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A dual catalytic strategy for carbon–phosphorus cross-coupling via gold and photoredox catalysis[†]

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coupling with the H-phosphonate nucleophile.

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A new method for the P-arylation of aryldiazonium salts with H-phosphonates via dual gold and photoredox

catalysis is described. The reaction proceeds smoothly at room temperature in the absence of base and/or

additives, and offers an efficient approach to arylphosphonates. The reaction is proposed to proceed

through a photoredox-promoted generation of an electrophilic arylgold(iii) intermediate that undergoes

also engage in coupling reactions with other nucleophilic species [eqn (3)].11



Results and discussions

To this end, we explored the dual photoredox/gold-catalyzed coupling reaction of p-tolyldiazonium12 with diethyl phosphite (Table 1). The initial screening of solvents found that the desired product was formed in 37% yield when acetonitrile was employed as solvent (Table 1, entry 1). Other solvents commonly employed in photocatalysis, such as DMF and EtOH, were also tested and afforded the product in 50% and 65%, respectively (Table 1, entries 2 and 3). In order to exploit the better solubility of diazonium salts and tautomerization of H-phosphonates13 in polar solvents, we explored whether a solvent mixture with ethanol might improve the reaction outcome. The co-solvent consisting of MeCN/EtOH (4:1) gave the best result, affording the arylphosphonate in 82% yield (Table 1, entries 4–7). Lower yields were obtained when $Ru(bpy)_3Cl_2$ or $Ir(ppy)_3$ were used as the photocatalyst (Table 1, entries 8 and 9). No product was observed with IPrAuCl as the gold catalyst (Table 1, entry 10), and reducing the amount of photocatalyst or gold catalyst both gave lower yields (Table 1, entries 11 and 12). Moreover, no product was detected when the reaction was performed in the

During the past decade, homogeneous gold reactions based on Au(1) or Au(111) catalysis have emerged as an extraordinary tool to create molecular complexity. In these reactions, gold mostcommonly acts as a redox-neutral and carbophilic π -acid that activates carbon-carbon multiple bonds towards nucleophilic attack.1 Alternatively, gold-catalyzed transformations employing a stoichiometric external oxidant, such as Selectfluor, have allowed entry into pathways involving Au(I)/Au(III);² however, the majority of these reactions still involve intermediates generated from activation of a carbon–carbon π -bond. The requirement for stoichiometric amounts of strong oxidizing reagents has generally limited the chemistry to π -bonds and aromatic compounds.3 Recently, stepwise oxidation of gold(I) complexes by photoredox-generated⁴ radical species has emerged as an strategy for accessing Au(I)/Au(III) coupling alternative reactions.5

Organophosphorus compounds have drawn increasing attention due to their broad applications in biological, pharmaceutical, and material sciences.6 These compounds are commonly accessed through transition metal-catalyzed coupling processes.⁷ More recently, the desired coupling has been achieved through the reaction of phosphonate esters8 or phosphine oxides⁹ with highly electrophilic arylcopper(III) intermediates¹⁰ generated from oxidation of copper(I) with diaryliodionium(m) salts [eqn (1)]. While the reported combined photoredox/gold-catalyzed reactions have relied on the intervention of carbon–carbon π -bonds [eqn (2)], we hypothesized that the gold(m) intermediates generated in this manner might



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Entry	Cat.	Photocatalyst	Solvent	Time (h)	Yield ^b (%)
1	Ph₃PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN	4	37
2	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	DMF	4	50
3	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	EtOH	4	65
4	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	DMF: EtOH = 4:1	4	49
5	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	82
6	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 1:1	4	61
7	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 9:1	4	58
8	Ph ₃ PAuCl	$Ru(bpy)_3Cl_2$	MeCN: EtOH = 4:1	4	77
9	Ph ₃ PAuCl	Ir(ppy) ₃	MeCN: EtOH = 4:1	4	24
10	IPrAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	0
11 ^c	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	73
12^d	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	54
13	_	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	0
14	Ph ₃ PAuCl		MeCN: EtOH = 4:1	4	<10
15^e	Ph ₃ PAuCl	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	<5
16	$Pd(OAc)_2$	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	4	43
17	AgNTf ₂	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0
18	$AgBF_4$	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0
19 ^f	$AgBF_4$	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0
20	AgOTf	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0
21	$Cu(OAc)_2$	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0
22	CuI	$Ru(bpy)_3(PF_6)_2$	MeCN: EtOH = 4:1	16	0

