Cite this: Chem. Commun., 2011, 47, 6719-6721

www.rsc.org/chemcomm

COMMUNICATION

Au(PPh₃)OPOF₂-catalyzed intramolecular [4+2] cycloaddition reaction of dienynes^{\dagger}

Soo Min Kim, Ji Hoon Park and Young Keun Chung*

Received 25th February 2011, Accepted 18th April 2011 DOI: 10.1039/c1cc11127b

Solvolysis of Au(PPh₃)PF₆ afforded Au(PPh₃)OPOF₂ which is an effective catalyst in the intramolecular [4+2] cycloaddition of unactivated dienynes bearing a terminal alkyne.

The development of effective cyclization reactions for the synthesis of carbocycles and heterocycles has been the subject of many extensive studies because of their relevance to biologically important and other functional materials. Among them, gold-catalyzed cyclization is one of the most popular branches of research in the formation of functionalized cyclic structures.^{1,2} In particular, the cycloisomerization of enynes, which produces novel intermediates is one of the most studied fields.³ In our continuous efforts to develop efficient catalytic reactions using gold complexes,⁴ we have also been studying the use of gold complexes in the catalytic cycloaddition of dienynes. In our attempt to make a cationic gold(I) complex $[Au(PPh_3)PF_6]$ to use as the catalyst in the cycloisomerization of dienyne 1, we isolated $Au(PPh_3)OPOF_2$ as the sole product. The formation of Au(PPh₃)OPOF₂ was confirmed by a combustion analysis and a X-ray diffraction study (Fig. 1). The anion PF_6^- was found to be hydrolyzed to $OPOF_2^-$. The solvolysis of the PF₆⁻ anion and the formation of the OPOF₂⁻ anion have already been reported for other systems.5

Fig. 1 X-Ray structure of $Au(PPh_3)OPOF_2$. Hydrogen atoms are omitted for clarity.

However, to the best of our knowledge, $Au(PPh_3)OPOF_2$ is first reported in this study (eqn (1)).⁶

$$\begin{array}{c|c} \mathsf{Ph}_3\mathsf{P}-\mathsf{Au}-\mathsf{CI} + \mathsf{AgPF}_6 & \xrightarrow{} & \mathsf{Ph}_3\mathsf{P}-\mathsf{Au}-\mathsf{OPOF}_2 \\ & \mathsf{CH}_2\mathsf{CI}_2 \\ & \mathsf{rt}, 1 \mathsf{h} & \mathsf{95\%} \end{array} (1)$$

In relation to gold-catalyzed [4+2] cycloaddition, Fürstner and Stimson have reported⁷ the [Au(PPh₃)Cl]/AgSbF₆catalyzed cycloaddition of unactivated alkynes and Echavarren group have reported⁸ the scope and mechanism of gold(1)-catalyzed intramolecular [4+2] cycloadditions of arylalkynes or 1,3-enynes with alkenes. Böhringer and Gagosz also used a gold(1)-catalyzed [4+2] reaction in the synthesis of functionalized bicyclo[4.3.0]nonenes.⁹ Very recently, we found that Au(PPh₃)OPOF₂ was also quite effective in the intramoleulcar [4+2] cycloaddition of dienynes. Herein, we report the Au(PPh₃)OPOF₂-catalyzed intramolecular [4+2]cycloaddition reaction of dienynes under very mild reaction conditions.

We investigated the gold(1)-catalyzed intramolecular [4+2] cycloaddition of a dienyne (1) bearing an *N*-Ts group (Table 1). We first screened neutral gold compounds, such as

 Table 1
 Screening the reaction conditions^a



^{*a*} 0.5 mmol of **1** was reacted with 5 mol% catalyst and 5 mol% of additive at room temperature. ^{*b*} Isolated yield. ^{*c*} 10 mol% AgSbF₆ was used. ^{*d*} 0.3 mol% catalyst used.

