

Cavitands | *Very Important Paper* |

VIP **Rational Design of a Metallocatalytic Cavitand for Regioselective Hydration of Specific Alkynes**

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Abstract: The synthesis of a functionalized supramolecular cavitand with inwardly oriented Au^I and P=O moieties was explored, including its catalytic proclivity in the selective hydration of internal alkynes. The cavitand works as a supramolecular flask device: Au^I coordinates to the triple bond, the P=O moiety

connects with a H₂O molecule, and the cavity favors folding of a single alkynyl side chain. Several tests of different substrate patterns indicated that the cavity was substrate specific, similar to enzymatic catalysis.

Introduction

Enzymes are attractive, appealing, and inviting compounds to synthetic chemists, because they catalyze highly selective transformations under rather mild conditions.^[1] There are two quintessential properties of enzymes that provide chemists a continuing challenge to mimic. One is to orient metal centers inwardly towards a somewhat isolated space: for example, multiple metals activate otherwise inert molecules inside enclosed cavities.^[2] The other is to prepare two or more active sites on the concave surface of the host that work synergistically to make a substrate guest more reactive and selective.^[3] Overcom-

ing these formidable challenges will perhaps allow synthetic chemists to make more significant contributions to new modes of chemical catalysis and transformations from the viewpoint of green chemistry that enzymes are already able to achieve.^[4,5] Recently, we reported the synthesis of an introverted bis-Au cavitand that was flanked by two quinoxaline walls and based on a resorcin[4]arene, and we found that it catalyzed the cross-dimerization of terminal alkynes.^[6] The cavitand set the two Au atoms symmetrically, but each Au trapped a different alkyne, which brought two alkynes together to result in a cross-dimerization event. Presumably, the enforced cavity confined fitting guests in a limited space and properly positioned them to stabi-

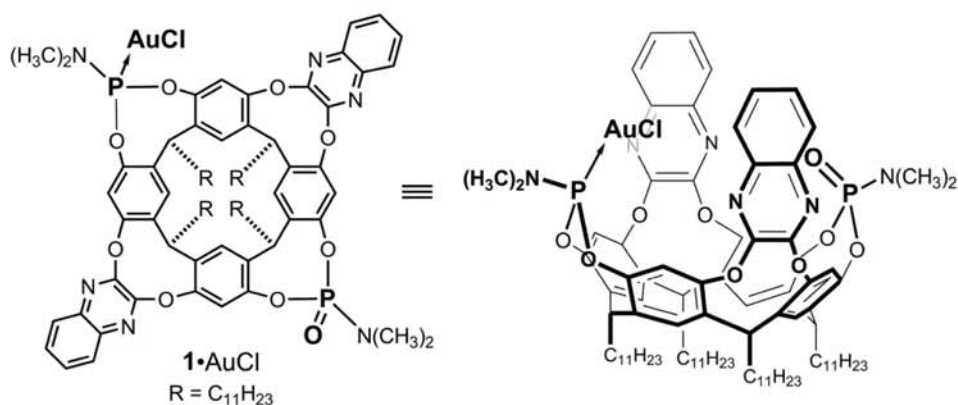


Figure 1. Mono-Au complex cavitand **1·AuCl** functionalized with PNMe₂ and O=PNMe₂ moieties in which the two P–N bonds point outside toward the cavity space. A part of the quinoxaline moiety is colored in gray for ease of viewing.

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lize the reactive species in the transition state. Such a positive effect drove us to develop new mono-Au complex **1·AuCl** (Figure 1) that is endowed with phosphoramidite (PNMe₂) and phosphoramidate (O=PNMe₂) moieties; the PNMe₂ group works as a supporting ligand for the Au metal, and the O=PNMe₂ groups acts as an electron-donating point for activation of the

