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Phosphate ligands in the gold(I)-catalysed activation of enynes†

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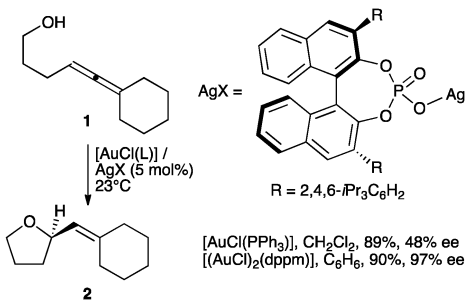
Gold(I) forms neutral complexes with binol phosphates that are unreactive in the catalytic cyclisation of enynes. Reaction in protic solvents or activation by silver(I) restores the catalytic activity.

The reactive gold(I) species $[AuL]^+$ in the catalytic activation of alkynes, allenes, and alkenes are often formed by chloride abstraction from [AuCl(L)] complexes using silver(I) salts.[1] In 2007, Toste and coworkers demonstrated that achiral complexes [AuCl(L)] became enantioselective catalysts upon activation with silver binol phosphate salts in the cyclisation of allenols such as **1** to form tetrahydrofuran **2** (Scheme 1) and in related transformations of allenyl sulfonamides,[2,3] as well as in the enantioselective synthesis of pyrazolidines, isoxazolidines and tetrahydrooxazines.[4] It was postulated that an ion pair $[Au(L)]^+X^-$ was formed *in situ* by reaction of [AuCl(L)] with the silver binol phosphate, although the resulting complexes were neither isolated nor characterized.[5] The importance of ion pairing has been recognized in other contexts in gold catalysis.[6] Complexes $[(AuX)_2(L–L)]$ and $[Au_2XCl(L–L)]$ (L–L = bidentate phosphine) were also active in the enantioselective cyclisation of hydroxy- and sulfonamidoallenes.[7] Chiral phosphoric acids in combination with gold complexes have also been used in other enantioselective transformations.[8,9]

Despite the success in enantioselective catalysis using allene derivatives,[2,4,7] this concept has not been extended to the activation of alkynes, the most general playground in gold catalysis.[1] In addition, the nature of the silver(I) and gold(I) binol phosphate complexes used in the activation of allenes was not well defined. Here we show that the binol phosphates form covalent species [AuX(L)]. Although these complexes activate allenes, terminal alkynes lead to alkynyl–gold(I) complexes that are catalytically inactive.



Scheme 1 Enantioselective cyclisation of allenols.[2]

Silver(I) phosphate complexes **5** and **6**, prepared by reaction of the binol phosphoric acids **3** and **4** with Ag_2O, showed ^{31}P NMR spectra consistent with the formation of dimeric species or higher aggregates (Scheme 2).[10] Thus, **5** shows an apparent triplet in CD_2Cl_2 or C_6D_6 at all concentrations. In diluted CD_2Cl_2 solutions, the ^{31}P NMR spectrum of **6** consists of a triplet that becomes a multiplet and then a broad singlet in more concentrated solutions. The formation of dimeric species was confirmed by X-ray diffraction of complex **5**, which showed a C_2 symmetrical structure with a Ag–Ag distance of 3.072 Å (Scheme 2).