Intelligent Textile System Research Center, and Department of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, Korea. E-mail: ykchung@snu.ac.kr; Fax: +82 (2)889 0310; Tel: +82 (2) 880 6662

[†] Electronic supplementary information (ESI) available: Detailed experimental procedure and properties of compounds. CCDC 740934–740936. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc11127b

View Article Online

[Au(PPh₃)Cl] and [Au(IPr)Cl], as catalysts (entries 1 and 2). The reaction of 1 with [Au(PPh₃)Cl] in dichloromethane afforded 1a and 1c in 13% and 7% yields, respectively. The use of [Au(IPr)Cl] as a catalyst gave 1a in 15% yield. In both of these reactions, 80% of 1 was recovered. Apparently, it is concluded that a neutral gold compound was not active enough as a catalyst for the [4+2] cycloaddition of 1.

We next screened an *in situ* generated cationic gold(1) species derived from Au(PPh₃)Cl/AgSbF₆. When 5 mol% of Au(PPh₃)Cl and 5 mol% of AgSbF₆ were used, a mixture of 1a, 1b, and 1c was obtained in 25%, 20%, and 29% yields, respectively (entry 3). The formation of the cycloisomerization products, 1b and 1c, was confirmed by a X-ray diffraction study.¹⁰ The silver salt is very hydroscopic, making it difficult to weigh. Thus, when the amount of AgSbF₆ was doubled (entry 4), most of the substrates were decomposed and 1a and 1c were obtained in 8% and 7% yields, respectively. When we screened a different counter anion, such as BF₄⁻, NTf₂⁻ and PF_6^{-} , a similar distribution of products was observed in all three cases (entries 5–7). However, when Au(PPh₃)OPOF₂ was used as a catalyst, the yield dramatically increased to 97% (entry 8). In solvents such as dichloromethane, toluene, and THF, a high yield (91-99%) of **1a** was obtained. Moreover, the amount of the catalyst used could be reduced to 0.3 mol% in compensation for the long reaction time (48 h) (entry 11). Considering the reaction time and yield, Au(PPh₃)OPOF₂ was chosen as the catalyst in other reactions.

Next, we studied the Au(PPh₃)OPOF₂-catalyzed intramolecular [4+2] cycloaddition of various dienynes in THF (Table 2). All the terminal dienynes (entries 1-4) were good substrates. They gave the expected products in quantitative yields. The reaction was not affected by tethers. Dienynes (entries 5–10) with substituent(s) on a diene moiety were still good substrates. Interestingly, when an alkene or diene was a part of a cyclic moiety, *i.e.*, a cyclohexenyl or cyclohexadienyl group (entries 11 and 12), a quite different result was observed. When a dienyne bearing a cyclohexenyl group was used as the substrate, a mixture of two tricyclic compounds, a [4+2]cycloaddition product 11a and the respective aromatized product, was obtained in 45% and 5% yields. However, when a diene was part of a cyclohexadienyl group, the yield was 97%. The catalytic [4+2] cycloaddition was also effective for 1,7-dienynes (entries 13 and 14) although they needed a long reaction time. When the chain length between an alkyne and *N*-Ts increased, the yield after 72 h of reaction time was 66%. A dienvne with a longer tether chain between a diene and N-Ts was a good substrate, yielding 92% yield of the product after 24 h of reaction time.

