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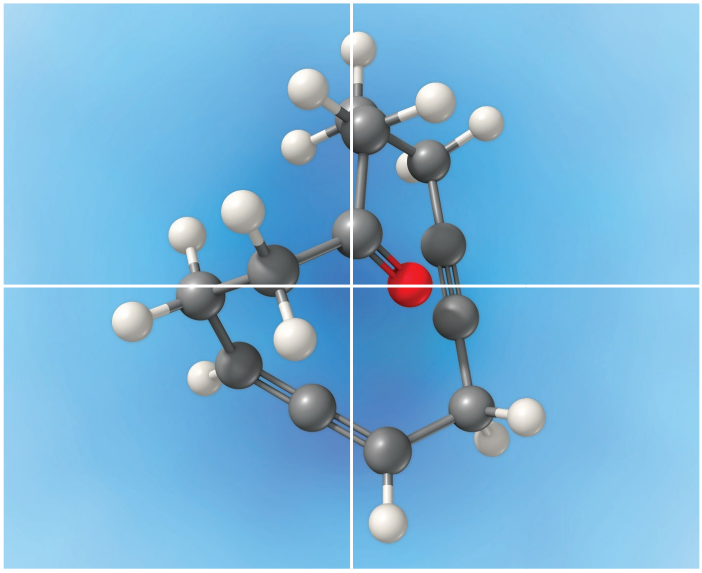

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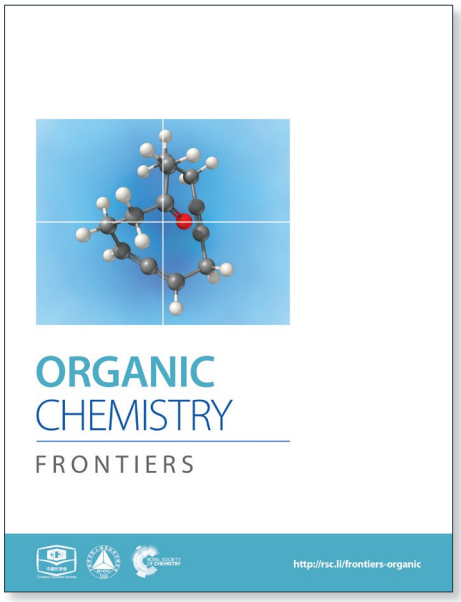

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Organic Chemistry Frontiers

RESEARCH ARTICLE

Selective Pd-catalyzed α- and β-Arylations of the Furan Rings of (ortho-Bromophenyl)furan-2-yl-methanones: C(CO)–C Bond Cleavage with a Furan Ring as a Leaving Group and Synthesis of Furan-derived Fluorenones

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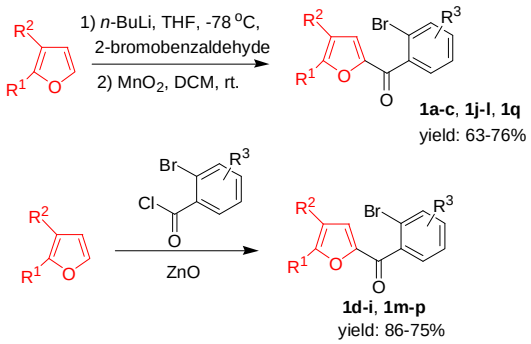
Selective palladium diacetate-catalyzed α- and β-arylations of the furan rings of (ortho-bromophenyl)furan-2-yl-methanones **1** under two different conditions are reported. In the presence of potassium tert-butoxide as a strong base and triphenylphosphine as a ligand, methanones **1** undergo α-arylation accompanied by C(CO)–C bond cleavage. In contrast, in the presence of potassium carbonate as the base and tricyclohexylphosphonium tetrafluoroborate as the ligand, methanones **1** undergo intramolecular β-arylation to afford furan-derived fluorenones in high yields from a wide variety of substrates. In addition, a one-pot protocol for the successive direct intramolecular β-arylation and intermolecular α-arylation of the furan rings of **1** has been achieved.

Furans are excellent building blocks not only because they can be readily prepared from biomass-derived synthetic platforms such as furfural and 5-hydroxymethylfurfural but also because they have unique reactivity both as electron-rich heteroaromatic compounds and as equivalents of alkenes, 1,3-dienes, alkynes, 1,4-diketones, and enol ethers.[1] Although the synthetic applications of furans have been greatly expanded, elucidation of new chemical properties and development of novel transformation of furans are still highly desirable goals,[2] given the current interest in sustainable chemistry.

