olefins (Fig. 3).<sup>19</sup> The ligand **3** could form the *N,O*-chelated rhodium intermediate **3-Rh** that disposes the metal center at the cavitand entrance to orientate two free coordination sites toward the cavity interior. The cavity size nicely discriminated between allylic and vinylic double bonds in the glucose substrate, which exclusively embraced the allyl group to afford a single product. In contrast, catalytic use of  $\text{PPh}_3$  indiscriminately reduced different two C=C double bonds.

More recently, the same group has constructed a new metal-bridged semi-capsule of *trans*-[PtCl<sub>2</sub>(**4**)]: **4** is bis-phosphorus ligand with widely separated P-centers and a core of which consists of two covalently linked resorcin[4]arenes (Fig. 4).<sup>20</sup> A crystal-

lographic analysis revealed that the chelate complex has wider two mouths of shell where the platinum two binding sites are fully or partially embedded inside. The styrene hydroformylation tests with the *trans*-[PtCl<sub>2</sub>(**4**)] and a *trans*-[PtCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>] of reference were carried out in the presence of SnCl<sub>2</sub> as an activator: the former produced benzaldehyde with a conversion of 55% and a regio-selectivity towards the branched product of 64%, and the latter gave less conversion and regio-selectivity. The metallo-container proved to be a good catalyst, with reactivity and selectivity towards the branched aldehyde superior to those observed for *trans*-[PtCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>] devoid of the capsular unit. The origin of this performance is likely to reflect the rigid and narrow space where reaction intermediates and transition states adopt somewhat distorted structures to avoid disfavored steric interactions between container walls and guest substructures. Consequently, the favored Pt-alkyl complex illustrated in Fig. 4 would be produced.

Iwasawa and co-workers have introduced a bis-Au approach as a strategy that makes apparent its introverted metal arrangement, where the two-quinoxaline walls flanked two sets of linear structured-Au arrays (Fig. 5).<sup>21,22</sup> The bis-phosphite **5** displayed the catalytic proclivity that efficiently catalyzes selective and direct dimerization of terminal alkynes to yield conjugated enynes in head-to-tailed fashion. The reaction progress features a predominant production of cross-coupled adduct more than homo-dimerized one, in which **5** makes ethynylbenzene as a nucleophilic donor to add to 1-octyne of an acceptor. The same

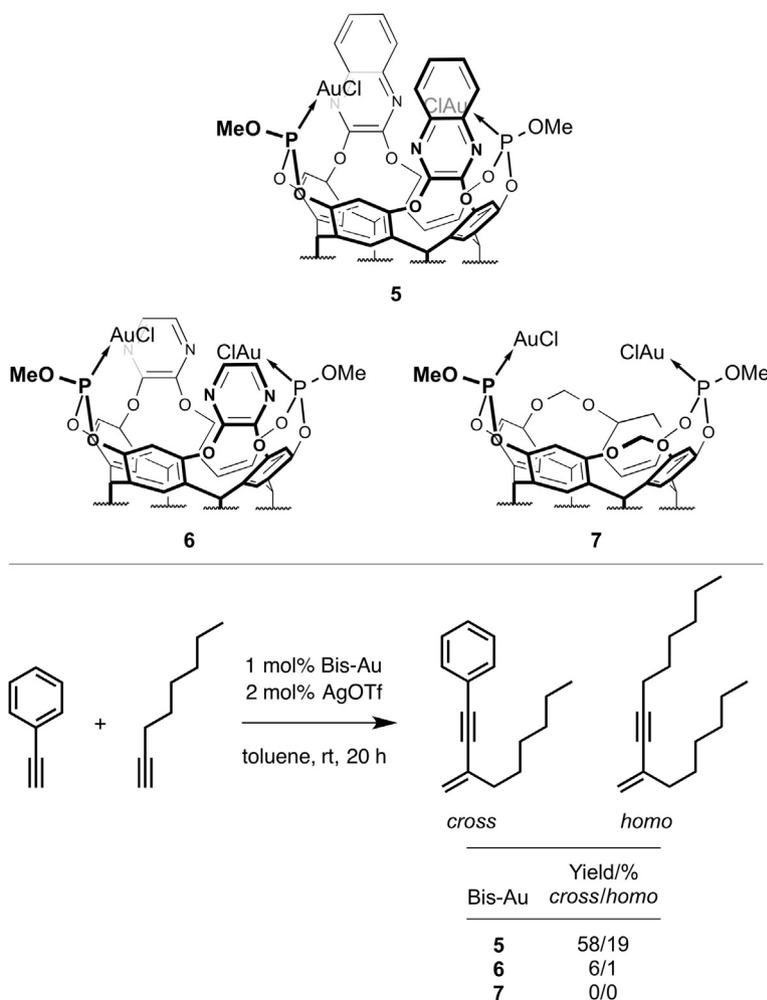


Fig. 5. Bis-gold complex-catalyzed dimerization of terminal alkynes in use of **5**, **6**, and **7**: the two Au supported by **5** enticed pairwise alkynes to undergo the selective coupling reactions.