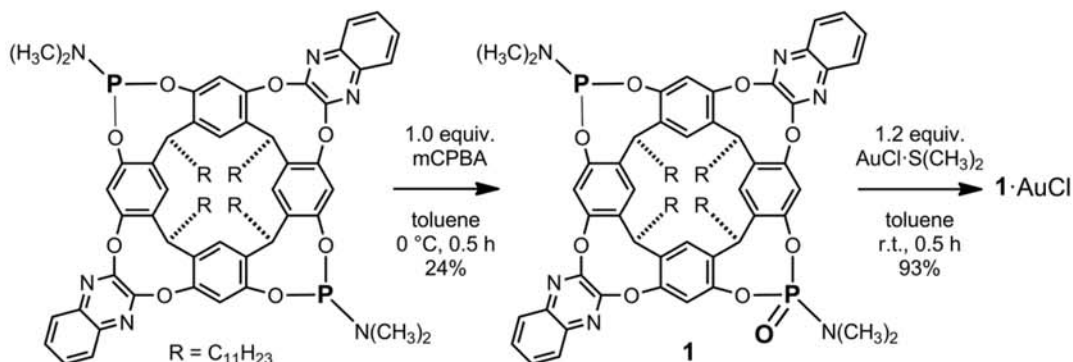
substrates.^[7] The question we continue to pursue is "can this new organometallic cavitant framework enable potent chemical transformations?"

Results and Discussion

We thus synthesized **1** in 24 % yield, which was the result of an oxidation reaction of the parent bis-phosphoramidite cavitant that was previously reported by our group with structure elucidation by crystallographic analysis (Scheme 1).^[8,6a] Double oxidation of the two phosphorus atoms was accomplished in 21 % yield, and 25 % of the unreacted parent bis-phosphoramidite cavitant remained. Upon reaction of **1** with AuCl·S(CH₃)₂, corresponding complex **1**·AuCl was prepared in 93 % yield.^[9] To bring out the hidden talent of **1**·AuCl, we investigated its performance in the hydration reaction of internal alkynes as a probe reaction.

The alkyne hydration reaction to construct a carbonyl motif with the use of water and alkynes is fundamentally important in modern organic synthesis, because it is typically atom economic and environmentally benign.^[10] Historically, strong acids such as H₂SO₄ and Hg^{II} salts were used to catalyze hydration;^[11] nonetheless, Nolan recently reported a method for the (IPr)Au^I-catalyzed acid-free hydration of alkynes [IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene].^[12,13] The method is highly efficient and useful for a wide range of alkynes; however, its fatal drawback is the production of terribly regioisomeric mixtures if unsymmetrical internal alkynes are used. For example, the (IPr)Au^I-catalyzed hydration of 2-octyne yielded mixtures including 51 % 2-octanone and 23 % 3-octanone. Thus, it is too difficult to discriminate between the two carbon atoms of the triple bond in 2-octyne. Here, a major challenge remains.

We wondered whether **1**·Au⁺ could be used to solve this profound challenge, and anticipated that **1**·Au⁺ has three roles in the hydration process (Figure 2): one, Lewis acidic Au⁺ coordinates to the carbon-carbon triple bond; two, Lewis basic O=P works as a hydrogen-bonding acceptor with a water molecule; three, the π-cloud cavity may show molecular recognition to help fold a single side chain of the alkyne, which could allow for the highly regioselective addition of H₂O to unsymmetrical triple bonds.



Scheme 1. Synthesis of **1**·AuCl derived from cavitant **1** prepared by *m*CPBA oxidation.

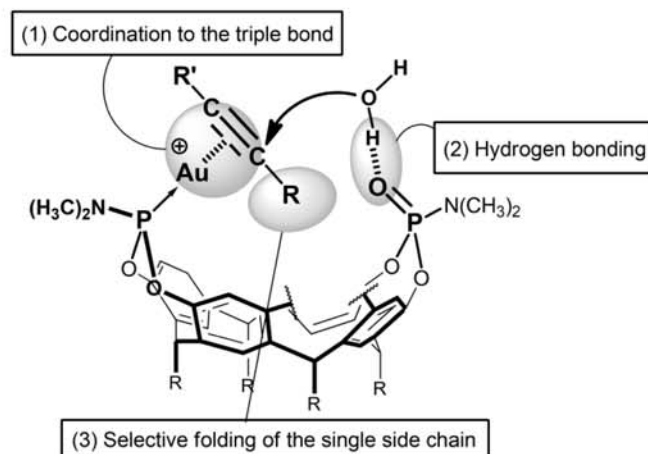
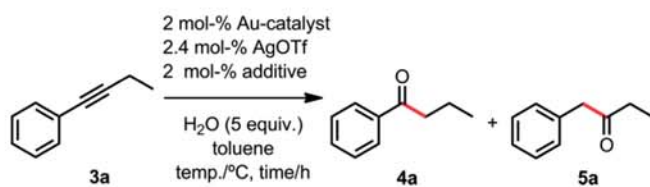


