

# Gold(III) Porphyrin-Catalyzed Cycloisomerization of Allenones

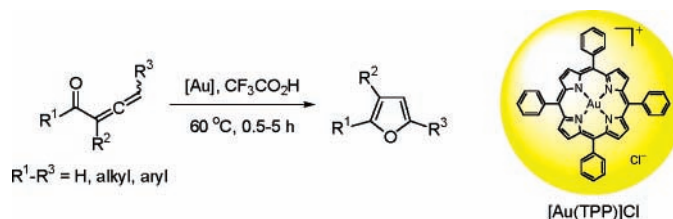
Cong-Ying Zhou, Philip Wai Hong Chan, and Chi-Ming Che\*

Department of Chemistry and Open Laboratory of Chemical Biology of the Institute of Molecular Technology for Drug Discovery and Synthesis, The University of Hong Kong, Pokfulam Road, Hong Kong

cmche@hku.hk

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## ABSTRACT



Gold(III) porphyrin-catalyzed cycloisomerization of allenones gave the corresponding furans in good to excellent yields (up to 98%) and with quantitative substrate conversions. By recovering the Au(III) catalyst, a recyclable catalytic system is developed with over 8300 product turnovers attained for the cycloisomerization of 1-phenyl-buta-2,3-dien-1-one. The versatility of the gold(III) porphyrin catalyst was exemplified by its application to the hydroamination and hydration of phenylacetylene in 73% and 87% yield, respectively.

Metalloporphyrin-mediated hydrocarbon functionalization has come under increasing scrutiny in recent years as an invaluable model system for biomimetic studies and potentially useful transformations in organic synthesis.<sup>1,2</sup> In the latter case, many of the studies have been focused on catalytic and stoichiometric C–C, C–N, and C–O bond formation reactions in the presence of porphyrinato complexes of Cr, Co, Fe, Mn, Os, Rh, and Ru.<sup>2</sup> In these organic transformations, manipulation of the steric and electronic properties of the porphyrin rings has been shown to result in unusually high selectivity including diastereo- and enantioselectivity and extremely high catalytic turnovers.<sup>2,3</sup> Despite these advances, examples of the use of metalloporphyrins in non-oxidative bond formation processes remain sparse; the recent examples are the applications of  $[\text{M}(\text{Por})(\text{L})]$  ( $\text{M} = \text{Fe, Cr, Ru}$ ;  $\text{Por} = \text{porphyrin}$ ,  $\text{L} = \text{neutral or anionic axial ligand}$ )

as Lewis acid catalysts for stereoselective epoxide ring opening<sup>4–6</sup> and imine cyclopropanation.<sup>7</sup>

The use of electrophilic gold(III) salts as Lewis acid catalysts for stereoselective C–X ( $\text{X} = \text{C, N, O, S}$ ) bond formation is currently receiving immense attention.<sup>8</sup> Although  $\text{AuCl}_3$  was noted to be a reactive catalyst, the challenge remains to develop a robust and highly chemoselective Au-catalyzed version of these reactions with high catalytic turnovers. In this context, we envision that Au(III) salts containing inexpensive tetraarylporphyrin ligands that are

(1) (a) Collman, J. P.; Boulatov, R.; Sunderland, C. J.; Fu, L. *Chem. Rev.* **2004**, *104*, 561. (b) Woggon, W.-D. *Acc. Chem. Res.* **2005**, *38*, 127.

(2) (a) Simonneaux, G.; Le Maux, P. *Coord. Chem. Rev.* **2002**, *228*, 43. (b) Che, C.-M.; Huang, J.-S. *Coord. Chem. Rev.* **2002**, *231*, 151. (c) Müller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905. (d) Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 8179 and references therein. (e) Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603.

(3) For selected examples, see: (a) Collman, J. P.; Fu, L.; Herrmann, P. C.; Zhang, X. *Science* **1997**, *275*, 949. (b) Gross, Z.; Galili, N.; Simkhovich, L. *Tetrahedron Lett.* **1999**, *40*, 1571. (c) Che, C.-M.; Huang, J.-S.; Lee, F.-W.; Li, Y.; Lai, T.-S.; Kwong, H.-L.; Teng, P.-F.; Lee, W.-S.; Lo, W.-C.; Peng, S.-M.; Zhou, Z.-Y. *J. Am. Chem. Soc.* **2001**, *123*, 4119. (d) Rose, E.; Ren, Q.-Z.; Andrioletti, B. *Chem. Eur. J.* **2004**, *10*, 224. (e) Chan, W.-K.; Wong, M.-K.; Che, C.-M. *J. Org. Chem.* **2005**, *70*, 4226. (f) Zhang, J.-L.; Che, C.-M. *Chem. Eur. J.* **2005**, *11*, 3899.