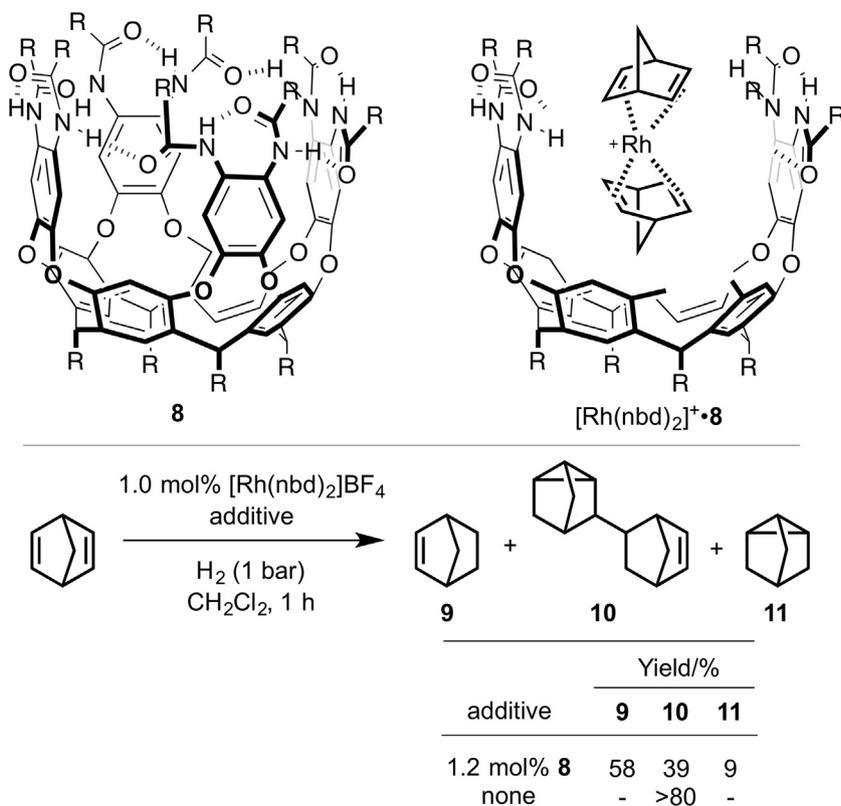


Fig. 6. Rhodium-catalyzed hydrogenation reactions of norbornadiene in the presence or absence of cavitand **8**.

group explored the effect of the cavity through a comparison with model catalysts that weakened cavity.<sup>23</sup> They synthesized two kinds of model compounds **6** and **7** in which one lacked two quinoxaline walls and the other had two pyrazine walls, and found that these exhibited much lower reactivity; thus, the two quinoxaline moieties play a quintessential role for the catalytic activity. They also checked the mono-Au complex as a control experiment, which showed no reactivity for the dimerization reaction.<sup>24</sup> This supramolecular effect would be strongly complemented by stabilization of reactive intermediates and reaction process, which are consequences inherent to such a limitedly  $\pi$ -clouded space.<sup>25</sup>

*Resorcin[4]arene-recessed metal catalysts by non-covalent host-guest interactions.* The metal catalysts described in this section were inclusion complexes of small catalyst centers inside the large self-assembled host molecules. The catalysts were bound inside the space with aid of supramolecular and hydrophobic interactions, and entropic increase by release of multiple solvent molecules resided in the cavity. Ballester and co-workers successfully demonstrated that an octa-amide cavitand **8** forms a stable encapsulation complex with  $[\text{Rh}(\text{nbd})_2]\text{BF}_4$  (nbd = norbornadiene) to give  $[\text{Rh}(\text{nbd})_2]^+\cdot\mathbf{8}$  in axial inclusion geometry (Fig. 6).<sup>26</sup> The catalytic activity of the complex  $[\text{Rh}(\text{nbd})_2]^+\cdot\mathbf{8}$  in the hydrogenation of norbornadiene was studied, which afforded 58% of norbornene **9**, 39% of dimer **10**, and 3% of **11**. When the cavitand **8** was absent from the reaction process, more than 80% of dimer **10** was produced. These results clearly inform the supramolecular encapsulation effect of **8**: this effect would be caused by  $[\text{Rh}(\text{nbd})_2](\text{CH}_2\text{Cl}_2)^+\cdot\mathbf{8}$  that was produced by replacement of one nbd ligand in  $[\text{Rh}(\text{nbd})_2]^+\cdot\mathbf{8}$  with two  $\text{CH}_2\text{Cl}_2$  molecules. In the  $[\text{Rh}(\text{nbd})(\text{CH}_2\text{Cl}_2)_2]^+\cdot\mathbf{8}$ , the cavitand loosely binds the central Rh through one molecular nbd ligand, and the partially exposed coordination site drove the unique catalysis that was not observed in the control catalyst of  $[\text{Rh}(\text{nbd})_2]\text{BF}_4$ .