However, the introduction of a substituent to the alkyne moiety was detrimental (Scheme 1). Thus, a dienyne (15) with a TMS-substituted internal alkyne gave the desilylated [4+2] cycloaddition product, 1a, in 64% yield after 24 h of reaction time with a 25% recovery of 15. Similarly, 16 also gave a desilylated [4+2] cycloaddition product, 2a, in 35% yield. Treatment of a dienyne (17) with a Me-substituted internal alkyne gave the cyclopropanated product, 17b, in 15% yield after 24 h of reaction time with a 51% recovery of the reactant. Based on the reactivity difference of terminal, silyl-substituted, and methyl-substituted alkynes, it seems that a desilyation

6720 | Chem. Commun., 2011, **47**, 6719–6721

Table 2Au(PPh_3)OPOF2-catalyzed intramolecular [4+2] cyclo-addition reaction of dienynes^a

| Entry | Reactant | | t/h | Product | | Yield ^b (%) |
|----------------|--|----|-----|--|-----|------------------------|
| 1 | TsN | 1 | 0.5 | TsN | 1a | 99 |
| 2 | MeO ₂ C MeO ₂ C | 2 | 0.5 | MeO ₂ C MeO ₂ C | 2a | 97 |
| 3 | MeO | 3 | 1.5 | Me O Me O | 3a | 99 |
| 4 | | 4 | 1 | K | 4a | 98 |
| 5 | | 5 | 2 | ····· | 5a | 90 ^c |
| 6 | TSN | 6 | 2 | TsN | 6a | 100 |
| 7 | TsN | 7 | 4 | TsN | 7a | 86 |
| 8 ^d | T sN | 8 | 2 | TsN | 8a | 96 |
| 9 | TsN | 9 | 24 | TsN | 9a | 97 |
| 10 | TsNPh | 10 | 6 | TsN | 10a | 96 |
| 11 | TsN | 11 | 24 | TsN | 11a | 45 ^e |
| 12 | TsN | 12 | 0.5 | TsN | 12a | 97 |
| 13 | TsN | 13 | 72 | TsN | 13a | 66 |
| 14 | TsN | 14 | 24 | TsN | 14a | 92 |

^{*a*} 0.5 mmol of the substrate was reacted with 5 mol% of Au(PPh₃)-OPOF₂ in THF at room temperature. ^{*b*} Yield of the isolated product. ^{*c*} A trace amount of an aromatized product was included. ^{*d*} The E/Z isomeric ratio 3:7 in **8** was retained in **8a**. ^{*e*} In addition, an aromatized product was isolated in 5% yield.

may happen slowly to generate a terminal alkyne under these reaction conditions and the resulting terminal alkyne undergoes a [4+2] cycloaddition reaction.

On the basis of the above results and previous reports,^{7,11} a plausible reaction mechanism was proposed (Scheme 2).



Scheme 1 Au(PPh₃)OPOF₂-catalyzed [4+2] cycloaddition of internal alkynes.



Scheme 2 Proposed mechanism.

We have demonstrated that $Au(PPh_3)OPOF_2$ is an effective catalyst in the intramolecular [4+2] cycloaddition of terminal dienynes. Further studies are needed to delineate the intimate mechanistic steps, and the origin of the high activity of $Au(PPh_3)OPOF_2$ is currently under investigation in our laboratory.

This work was supported by the National Research Foundation of Korea (NRF) (2010-0029663) and the Basic Science Research Program through the NRF funded by the Ministry of Education, Science and Technology (R11-2005-065).

Notes and references

- For reviews, see: (a) N. Krause and C. Winter, Chem. Rev., 2011, 111, 1994; (b) M. Bandini, Chem. Soc. Rev., 2011, 40, 1358; (c) A.
 - S. K. Hashmi, Angew. Chem., Int. Ed., 2010, 49, 5232;

(*d*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326; (*e*) L. Zhang, J. Sun and S. A. Kozmin, *Adv. Synth. Catal.*, 2006, **348**, 2271; (*f*) C. Nieto-Oberhuber, S. López, E. Jiménez-Núñez and A. M. Echavarren, *Chem.-Eur. J.*, 2006, **12**, 5916.