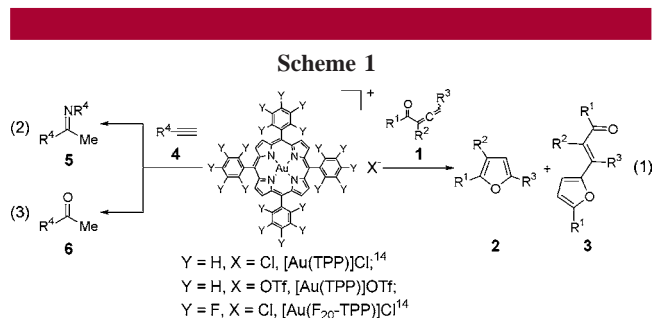
(4) Chen, J.; Che, C.-M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4950.

(5) (a) Suda, K.; Baba, K.; Nakajima, S.-I.; Takanami, T. *Chem. Commun.* **2002**, 2570. (b) Suda, K.; Kikkawa, T.; Nakajima, S.-I.; Takanami, T. *J. Am. Chem. Soc.* **2004**, *126*, 9554.

(6) Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426.

(7) Li, Y.; Chan, P. W. H.; Zhu, N.-Y.; Che, C.-M.; Kwong, H.-L. *Organometallics* **2004**, *23*, 54.

sterically bulky could hold promise for developing chemoselective Lewis acid catalysis. Although the physical<sup>9</sup> and biological<sup>10</sup> properties of gold(III) porphyrins have been studied, there are no reports on their use as catalysts for organic transformations. Herein, we describe the first metalloporphyrin-catalyzed cycloisomerization of allenones<sup>11</sup> in yields up to 98% and with >99% substrate conversion (reaction 1 in Scheme 1). The notable features of this



intramolecular C–O bond formation process are (1) the chemoselective formation of only the furan product and (2) the development of a recyclable catalytic system with a total product turnover number of 8300 attained. The first metalloporphyrin-catalyzed hydroamination<sup>12</sup> and hydration<sup>13</sup> of alkynes in yields up to 87% and with >99% substrate conversion (reactions 2 and 3 in Scheme 1) are also presented.

At the outset of this study, we found that treatment of **1a** (1 equiv) with 1 mol %  $[\text{Au}(\text{TPP})\text{Cl}]^{14}$  and 0.1 equiv  $\text{CF}_3\text{CO}_2\text{H}$  in acetone at 60 °C for 0.5 h gave the best result (see Table S1 in Supporting Information), furnishing **2a** in 88% yield with >99% substrate conversion (Table 1, entry 1). The analogous reactions conducted with  $\text{AuCl}_3$ ,  $\text{AuPPh}_3\text{Cl}$ ,

**Table 1.**  $[\text{Au}(\text{TPP})\text{Cl}]$ -catalyzed Cycloisomerization of Allenones **1a–w**<sup>a</sup>

entry	substrate	product	% yield <sup>d</sup>
1		<b>2a</b> , R = H	88
2		<b>2b</b> , R = <i>p</i> -Me	84
3		<b>2c</b> , R = <i>p</i> -OMe	81
4		<b>2d</b> , R = <i>p</i> -Br	85
5		<b>2e</b> , R = <i>m</i> -Br	87
6		<b>2f</b> , R = <i>o</i> -Br	98
7		<b>2g</b> , R = <i>p</i> -Cl	86
8 <sup>c</sup>		<b>2h</b> , R = <i>p</i> -CO <sub>2</sub> Me	92
9 <sup>e</sup>		<b>2i</b> , R = <i>p</i> -NO <sub>2</sub>	91
10		<b>2j</b> , R = H	80
11		<b>2k</b> , R = Br	85
12 <sup>c</sup>		<b>2l</b> , R = CO <sub>2</sub> Me	88
13			84
14 <sup>c</sup>			73
15			82
16	<b>1o–p</b>	<b>2o–p</b> , X = S	78
17		<b>2q</b> , R = Me	89 <sup>d</sup>
18	<b>1q–r</b>	<b>2r</b> , R = <sup>t</sup> Bu	92
19			90
20			97
21		<b>2u</b> , R = H	95
22 <sup>c</sup>	<b>1u–v</b>	<b>2v</b> , R = <sup>t</sup> Bu	93
23 <sup>c</sup>			90

<sup>a</sup> All reactions were performed in acetone at 60 °C for 0.5 h with ratio of  $[\text{Au}(\text{TPP})\text{Cl}]/\text{CF}_3\text{CO}_2\text{H}/\text{allenone} = 1:10:100$ . <sup>b</sup> Isolated yields with >99% conversions based on <sup>1</sup>H NMR analysis. <sup>c</sup> Reaction time = 2 h. <sup>d</sup> Yield by <sup>1</sup>H NMR. <sup>e</sup> Reaction time = 5 h.