Reek, Scarso and co-workers found that a metal complex of (*i*-Pr-NHC)Au(OTf) is involved in encapsulation process of reversibly self-assembled resorcin[4]arene-based-hexamers of  $(\mathbf{12})_6\cdot 8\text{H}_2\text{O}$  in water-saturated benzene  $d_6$  solvent (Fig. 7).<sup>27</sup> The resultant cationic (*i*-Pr-NHC)Au<sup>+</sup> of  $\sim 400 \text{ \AA}^3$  resides in the capsule  $(\mathbf{12})_6\cdot 8\text{H}_2\text{O}$  of  $1375 \text{ \AA}^3$  along with two to four extra solvents in agreement with the 55% occupancy rule,<sup>28</sup> where such solvent molecules are readily exchanged with substrate molecules of suitable size and shape. The hydration reaction of 4-phenyl-1-butyne carried out with free (*i*-Pr-NHC)Au(OTf) in water saturated benzene  $d_6$  completed in 30 min, and yielded quantitative formation of the corresponding methyl ketone **13**. In contrast, the encapsulated catalyst was much slower than non-encapsulated catalyst since the substrates have to sneak into the cavity through the seam of hydrogen bonds of  $(\mathbf{12})_6\cdot 8\text{H}_2\text{O}$ , but gave rise to a different product distribution in 400 min: ketone **13**, aldehyde **14** and dihydronaphthalene **15** were given in 12%, 4%, and 12% yields, respectively. The hexameric-assembled capsule imposed a barrier for the entrance of water, making the intramolecular reaction relatively slow. Alternatively, the sterically constrained environment inside the capsule forced the unusual intramolecular transformation like as the *anti*-Markovnikov hydration and Friedel-Crafts type cyclization, giving **14** and **15**.

After a while, Strukul, Scarso, Reek and co-workers assessed the substrate selectivity imparted by the residual cavity left by (*i*-Pr-NHC)Au<sup>+</sup> in hexameric capsule  $(\mathbf{12})_6\cdot 8\text{H}_2\text{O}$ , because they anticipated that the sterically and geometrically insulated space hosts only nice-fitting substrate for chemical transformation like enzymatic catalysis regardless of substrate original reactivity (Fig. 8).<sup>29</sup> They demonstrated experiments of hydration reactions in which homologous three alkynes were delivered all together to the 5 mol% catalysts of (*i*-Pr-NHC)Au<sup>+</sup>@ $(\mathbf{12})_6\cdot 8\text{H}_2\text{O}$  or (*i*-Pr-NHC)Au(OTf), considering the initial rate of the reactions.

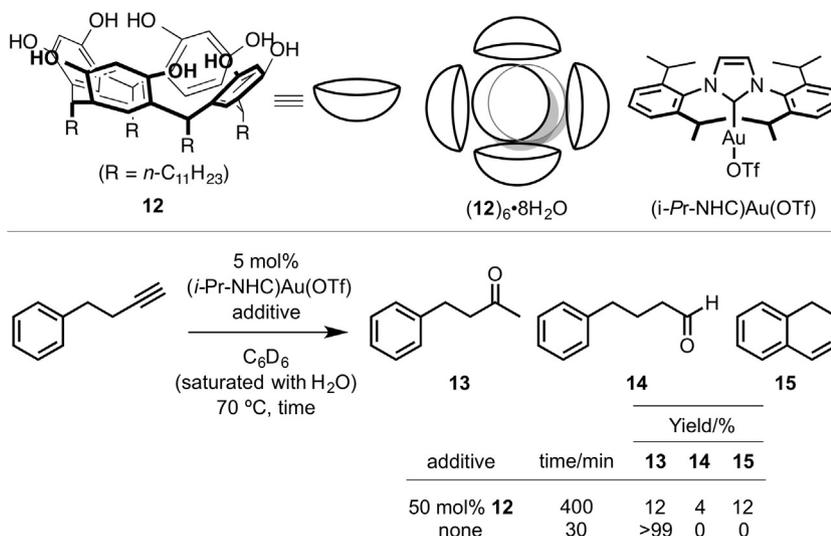


Fig. 7. Gold-catalyzed transformation of 4-phenyl-1-butyne in the presence or absence of hexameric resorcin[4]arene-based assembly of  $(\mathbf{12})_6 \cdot 8\text{H}_2\text{O}$ .