- For recent gold-catalyzed reactions, see: (a) H. Faustino, F. López, L. Castedo and J. L. Mascareñas, Chem. Sci., 2011, 2, 633; (b) C. Li, Y. Zeng, H. Zhang, J. Feng, Y. Zhang and J. Wang, Angew. Chem., Int. Ed., 2010, 49, 6413; (c) H. J. Bae, W. Jeong, J. H. Lee and Y. H. Rhee, Chem.-Eur. J., 2011, 17, 1433; (d) A. Escribano-Cuesta, V. López-Carrillo, D. Janssen and A. M. Echavarren, Chem.-Eur. J., 2009, 15, 5646; (e) P. Mauleón, R. M. Zeldin, A. Z. González and F. D. Toste, J. Am. Chem. Soc., 2009, 131, 6348; (f) R. A. Widenhoefer, Chem.-Eur. J., 2008, 14, 5382.
- 3 For recent papers, see: (a) H. Kusama, Y. Karibe, Y. Onizawa and N. Iwasawa, Angew. Chem., Int. Ed., 2010, 49, 4269; (b) Y. Matsumoto, K. B. Selim, H. Nakanishi, K.-I. Yamada, Y. Yamamoto and K. Tomioka, Tetrahedron Lett., 2010, 51, 404; (c) I. D. G. Watson, S. Ritter and F. D. Toste, J. Am. Chem. Soc., 2009, 131, 2056; (d) Y. Odabachian and F. Gagosz, Adv. Synth. Catal., 2009, 351, 379; (e) F.-D. Boyer, X. L. Goff and I. Hanna, J. Org. Chem., 2008, 73, 5163.
- 4 (a) S. M. Kim, J. H. Park, Y. K. Kang and Y. K. Chung, Angew. Chem., Int. Ed., 2009, 48, 4532; (b) S. M. Kim, J. H. Park, S. Y. Choi and Y. K. Chung, Angew. Chem., Int. Ed., 2007, 46, 6172; (c) S. I. Lee, S. M. Kim, M. R. Choi, S. Y. Kim and Y. K. Chung, J. Org. Chem., 2006, 71, 9366.
- F. L. Wimmer and M. R. Snow, Aust. J. Chem., 1978, 31, 267;
 M. A. Bennett, T. W. Matheson, G. B. Robertson, W. L. Steffen and T. W. Turney, J. Chem. Soc., Chem. Commun., 1979, 32; (c) G. Smith, D. J. Cole-Hamilton, A. C. Gregory and N. G. Gooden, Polyhedron, 1982, 1, 97; (d) R. Fernandez-Galan, B. R. Manzano, A. Otero, M. Lanfranchi and M. A. Pellinghelli, Inorg. Chem., 1994, 33, 2309.
- 6 We took ¹H and ³¹P NMR spectra of Au(PPh₃)PF₆ prepared in a glove box. Initially, we only observed the peak due to the phenyl group and no water peak in the ¹H NMR spectrum. However, as time passed, we could see the transformation of PF₆ into PF₂O₂ in ³¹P NMR spectra. The result of NMR experiments is deposited in ESI[†].
- 7 A. Fürstner and C. C. Stimson, Angew. Chem., Int. Ed., 2007, 46, 8845.
- 8 (a) C. Nieto-Oberhuber, P. Pérez-Galán, E. Herrero-Gómez, T. Lauterbach, C. Rodríguez, S. López, C. Bour, A. Rosellón, D. J. Cárdenas and A. M. Echavarren, J. Am. Chem. Soc., 2008, 130, 269; (b) C. Nieto-Oberhuber, S. López and A. M. Echavarren, J. Am. Chem. Soc., 2005, 127, 6178.
- 9 S. Böhringer and F. Gagosz, Adv. Synth. Catal., 2008, 350, 2617.
- 10 ESI†.
- (a) N. Cabello, E. Jiménez-Núñez, E. Buñuel, D. J. Cárdenas and A. M. Echavarren, *Eur. J. Org. Chem.*, 2007, 4217; (b) C. Nieto-Oberhuber, M. P. Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem.-Eur. J.*, 2006, **12**, 1677.