(8) For recent reviews, see: (a) Dyker, G. *Angew. Chem., Int. Ed.* **2000**, 39, 4237. (b) Hashmi, A. S. K. *Gold Bull.* **2004**, 37, 51. (c) Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, 104, 2127. (d) Hoffmann-Röder, A.; Krause, N. *Org. Biomol. Chem.* **2005**, 3, 387. (e) Brown, R. C. D. *Angew. Chem., Int. Ed.* **2005**, 44, 850. For selected examples, see: (f) Ito, Y.; Sawamura, M.; Hayashi, T. *J. Am. Chem. Soc.* **1986**, 108, 6405. (g) Fukuda, Y.; Utimoto, K. *J. Org. Chem.* **1991**, 56, 3729. (h) Teles, J. H.; Brode, S.; Chabanas, M. *Angew. Chem., Int. Ed.* **1998**, 37, 1415. (i) Asao, N.; Takahashi, K.; Lee, S.; Kasahara, T.; Yamamoto, Y. *J. Am. Chem. Soc.* **2002**, 124, 12650. (j) Zhang, L.; Kozmin, S. A. *J. Am. Chem. Soc.* **2005**, 127, 6962. (k) Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2005**, 127, 6966. (l) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, 127, 11260.

(9) Eng, M. P.; Ljungdahl, T.; Andréasson, J.; Mårtensson, J.; Albinsson, B. *J. Phys. Chem. A* **2005**, 109, 1776 and references therein.

(10) For recent examples, see: (a) Che, C.-M.; Sun, R. W.-Y.; Yu, W.-Y.; Ko, C.-B.; Zhu, N.; Sun, H. *Chem. Commun.* **2003**, 1718. (b) Sun, R. W.-Y.; Yu, W.-Y.; Sun, H.; Che, C.-M. *ChemBioChem* **2004**, 5, 1293. (c) Nyarko, E.; Hara, T.; Grab, D. J.; Habib, A.; Kim, Y.; Nikolskaia, O.; Fukuma, T.; Tabata, M. *Chem.-Biol. Interact.* **2004**, 148, 19.

(11) For  $\text{AuCl}_3$ -catalyzed reactions, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, 39, 2285. (b) Sromek, A. W.; Rubina, M.; Gevorgyan, V. *J. Am. Chem. Soc.* **2005**, 127, 10500. For Ag(I)- and Rh(II)-catalyzed reactions, see: (c) Marshall, J. A.; Robinson, E. D. *J. Org. Chem.* **1990**, 55, 3450. (d) Marshall, J. A.; Wallace, E. M.; Coan, P. S. *J. Org. Chem.* **1995**, 60, 796 and references therein.

(12) Mizushima, E.; Hayashi, T.; Tanaka, M. *Org. Lett.* **2003**, 5, 3349.

(13) Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. *Angew. Chem., Int. Ed.* **2002**, 41, 4563.

(14) (a)  $\text{H}_2(\text{TPP}) = \text{meso-tetraphenylporphyrin}$ . (b)  $\text{H}_2(\text{F}_{20}\text{-TPP}) = \text{meso-tetrakis(pentafluorophenyl)porphyrin}$ . (c)  $\text{H}_2(\text{salen}) = N,N'$ -bis(salicylidene)-ethylenediamine.

$[\text{Au}(\text{salen})\text{Cl}]^{14}$  or  $\text{AgNO}_3$  as catalyst and acids other than  $\text{CF}_3\text{CO}_2\text{H}$  such as  $\text{TsOH}$  and  $\text{CH}_3\text{CO}_2\text{H}$  were found to proceed in lower product yields (17–87%, see Table S1 in Supporting Information). On the other hand, reactions of a series of allenones **1b–w** that include disubstituted and trisubstituted ones, under the optimal conditions mentioned earlier, afforded the corresponding furans **2b–w** in 73–98% yield and with >99% substrate conversion (entries 2–23). Notably, for each reaction shown in Table 1, no byproducts that could be attributed to formation of the dimer **3** were detected. For the  $\text{AuCl}_3$ -catalyzed reactions of **1i** and **1q**, such byproducts were isolated in yields up to 47%.<sup>11a</sup> In one case, where it was envisaged that the presence of two allenone groups on the substrate as in **1n** may lead to competitive side reactions, **2n** was obtained in 73% yield (entry 14). These findings highlight the uniqueness of gold(III) porphyrin catalyst, which is undoubtedly due to the sterically encumbered porphyrin ligand.