Silver(I) complexes **5** and **6** reacted with $[AuCl(PPh_3)]$ to give gold(I) complexes **7** and **8** in good yields (Scheme 2). These gold(I) phosphate complexes are very robust and can be purified by flash chromatography on SiO_2. Long-range ^{31}P–^{31}P coupling could be observed in the ^{31}P NMR spectra of **7** and **8** (3.6 and 2.6 Hz, respectively), which shows that the phosphate is covalently bound to Au(I). Their covalent structures were confirmed by the X-ray structure of complex **7**·$CHCl_3$, which shows an almost linear P–Au–O bond (172.7°). The Au–O distance of 2.056 Å is in line with reported data for other well-characterized phosphine–Au(I) phosphate complexes (2.06 Å).[7a,11] The $CHCl_3$ molecule is hydrogen bonded to the P=O group (*ca.* 1.93 Å). A second solvate containing water and methanol was obtained by crystallizing **7** from methanol in which the Au–O bond is lengthened from 2.056 Å in **7**·$CHCl_3$ to 2.101 Å in the **7**·MeOH/H_2O solvate. The P=O distance in **7**·MeOH/H_2O is also longer than that in **7**·$CHCl_3$ (1.493 *vs.* 1.463 Å). Additionally, under concentrations comparable to the ones employed in catalysis, the molar conductivity of **7** in CH_2Cl_2 is two orders of magnitude lower than that of cationic gold(I) complex [Au(*o*-biphenP*t*Bu$_2$)(MeCN)]SbF_6 (**9a**),[12] which supports the covalent nature of **7** in solution.

Well-characterized **7** and **8** (5 mol%) catalysed the cyclisation of allenol **1** into tetrahydrofuran **2** (80%, 3 h, 24% ee and 73% yield, 30 min, 48% ee, respectively) (Scheme 1) in total agreement with the results reported by Toste with the complexes formed *in situ*. Surprisingly, **7** and **8** were inactive in the cyclisation of **10**, a highly reactive 1,6-enyne in gold(I)-catalyzed reactions.[12,13] This enyne has been reported to form the product of single cleavage rearrangement **11** almost quantitatively with only

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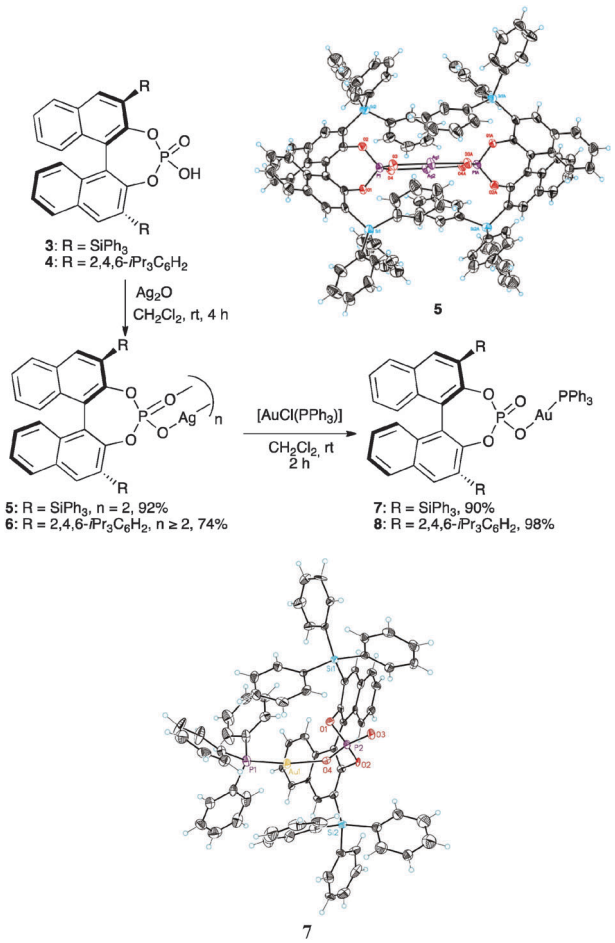
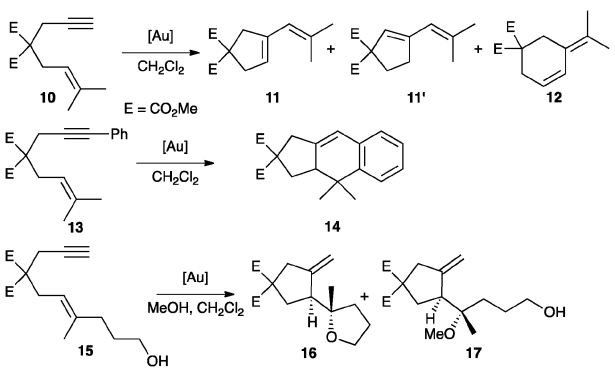
† Electronic supplementary information (ESI) available: Synthesis of starting substrates, characterization and X-ray crystallographic data. CCDC 841519 (**5**), 841517 (**7**·$CHCl_3$), and 841518 (**7**·MeOH/H_2O). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1cc15739f