^{*a*} Reactions were carried out at room temperature with a 26 W household bulb, **1a** (0.3 mmol), **2a** (0.1 mmol), cat. (10 mol%), photocatalyst (2 mol%), degassed solvent (0.5 ml), N₂ atmosphere, rt. ^{*b*} Isolated yields. ^{*c*} 1 mol% Ru(bpy)₃(PF₆)₂ was used. ^{*d*} 5 mol% Ph₃PAuCl was used. ^{*e*} Reaction run in the dark. ^{*f*} 10 mol% PPh₃ was used as the ligand.

absence of the gold catalyst (Table 1, entry 13) and significantly reduced yields of **3a** were observed in the absence of the $Ru(bpy)_3(PF_6)_2$ and/or light (Table 1, entries 14 and 15). We also examined replacing the gold catalyst with those derived from palladium, silver or copper salts; however, only moderate yield was obtained when $Pd(OAc)_2$ was used (Table 1, entry 16), and no product was detected with other catalysts even when the reaction time was prolonged to 16 h (Table 1, entries 17–22).

With the optimized conditions in hand, we investigated the scope of the diazonium substrates. Aryldiazoniums salts bearing electron-donating groups at their para-positions, such as methyl, phenyl and methoxy, were coupled with diethyl phosphite affording the corresponding products in good to excellent yields (Table 2, compounds 3a-3c). However, the reactivity was dramatically decreased when aryldiazoniums salts containing strong withdrawing groups such as -CF3 and -NO₂ were used (Table 2, compounds 3k and 3l). As expected, the P-arylation using aryl diazoniums with halogen in their para and meta positions proceeded efficiently, and yields of 71-86% were obtained (Table 2, compounds 3e-3g). However, 2-bromophenyl diazonium was less reactive comparatively and 37% yield of the product was obtained (Table 2, compound 3h). The naphthyl phosphonate was isolated in 72% yield under the standard reaction conditions (Table 2, compound 3i).

We next turned our attention to an evaluation of the scope and limitations of our reaction with different types of P(O)Hcompounds. As seen in Table 3, aryl diazonium salts with electron-donating, electron-withdrawing and halogen substituents reacted with *H*-phosphonate diesters bearing different alkyl groups efficiently, and yields of 74–90% were obtained (Table 3, entries 1–5). The reaction also proceeded smoothly with dibenzyl and ethyl phenylphosphinate as coupling partners (Table 3, entries 6 and 8). The more challenging coupling of *H*-phosphonate diphenylester also occurred under the gold-catalyzed reaction conditions, albeit it in diminished yield (Table 3, entry 7).

Interestingly, phenyl phosphinic acid was also a competent nucleophile for this reaction yielding products of a threecomponent coupling between the diazonium salt, arylphosphinic acid and the alkyl alcohol solvent [eqn (4)].

Additionally, the intermediate aryl diazonium salt can be generated without purification from the corresponding aniline. For example, **3e** was obtained in 69% through one-pot, two-step procedure for the diazotization and *P*-arylation of 4-fluoroaniline, compared with 86% under standard conditions [eqn (5)].

Table 2 P-arylation of various aryldiazoium salts with diethyl phosphite^a



^a Reaction conditions: 1 (0.3 mmol), 2a (0.1 mmol), Ph₃PAuCl (10 mol%), Ru(bpy)₃(PF₆)₂ (2 mol%), degassed MeCN : EtOH = (4:1) (0.5 ml), N₂ atmosphere, visible light, rt. for 4h, isolated yields for all products. b 1 (9 mmol), 2a (3 mmol), Ph₃PAuCl (8 mol%), $Ru(bpy)_3(PF_6)_2$ (2 mol%); isolated yields.