Figure 2. Three strategies of **1**·Au⁺ in the selective hydration of internal alkynes (the two quinoxaline walls are omitted for ease of viewing): (1) coordination of Au⁺ toward the triple bond, (2) hydrogen bonding between P=O and H₂O, and (3) the inner space favorably includes one side of the alkyne substituents.

We started to evaluate the proclivity of **1**·AuCl to catalyze the hydration of commercially available 1-phenyl-1-butyne (**3a**): reactions with **1**·AuCl (2 mol-%) and silver trifluoromethanesulfonate (AgOTf, 2.4 mol-%) were carried out in toluene by including distilled water (5 equiv.).^[14] These results are summarized in Table 1, noting the results of (IPr)AuCl and **2**^[15] (Figure 3). Initially, **1**·AuCl consumed the entire amount of **3a** in 1 h at the mild temperature of 50 °C and predominantly produced **5a** in 98 % yield (Table 1, entry 1). Increasing the temperature to 80 °C resulted in a loss of selectivity, and a **4a**/**5a** ratio of 3:86 was obtained (Table 1, entry 2). The reactivity of mono-AuCl **2** flanked by a triquinoxaline-spanned resorcin[4]arene was evaluated: **2** lacks the P=O moiety in **1**, and its sealing abilities are increased relative to those of **1** (Table 1, entries 3–6). Surprisingly, the hydration reaction hardly occurred: more than 78 % **3a** remained unreacted, and the ketones were scarcely produced (Table 1, entries 3 and 4). Upon increasing the temperature to 80 °C (Table 1, entries 5 and 6), the reaction efficiency did not improve. From the viewpoint of structure-activity relationships, the P=O moiety of **1** was proven to be important for catalysis, which indicates that the proximity effect in **1**·Au⁺ between the alkyne and water would accelerate

hydration. For reactions performed with (IPr)AuCl (Table 1, entries 7–10), the aid of the Ph₃PO moiety resulted in 68 % yield (Table 1, entry 9); however, prolonging the reaction time to 4 h gave a terrible mixture of 16 % **4a** and 68 % **5a** with 7 % unreacted **3a**. The representative Au precursors of AuCl·PPh₃ (Table 1, entries 11 and 12) and AuCl·SMe₂ (Table 1, entries 13 and 14) were not effective.

Table 1. Evaluation of the reactivity of **1**·AuCl in the selective hydration of 1-phenyl-1-butyne (**3a**) compared to several Au catalysts.^[a]



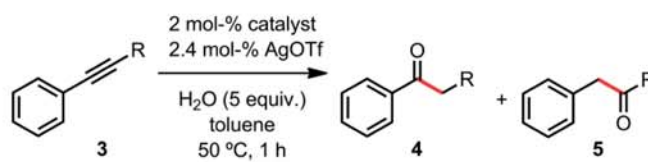
Entry	Au catalyst	Additive	T [°C]	t [h]	Yield ^[b] [%]		
					3a ^[c]	4a	5a
1	1 ·AuCl	–	50	1	0	<2	98
2	1 ·AuCl	–	80	0.5	0	3	86
3	2	–	50	1	82	3	1
4	2	Ph ₃ PO	50	1	78	3	1
5	2	–	80	0.5	70	11	4
6	2	Ph ₃ PO	80	0.5	72	10	5
7	(IPr)AuCl	–	50	4	9	18	56
8	(IPr)AuCl	–	80	0.5	20	12	44
9	(IPr)AuCl	Ph ₃ PO	50	4	7	16	68
11	(IPr)AuCl	Ph ₃ PO	50	4	72	0	0
12	AuCl·PPh ₃	–	50	4	78	1	1
13	AuCl·PPh ₃	Ph ₃ PO	50	4	94	<1	<1
14	AuCl·SMe ₂	–	50	4	72	0	0
15	AuCl·SMe ₂	Ph ₃ PO	50	4	92	0	0