The Pd-catalyzed arylation of furans is a powerful tool for the construction of arylfurans,[3] some of which display interesting bioactivities and physical properties.[4] Among the methods used to accomplish this transformation, the direct arylation of furyl C–H bonds with aryl halides is of special interest because it does not require preactivation of the substrates. This reaction usually occurs regioselectively at the more reactive α-position of the furan ring.[5] Direct arylation at the less reactive β-position is more challenging, and there are only a few reports of this reaction. Specifically, β-Arylation of furans occurs only when both of the α-positions are substituted[6] or when a furan 2-carboxamide is used as the substrate; in the latter case, chelation-assisted regioselective functionalization of the *ortho*-C–H bonds occurs with the amide as the directing group.[7] In addition, a protocol involving Pd-catalyzed α-arylation of 2-furoic acid substrates with aryl halides accompanied by C–C(O)OH bond cleavage (decarboxylation) has also received much attention because of the ready availability of 2-furoic acid.[8] To our knowledge, direct β-arylation of furan rings substituted with an electron-withdrawing benzoyl group and α-arylation of α-substituted furan rings accompanied by C(CO)–C bond cleavage have never previously been reported.

Owing to our ongoing interest in synthetic applications of furans[9] and given that fluorenones have important biological activities and are useful synthetic intermediates,[10] we wished to develop a route to unexplored furan-derived fluorenones **3** starting from simple (*ortho*-bromophenyl)furan-2-yl-methanones **1** via palladium-catalyzed direct β-arylation of the furan ring.[11,12] Substrates **1** were prepared easily either by the reactions of lithium furyl compounds with 2-bromobenzaldehydes followed by MnO_2 oxidation of the resultant alcohols or by Friedel–Crafts reactions of furans with acyl chlorides (Scheme 1).



Scheme 1. Syntheses of **1**

Initially, we attempted to produce **3a** by treatment of **1a** with NaO^{t}Bu in the presence of $Pd(OAc)_2$ as a catalyst, PPh_3 as a ligand, and KI as an additive to activate the aryl bromide. However, only a trace of **3a** was obtained, along with a substantial amount of protonated product **2a** (Scheme 2). Interestingly, an unexpected product, [2-(5-methyl-furan-2-yl)phenyl]methanone (**4a**), was also obtained, albeit in a low

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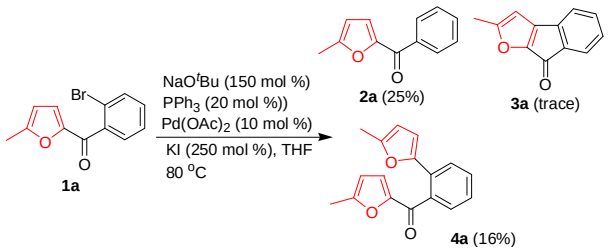
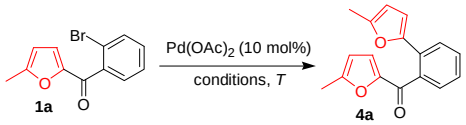
yield (16%). The presence of the newly introduced furyl group at the *ortho*-position of the phenyl ring of **4a** clearly indicated the occurrence of a novel α-arylation reaction of the α-substituted furan and an interesting palladium-catalyzed C(CO)–C bond cleavage with a furan ring as a leaving group.[13] To improve the yield of **4a** and gain insight into the mechanism of this reaction, we directed our efforts at optimizing the reaction parameters (additive, base, ligand, and solvent).



Scheme 2. Palladium-catalyzed transformations of **1a** in the presence of NaO^{t}Bu

As shown in Table 1, when **1a** was subjected to the above-mentioned conditions in the absence of Pd(OAc)$_2$, no **4a** formed (entry 1), which indicated that Pd(OAc)$_2$ was essential for C–C bond cleavage. Screening of various bases revealed that KO^{t}Bu was optimal (entries 2–7). The presence of additives clearly influenced the reaction. Several potassium salts were screened, and KCl gave the highest yield (43%; entries 2, 8–11). The use of various chloride salts including NaCl, LiCl, and tetrabutylammonium chloride did not further improve the yield (entries 12–14). Various other ligands were examined (**L$_1$**–**L$_6$**), but none were found to be better than PPh$_3$ (entries 15–20). Of the various solvents that were evaluated, the aprotic solvent toluene was the best, providing **4a** in 66% yield (entry 22).