Ph₂PAuC ۱₂BF Ru(bpy)₃(PF₆)₂ OR2 ·OR₂ R₃ R₃ MeCN:EtOH= 4:1 visible light,RT R4 2 3m-3t Yield^b (%) P(O)H compounds Entry R_1 1^c OMe 3m, 90 20 F **3n**, 74 3^c COOMe **30**, 88 4^d ОМе 3p, 81 5^d F 3q, 84 0 6 OMe 3r, 50 o^{,Ph} 7 OMe 3s, 31 8 OMe 3t, 82

Table 3 Scope studies of various P(O)H compounds and aryldiazo-

nium salts^a

^a Reaction conditions: 1 (0.3 mmol), 2 (0.1 mmol), Ph₃PAuCl (10 mol%), $Ru(bpy)_3(PF_6)_2$ (2 mol%), degassed MeCN : EtOH = (4 : 1) (0.5 ml), N₂ atmosphere, visible light, rt. for **4h**. ^{*b*} Isolated yield. ^{*c*} MeCN : MeOH = (4:1)(0.5 m) as the solvent. ^{*d*} MeCN : ^{*i*}PrOH = (4:1)(0.5 m) as the solvent.

Conclusions

In conclusion, we have developed the first gold-catalyzed oxidative P-arylation of H-phosphonates promoted by visible light photoredox catalysis. The reaction proceeds under mild reaction conditions (room temperature, no base) and shows excellent substrate scope, including the use of phosphinic acids as coupling partners. More broadly, the use of photoredox catalysis to achieve the oxidation event required for crosscoupling,^{5,14} avoids the need for strong oxidants associated with known gold-catalyzed coupling reactions.15 This feature putatively allows for increased functional group compatibility, as clearly demonstrated by the gold-catalyzed formation of alkynesubstituted phosphinate ester 3v, in which the potentially reactive carbon-carbon π -bond¹⁶ is left intact, and can subsequently be engaged in a copper-catalyzed alkyne-azide click reaction¹⁷ [eqn (6)]. The development of this strategy for crosscoupling and detailed mechanistic studies is ongoing in our group.



