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Synthesis of unsymmetrical benzils *via* palladium-catalysed α-arylation–oxidation of 2-hydroxyacetophenones with aryl bromides†

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A diverse set of unsymmetrically substituted benzils were facilely synthesised by a cross-coupling reaction between 2-hydroxyacetophenones and aryl bromides in the presence of a palladium catalyst. Experimental studies suggested a reaction mechanism involving a one-pot tandem palladium-catalysed α-arylation and oxidation, where aryl bromides play a dual role as mild oxidants as well as arylating agents.

Introduction

1,2-Diketones are members of an important class of molecules with diverse application potential in various fields. They are useful building blocks for the synthesis of a range of carbo- and heterocyclic compounds,[1] and 1,2-diketone-derived compounds have been utilised as ligands for transition metals.[2] Among these 1,2-diketones, benzils (diphenylethanediones) are recognised as privileged scaffolds that have distinct properties, and they can be converted into compounds with vicinal diphenyl groups. Benzils are generally synthesised *via* oxidation of the corresponding benzoins,[3] diarylacetylenes,[4] or other 1,2-diphenyl derivatives.[5] Thus, the traditional synthesis of unsymmetrical benzils necessitates the preparation of unsymmetrical starting materials, which can complicate the process considerably. In this context, significant advances have recently been made, whereby coupling strategies offer a viable and effective procedure for the synthesis of unsymmetrical benzils.[6,7] In particular, a reaction employing an aryl halide as the aryl source would be advantageous, as a large number of aryl halides are currently commercially available and relatively inexpensive.

Palladium-catalysed α-arylation of ketones with aryl halides, enabling cross-coupling between an electrophilic aryl group and a nucleophilic ketone enolate, represents a versatile and robust method for the synthesis of α-aryl ketones.[8] Although the α-arylation of other carbonyl compounds, such as esters and aldehydes, as well as nitriles, and nitroalkanes has been well established,[9] to date, there have been no reports on a reaction utilizing α-hydroxy ketones as nucleophiles. In this paper, we report that palladium(0)-catalysed α-arylation of 2-hydroxyacetophenones with aryl bromides produces benzoins, which are subsequently oxidised to benzils through the action of aryl bromides as mild oxidants, under catalytic conditions. In reactions of α-hydroxy ketones with two nucleophilic sites, *C*-arylation is particularly favoured over *O*-arylation.[10] Moreover, a control experiment revealed that 2-hydroxyacetophenones are more prone to α-arylation than acetophenone.

Results and discussion

2-Hydroxyacetophenone (**1a**) and 4-bromotoluene (**2a**, 2 equiv.) were heated in toluene at 100 °C in the presence of 10 mol% $Pd(PPh_3)_4$ as the catalyst and NaO*t*-Bu as a base for 24 h (Table 1, entry 1). The reaction primarily resulted in a reductive homocoupling to afford a biaryl, and no cross-coupling was observed. In contrast, when $[PdCl(allyl)]_2$ was employed as the catalyst, cross-coupling between **1a** and **2a** occurred, but the benzil product **3aa** was isolated in only 9% yield (entry 2). The anticipated α-arylation product, benzoin, was not detected in the reaction mixture, indicating that oxidation had occurred concomitantly during the reaction. To increase the product yield, we examined various phosphine ligands and found that XPhos[11] was the most effective (36% yield) among those examined (entries 3–8). As for the palladium complexes, $[PdCl(allyl)]_2$ was found to be the complex of choice for this reaction (entries 8–11).

As the decomposition of benzil **3aa** was observed with longer reaction times under the conditions employing NaO*t*-Bu, further optimisation was performed (Table 2). An extensive investigation into the choice of base (entries 1–6) indicated that the use of K_3PO_4 resulted in a cleaner reaction, furnishing **3aa** in 62% yield within 6 h;[12] the yield was further improved