[a] Reaction conditions: **3a** (0.07 mL, 0.5 mmol), H₂O (0.05 mL, 2.5 mmol), Au catalyst (0.01 mmol), AgOTf (3.0 mg, 0.012 mmol), additive (0.01 mmol), toluene (1 mL); for entries 1, 2, and 7–9, the yields are the averages of two runs. [b] Determined by ¹H NMR spectroscopy analysis of samples purified by short-plug silica gel column chromatography (toluene only). The ¹H NMR spectra of **4a** and **5a** were identical to those of commercially available 1-phenyl-2-butanone and 1-phenyl-1-butanone, respectively. Compound **3a** is volatile owing to the low boiling point of hydrocarbons, and so samples were carefully dried to obtain the yields. [c] Unreacted **3a**.

Next, we studied the influence of alkyl groups joined to the 1-phenyl-1-ethynyl moieties to evaluate the abilities of catalyst **1**·AuCl (Table 2). The yields and selectivities at 50 °C for 1 h were evaluated for aliphatic methyl, ethyl, *n*-propyl, *n*-butyl, and

n-heptyl substituents. Although **1**·Au⁺ could not coordinate to the terminal triple bond of **3b** (Table 2, entries 1 and 7) owing to electron deficiency, **1**·AuCl hydrated **3c** (Table 2, entry 2) and **3a** (Table 2, entry 3) with near-perfect selectivities to the products and afforded **5c** and **5a**, respectively, each in 98 % yield. Elongated substrates **3d** and **3e** gave lower conversion ratios, and finally, **3f** remained intact. On the other hand, upon using (IPr)AuCl, neither the reaction progress nor the product distribution was good under these mild conditions (Table 2, entries 8–12). These results explain that **1**·AuCl is specific for its reactivity and selectivity in the hydration of **3c** and **3a**, which would suggest that methyl and ethyl groups fit well inside the cavity of **1**·Au⁺. Indeed, as illustrated in Scheme 2, the **1**·AuCl-catalyzed hydration of 1-methyl-4-(phenylethynyl)benzene un-

Table 2. Influence of aliphatic substituents joined to the 1-phenyl-1-ethynyl moiety on the Au-catalyzed selective hydration.^[a]



Entry	Catalyst	R	Alkyne 3	Yield ^[b] [%]		
				3 ^[c]	4	5
1	1 ·AuCl	H	3b	100	0	0
2	1 ·AuCl	CH ₃	3c	0	2	98
3	1 ·AuCl	C ₂ H ₅	3a	0	2	98
4	1 ·AuCl	<i>n</i> C ₃ H ₇	3d	51	16	33
5	1 ·AuCl	<i>n</i> C ₄ H ₉	3e	87	10	3
6	1 ·AuCl	<i>n</i> C ₇ H ₁₅	3f	100	0	0
7	(IPr)AuCl, Ph ₃ PO	H	3b	100	0	0
8	(IPr)AuCl, Ph ₃ PO	CH ₃	3c	98	2	2
9	(IPr)AuCl, Ph ₃ PO	C ₂ H ₅	3a	70	4	17
10	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₃ H ₇	3d	88	5	7
11	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₄ H ₉	3e	61	11	28
12	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₇ H ₁₅	3f	94	3	3

[a] Reaction conditions: alkyne (0.5 mmol), H₂O (0.05 mL, 2.5 mmol), catalyst [18 mg of **1**·AuCl, 6 mg of (IPr)AuCl, and 3 mg of Ph₃PO, 0.02 mmol], AgOTf (3.0 mg, 0.012 mmol), toluene (1 mL). [b] Determined by ¹H NMR spectroscopy analysis of samples purified by short-plug silica gel column chromatography ([D₂]toluene only). The ¹H NMR spectra of **4c**, **5d**, **4e**, and **5e** were identical to those of commercially available propiophenone, valerophenone, hexanophenone, and benzyl butyl ketone, respectively. The spectra of **5c** and **4d** were inferred from ChemDraw-estimated charts. [c] Unreacted **3a**.