Scheme 2 Synthesis and structures of Ag(I)–Au(I)–phosphate complexes.

0.01 mol% of neutral complex $[Au(NTf_2)(PPh_3)]$ in 30 min,[14] whereas cationic catalyst $[Au(o\text{-biphenPCy}_2)(MeCN)]SbF_6$ led to **11** at temperatures as low as −63 °C[12] (Scheme 3). In contrast, no reaction was observed after 3 days at 23 °C in the presence of complex **7**. Similarly, no cyclisation of **13** into **14**[15] was observed even after heating at 40 °C in CH_2Cl_2 (microwave irradiation) with complexes **7** or **8** for 12 h. These reactions also failed with gold(I) phosphate complexes generated *in situ* by mixing Ag(I) complex **5** (2.5 mol%) with $[AuCl(PPh_3)]$ (5 mol%), $[AuCl(o\text{-biphenPCy}_2)]$ (5 mol%), $[(AuCl)_2(dppm)]$ (2.5 mol%), or $[(AuCl)_2(binap)]$ (2.5 mol%). Furthermore, no reaction was observed when enynol **15** was treated with **7** (5 mol%) in CH_2Cl_2 at 23–40 °C, whereas $[Au(PPh_3)Cl]$ and $AgSbF_6$ (3 mol% each) catalysed the transformation of **15** into **16**[12] in 45 min (76% yield) (Scheme 3). The catalytic activity of **7** (5 mol%) was restored in the presence of MeOH (55 equivalents), leading to **16** (19%) and **17** (44%) after 48 h at 23 °C.



Scheme 3 Gold(I)-catalysed cyclisations of selected 1,6-enynes.

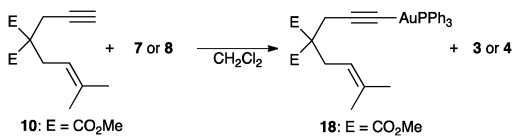
Addition of an equimolar amount of $[Ag(NCMe)_2]SbF_6$[16] to complex **7** (5 mol%) also restores the catalytic activity in the skeletal rearrangement of 1,6-enyne **10**, yielding a 9 : 1 ratio of **11** and **12** after 20 min in quantitative yield at 23 °C. The formal intramolecular [4 + 2] cycloaddition of **13** also proceeded satisfactorily in the presence of $[Ag(NCMe)_2]SbF_6$ to give racemic **14** in 81% yield after 6 h. Presumably, under these conditions, catalytically active gold(I) complex $[Au(PPh_3)(MeCN)]SbF_6$ along with silver(I) salt **5** are formed.

Gold(I)–phosphate complexes **7** and **8** catalysed the hydration of 1-octyne in aqueous methanol at 23 °C (1 mol% catalysts, 67 h) leading to 2-octanone (43% and 100% yields with **7** and **8**, respectively).[17] Surprisingly, monitoring the reaction by ^1H NMR revealed that deuterium exchange at the alkyne proton is much faster than the hydration reaction.