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Notes and references

- 1 For selected reviews: (a) N. D. Shapiro and F. D. Toste, Synlett, 2010, 675-691; (b) A. Fürstner, Chem. Soc. Rev., 2009, 38, 3208-3221; (c) D. J. Gorin, B. D. Sherry and F. D. Toste, Chem. Rev., 2008, 108, 3351-3378; (d) D. J. Gorin and F. D. Toste, Nature, 2007, 446, 395-403; (e) M. N. Hopkinson, A. D. Gee and V. Gouverneur, Chem.-Eur. J., 2011, 17, 8248-8262; (f) H. A. Wegner and M. Auzias, Angew. Chem., Int. Ed., 2011, 50, 8236-8247; (g) A. S. K. Hashmi and G. J. Hutchings, Angew. Chem., Int. Ed., 2006, 45, 7896-7936.
- 2 (a) G. Z. Zhang, Y. Peng, L. Cui and L. M. Zhang, Angew. Chem., Int. Ed., 2009, 48, 3112-3115; (b) G. Z. Zhang, L. Cui, Y. Z. Wang and L. M. Zhang, J. Am. Chem. Soc., 2010, 132, 1474-1475; (c) W. E. Brenzovich, D. Benitez, D. Lackner, H. P. Shunatona, E. Tkatchouk, A. W. A. Goddard and F. D. Toste, Angew. Chem., Int. Ed., 2010, 49, 5519-5522; (d) A. D. Melhado, W. E. Brenzovich, A. D. Lackner and F. D. Toste, J. Am. Chem. Soc., 2010, 132, 8885-8886; (e) N. P. Mankad and F. D. Toste, J. Am. Chem. Soc., 2010, 132, 12859-12861; (f) M. N. Hopkinson, A. Tessier, A. Salisbury, G. T. Giuffedi, L. E. Combettes, A. D. Gee and V. Gouverneur, Chem.-Eur. J., 2010, 16, 4739-4743; (g) W. E. Brenzovich, J. F. Brazeau and F. D. Toste, Org. Lett., 2010, 12, 4728-4731; (h) L. T. Ball, M. Green, G. C. Lloyd-Jones and C. A. Russel, Org. Lett., 2010, 12, 4724-4727; (i) M. N. Hopkinson, J. E. Ross, G. T. Giuffredi, A. D. Gee and V. Gouverneur, Org. Lett., 12, 4904–4907; (j) W. Wang, J. Jasinski, 2010. G. B. Hammond and B. Xu, Angew. Chem., Int. Ed., 2010, 49, 7247-7252; (k) T. de Haro and C. Nevado, Angew. Chem., Int. Ed., 2011, 50, 906-910; (l) G. Z. Zhang, Y. D. Luo, Y. Z. Wang and L. M. Zhang, Angew. Chem., Int. Ed., 2011, 50, 4450-4454; (m) A. Leyva-Pérez, A. Doménech, S. I. Al-Resayes and A. Corma, ACS Catal., 2012, 2, 121-126; (n) A. Arcadi, E. Pietropaolo, A. Alvino and V. Michelet, Org. Lett., 2013, 15, 2766-2769; (o) R. Zhang, Q. Xu, K. Chen, P. Gu and M. Shi, Eur. J. Org. Chem., 2013, 2013, 7366-7371; (p) For an approach using iodine(m) as an oxidant see: L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, Chem.-Eur. J., 2012, 18, 2931-2937.
- 3 (a) J. P. Brand, J. Charpentier and J. Waser, Angew. Chem., Int. Ed., 2009, 48, 9346–9349; (b) T. de Haro and C. Nevado, J. Am. Chem. Soc., 2010, 132, 1512–1513; (c) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, Science, 2012, 337, 1644–1648; (d) J. P. Brand and J. Waser, Org. Lett., 2012, 14, 744–747; (e) L. T. Ball, G. C. Lloyd-Jones and C. A. Russell, J. Am. Chem. Soc., 2014, 136, 254–264.