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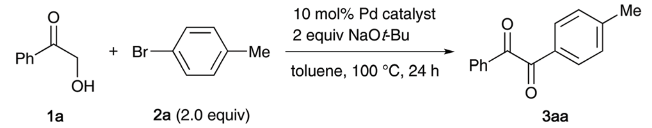
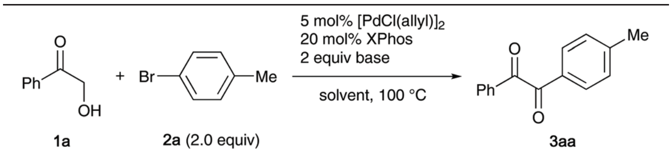
Table 1 Screening of palladium complexes and phosphine ligands for the palladium-catalysed coupling of 2-hydroxyacetophenone (**1a**) with 4-bromotoluene (**2a**)[a]



Entry	Pd catalyst (mol%)	Yield[b] (%)
1	$Pd(PPh_3)_4$ (10)	<5
2	$[PdCl(allyl)]_2$ (5)	9
3	$[PdCl(allyl)]_2/PPh_3$ (5/20)	<5
4	$[PdCl(allyl)]_2$/DPPE (5/10)	14
5	$[PdCl(allyl)]_2$/XANTPHOS (5/10)	5
6	$[PdCl(allyl)]_2$/DavePhos (5/20)	20
7	$[PdCl(allyl)]_2$/JohnPhos (5/10)	35
8	$[PdCl(allyl)]_2$/XPhos (5/20)	36
9	$Pd(OAc)_2$/XPhos (10/20)	21
10	$Pd(OCOCF_3)_2$/XPhos (10/20)	31
11	$Pd_2(dba)_3$/XPhos (5/20)	33

[a] Reaction conditions: **1a** (0.100 mmol), **2a** (0.200 mmol), Pd complex (10 mol%), phosphine ligand (20/10 mol% for monodentate/bidentate), NaO*t*-Bu (0.200 mmol), and toluene (0.5 mL) at 100 °C for 24 h. [b] Isolated yield.

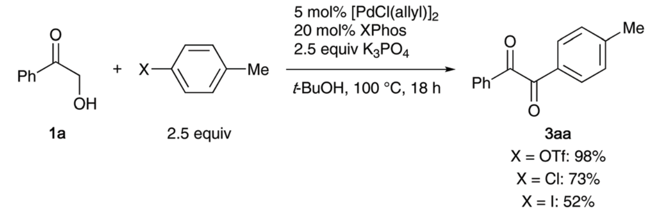
Table 2 Screening of bases and solvents[a]



Entry	Base	Solvent	Time (h)	Yield[b] (%)
1	NaO*t*-Bu	Toluene	6	56
2	KO*t*-Bu	Toluene	6	22
3	$NaN(SiMe_3)_2$	Toluene	6	32
4	Cs_2CO_3	Toluene	6	33
5	K_2CO_3	Toluene	6	35
6	K_3PO_4	Toluene	6	62
7	K_3PO_4	Toluene	18	80
8	K_3PO_4	1,4-Dioxane	18	72
9	K_3PO_4	THF	18	70
10	K_3PO_4	$ClCH_2CH_2Cl$	18	33
11	K_3PO_4	DMF	18	25
12	K_3PO_4	EtOH	18	33
13	K_3PO_4	*t*-BuOH	18	80
14[c]	K_3PO_4	*t*-BuOH	18	90
15[c,d]	K_3PO_4	*t*-BuOH	18	83
16[c,e]	K_3PO_4	*t*-BuOH	18	25
17[c,f]	K_3PO_4	*t*-BuOH	18	91

[a] Reaction conditions: **1a** (0.100 mmol), **2a** (0.200 mmol), $[PdCl(allyl)]_2$ (0.005 mmol, 10 mol% Pd), XPhos (0.020 mmol, 20 mol%), base (0.200 mmol) and solvent (0.5 mL) at 100 °C for the indicated time unless otherwise noted. [b] Isolated yield. [c] 2.5 equiv. (0.250 mmol) each of **2a** and K_3PO_4 were used. [d] 2.5 mol% $[PdCl(allyl)]_2$ (5.0 mol% Pd) was used. [e] 1.0 mol% $[PdCl(allyl)]_2$ (2.0 mol% Pd) was used. [f] **1a** (6.00 mmol) was reacted under reflux.