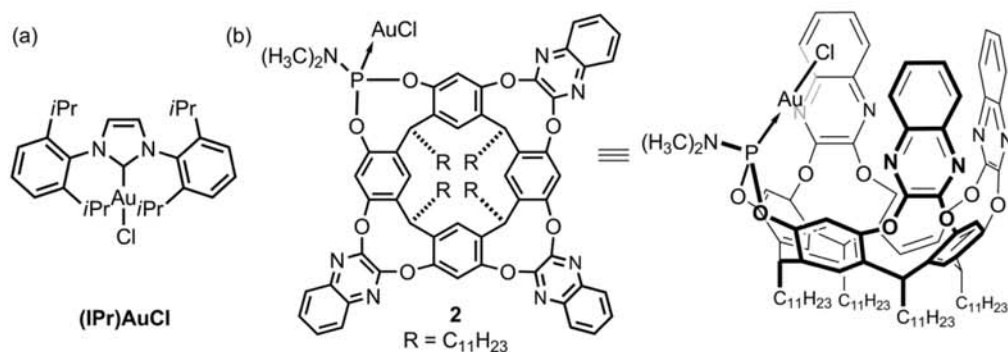
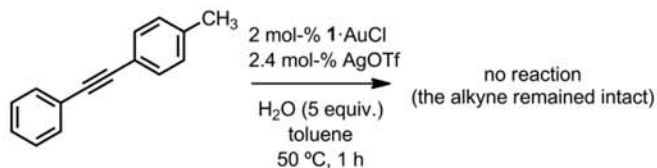


Figure 3. (IPr)AuCl, and mono-AuCl **2** tethered to a triquinoline-spaced resorcin[4]arene. A part of the quinoxaline moiety is colored in gray for ease of viewing.

der the same conditions was not observed at all. Thus, the phenyl moiety in **3a–f** is too large to reside in the inner space.



Scheme 2. Reactivity of 1-methyl-4-(phenylethynyl)benzene at 50 °C in the presence of **1**-AuCl.

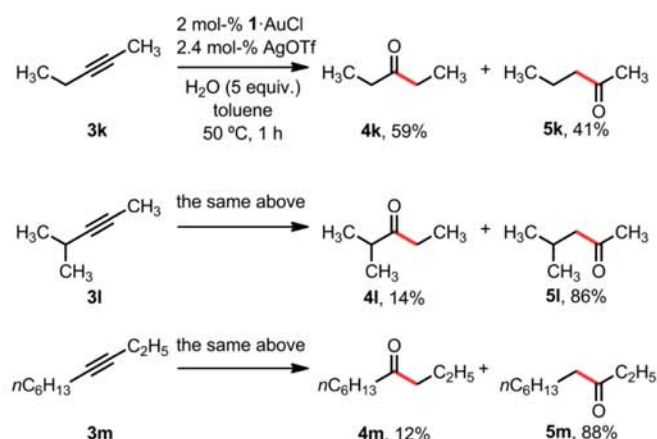
In the same vein, we assessed the shapes of various octynes, including unsymmetrical 3-octyne, 2-octyne, 1-octyne, and symmetrical 4-octyne (Table 3). Alkynes **3g** ($R^2 = C_2H_5$) and **3h** ($R^2 = CH_3$) were totally converted into the corresponding ketones with predominant formation of **5g** (91 %) and **5h** (82 %) (Table 3, entries 1 and 2). In contrast, with the use of terminal alkyne **3i**, no reaction was observed (Table 3, entry 3). On the other hand, upon using (IPr)AuCl, the reactions did not go to completion and horrible mixtures of **4g/5g** (13/23 %) and **4h/5h** (21/39 %) were obtained (Table 3, entries 5–7). With the use of 4-octyne, **1**-AuCl achieved a high-yielding transformation of 96 % in contrast to (IPr)AuCl, which gave the product in less than 75 % yield (Table 3, entries 4 and 8). These results strongly suggest that the different distributions of products **4/5** by **1**-AuCl can be attributed to the different strengths of host-guest interactions between the alkyl moiety and the cavity space. Particularly, methyl and ethyl moieties immediately adjacent to the triple bond seem to have a strong affinity with the space, and this would fix the geometry of the nucleophilic attack of the water molecule to give the ketone products with high regioselectivity. The outstanding product distributions in **3a**, **3c**, **3g**, and **3h** imply that the cavity has substrate specificity for alkynyl methyl and ethyl groups.