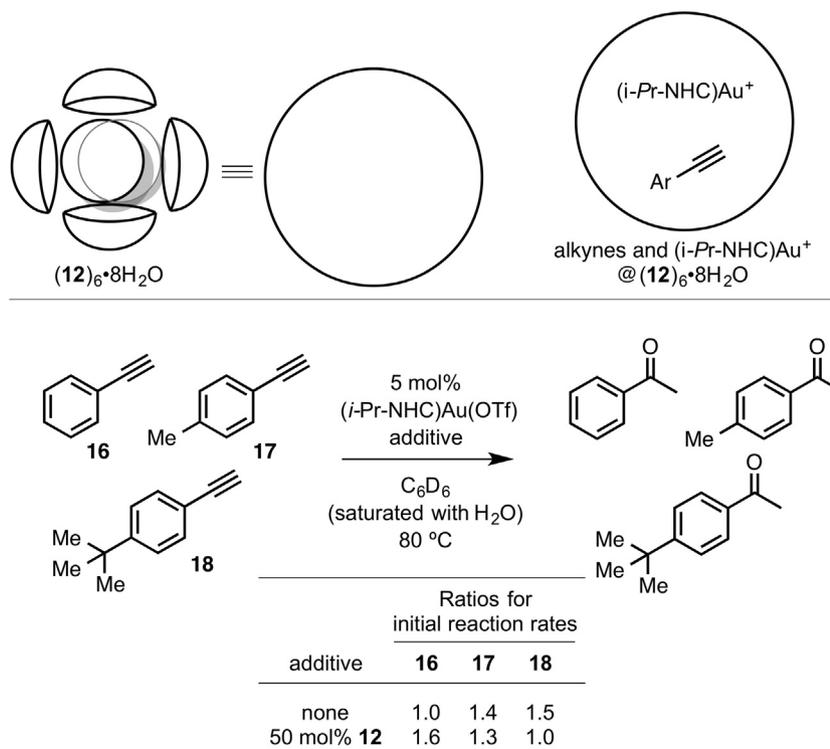
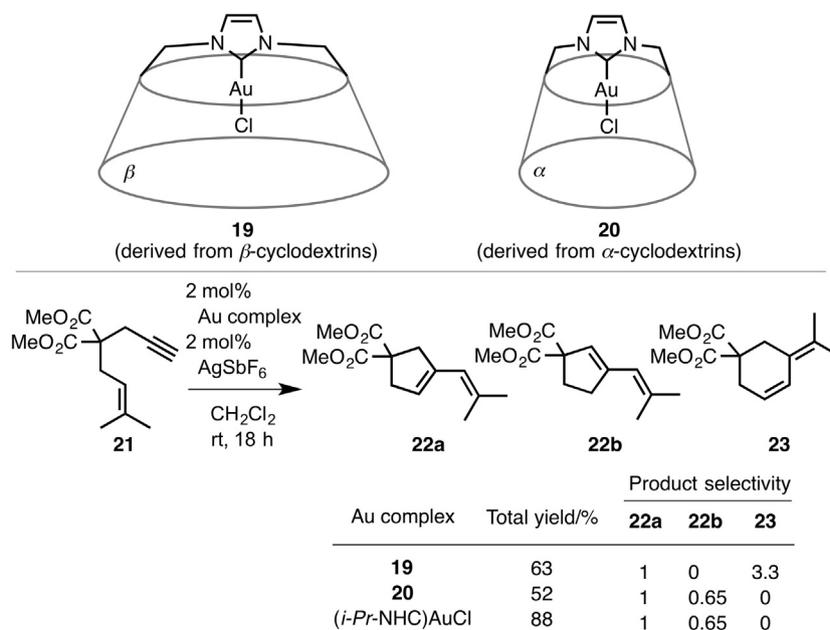


Fig. 8. Substrate selectivity in the competitive hydration reactions of homologous alkynes mediated by NHC-Au(I) catalyst wrapped with or without hexameric resorcin[4]arene capsule  $(\mathbf{12})_6 \cdot 8\text{H}_2\text{O}$ .

The  $(i\text{-Pr-NHC})\text{Au}^+$  wrapped with  $(\mathbf{12})_6 \cdot 8\text{H}_2\text{O}$  scored 1.6:1.3:1.0 for **16:17:18**, although the free complex  $(i\text{-Pr-NHC})\text{Au}(\text{OTf})$  provided a contrary slope of 1.0:1.4:1.5 for the alkynes **16:17:18**. Apart from an expected difference in activity between these two catalysts, completely reversed substrate selectivity was observed. The result in the use of free complex was reasonable because the more electron-rich **18** showed high affinity to the central  $\text{Au}^+$  than non-*para*-substituted **16**. On the other hand, the residual space in the  $(i\text{-Pr-NHC})\text{Au}^+@(\mathbf{12})_6 \cdot 8\text{H}_2\text{O}$  made extra steric constrain for the guest substrate to interact with the  $\text{Au}^+$ , which favored the smaller ethynylbenzene **16** that is less reactive.