These results point to a facile deprotonation of the terminal alkyne by the gold(I) phosphate leading to the formation of the corresponding gold(I)–acetylide.[18] Indeed, 1,6-enyne **10** reacted with **7** and **8** (5 mol%) in CH_2Cl_2 at 23 °C to form gold(I)–acetylide **18** and phosphoric acids **3** and **4** (43–47% conversion after 33 h). Phenylacetylene reacted similarly with complexes **7** and **8** to give $PhC{\equiv}C{-}AuPPh_3$ (24–32% conversion after 17–25 h). Whereas acetylide **18**, prepared from **10** and $[Au(PPh_3)Cl]$ in the presence of NaOEt, was stable in solution, the addition of 1 equivalent of TfOH or Tf_2NH in $CDCl_3$ led to the formation of **11** and **12**, along with isomerized diene **11′**[19,20] (86%, 30 min and 80%, 90 min, respectively) (Scheme 4).

Neutral difluorophosphate complex $[Au(OPOF_2)(PPh_3)]$ (**19**) has been recently prepared by reaction of $[Au(PPh_3)Cl]$ with $AgPF_6$ in wet CH_2Cl_2.[11,21] Cyclisation of 1,6-enyne **10** with **19** as catalyst proceed very sluggishly under standard conditions (*ca.* 7% conversion after 1 h with 5 mol% **19** at 23 °C). This is somewhat surprising considering that the difluorophosphate anion is considerably less basic than the binol phosphates.[22] For comparison, complexes $[Au(PPh_3)(MeCN)]SbF_6$ and $[Au(NTf_2)(PPh_3)]$ (1 mol%) gave quantitatively **11**, **11′**, and **12** (2 : 1 : 2 ratio) in only 30 min. To further confirm the poor catalytic reactivity of covalently bound gold(I) phosphate complexes, we prepared cationic and neutral gold(I) complexes **9b** and **9c** (Fig. 1) and compared their reactivity in the cyclisation of **10**. Thus, whereas **9b** (5 mol%) led to quantitative conversions after 30 min, reaction with **9c** required 17 h to give a different mixture of products.[23,24]

Gold(I) complexes [AuX(L)] with phosphates and other anionic X ligands that are sufficiently basic form alkynyl–gold(I) complexes **II** and/or binuclear derivatives resulting from coordination of AuL^+ to **II**,[18a,d,f] which are catalytic dead ends (Scheme 5).



Scheme 4 Formation of gold(I)–acetylide complex **18** from enyne **10**.

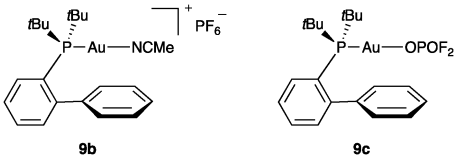
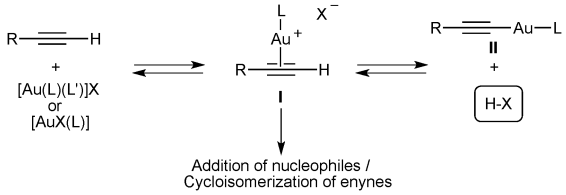


Fig. 1 Cationic and neutral gold(I)–phosphate complexes **9b–c**.



Scheme 5 General pathways in the gold(I)-activation of terminal alkynes.

In contrast, these species probably play a minor role in catalysis with complexes [AuX(L)] or [Au(L)(L′)]X whose anionic ligands are the conjugate bases of very strong acids, such as $HSbF_6$, HBF_4, or Tf_2NH. In these cases, the released strong Brønsted acid HX shifts the equilibrium towards **I** and does not act as a catalyst in the cyclisation as demonstrated by control experiments carried out with HBF_4, TfOH, and Tf_2NH and enynes **10** and **13**.[25]

In the case of gold(I)–phosphate complexes the use of a protic solvent such as methanol restores the catalytic activity presumably by facilitating the associative ligand substitution step[12] through activation of the phosphate ligand by an H-bond and by lowering the basicity of the phosphate anions by solvation. The lack of reactivity of enyne **13** in the presence of **7** and **8** shows that the first step of the catalytic cycle that forms cationic species **I** is much slower with these neutral complexes than with cationic gold(I) catalysts $[Au(L)(L')]^+X^-$ (L′ = weakly coordinating ligand).