Table 3. Influence of isomeric octynes on catalytic hydration with **1**-AuCl and (IPr)AuCl.^[a]

Entry	Catalyst	R ¹	R ²	Octyne 3	Yield ^[b] [%] 4	5
1	1 -AuCl	<i>n</i> C ₄ H ₉	C ₂ H ₅	3g	0	91
2	1 -AuCl	<i>n</i> C ₅ H ₁₁	CH ₃	3h	0	82
3	1 -AuCl	<i>n</i> C ₆ H ₁₃	H	3i	100	0
4	1 -AuCl	<i>n</i> C ₃ H ₇	<i>n</i> -C ₃ H ₇	3j	4	96
5	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₄ H ₉	C ₂ H ₅	3g	64	13
6	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₅ H ₁₁	CH ₃	3h	40	21
7	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₆ H ₁₃	H	3i	74	26
8	(IPr)AuCl, Ph ₃ PO	<i>n</i> C ₃ H ₇	<i>n</i> -C ₃ H ₇	3j	25	75

[a] Reaction conditions: octyne (55 mg, 0.5 mmol), H₂O (0.05 mL, 2.5 mmol), catalyst [18 mg of **1**-AuCl, 6 mg of (IPr)AuCl, and 2.8 mg of Ph₃PO, 0.01 mmol], AgOTf (3.0 mg, 0.012 mmol), toluene (1 mL). [b] Determined by ¹H NMR spectroscopy analysis of samples purified by short-plug silica gel column chromatography ([D₈]toluene only). The ¹H NMR spectra of **4g** (= **4j**), **5g** (= **4h**), and **5h** (= **4i**) were identical to those of commercially available 4-octanone, 3-octanone, and 2-octanone, respectively. [c] Unreacted **3a**.

Additionally, as depicted in Scheme 3, we verified the quality of this specificity in the hydration of 2-pentyne (**3k**), 4-methyl-2-pentyne (**3l**), and 3-decyne (**3m**). For **3k**, the chemical yields of **4k** and **5k** were 59 and 41 %, respectively.^[16] Thus, there is not much difference in the affinity to the cavity between the methyl and ethyl groups. For **3l**, the product distribution was reasonably good and **5l** was obtained in 86 % yield, which implies that the methyl group fits into the cavity much better than the isopropyl group. For **3m**, a high selectivity of 12:88 was obtained, as expected, because the *n*-C₆H₁₃ group in **5m** is longer than the C₂H₅ group and is not a suitable guest for the cavity.



Scheme 3. Ability of **1**-AuCl to catalyze the selective hydration of 2-pentyne (**3k**), 4-methyl-2-pentyne (**3l**), and 3-decyne (**3m**). Yields were determined by ¹H NMR spectroscopy analysis of samples purified by short-plug silica gel column chromatography eluting with [D₈]toluene. The ¹H NMR spectra of **4k**, **5k**, **4l**, and **5l** were inferred from ChemDraw-estimated charts. The ¹H NMR spectra of **4m** and **5m** were identical to those of commercially available 4-decanone and 3-decanone, respectively.

These results allow us to illustrate the mechanism for hydration shown in Figure 2. The narrow space welcomes small groups such as alkynyl-CH₃ and alkynyl-CH₃CH₂ groups, even under mild conditions,^[17] however, the entrance of larger substituents such as *n*-butyl, isopropyl, and phenyl moieties is unfavorable. This molecular recognition leads to the formation of a significant host-guest complex, which precisely approaches a hydrogen-bonded water molecule toward one side of the two carbon atoms in the carbon-carbon triple bond.

Conclusions

In conclusion, the inward arrangement of the P-Au and P=O moieties in **1**-AuCl provides a new functional architecture for the selective hydration of simple internal alkynes. The supramolecular catalyst is a cutting-edge solution for which host-guest interactions enable the two side chains of internal alkynes to be distinguished. Comparison with model catalysts such as **2** and (IPr)AuCl strongly indicates that **1**-Au⁺ activates the triple bond through cationic Au by trapping molecular water with its O=P moiety and selectively folding one of the two alkynyl side chains. The **1**-Au⁺ catalyst specifically welcomes

methyl and ethyl groups inside the cavity, simultaneously orienting its paired moiety outwards.^[18] These results emphasize the relevance of the quinoxaline-spanned resorcin[4]arene structure to design highly effective cavitand catalysts and to achieve new and potent chemical transformations not achievable heretofore.^[19,20] Further development of new selective transformations is ongoing and will be reported in due course.