- 4 For reviews on visible-light photoredox catalysis, see: (a)
 K. Zeitler, Angew. Chem., Int. Ed., 2009, 48, 9785-9789; (b)
 T. P. Yoon, M. A. Ischay and J. Du, Nat. Chem., 2010, 2, 527-532; (c) J. M. R. Narayanam and C. R. J. Stephenson, Chem. Soc. Rev., 2011, 40, 102-113; (d) M. A. Ischay and
 T. P. Yoon, Eur. J. Org. Chem., 2012, 2012, 3359-3372; (e)
 J. W. Tucker and C. R. J. Stephenson, J. Org. Chem., 2012, 77, 1617-1622; (f) J. Xuan and W. J. Xiao, Angew. Chem., Int. Ed., 2012, 51, 6828-6838; (g) C. K. Prier, D. A. Rankic and
 D. W. C. MacMillan, Chem. Rev., 2013, 113, 5322-5363; (h)
 Y. M. Xi, H. Yi and A. W. Lei, Org. Biomol. Chem., 2013, 11, 2387-2403; (i) M. N. Hopkinson, B. Sahoo, J. L. Li and
 F. Glorius, Chem.-Eur. J., 2014, 20, 3874-3886.
- 5 (a) B. Sahoo, M. N. Hopkinson and F. Glorius, J. Am. Chem. Soc., 2013, 135, 5505–5508; (b) X. Z. Shu, M. Zhang, Y. He, H. Frei and F. D. Toste, J. Am. Chem. Soc., 2014, 136, 5844– 5847; (c) M. S. Winston, W. J. Wolf and F. D. Toste, J. Am. Chem. Soc., 2014, 136, 7777–7782.
- 6 For selected reviews: (a) A. Skarżyńska, Coord. Chem. Rev., 2013, 257, 1039–1048; (b) J. L. Montchamp, Acc. Chem. Res., 2014, 47, 77–87; (c) C. Queffélec, M. Petit, P. Janvier, D. A. Knight and B. Bujoli, Chem. Rev., 2012, 112, 3777–3807; (d) C. S. Demmer, N. Krogsgaard-Larsen and L. Bunch, Chem. Rev., 2011, 111, 7981–8006; (e) L. Kollár and G. Keglevich, Chem. Rev., 2010, 110, 4257–4302; (f) S. Van der Jeught and C. V. Stevens, Chem. Rev., 2009, 109, 2672–2702; (g) W. Tang and X. Zhang, Chem. Rev., 2003, 103, 3029–3069.
- 7 For recent examples, see: (a) G. Hu, W. Chen, T. Fu, Z. Peng, H. Qiao, Y. Gao and Y. Zhao, Org. Lett., 2013, 15, 5362-5365;
 (b) O. Berger, C. Petit, E. L. Deal and J. L. Montchamp, Adv. Synth. Catal., 2013, 355, 1361-1373; (c) K. Xu, H. Hu, F. Yang and Y. Wu, Eur. J. Org. Chem., 2013, 2013, 319-325;
 (d) A. J. Bloomfield and S. B. Herzon, Org. Lett., 2012, 14, 4370-4373; (e) S. M. Rummelt, M. Ranocchiari and J. A. van Bokhoven, Org. Lett., 2012, 14, 2188-2190; (f) C. R. Shen, G. Q. Yang and W. B. Zhang, Org. Biomol. Chem., 2012, 10, 3500-3505; (g) E. L. Deal, C. Petit and J. L. Montchamp, Org. Lett., 2011, 13, 3270-3273.
- 8 M. Fañanás-Mastral and B. L. Feringa, J. Am. Chem. Soc., 2014, 136, 9894-9897.
- 9 J. Xu, P. B. Zhang, Y. Z. Gao, Y. Y. Chen, G. Tang and Y. F. Zhao, *J. Org. Chem.*, 2013, **78**, 8176–8183.
- 10 (a) A. J. Walkinshaw, W. Xu, M. G. Suero and M. J. Gaunt, J. Am. Chem. Soc., 2013, 135, 12532–12535; (b) M. G. Suero, E. D. Bayle, B. S. L. Collins and M. J. Gaunt, J. Am. Chem. Soc., 2013, 135, 5332–5335.
- 11 We have previously observed C–P reductive elimination in the formation of tertaarylphosphonium salt by-products of the dual photoredox/gold-catalyzed process reported in ref. 5b.
- 12 For recent reviews on the reactions of aryldiazonium salts, see: (a) D. P. Hari and B. König, *Angew. Chem., Int. Ed.*, 2013, 52, 4734–4743; (b) F. Y. Mo, G. B. Dong, Y. Zhang and J. B. Wang, *Org. Biomol. Chem.*, 2013, 11, 1582–1593.
- 13 J. Stawinski and A. Kraszewski, Acc. Chem. Res., 2002, 35, 952–960.

- 14 (a) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt and M. S. Sanford, *J. Am. Chem. Soc.*, 2011, 133, 18566–18569;
 (b) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle and D. W. C. MacMillan, *Science*, 2014, 345, 437–440; (c) J. C. Tellis, D. N. Primer and G. A. Molander, *Science*, 2014, 345, 433–436.
- 15 M. D. Levin and F. D. Toste, Angew. Chem., Int. Ed., 2014, 53, 6211–6215.
- 16 Carbon–carbon π-bonds as reactive towards the previously employed selectfluor oxidant. For example, the Agcatalyzed phosphonofluorination of π-bonds: C. Zhang, Z. Li, L. Zhu, L. Yu, Z. Wang and C. Li, *J. Am. Chem. Soc.*, 2013, 135, 14082–14085.
- 17 V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596–2599.