to 80% when the reaction time was 18 h (entry 7). Notably, the reaction proceeded smoothly without the need for stronger bases, such as alkoxides. Solvent screening confirmed that *t*-BuOH was the optimal solvent, giving superior results in terms of the prevention of decomposition of α-hydroxy ketone **1a** (entries 7–13). Finally, the use of 2.5 equiv. of both the aryl bromide **2a** and the base afforded **3aa** in 90% yield (entry 14). The reaction with 5 mol% catalyst loading provided a comparable yield, while the yield deteriorated with further catalyst loading reduction to 2 mol% (entries 15 and 16). The coupling was successfully performed on a gram scale to furnish 1.2 g of **3aa** in 91% yield (entry 17).



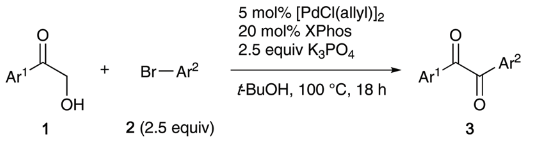
Scheme 1 Comparison of the reactivity of aryl halides and triflate.

The reaction proved efficient using an aryl triflate, providing **3aa** in 98% yield (Scheme 1). A slight decrease in yield was observed for aryl chlorides. In the case of an aryl iodide, however, the yield was reduced to 52% due to the competing biaryl homocoupling.

With the optimised conditions in hand, we investigated the scope of the coupling reaction and found that a diverse array of unsymmetrical benzils, as well as the parent benzil could be effectively synthesised (Table 3). Coupling of **1a** with bromobenzenes **2c–g** bearing electron-donating and electron-withdrawing substituents at the *meta*- or *para*-positions afforded the corresponding benzils **3ac–ag** in 61–98% yields (entries 2–6). Moreover, it was established that the reaction was effective in the presence of heteroatom substituents (entries 7–10). The reaction using 2- and 1-naphthyl bromides **2l** and **2m** delivered 1,2-diketones **3al** and **3am** in 79% and 58% yields, respectively, (entries 11 and 12). However, the yields of **3** declined considerably when *ortho*-substituted bromobenzenes **2n** and **2o** were used (entries 13 and 14). The attempted reaction with 4-bromophenol afforded only a trace amount of the desired product, and the formation of complex product mixtures was observed with 1-bromo-3-nitrobenzene and 3′-bromoacetophenone.[13] Furthermore, a variety of α-hydroxy ketones **1b–k**, including naphthyl and heteroaryl ketones, also underwent the coupling reaction with **2a** to deliver **3ba–ka** (entries 15–24).[14] Finally, it was demonstrated that additional unsymmetrical benzils, including highly electronically biased **3ee**, could be obtained by the coupling protocol (entries 25–31).

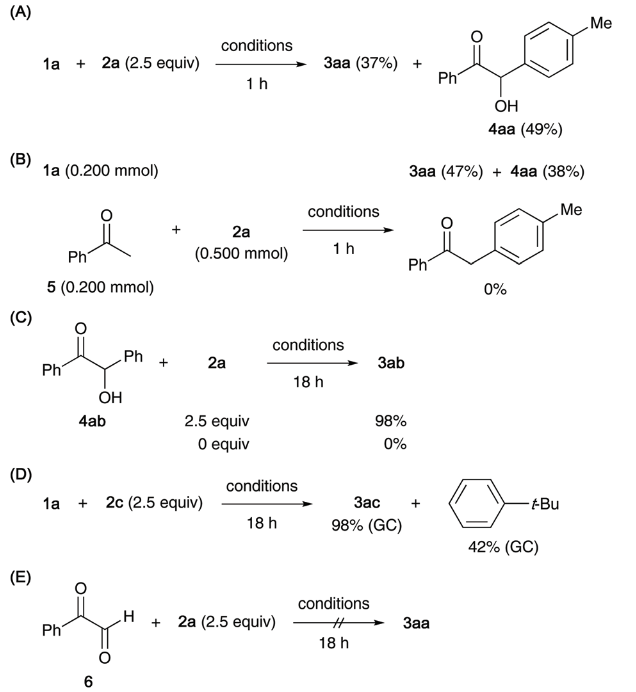
Several control experiments were conducted to elucidate the mechanistic aspects of the coupling reaction (Scheme 2). When the reaction was terminated after 1 h, benzoin **4aa** was isolated in 49% yield in addition to benzil **3aa** (37%), suggesting that **4aa** is the initial product, and that **3aa** is subsequently formed by the oxidation of **4aa** (Scheme 2A). The preference of α-arylation of α-hydroxy ketone **1a** over acetophe-