This work shows that in order to extend the chiral counter-ion concept to gold(I)-catalysed activation of alkynes, anionic ligands less basic than phosphates should be used.

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Notes and references

1 (*a*) E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326–3350; (*b*) D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351–3378; (*c*) A. Fürstner, *Chem. Soc. Rev.*, 2009, **38**, 3208–3221.
2 G. L. Hamilton, E. J. Kang, M. Mba and F. D. Toste, *Science*, 2007, **317**, 496–499.
3 Enantioselective cyclisation of allenyl sulfonamides with (*R*)-xylyl-BINAP(AuOPNB)$_2$ (PNB = *p*-nitrobenzoate): (*a*) R. L. LaLonde, B. D. Sherry, E. J. Kang and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 2452–2453; (*b*) J. H. Kim, S.-W. Park, S. R. Park, S. Lee and E. J. Kang, *Chem.–Asian J.*, 2011, **6**, 1982–1986.
4 R. L. La Londe, Z. J. Wang, M. Mba, A. D. Lackner and F. D. Toste, *Angew. Chem., Int. Ed.*, 2010, **49**, 598–601.
5 Review on the use of chiral anions in stereoselective synthesis: J. Lacour and D. Moraleda, *Chem. Commun.*, 2009, 7073–7089.
6 D. Zuccaccia, L. Belpassi, F. Tarantelli and A. Macchioni, *J. Am. Chem. Soc.*, 2009, **131**, 3170–3171.
7 (*a*) K. Aikawa, M. Kojima and K. Mikami, *Angew. Chem., Int. Ed.*, 2009, **48**, 6073–6077; (*b*) K. Aikawa, M. Kojima and K. Mikami, *Adv. Synth. Catal.*, 2010, **352**, 3131–3135.
8 (*a*) X.-Y. Liu and C.-M. Che, *Org. Lett.*, 2009, **11**, 4204–4207; (*b*) Z.-Y. Han, H. Xiao, X.-H. Chen and L.-Z. Gong, *J. Am. Chem. Soc.*, 2009, **131**, 9182–9183; (*c*) M. E. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt and D. J. Dixon, *J. Am. Chem. Soc.*, 2009, **131**, 10796–10797; (*d*) C. Wang, Z.-Y. Han, H.-W. Luo and L.-Z. Gong, *Org. Lett.*, 2010, **12**, 2266–2269; (*e*) A. S. K. Hashmi and C. Hubbert, *Angew. Chem., Int. Ed.*, 2010, **49**, 1010–1012.
9 Review on binol-derived phosphoric acids and amides as Brønsted acid catalysts: M. Rueping, B. J. Nachtsheim, W. Ieawsuwan and I. Atodiresei, *Angew. Chem., Int. Ed.*, 2011, **50**, 6706–6720.
10 X-Ray structure of a related complex: M. Rueping, R. M. Koenigs and I. Atodiresei, *Chem.–Eur. J.*, 2010, **16**, 9350–9365.
11 S. M. Kim, J. H. Park and Y. K. Chung, *Chem. Commun.*, 2011, **47**, 6719–6721.
12 C. Nieto-Oberhuber, S. López, M. P. Muñoz, D. J. Cárdenas, E. Buñuel, C. Nevado and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2005, **44**, 6146–6148.
13 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**, 1677–1693.
14 N. Mézailles, L. Ricard and F. Gagosz, *Org. Lett.*, 2005, **7**, 4133–4136.
15 (*a*) C. Nieto-Oberhuber, S. López and A. M. Echavarren, *J. Am. Chem. Soc.*, 2005, **127**, 6178–6179; (*b*) 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**, 269–279.