**Cyclodextrin-recessed metal catalysts.** Cyclodextrins (CDs) are used to mimic enzymatic catalysis because their interior is carpeted with hydrogen atoms, which artificially confer hydrophobicity and introduce additional van der Waals interactions. If the metal can be deeply encapsulated inside the cyclodextrin pocket, this set mimics the environment of a metal buried within a folded metallo-enzymes.<sup>30,31</sup> Sollogoub and co-workers developed NHC-capped  $\alpha$ - and  $\beta$ -CD toruses (Fig. 9) that bind with Au and hang the Au in the middle of the cavity where these metallo-cyclodextrins induce a strong de-shielding effect on a pair of CD's H-5 atoms.<sup>32</sup> To probe the possibility of the unique catalytic activity,

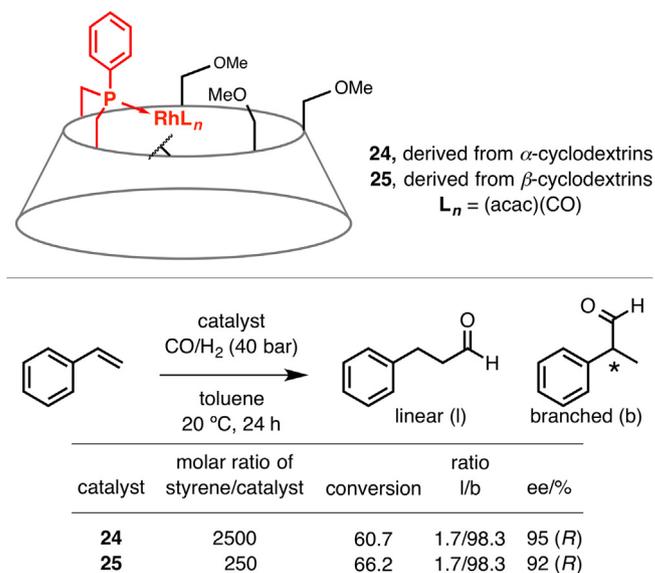


**Fig. 9.** Gold-catalyzed cyclization of **21** in the presence of  $\beta$ -CD sphere **19** favorably afforded **23**, whereas **22a** was predominantly formed in the presence of  $\alpha$ -CD sphere **20** and (*i-Pr-NHC*)AuCl.

they compared the capped gold complexes **19** derived from  $\beta$ -CD, **20** derived from  $\alpha$ -CD, and non-capped (*i-Pr-NHC*)AuCl in a cyclization of enyne **21**. Whereas the reaction with  $\beta$ -version **19** predominantly produced the six-membered ring **23**, the  $\alpha$ -version **20** and conventional (*i-Pr-NHC*)AuCl bifurcated different process to give two kinds of 5-membered rings **22a** and **22b**. The difference in product selectivity clearly demonstrates the effect of the cavity on the outcome of the reaction. Not only the shape and size of bowl-like pocket of **19** but also its unusual electronic natures including supramolecular interactions will influence the product selectivity.<sup>33</sup>

In a similar vein, Matt, Armspach and co-workers elegantly showed rhodium-phosphorus complex catalysts in which regio- and *enantio*-selectivities were controlled by the second coordination sphere attached to  $\alpha$ - and  $\beta$ -cyclodextrins **24** and **25** (Fig. 10).<sup>34</sup> These metallo-cyclodextrins tightly embrace the central Rh metals to form square planar, and strictly prevent coordination of the second phosphorus atom. Interestingly, the  $\alpha$ -**24** has acac ligand outside the cavity and CO ligand inside, while **25** confines the acac to orient CO toward the exterior of the space. In the catalytic use for hydroformylation of styrene, both complexes achieved high 98.3% selectivity for producing the branched aldehyde and singly construction of a chiral carbon (up to 95% ee). The  $\alpha$ -**24** was activated with CO/H<sub>2</sub> to give an important active species of phosphine-coordinated RhH(CO)<sub>3</sub> complex, in which the phosphorus atom exclusively located in *trans* to the hydride concomitant with implantation inside the cavity. This rigid geometry will ensure unprecedented chirality transfer, because there is no other example of a monodentate phosphorus ligand performing simultaneously high chiral induction and high isoregio-selectivity.