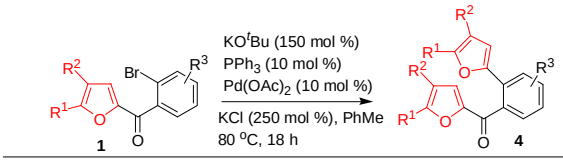
Table 1. Optimization of the reaction conditions for synthesis of **4a**[a]

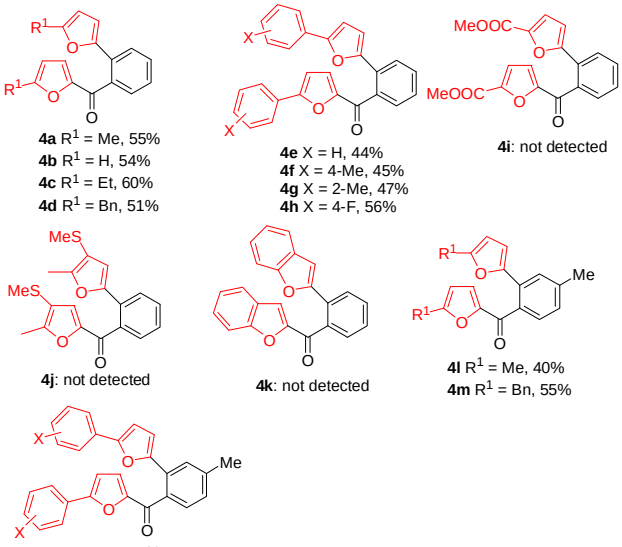


Entry	Conditions				Yield (%)[b]
	Additive	Base	L	Solvent	
1[c]	KI	NaO^{t}Bu	PPh$_3$	THF	ND
2	KI	KO^{t}Bu	PPh$_3$	THF	25
3	KI	NaO^{t}Bu	PPh$_3$	THF	16
4	KI	LiO^{t}Bu	PPh$_3$	THF	ND
5	KI	K_2CO_3	PPh$_3$	THF	ND
6	KI	Cs_2CO_3	PPh$_3$	THF	ND
7	KI	Et_3N	PPh$_3$	THF	NR
8	KF	KO^{t}Bu	PPh$_3$	THF	ND
9	KBr	KO^{t}Bu	PPh$_3$	THF	26
10	KCl	KO^{t}Bu	PPh$_3$	THF	43
11	K_3PO_4	KO^{t}Bu	PPh$_3$	THF	27
12	NaCl	KO^{t}Bu	PPh$_3$	THF	40
13	LiCl	KO^{t}Bu	PPh$_3$	THF	ND
14	TBAC	KO^{t}Bu	PPh$_3$	THF	trace
15	KCl	KO^{t}Bu	**L$_1$**	THF	ND
16	KCl	KO^{t}Bu	**L$_2$**	THF	ND
17	KCl	KO^{t}Bu	**L$_3$**	THF	40
18	KCl	KO^{t}Bu	**L$_4$**	THF	trace
19	KCl	KO^{t}Bu	**L$_5$**	THF	13
20	KCl	KO^{t}Bu	**L$_6$**	THF	8
21	KCl	KO^{t}Bu	PPh$_3$	DMF	ND
22	**KCl**	**KO^{t}Bu**	**PPh$_3$**	**PhMe**	**66**
23	KCl	KO^{t}Bu	PPh$_3$	DMSO	ND
24	KCl	KO^{t}Bu	PPh$_3$	1,4-dioxane	40

[a]Reaction conditions, unless otherwise noted: **1a** (0.5 mmol), Pd(OAc)$_2$ (0.05 mmol), additive (1.25 mmol), base (0.75 mmol), ligand (0.1 mmol), solvent (5 mL), 80 °C under N$_2$ for 16 h. TBAC = tetrabutylammonium chloride; **L$_1$** = tri-*tert*-butylphosphine; **L$_2$** = tricyclohexylphosphine; **L$_3$** = tri-*p*-tolylphosphine; **L$_4$** = tri(2-furyl)phosphine; **L$_5$** = (±)-2,2'-bis(diphenylphosphino)-1,1'-binaphthalene; **L$_6$** = 1,1'-bis(diphenylphosphino)ferrocene; ND = not detected; NR = no reaction. [b]Isolated yield **(4a** was produced from 2 equiv of **1a)**. [c]No Pd(OAc)$_2$ was used.

Table 2. Investigation of the substrate scope of the reaction[a]