16 M. Raducan, C. Rodríguez-Escrich, X. C. Cambeiro, E. Escudero-Adán, M. A. Pericàs and A. M. Echavarren, *Chem. Commun.*, 2011, **47**, 4893–4895.
17 (*a*) N. Marion, R. S. Ramón and S. P. Nolan, *J. Am. Chem. Soc.*, 2009, **131**, 448–449; (*b*) A. Leyva and A. Corma, *J. Org. Chem.*, 2009, **74**, 2067–2074.
18 (*a*) P. H.-Y. Cheong, P. Morganelli, M. R. Luzung, K. N. Houk and F. D. Toste, *J. Am. Chem. Soc.*, 2008, **130**, 4517–4526; (*b*) Y. Odabachian, X.-F. Le Goff and F. Gagosz, *Chem.–Eur. J.*, 2009, **15**, 8966–8970; (*c*) S. Gaillard, A. M. Z. Slawin and S. P. Nolan, *Chem. Commun.*, 2010, **46**, 2742–2744; (*d*) T. N. Hooper, M. Green and C. A. Russell, *Chem. Commun.*, 2010, **46**, 2313–2315; (*e*) G. C. Fortman, A. Poater, J. W. Levell, S. Gaillard, A. M. Z. Slawin, I. D. W. Samuel, L. Cavallo and S. P. Nolan, *Dalton Trans.*, 2010, **39**, 10382–10390; (*f*) A. Simonneau, F. Jaroschik, D. Lesage, M. Karanik, R. Guillot, M. Malacria, J.-C. Tabet, J.-P. Goddard, L. Fensterbank, V. Gandon and Y. Gimbert, *Chem. Sci.*, 2011, DOI: 10.1039/c1sc00478f; (*g*) M. C. Blanco, J. Cámara, M. C. Gimeno, P. G. Jones, A. Laguna, J. M. López de Luzuriaga, M. E. Olmos and M. D. Villacampa, *Organometallics*, 2011, DOI: 10.1021/om200397t; (*h*) T. J. Brown and R. A. Widenhoefer, *Organometallics*, 2011, DOI: 10.1021/om200840g.
19 C. Nieto-Oberhuber, M. Paz Muñoz, S. López, E. Jiménez-Núñez, C. Nevado, E. Herrero-Gómez, M. Raducan and A. M. Echavarren, *Chem.–Eur. J.*, 2006, **12**, 1677–1693.
20 In addition, products assigned to the addition of TfOH or Tf_2NH to the 1,6-enyne were also observed in the crude reaction mixtures.
21 Complex **19** shows two signals in the ^{31}P NMR ($CDCl_3$) at δ 30.54 (s, PPh_3) and −10.28 (t, $J(^{31}P–^{19}F)$ = 973.0 Hz, PO_2F_2).
22 (*a*) A pK_a of 0.3 has been reported for difluorophosphoric acid in water: J. W. Larson and B. Su, *J. Chem. Eng. Data*, 1994, **39**, 33–35; (*b*) A pK_a of 4.2 has been determined for phosphoric acid **6** in DMSO: P. Christ, A. G. Lindsay, S. S. Vormittag, J.-M. Neudörf, A. Berkessel and A. C. O'Donoghoue, *Chem.–Eur. J.*, 2011, **17**, 8524–8528.
23 See ESI† for details.
24 (*a*) A pK_a of 4.2 has been determined for phosphoric acid **6** in DMSO: P. Christ, A. G. Lindsay, S. S. Vormittag, J.-M. Neudörf, A. Berkessel and A. C. O'Donoghoue, *Chem.–Eur. J.*, 2011, **17**, 8524–8528; (*b*) The pK_a of benzoic acid in DMSO is 11: W. N. Olmstead and F. D. Bordwell, *J. Org. Chem.*, 1980, **45**, 3299–3305.
25 No reaction was observed with **10** or **13** using HBF_4, TfOH, and Tf_2NH (1 and 5 mol%, respectively, 24 h in $CDCl_3$).