It is noteworthy that employment of  $\text{CF}_3\text{CO}_2\text{H}$  and a temperature of 60 °C for the cycloisomerization reaction is essential. Conducting the reaction at room temperature with

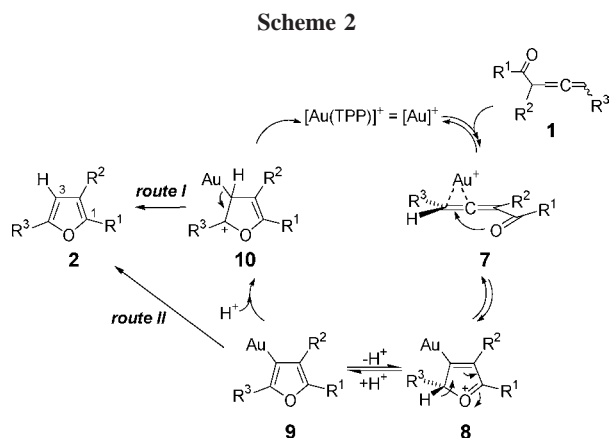
[Au(TPP)]Cl as catalyst gave **2a** in 28% yield with 31% substrate conversion and no reaction in the absence of CF<sub>3</sub>-CO<sub>2</sub>H with either [Au(TPP)]Cl or [Au(TPP)]OTf as catalyst (see Supporting Information). In contrast, by employing the optimal conditions mentioned earlier and recycling the Au(III) catalyst, a high turnover number could be achieved. With 0.1 mol % [Au(TPP)]Cl and CF<sub>3</sub>CO<sub>2</sub>H (0.1 equiv), reaction of **1a** gave **2a** in 85% yield, >99% substrate conversion and with 850 turnovers. The [Au(TPP)]Cl catalyst was recovered and subjected to another consecutive nine runs (see Supporting Information for details); the results are listed in Table 2. *No apparent loss of catalytic activity was observed, and a total product turnover of 8300 was attained.*

**Table 2.** Recyclable [Au(TPP)]Cl Catalyst for Cycloisomerization of **1a**<sup>a</sup>

entry	yield (%) <sup>b,c</sup>	turnovers
1	85	850
2	85	850
3	84	840
4	84	840
5	84	840
6	83	830
7	82	820
8	82	820
9	81	810
10	80	800

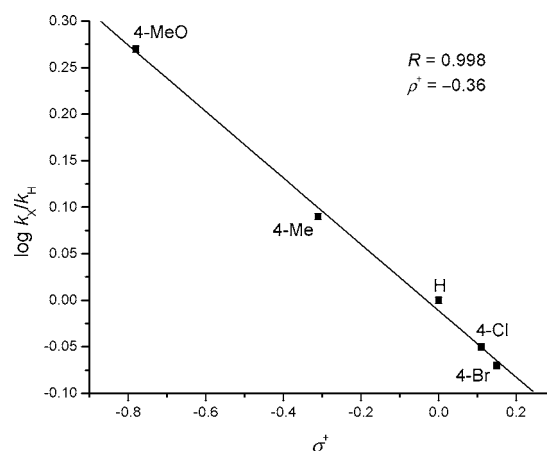
<sup>a</sup> Reactions were performed in acetone at 60 °C for 0.5 h with [Au(TPP)]Cl/CF<sub>3</sub>CO<sub>2</sub>H/allenone ratio of 1:100:1000. <sup>b</sup> Yield by <sup>1</sup>H NMR. <sup>c</sup> All substrate conversions were quantitative on the basis of <sup>1</sup>H NMR analysis.