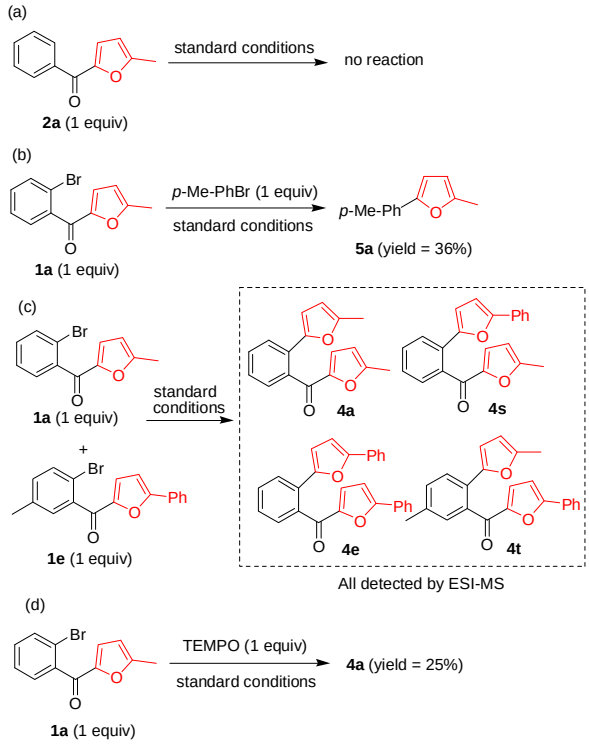




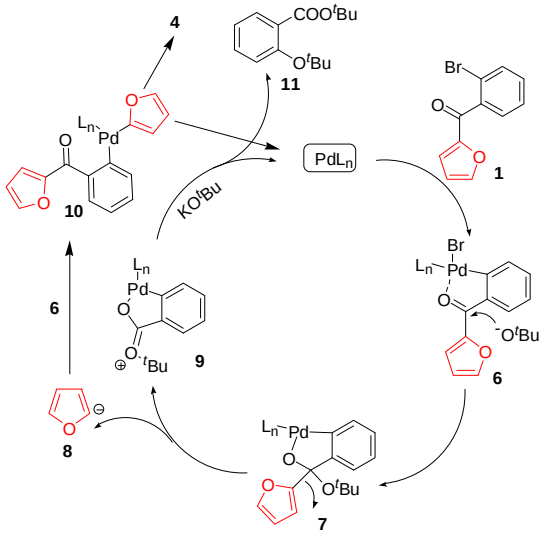
[a]**1** (0.5 mmol), Pd(OAc)$_2$ (0.05 mmol), PPh$_3$ (0.05 mmol), KO^{t}Bu (0.75 mmol), KCl (1.25 mmol), and PhMe (5 mL) at 80 °C under N$_2$ for 18 h. All yields are isolated yields.

Next we investigated the reaction scope by subjecting numerous furfuryl phenyl ketones **1** to the optimized conditions (Table 2). The electron density of the furan ring markedly influenced the reaction. When R^3 = R^2 = H, R^1 could be a H, an alkyl group (Me, Et, or Bn), an unsubstituted phenyl group, or a phenyl group with an electron-donating or electron-withdrawing substituent; the reactions of these substrates afforded **4a**–**4h** in moderate to good yields. However, the reaction of a substrate in which R^1 was an electron-withdrawing ester group did not give the expected

product (**4i**). A substrate with two electron-donating groups (R^1 = Me, R^2 = SMe) also did not give the expected product (**4j**), and a benzofuran-type substrate did not give the product of C–C bond cleavage (**4k**). When R^1 was a methyl group, the reactions gave the corresponding products (**4l–4p**) in moderate yields.



Scheme 3. Control experiments



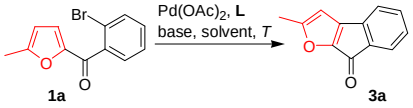
Scheme 4. Proposed reaction mechanism

The mechanism of this transformation was explored by means of four control experiments (Scheme 3). Ketone **2a** did not react under the standard conditions, indicating that the aryl bromide moiety was essential for C–C bond cleavage (Scheme 3a). That the reaction of **1a** with *p*-methylphenyl bromide gave **5a** clearly demonstrated that the cleaved furan ring could be trapped by a phenyl bromide (Scheme 3b). This was confirmed by the results of a cross reaction between **1a** and **1e** under the standard reaction conditions, which afforded cross products **4s** and **4t**, as indicated by ESI/MS (Scheme 3c). When the radical scavenger 2,2,6,6-tetramethyl piperidinyloxy was added under the standard conditions, **4a** was obtained in 25% isolated yield, suggesting that the reaction did not proceed by a radical-mediated mechanism (Scheme 3d).

On the basis of the above-described results, we propose the mechanism outlined in Scheme 4. Oxidative addition of PdL_n to **1** provides complex **6**, which undergoes nucleophilic addition by KO^{t}Buto afford **7**. Complex **7** is then cleaved to produce furyl anion **8** and cation **9**. Reaction of **8** with **6** produces complex **10**, which undergoes reductive elimination to generate **4**; and reaction of **9** with KO^{t}Bu affords **11** detected by ESI/MS.