Table 3 Scope of palladium-catalysed α-arylation–oxidation of **1** with **2**[a]

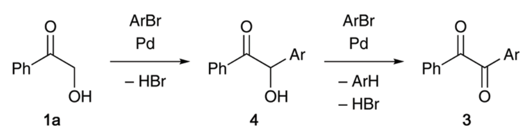


Entry	1 (Ar[1])	2 (Ar[2])	3	Yield[b] [%]
1	**1a** (Ph)	**2b** (Ph)	**3ab**	88
2	**1a** (Ph)	**2c** (4-*t*-BuC$_6$H$_4$)	**3ac**	86
3	**1a** (Ph)	**2d** (3-MeC$_6$H$_4$)	**3ad**	98
4	**1a** (Ph)	**2e** (4-MeOC$_6$H$_4$)	**3ae**	78
5	**1a** (Ph)	**2f** (4-F$_3$CC$_6$H$_4$)	**3af**	70
6	**1a** (Ph)	**2g** (3-MeO$_2$CC$_6$H$_4$)	**3ag**	61
7	**1a** (Ph)	**2h** (4-FC$_6$H$_4$)	**3ah**	89
8	**1a** (Ph)	**2i** (4-Me$_3$SiC$_6$H$_4$)	**3ai**	98
9	**1a** (Ph)	**2j** (3-MeSC$_6$H$_4$)	**3aj**	76
10	**1a** (Ph)	**2k** (3-(dan)BC$_6$H$_4$)[c]	**3ak**	49
11	**1a** (Ph)	**2l** (2-naphthyl)	**3al**	79
12	**1a** (Ph)	**2m** (1-naphthyl)	**3am**	58
13	**1a** (Ph)	**2n** (2-MeC$_6$H$_4$)	**3an**	45
14	**1a** (Ph)	**2o** (2-MeOC$_6$H$_4$)	**3ao**	44
15	**1b** (4-MeC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3ba**	92
16	**1c** (3-MeC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3ca**	95
17	**1d** (3-MeOC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3da**	78
18	**1e** (4-F$_3$CC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3ea**	64
19	**1f** (4-FC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3fa**	79
20	**1g** (2-MeC$_6$H$_4$)	**2a** (4-MeC$_6$H$_4$)	**3ga**	71
21	**1h** (2-naphthyl)	**2a** (4-MeC$_6$H$_4$)	**3ha**	74
22	**1i** (1-naphthyl)	**2a** (4-MeC$_6$H$_4$)	**3ia**	72
23	**1j** (2-furyl)	**2a** (4-MeC$_6$H$_4$)	**3ja**	55
24	**1k** (2-thienyl)	**2a** (4-MeC$_6$H$_4$)	**3ka**	76
25	**1d** (3-MeOC$_6$H$_4$)	**2e** (4-MeOC$_6$H$_4$)	**3de**	71
26	**1e** (4-F$_3$CC$_6$H$_4$)	**2e** (4-MeOC$_6$H$_4$)	**3ee**	59
27	**1g** (2-MeC$_6$H$_4$)	**2f** (4-F$_3$CC$_6$H$_4$)	**3gf**	65
28	**1g** (2-MeC$_6$H$_4$)	**2l** (2-naphthyl)	**3gl**	70
29	**1h** (2-naphthyl)	**2f** (4-F$_3$CC$_6$H$_4$)	**3hf**	62
30	**1i** (1-naphthyl)	**2f** (4-F$_3$CC$_6$H$_4$)	**3if**	61
31	**1k** (2-thienyl)	**2l** (2-naphthyl)	**3kl**	82

[a] Reaction conditions: **1** (0.200 mmol), **2** (0.500 mmol), [PdCl(allyl)]$_2$ (0.010 mmol, 10 mol% Pd), XPhos (0.040 mmol, 20 mol%), K$_3$PO$_4$ (0.500 mmol) and *t*-BuOH (0.5 mL) at 100 °C for 18 h. [b] Isolated yield. [c] B(dan) = naphtho[1,8-*de*][1,3,2]diazaborinin-2-yl.