**Hemicryptophane-recessed metal catalysts.** A metal-hemicryptophane complex as a catalyst has a central metal embedded in the capsule that was formed with two substructures of a cyclotrimer-arylene cap and an atrane ligand.<sup>35</sup> Three alkyl chains link between these two moieties, which gives a relatively flexible conformation as a significant feature of this molecule as compared to other catalytic cavities endowed with high rigidity. Dutasta group reported the first example of metal-hemicryptophane in 2009.<sup>36,37</sup> They prepared hemicryptophane-oxidovanadium com-



**Fig. 10.** Rhodium-catalyzed asymmetric hydroformylation of styrene with cyclodextrin-folded mono-phosphorus ligands **24** and **25**.

plex **26**, which was tested in the oxidation of sulfide to sulfoxide (Fig. 11). With 10 mol% of **26** and cumene hydroperoxide as an oxidant, the oxidation of thioanisole and benzyl phenyl sulfide proceeded in 95% and 90% yields. In the same condition, the model complex **27** catalyst that lacks cavity shaped by the cyclotrimer-arylene part, oxidized thioanisole and benzyl phenyl sulfide in only 40% and 28%, respectively: this differences in catalytic activity between **26** and **27** indicates a positive supramolecular effect. From the viewpoint of reaction rates, **26** performed those oxidations in up to sixfold faster than **27**. When decreasing the catalyst loading of **26** to 0.5 mol%, a turnover number reached to 180. The high efficiency caused by the existence of cage was attributed to not only encapsulation of guest substrate but also the structural flexibility of the complex **26**.

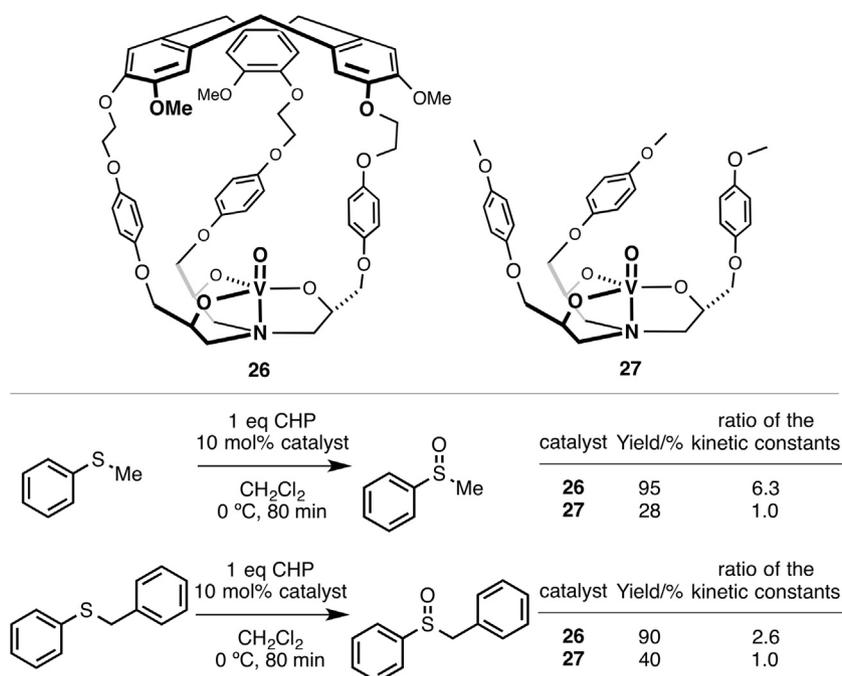


Fig. 11. Oxidovanadium(V)-catalyzed oxidation reactions of thioanisole and phenyl benzyl sulfide using **26** and the corresponding model **27** (CHP = cumene hydroperoxide).

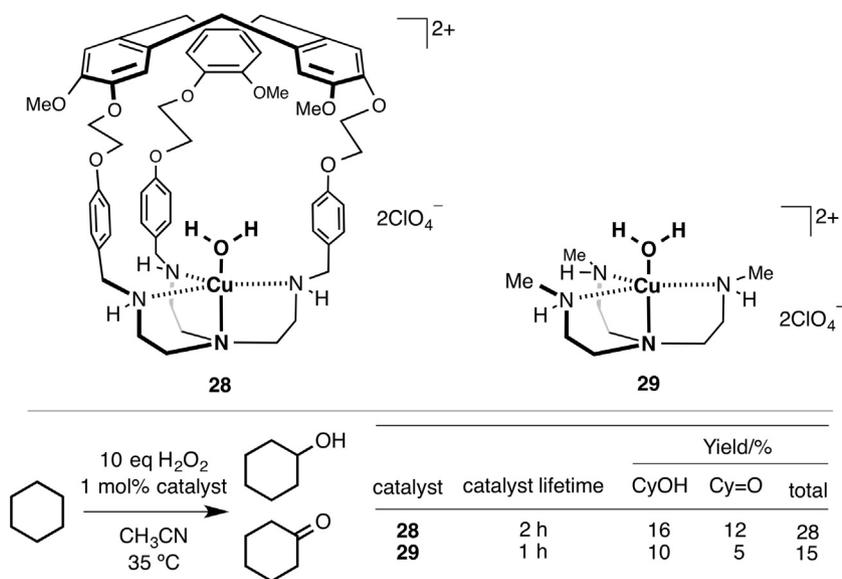


Fig. 12. Copper-catalyzed C–H oxidation of cyclohexane by H<sub>2</sub>O<sub>2</sub> utilizing a copper-hemicryptophane complex **28** and the corresponding model **29**.