Having investigated the α-arylation accompanied by C–C bond cleavage, we next searched for suitable conditions for achieving intramolecular β-arylation to synthesize **3** via suppression of C–C bond cleavage and protonation. Considering that cleavage of the C–C bond of **1** may have resulted from the nucleophilicity of the KO^{t}Bu or from the presence of KCl, we hypothesized that using a weakly nucleophilic base and omitting the KCl might minimize C–C bond cleavage. In addition, because the formation of a protonated product might have resulted from the weak acidity of the β-H of the furan ring, we suspected that rescreening of various ligands and reaction temperatures would be helpful. We began by screening a series of bases in reactions at 80 °C with $Pd(OAc)_2$ as the catalyst, PPh_3 as the ligand, and THF as the solvent in the absence of an additive (Table 3). Among the relatively weak bases (entries 1–4), K_2CO_3 provided **3a** in the best yield (20%), and **4a** was not detected. Of the various ligands that were evaluated (entries 5–10), $PCy_3{\cdot}HBF_4$ was the best, providing **3a** in 68% yield (entry 10). We suggest that BF_4^- may have coordinated with the carbonyl group, thus increasing the acidity of the β-H. Changing the solvent from THF to mesitylene, which is less polar, increased the yield to 77% (entry 13), and elevating the reaction temperature to 150 °C resulted in a 95% yield (entry 16).

Table 3. Optimization of conditions for synthesis of fluorenone **3a**[a]

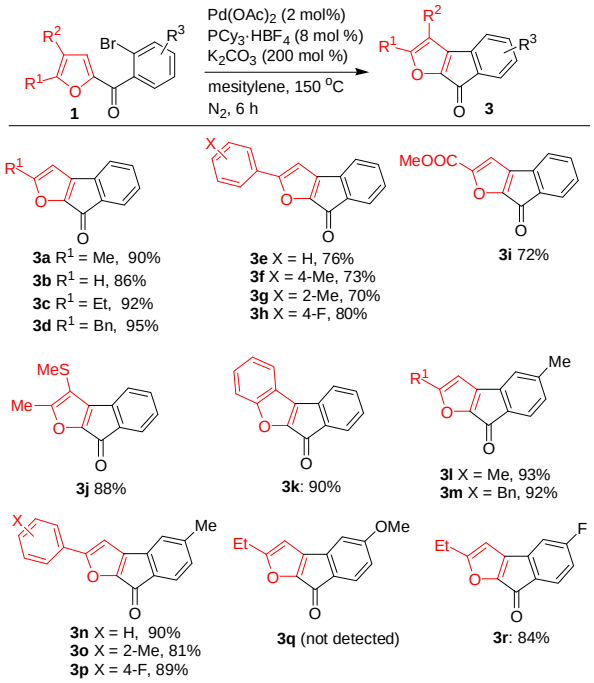


Entry	L	Base	Solvent	Yield (%)[b]
1	PPh_3	K_2CO_3	THF	20
2	PPh_3	Cs_2CO_3	THF	15
3	PPh_3	Na_2CO_3	THF	8
4	PPh_3	K_3PO_4	THF	trace
5	**L$_7$**	K_2CO_3	THF	32
6	PCy_3	K_2CO_3	THF	35
7	**L$_1$**	K_2CO_3	THF	NR
8	dppf	K_2CO_3	THF	48
9	BINAP	K_2CO_3	THF	54
10	**L$_8$**	K_2CO_3	THF	68
11	**L$_8$**	K_2CO_3	DMF	ND
12	**L$_8$**	K_2CO_3	Tol	65

13	**L$_8$**	K_2CO_3	Mes	77
14[c]	**L$_8$**	K_2CO_3	Mes	84
15[d]	**L$_8$**	K_2CO_3	Mes	88
16[e]	**L$_8$**	K_2CO_3	Mes	95

[a]Reaction conditions, unless otherwise noted: **1** (0.5 mmol), $Pd(OAc)_2$ (0.01 mmol), ligand (0.04 mmol), base (1.0 mmol), solvent (5 mL), *T* = 80 °C. dppf = bis(diphenylphosphino)ferrocene; BINAP = (±)-2,2'-bis(diphenylphosphino)-1,1'-binaphthalene; **L$_7$**, tris(4-methylphenyl)phosphine; **L$_8$**, $PCy_3{\cdot}HBF_4$; Tol = toluene; Mes = mesitylene. [b]All yields are isolated yields. NR = no reaction; ND = not detected. [c]*T* = 110 °C. [d]*T* = 130 °C. [e]*T* = 150 °C.

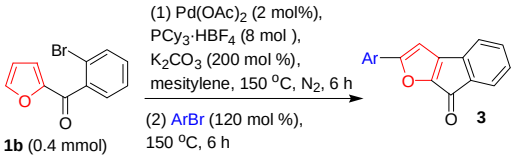
Table 4. Syntheses of fluorenones **3**[a]



[a]All yields are isolated yields.