Scheme 2 Control experiments (conditions: 5 mol% [PdCl(allyl)]$_2$, 20 mol% XPhos, 2.5 equiv. K$_3$PO$_4$, *t*-BuOH, 100 °C).



Scheme 3 Mechanism for α-arylation–oxidation.

none (**5**) was confirmed by a competition experiment with equimolar amounts of **1a** and **5** under the standard conditions. After 1 h, **3aa** and **4aa** were isolated in 85% combined yield while **5**, lacking the hydroxyl group, remained intact (Scheme 2B). Palladium-catalysed oxidation of alcohols using aryl halides as oxidants has been reported.[15] Indeed, oxidation of benzoin (**4ab**) with **2a** in the presence of the Pd–XPhos catalyst and K$_3$PO$_4$ in *t*-BuOH furnished benzil (**3ab**) in a high yield, whereas the oxidation of **4ab** failed to occur in the absence of **2a** (Scheme 2C). In the case of the reaction with 1-bromo-4-(*tert*-butyl)benzene (**2c**), the formation of *tert*-butylbenzene (42%) was detected by GC along with the quantitative formation of benzil **3ac** (Scheme 2D). Another possible scenario involving an initial oxidation of an α-hydroxy ketone to a glyoxal, which is subsequently arylated, was excluded, and no arylation of phenylglyoxal (**6**) was observed under our conditions (Scheme 2E).[16]

Based on these experimental observations, we conclude that the present reaction involves an initial α-arylation of 2-hydroxyacetophenone (**1a**) followed by oxidation of the resulting benzoin **4** to benzil **3**, both of which are catalysed by a palladium complex equipped with XPhos; two equivalents of aryl bromide are consumed during the process (Scheme 3).[17]

Conclusions

In summary, we have developed a novel synthetic method for accessing unsymmetrical benzils starting from 2-hydroxyacetophenones, achieved by a tandem α-arylation–oxidation sequence, both of which are catalysed by a palladium–XPhos system. Readily available aryl bromides initially function as arylating agents to form C–C bonds, and then subsequently oxidise the resulting benzoins to benzils, with concomitant hydrodebromination. The widely applicable transformation can be conducted under mild and virtually redox-neutral conditions.[18]

Conflicts of interest

There are no conflicts to declare.

Notes and references

1 (*a*) C. Rogers, W. S. Perkins, G. Veber, T. E. Williams, R. R. Cloke and F. R. Fischer, *J. Am. Chem. Soc.*, 2017, **139**, 4052–4061; (*b*) S. Sundar and R. Rengan, *Org. Biomol. Chem.*, 2019, **17**, 1402–1409; (*c*) A. Y. Dubovtsev, D. V. Dar'in, M. Krasavin and V. Y. Kukushkin, *Eur. J. Org. Chem.*, 2019, 1856–1864; (*d*) Y. Nakagawa, R. Sekiguchi, J. Kawakami and S. Ito, *Org. Biomol. Chem.*, 2019, **17**, 6843–6853; (*e*) A. Rashidizadeh, H. Ghafuri, H. R. E. Zand and N. Goodarzi, *ACS Omega*, 2019, **4**, 12544–12554; (*f*) G. Li, Y. Han, Y. Zou, J. J. C. Lee, Y. Ni and J. Wu, *Angew. Chem., Int. Ed.*, 2019, **58**, 14319–14326; (*g*) T. T. Nguyen, N.-P. T. Le, T. T. Nguyen and P. H. Tran, *RSC Adv.*, 2019, **9**, 38148–38153.