Experimental Section

Synthesis of 1: Under an argon atmosphere, a two-necked flask was charged with a solution of the starting parent bis-phosphoramidite molecule in Scheme 1 (600 mg, 0.4 mmol) in dry toluene (16 mL). A solution of *m*CPBA (92 mg, 0.4 mmol) in toluene (8 mL) was then added dropwise at 0 °C over 10 min. After stirring at 0 °C for 30 min, the reaction was quenched by the addition of satd. aq. NaHCO₃ (8 mL) over 10 min. The organic layer was washed with water (3 × 20 mL) and brine (20 mL), dried with Na₂SO₄, and concentrated in vacuo to give a crude, white solid material (585 mg). Purification by silica gel column chromatography (toluene/EtOAc = 9:1–4:1) afforded **1** (147 mg, 24 %) as a yellowish white solid material. Further reprecipitation from CH₂Cl₂/CH₃OH (1:8) whitened **1** (134 mg, 22 %). *R*_f = 0.16 (toluene/EtOAc = 9:1). ¹H NMR (400 MHz, CDCl₃): δ = 7.83–7.78 (m, 4 H), 7.51–7.50 (m, 4 H), 7.41 (s, 2 H), 7.33 (s, 2 H), 7.22 (s, 2 H), 7.14 (s, 2 H), 5.72 (t, *J* = 8.1 Hz, 2 H), 4.60–4.56 (m, 2 H), 2.91 (d, ³*J*_{PH} = 10.9 Hz, 6 H), 2.84 (d, ³*J*_{PH} = 10.5 Hz, 6 H), 2.28–2.22 (m, 8 H), 1.45–1.28 (m, 72 H), 0.90–0.87 (m, 12 H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 153.2, 153.1, 152.6 (d, *J*_{CP} = 1.4 Hz), 152.4, 150.3 (d, *J*_{CP} = 4.8 Hz), 146.6 (d, *J*_{CP} = 8.3 Hz), 140.1 (two signals overlapped), 137.3 (d, *J*_{CP} = 2.2 Hz), 136.7 (d, *J*_{CP} = 2.1 Hz), 134.4 (d, *J*_{CP} = 3.6 Hz), 134.1, 129.7, 129.6, 128.5, 128.2, 123.2, 122.5, 117.7, 117.3 (d, *J*_{CP} = 4.1 Hz), 37.2 (d, *J*_{CP} = 3.1 Hz), 36.2, 36.0, 35.4 (d, *J*_{CP} = 18.6 Hz), 34.3, 32.3 (many signals overlapped), 32.0, 31.9, 31.4, 30.1 (many signals overlapped), 29.8 (many signals overlapped), 28.4, 28.3, 23.1 (many signals overlapped), 14.5 (many signals overlapped) ppm. ³¹P NMR (162 MHz, CDCl₃): δ = 140.6, –1.5 ppm. IR (neat): ν̄ = 2922, 2851, 1482, 1271, 1119, 1068, 868 cm⁻¹. HRMS (MALDI-TOF): calcd. for C₉₂H₁₂₅N₆O₉P₂ [M+H]⁺ 1519.8983; found 1519.9099. C₉₂H₁₂₄N₆O₉P₂ (1519.97): calcd. C 72.70, H 8.22, N 5.53; found C 72.66, H 8.20, N 5.44.