A library of furan-derived fluorenones **3** was synthesized from various substrates **1** under the optimized reaction conditions (Table 4). Despite the high reaction temperature, the reaction tolerated a wide variety of functional groups, and the electron density of the furan ring had only a slight influence on the outcome of the reaction. When $R^3 = R^2 = H$, R^1 could be a H, an alkyl group (Me, Et, or Bn), or a phenyl group, either unsubstituted or with an electron-donating or electron-withdrawing substituent; and **3a–3h** were produced in good to excellent yields. Substrates with a phenyl R^1 group generally gave lower yields than substrates with an alkyl R^1 group. A substrate with an electron-withdrawing ester group as R^1 also gave the expected product (**3i**) in a good yield (72%). A substrate with two electron-donating groups (R^1 = Me, R^2 = SMe) on the furan ring afforded **3j** in 88% yield, and benzofuran-type product **3k** was obtained in 90% yield. R^3 could be an electron-neutral H atom (**3a–3k**), an electron-donating methyl group (**3l–3p**), or an electron-withdrawing fluorine atom (**3r**). In contrast, a substrate with a strongly electron-donating 4-methoxyl group did not give the desired product (**3q**).

Encouraged by the above-described results, we next investigated a one-pot procedure for successive direct intramolecular β-arylation and intermolecular α-arylation of the furan ring of **1b** by means of double C–H activation of the ring (Scheme 5). After completion of the β-arylation reaction was detected by TLC, 1.2 equiv of an aryl bromide was added to the reaction mixture under a nitrogen atmosphere, and the reaction was continued for 6 h at 150 °C; this protocol resulted in the formation of di-arylated products **3e, 3f, 3h**, and **3s** in moderate to good isolated yields.



3e: 65%; **3f**: 68%; **3h**: 66%; **3s** (Ar = *p*-MeO-Ph): 72%

Scheme 5. One-pot synthesis of **3e, 3f, 3h,** and **3s** from **1b**

In summary, we have developed a protocol for selective α- and β-arylations of the furan rings of (*ortho*-bromophenyl)furan-2-yl-methanones. The α-arylation involved a novel palladium-catalyzed C(CO)–C bond cleavage with a furan ring as a leaving group in the presence of KO^tBu and the subsequent coupling of the cleaved furan ring with an aryl bromide. This transformation might be useful for the development of new reactions involving C–C bond cleavage. We achieved intramolecular β-arylation of the furan ring by suppressing the C(CO)–Cbond cleavage using K_2CO_3 as the base and $PCy_3{\cdot}HBF_4$ as the ligand, and these reaction conditions were used to synthesize furan-derived fluorenones in high yields from a wide variety of substrates. In addition, a one-pot protocol for successive direct intramolecular β-arylation and intermolecular α-arylation of the furan ring was developed. This protocolmay be useful for the synthesis of biologically interesting fluorenones derivatives.

Acknowledgements

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References

1 For reviews on the conversion of furans, see: (a) B. H. Lipshutz, *Chem. Rev.* 1986, **86**, 795; (b) F. W. Lichtenthaler, *Acc. Chem. Res.* 2002, **35**, 728; (c) S. K. Bur, A. Padwa, *Chem. Rev.* 2004, **104**, 2401; (d) A. A. Rosatella, S. P. Simeonov, R. F. M. Frade, C. A. M. Afonso, *Green Chem.* 2011, **13**, 754; (e) P. Gallezot, *Chem. Soc. Rev.* 2012, **41**, 1538; (f) R. -J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, J. G. de Vries, *Chem. Rev.* 2013, **113**, 1499; (g) I. V. Trushkov, M. G. Uchuskin, A. V. Butin, *Eur. J. Org. Chem.* **2015**, 2999.

2 For selected recent examples, see: (a) L. I. Palmer, J. Read de Alaniz, *Angew. Chem. Int. Ed*. 2011, **50**, 7167; (b) G. K. Veits, D. R. Wenz, J. Read de Alaniz, *Angew. Chem. Int. Ed*. 2010, **49**, 9484; (c) J.-Q. Dong, H. N. C. Wong, *Angew. Chem. Int. Ed*. 2009, **48**, 2351; (d) K. C. Nicolaou, C. R. H. Hale, C. Ebner, C. Nilewski, C. F. Ahles, D. Rhoades, *Angew. Chem. Int. Ed*. 2012, **51**, 4726; (e) V. T. Abaev, A. T. Plieva, P. N. Chalikidi, M. G. Uchuskin, I. V. Trushkov, A. V. Butin, *Org. Lett.* 2014, **16**, 4150; (f) A. Kuznetsov, A. Makarov, A. E. Rubtsov, A. V. Butin, V. Gevorgyan, *J. Org. Chem*. 2013, **78**, 12144.