2 (*a*) K. Ohta, Y. Inagaki-Oka, H. Hasebe and I. Yamamoto, *Polyhedron*, 2000, **19**, 267–274; (*b*) J. L. Dempsey, B. S. Brunschwig, J. R. Winkler and H. B. Gray, *Acc. Chem. Res.*, 2009, **42**, 1995–2004; (*c*) F. Wang and C. Chen, *Polym. Chem.*, 2019, **10**, 2354–2369.

3 For recent examples, see: (*a*) P. Muthupandi and G. Sekar, *Tetrahedron Lett.*, 2011, **52**, 692–695; (*b*) Y. Yu, C. Lin, B. Li, P. Zhao and S. Zhang, *Green Chem.*, 2016, **18**, 3647–3655; (*c*) A. Saha, S. Payra and S. Banerjee, *New J. Chem.*, 2017, **41**, 13377–13381; (*d*) A. R. Patel, G. Patel and S. Banerjee, *ACS Omega*, 2019, **4**, 22445–22455.

4 For recent examples, see: (*a*) J.-W. Xue, M. Zeng, X. Hou, Z. Chen and G. Yin, *Asian J. Org. Chem.*, 2018, **7**, 212–219; (*b*) S. W. Kim, T.-W. Um and S. Shin, *J. Org. Chem.*, 2018, **83**, 4703–4711; (*c*) J. Zhou, X.-Z. Tao, J.-J. Dai, C.-G. Li, J. Xu, H.-M. Xu and H.-J. Xu, *Chem. Commun.*, 2019, **55**, 9208–9211; (*d*) W. Yang, Y. Chen, Y. Yao, X. Yang, Q. Lin and D. Yang, *J. Org. Chem.*, 2019, **84**, 11080–11090; (*e*) A. Y. Dubovtsev, N. V. Shcherbakov, D. V. Dar'in and V. Y. Kukushkin, *J. Org. Chem.*, 2020, **85**, 745–757.

5 For recent examples, see: (*a*) X. Liu and W. Chen, *Organometallics*, 2012, **31**, 6614–6622; (*b*) X. Zeng, C. Miao, S. Wang, C. Xia and W. Sun, *RSC Adv.*, 2013, **3**, 9666–9669; (*c*) J.-W. Yu, S. Mao and Y.-Q. Wang, *Tetrahedron Lett.*, 2015, **56**, 1575–1580; (*d*) R. Chebolu, A. Bahuguna, R. Sharma, V. K. Mishra and P. C. Ravikumar, *Chem. Commun.*, 2015, **51**, 15438–15441; (*e*) J. M. Khurana, A. Lumb and A. Chaudhary, *Monatsh. Chem.*, 2017, **148**, 381–386.

6 For oxidative coupling reactions, see: (*a*) Q. Zhang, C.-M. Xu, J.-X. Chen, X.-L. Xu, J.-C. Ding and H.-Y. Wu, *Appl. Organomet. Chem.*, 2009, **23**, 524–526; (*b*) X. Guo, W. Li and Z. Li, *Eur. J. Org. Chem.*, 2010, 5787–5790; (*c*) M. R. Rohman, I. Kharkongor, M. Rajbangshi, H. Mecadon, B. M. Laloo, P. R. Sahu, I. Kharbangar and B. Myrboh, *Eur. J. Org. Chem.*, 2012, 320–328; (*d*) Y. Su, X. Sun, G. Wu and N. Jiao, *Angew. Chem., Int. Ed.*, 2013, **52**, 9808–9812; (*e*) W.-X. Lv, Y.-F. Zeng, S.-S. Zhang, Q. Li and H. Wang, *Org. Lett.*, 2015, **17**, 2972–2975; (*f*) J. B. Bharate, S. Abbat, R. Sharma, P. V. Bharatam, R. A. Vishwakarma and S. B. Bharate, *Org. Biomol. Chem.*, 2015, **13**, 5235–5242; (*g*) P. Hirapara, D. Riemer, N. Hazra, J. Gajera, M. Finger and S. Das, *Green Chem.*, 2017, **19**, 5356–5360; (*h*) Y. Kumar, Y. Jaiswal and A. Kumar, *Eur. J. Org. Chem.*, 2018, 494–505.