Martinez and co-workers prepared a hemicryptophane copper (II) complex **28** in which a tris(2-aminoethylamine) ligand (namely, tren) took hold of the central copper metal at the inner space and a guest substrate is sufficiently accommodated (Fig. 12).<sup>38</sup> The complex **28** achieved cyclohexane (Cy) C–H bond oxidation with H<sub>2</sub>O<sub>2</sub> to give CyOH and Cy=O: with 1 mol% of **28**, the total yields of CyOH and Cy=O reached 28% in 2 h. On the other hand, the use of corresponding model **29** stopped the oxidation in 1 h, giving 14% yield of oxidized products. The initial reaction rate of **28** was comparable to that of **29**, which explains that the existence of cavity in **28** prolonged the catalyst lifetime and played a role of protecting group. The lack of the cavity in **29** readily caused loss of the catalytic activity owing to degradation of the metal center. In addition, the competitive oxidation experiments between cyclohexane, cyclooctane or adamantane revealed that the cavity

of **28** more favorably fold CyH compared to cyclooctane or adamantane unlike the corresponding model **29**. Thus, the oxidation event positively occurs inside the catalytic cavitation like as enzymatic catalysis.

Makita and co-workers synthesized a zinc(II)-induced hemicryptophane **30** from Zn(OAc)<sub>2</sub> in which three aromatic rings connected with a cyclotrimeratrylene and a tren ligand (Fig. 13).<sup>39,40</sup> The aromatic linkers invests the complex with relative rigidity compared to Dutasta's hemicryptophane **26**. The corresponding model **31** that removes the cyclotrimeratrylene was also prepared, and the differences in the observed rate constants (*k*<sub>obs</sub>) between **30** and **31** were studied on catalytic hydrolysis reactions of alkyl *para*-nitrophenyl carbonates. The capped **30** accelerated the hydrolysis of most of substrates up to 3.5-fold faster than uncapped **31**. However, the hydrolysis of *tert*-Bu

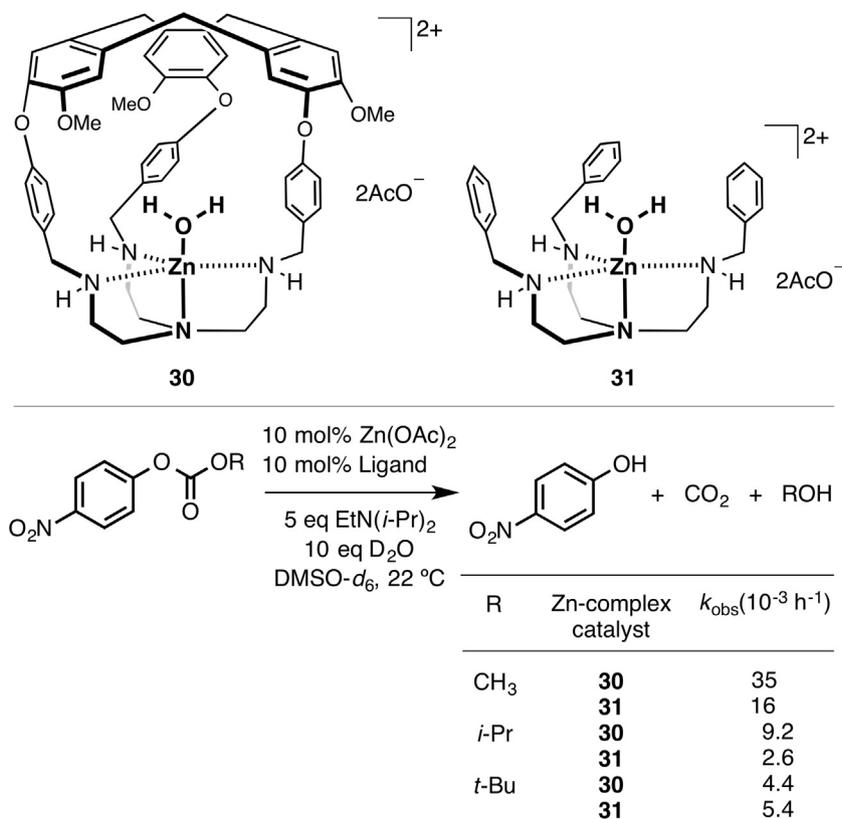


Fig. 13. Zinc-catalyzed hydrolysis reactions of alkyl *para*-nitrophenyl carbonate using the capped **30** and the uncapped **31**.