3 For selected reviews on C–H arylations of furans, see: (a) D. A. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* 2007, **107**, 174; (b) F. Bellina, R. Rossi, *Tetrahedron* 2009, **65**, 10269; (c) J. Roger, A. L. Gottumukkala, H. Doucet, *ChemCatChem* 2010, **2**, 20; (d) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* 2009, **48**, 9792.

4 For selected examples of biologically activities and physical properties of C-3-arylated furan derivatives, see: (a) S. Jiang, S. R. Tala, H. Lu, N. E. Abo-Dya, I. Avan, K. Gyanda, L. Lu, A. R. Katritzky, A. K. Debnath, *J. Med. Chem*. 2011, **54**, 572; (b) R. B. de Oliveira, E. M. de Souza-Fagundes, H. A. J. Siqueira, R. S. Leite, C. L. Donnici, C. L. Zani, *Eur. J. Med. Chem*. 2006, **41**, 756; (c) G. Wang, X. Wang, H. Yu, S. Wei, N. Williams, D. Holmes, R. Halfmann, J. Naidoo, L. Wang, L. Li, S. Chen, P. Harran, X. Lei, X. Wang, *Nat. Chem. Biol.* 2013, **9**, 84; (d) Q.-Q. Huang, M. Huang, F.-J. Nan, Q.-Z. Ye, *Bioorg. Med. Chem. Lett.* 2005, **15**, 5386; (e) M. E. Kort, I. Drizin, R. J. Gregg, M. J. C. Scanio, L. Shi, M. F. Gross, R. N. Atkinson, M. S. Johnson, G. J. Pacofsky, J. B. Thomas, W. A. Carroll, M. J. Krambis, D. Liu, C.-C. Shieh, X. Zhang, G. Hernandez, J. P. Mikusa, C. Zhong, S. Joshi, P. Honore, R. Roeloffs, K. C. Marsh, B. P. Murray, J. Liu, S. Werness, C. R. Faltynek, D. S. Krafte, M. F. Jarvis, M. L. Chapman, B. E. Marron, *J. Med. Chem*. 2008, **51**, 407; (f) X.-H. Jin, D. Sheberla, L. J. W. Shimon, M. Bendikov, *J. Am. Chem. Soc*. 2014, **136**, 2592; (g) J. C. Bijleveld, B. P. Karsten, S. G. J. Mathijssen, M. M. Wienk, D. M. de Leeuw, R. A. J. Janssen, *J. Mater. Chem*. 2011, **21**, 1600; (h) C. H. Woo, P. M. Beaujuge, T. W. Holcombe, O. P. Lee, J. M. J. Fréchet, *J. Am. Chem. Soc*. 2010, **132**, 15547.

5 For selcted recent examples, see: (a) E. Ö. Karaca, N. Gürbüz, İ. Özdemir, H. Doucet, O. Şahin, O. Büyükgüngör, B. Çetinkaya, *Organometallics* 2015, **34**, 2487; (b) A. Jakab, Z. Dalicsek, T. Soós, *Eur. J. Org. Chem.* **2015**, 56; (c) R. Matsidik, J. Martin, S. Schmidt, J. Obermayer, F. Lombeck, F. Nübling, H. Komber, D. Fazzi, M. Sommer, *J. Org. Chem*. 2015, **80**, 980; (d) G. Erickson, J. Guo, M. McClure, M. Mitchell, M.-C. Salaun, A. Whitehead, *Tetrahedron Lett.* 2014, **55**, 6007; (e) L. Chen, C. Bruneau, P. H. Dixneuf, H. Doucet, *ChemCatChem* 2013, **5**, 1956; (f) L. Chen, C. Bruneau, P. H. Dixneuf, H. Doucet, *Tetrahedron* 2013, **69**, 4381; (g) S. Bensaid, H. Doucet, *ChemSusChem* 2012, **5**, 1559; (h) L. Chen, J. Roger, C. Bruneau, P. H. Dixneuf, H. Doucet, *Adv. Synth. Catal*. 2011, **353**, 2749.

6 (a) T. Nishikata, Y. Yamane, Y. Yamaguchi, S. Ishikawa, *Asia. J. Org. Chem* 2016, **5**, 466; (b) S. Ishikawa, Y. Noda, M. Wada, T. Nishikata, *J. Org. Chem* 2015, **80**, 7555; (c) By Piller, Fabian M. and Knochel, Paul, From *Synthesis*, **2011**, 1751; (d) A. L. Gottumukkala, H. Doucet, *Adv. Synth. Catal*. 2008, **350**, 2183; (e) H. Cao, D. Shen, H. Zhan, L. Yang, *Synlett* **2011**, 1472.