Acknowledgments

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Keywords: Cavitands · Regioselectivity · Supramolecular chemistry · Gold · Hydration reactions

- [1] A. Fersht, *Enzyme Structure and Mechanism*, Freeman, New York, **1984**, p. 47–97.
- [2] a) F. A. Tezcan, J. T. Kaiser, D. Mustafi, M. Y. Walton, J. B. Haward, D. C. Rees, *Science* **2005**, *309*, 1377–1380; b) T. Spatzal, M. Aksoyoglu, L. Zhang, S. L. A. Andrade, E. Schleicher, S. Weber, D. C. Rees, O. Einsle, *Science* **2011**, *334*, 940; c) K. M. Lancaster, M. Roemelt, P. Ettenhuber, Y. Hu, M. W. Ribbe, F. Neese, U. Bergmann, S. DeBeer, *Science* **2011**, *334*, 974–977.
- [3] a) G. Varani, *Annu. Rev. Biophys. Biomol. Struct.* **1995**, *24*, 379–404; b) M. V. Rodnina, W. Wintermeyer, *Curr. Opin. Struct. Biol.* **2003**, *13*, 334–340; c) K. Shen, A. C. Hines, D. Schwarzer, K. A. Pickin, P. A. Cole, *Biochim. Biophys. Acta Proteins Proteomics* **2005**, *1754*, 65–78.
- [4] a) P. Molenveld, J. F. J. Engbersen, D. N. Reinhoudt, *Chem. Soc. Rev.* **2000**, *29*, 75–86; b) M. Shibasaki, N. Yoshikawa, *Chem. Rev.* **2002**, *102*, 2187–2209; c) M. Terada, T. Komuro, Y. Toda, T. Korenaga, *J. Am. Chem. Soc.* **2014**, *136*, 7044–7057.
- [5] T. Iwasawa, *Tetrahedron Lett.* **2017**, *58*, 4217–4226 and references cited therein.
- [6] a) N. Endo, M. Kanaura, M. P. Schramm, T. Iwasawa, *Eur. J. Org. Chem.* **2016**, *2016*, 2514–2521; b) M. Kanaura, N. Endo, M. P. Schramm, T. Iwasawa, *Eur. J. Org. Chem.* **2016**, 4970–4975.
- [7] Y. Hamashima, D. Sawada, M. Kanai, M. Shibasaki, *J. Am. Chem. Soc.* **1999**, *121*, 2641–2642.
- [8] T. Iwasawa, Y. Nishimoto, K. Hama, T. Kamei, M. Nishiuchi, Y. Kawamura, *Tetrahedron Lett.* **2008**, *49*, 4758–4762.
- [9] H. Teller, S. Flügge, R. Goddard, A. Fürstner, *Angew. Chem. Int. Ed.* **2010**, *49*, 1949–1953; *Angew. Chem.* **2010**, *122*, 1993.
- [10] *Modern Carbonyl Chemistry* (Ed.: J. Otera), Wiley-VCH, Weinheim, Germany, **2000**.
- [11] L. Hintermann, A. Labonne, *Synthesis* **2007**, 1121–1150.
- [12] N. Marion, R. S. Ramon, S. P. Nolan, *J. Am. Chem. Soc.* **2009**, *131*, 448–449.
- [13] P. Roembke, H. Schmidbaur, S. Cronje, H. Raubenheimer, *J. Mol. Catal. A* **2004**, *212*, 35–42.
- [14] With the use of 1 mol-% of 1·AuCl, unreacted **3a** remained in ≈ 10 %.
- [15] M. P. Schramm, M. Kanaura, K. Ito, M. Ide, T. Iwasawa, *Eur. J. Org. Chem.* **2016**, 813–820.
- [16] A sealed tube was used as the reaction vessel owing to the low boiling point of 2-pentyne (56 °C).
- [17] We tried to obtain evidence of host–guest complexes by NMR spectroscopy techniques; however, unfortunately, we did not obtain any such evidence.
- [18] J. Rebek Jr., *Hydrogen-Bonded Capsules: Molecular Behavior in Small Spaces*, World Scientific Publishing Co. Pte Ltd., Imperial College Press, UK, **2016**.
- [19] A. Galan, P. Ballester, *Chem. Soc. Rev.* **2016**, *45*, 1720–1737.
- [20] a) S. Mosca, Y. Yu, J. V. Gavette, K.-D. Zhang, J. Rebek Jr., *J. Am. Chem. Soc.* **2015**, *137*, 14582–14583; b) D. M. Kaphan, F. D. Toste, R. G. Bergman, K. N. Raymond, *J. Am. Chem. Soc.* **2015**, *137*, 9202–9205; c) T. Iwasawa, R. J. Hooley, J. Rebek Jr., *Science* **2007**, *317*, 493–496.

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