*para*-nitrophenyl carbonate with **30** was slower than the model **31**, which strongly indicates the bulky *tert*-Bu group hindered smooth access to the inner active water molecule coordinated to zinc. Hence, the acceleration effect is due not only to a property of being close between guest and zinc inside the capsule, but also to a regulation of DMSO coordination with the inner zinc site.

The Makita team also performed ruthenium **32**-catalyzed oxidation of primary alcohols with CAN (cerium(IV) ammonium nitrate) as a stoichiometric oxidant, employing the same framework of hemicryptophane **30** (Fig. 14).<sup>41</sup> A simple tren-derived complex **33** oxidized 1-octanol to yield a mixture of 1-octanal and 1-octanoic acid in 18% and 82%, whereas **32** afforded

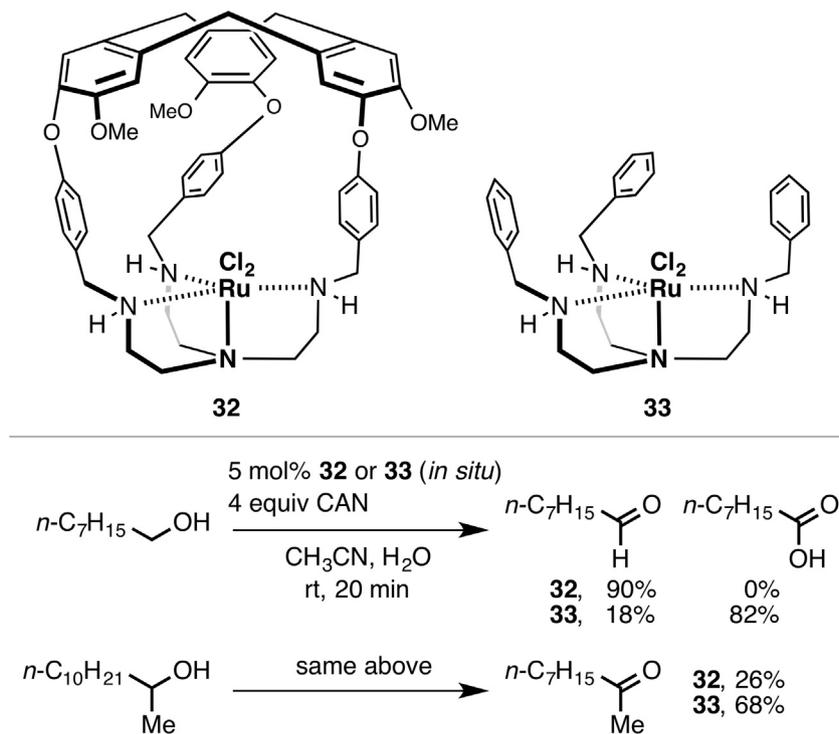


Fig. 14. Ruthenium-catalyzed selective oxidation reactions of alcohols in the presence of hemicryptophane complex **32** and its corresponding model **33**.

amazingly exclusive formation of 1-octanal in 90% and totally suppressed production of 1-octanoic acid. The prolonged reaction time never produced 1-octanoic acid: this means that oxidation stopped completely. In contrast, with a secondary alcohol of 2-dodecanol, the model **33** showed a better catalytic activity in 68% yield than **32** of 26% yield. These results indicate that the compartment of **32** controls entrance of guest substrates, recognizing differences between alcohol and aldehyde as well as between primary and secondary alcohols.

To conclude, this Digest focuses on metal catalysts that have the metal centers at the cavitand recesses: the selected cavitands are resorcin[4]arenes, cyclodextrins, and hemicryptophanes (cyclotrimeratrylenes). The catalysts have two salient features: One, the half-opened shape enables guests to approach the space readily and allows products to exit from the place smoothly, which achieves the catalytic cycle in marked contrast with fully closed molecular containers. Two, the restricted space forcibly determines the arrangement and geometry of molecules inside, which limits the conformations of transition states and reaction intermediates to bring prominent reactivity and selectivity untouched in bulk solution. These features remind us of enzymatic catalysis, and inspire us to try out a development of greener artificial enzyme as much as possible. The current situation of cavitand-recessed type metal catalysts is still immature obviously as a synthetic tool in organic synthesis field. Yet, in this endeavor, the future direction where we head will locate in creating artificial nitrogenase to permit activation of atmospheric nitrogen: the real approach to overcome such a truly important challenge is what we chemists put our hope on. During the course of such a research, future chemistry will act up to green chemistry principals with real saving energy and cause paradigm shift in homogeneous transition metal catalysis. We hope that this Digest will increase awareness of *cavitand-recessed type metal catalysts* and accelerate the development of green chemistry based on these interesting supramolecules.

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