As depicted in Scheme 2, we postulate that [Au(TPP)]<sup>+</sup> reversibly binds to the C=C=C moiety; such binding facilitates nucleophilic attack by the carbonyl oxygen at the terminal allene carbon. The short-lived furyl-gold species **9** undergoes acid-catalyzed demetalation via route I or II to give the furan product.<sup>15</sup> The role of CF<sub>3</sub>CO<sub>2</sub>H in facilitating demetalation is supported by the fact that no furan product was detected for the reaction of **1a** in the absence of CF<sub>3</sub>-



CO<sub>2</sub>H mentioned earlier and the following deuterium labeling experiments. Heating a *d*<sub>6</sub>-acetone–D<sub>2</sub>O (15:1 v/v) solution containing CF<sub>3</sub>CO<sub>2</sub>D (0.1 equiv) and either **1r** or **2r** at 60 °C for 30 min did not cause any observable deuterium exchange based on <sup>1</sup>H NMR analysis. Upon addition of [Au(TPP)]Cl catalyst, cycloisomerization of **1r** gave **2r** in 84% yield with >99% substrate conversion and with a deuterium content of 83% incorporated at C-3 as determined by <sup>1</sup>H NMR analysis and verified by mass spectrometry (see Supporting Information for details). The highly chemoselective nature of the present reaction should be due to a rapid irreversible demetalation step resulting from unfavorable steric interactions between the porphyrin ring and the newly formed furyl moiety. Previously, the susceptibility of such furyl-gold species to undergo Michael addition with the allenone substrate was proposed to account for the competitive formation of byproducts.<sup>11a</sup>

In this work, we performed competition experiments on the cycloisomerizations of *p*-X-C<sub>6</sub>H<sub>4</sub>C(O)CH=C=CH<sub>2</sub> [X = H (**1a**), Me (**1b**), OMe (**1c**), Br (**1d**) and Cl (**1g**)]. This revealed that allenones substituted with an electron-donating group are more reactive than **1a**, whereas those with electron-withdrawing *para*-substituents retard reaction (see Supporting Information for details). Fitting (by least-squares method) the log *k*<sub>X</sub>/*k*<sub>H</sub> data to the σ<sup>+</sup> scale gave rise to good linearity (*R* = 0.998) with a ρ<sup>+</sup> value of –0.36 (Figure 1). The small



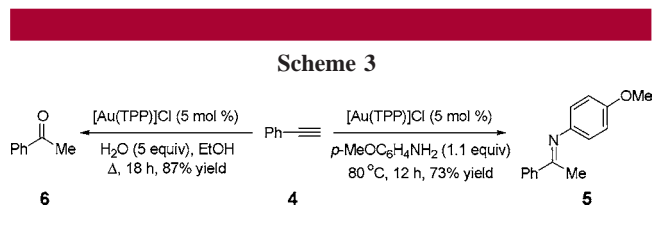
**Figure 1.** Linear free-energy correlation of log *k*<sub>X</sub>/*k*<sub>H</sub> vs σ<sup>+</sup> plot for cycloisomerization of *para*-substituted allenones *p*-X-C<sub>6</sub>H<sub>4</sub>C(O)CH=C=CH<sub>2</sub> **1a–d** and **1g** catalyzed by [Au(TPP)]Cl.

and negative ρ<sup>+</sup> value indicates minimal positive-charge development on the allenone substrate and electrophilic nature of the active Au(III) species. This might imply rate-limiting formation of the allenone-gold(III) intermediate **7** and explain the need for longer reaction times for complete substrate conversion of **1h–i**, **1l**, **1n**, **1v**, and **1w** (which

(15) See ref 11c,d and (a) Hashmi, A. S. K.; Ruppert, T. L.; Knöfel, T.; Bats, J. W. *J. Org. Chem.* **1997**, *62*, 7295. (b) Hoffmann-Röder, A.; Krause, N. *Org. Lett.* **2001**, *3*, 2537.

contain strongly electron-withdrawing or sterically bulky groups) shown in Table 1.

To highlight that gold(III) porphyrins could be a versatile class of catalysts for organic transformations, we examined the catalytic alkyne hydroamination<sup>12</sup> and hydration<sup>13</sup> reactions. Thus, by employing the conditions depicted in Scheme 3, [Au(TPP)]Cl-catalyzed hydroamination and hydration of



**4** gave **5** and **6** in 73% and 87% yield, respectively, with >99% substrate conversion on the basis of <sup>1</sup>H NMR analysis.

In summary, we report the first examples on the use of gold(III) porphyrins as practical catalysts for organic transformations. Given the diverse structures of porphyrin ligands known and the high reactivities of Au(III), the gold(III) porphyrins should present a new class of robust Lewis acid catalysts with useful applications.

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**Supporting Information Available:** Detailed experimental procedures and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>. OL052696C