7 For one-pot syntheses via Sonogashira/Heck coupling–oxidation, see: (*a*) H. Min, T. Palani, K. Park, J. Hwang and S. Lee, *J. Org. Chem.*, 2014, **79**, 6279–6285; (*b*) D. Saberi, H. Hashemi and K. Niknam, *Asian J. Org. Chem.*, 2017, **6**, 169–173; (*c*) V. G. Jadhav, S. A. Sarode and J. M. Nagarkar, *Tetrahedron Lett.*, 2017, **58**, 1834–1838; (*d*) P. Niesobski, I. S. Martínez, S. Kustosz and T. J. J. Müller, *Eur. J. Org. Chem.*, 2019, 5214–5218.

8 (*a*) M. Palucki and S. L. Buchwald, *J. Am. Chem. Soc.*, 1997, **119**, 11108–11109; (*b*) B. C. Hamann and J. F. Hartwig, *J. Am. Chem. Soc.*, 1997, **119**, 12382–12383.

9 (*a*) W. A. Moradi and S. L. Buchwald, *J. Am. Chem. Soc.*, 2001, **123**, 7996–8002; (*b*) S. Lee, N. A. Beare and J. F. Hartwig, *J. Am. Chem. Soc.*, 2001, **123**, 8410–8411; (*c*) E. M. Vogl and S. L. Buchwald, *J. Org. Chem.*, 2002, **67**, 106–111; (*d*) D. A. Culkin and J. F. Hartwig, *J. Am. Chem. Soc.*, 2002, **124**, 9330–9331; (*e*) R. Martín and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2007, **46**, 7236–7239; (*f*) G. D. Vo and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2008, **47**, 2127–2130. For a review on α-arylation, see: (*g*) C. C. C. Johansson and T. J. Colacot, *Angew. Chem., Int. Ed.*, 2010, **49**, 676–707.

10 (*a*) M. Palucki, J. P. Wolfe and S. L. Buchwald, *J. Am. Chem. Soc.*, 1997, **119**, 3395–3396; (*b*) K. E. Torraca, X. Huang, C. A. Parrish and S. L. Buchwald, *J. Am. Chem. Soc.*, 2001, **123**, 10770–10771; (*c*) H. Zhang, P. Ruiz-Castillo and S. L. Buchwald, *Org. Lett.*, 2018, **20**, 1580–1583.

11 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl.

12 The use of organic bases, such as Et_3N and DBU resulted in virtually no reaction.

13 The reaction of **1a** with 2-bromopyridine led to decomposition of the starting materials.

14 The attempted coupling of ethyl hydroxyacetate with **2a** failed, producing a complex mixture of products. Hydroxyacetone was not suitable for the reaction.

15 (*a*) A. S. Guram, X. Bei and H. W. Turner, *Org. Lett.*, 2003, **5**, 2485–2487; (*b*) C. Berini, D. F. Brayton, C. Mocka and O. Navarro, *Org. Lett.*, 2009, **11**, 4244–4247; (*c*) Q. Gao and S. Xu, *Org. Biomol. Chem.*, 2018, **16**, 208–212; (*d*) M. Kuriyama, S. Nakashima, T. Miyagi, K. Sato, K. Yamamoto and O. Onomura, *Org. Chem. Front.*, 2018, **5**, 2364–2369.

16 Syntheses of benzophenones by the palladium-catalysed coupling of benzaldehydes with aryl halides have been reported. (*a*) B. Suchand and G. Satyanarayana, *J. Org. Chem.*, 2016, **81**, 6409–6423; (*b*) T. Wakai, T. Togo, D. Yoshidome, Y. Kuninobu and M. Kanai, *ACS Catal.*, 2018, **8**, 3123–3128.

17 The reaction with 1.2 equiv. **2a** under air afforded **3a** in 45% yield, indicating that aerobic oxidation was impractical under our conditions. See ref. 6a.

18 For an account on the synthesis 1,2-diketones from α-hydroxy ketones, see: H. Liang, H. Liu and X. Jiang, *Synlett*, 2016, 2774–2782.