7 (a) K. S. Larbi, H. Y. Fu, N. Laidaoui, K. Beydoun, A. Miloudi, D. E. Abed, S. Djabbar, H. Doucet, *ChemCatChem* 2012, **4**, 815; (b) R. Padmavathi, R. Sankar, B. Gopalakrishnan, R. Parella, S. A. Babu, *Eur. J. Org. Chem.* **2015**, 3727.

8 (a) F. Bilodeau, M.-C. Brochu, N. Guimond, K. H. Thesen, P. Forgione, *J. Org. Chem*. 2010, **75**, 1550; (b) L. J. Gooßen, B. Zimmermann, C. Linder, N. Rodríguez, P. P. Lange, J. Hartung, *Adv. Synth. Catal*. 2009, **351**, 2667; (c) G. Cahiez, A. Moyeux, O. Gager, M. Poizat, *Adv. Synth. Catal*. 2013, **355**, 790; (d)J.-J. Dai, J.-H. Liu, D.-F. Luo, L. Liu, *Chem. Commun*. 2011, **47**, 677; (e) H. Y. Fu, H. Doucet, *Eur. J. Org. Chem.* **2011**, 7163.

9 (a) B.-L. Yin, J.-Q. Lai, Z.-R. Zhang, H.-F. Jiang, *Adv. Synth. Catal*. 2011, **353**, 1961; (b) B. Yin, G. Zeng, C. Cai, F. Ji, L. Huang, Z. Li, H. Jiang, *Org. Lett*. 2012, **14**, 616; (c) B. Yin, C. Cai, G. Zeng, R. Zhang, X. Li, H. Jiang, *Org. Lett*. 2012, **14**, 1098; (d) B. Yin, L. Huang, X. Wang, J. Liu, H. Jiang, *Adv. Synth. Catal*. 2013, **355**, 370; (e) B. Yin, X. Zhang, J. Liu, X. Li, H. Jiang, *Chem. Commun*. 2014, **50**, 8113; (f) B. Yin, X. Zhang, X. Zhang, H. Peng, W. Zhou, B. Liu, H. Jiang, *Chem. Commun*. 2015, **51**, 6126; (g) J. Liu, X. Zhang, H. Peng, H. Jiang, B. Yin, *Adv. Synth. Catal*. 2015, **357**, 727; (h) F. Ji, H.peng, X. Zhang, W. Lu, S. Liu, H. Jiang, B. Yin, *J. Org. Chem.* 2015, **80**, 2092; (i) H. Peng, J. Li, F. Wang, B. Liu, B. Yin, *J. Org. Chem.* 2016, **81**, 4939; (j) J. Li, H. Peng, F. Wang, X. Wang, H. Jiang, B. Yin, *Org. Lett*. 2016, **18**, 3226.

10 For the bioactivities of fluorenones and their derivatives, see: (a) M. L. Greenlee, J. B. Laub, G. P. Rouen, F. DiNinno, M. L. Hammond, J. L. Huber, J. G. Sundelof, G. G. Hammond, *Bioorg. Med. Chem. Lett*., 1999, **9**, 3225; (b) P. J. Perry, M. A. Read, R. T. Davies, S. M. Gowan, A. P. Reszka, A. A. Wood, L. R. Kelland, S. Neidle, *J. Med. Chem*., 1999, **42**, 2679; (c) C.-C. Lee, D.-M. Chang, K.-F. Huang, C.-L. Chen, T.-C. Chen, Y. Lo, J.-H. Guh, H.-S. Huang, *Bioorg. Med. Chem*. 2013, **21**, 7125; (d) X. Zhang, J.-K. Xu, J. Wang, N.-L. Wang, H. K., S. Kitanaka, X.-S. Yao, *J. Nat. Prod*. 2007, **70**, 24; (e) H. O. Saxena, U. Faridi, S. Srivastava, J. K. Kumar, M. P. Darokar, S. Luqman, C. S. Chanotiya, V. Krishna, A. S. Negi, S. P. S. Khanuja, *Bioorg. Med. Chem. Lett*. 2008, **18**, 3914; (f) R. Romagnoli, P. G. Baraldi, M. D. Carrion, C. L. Cara, O. Cruz-Lopez, M. Tolomeo, S. Grimaudo, A. D. Cristina, M. R. Pipitone, J. Balzarini, N. Zonta, A. Brancale, E. Hamel, *Bioorg. Med. Chem*. 2009, **17**, 6862. (g) S. Lee, C. Esteva-Font, P.-W. Phuan, M. O. Anderson, A. S. Verkman, *MedChemComm* 2015, **6**, 1278.

11 For examples of the synthesis of fluorenones and their derivatives via direct palladium-catalyzed intramolecular arylation of 2-bromoarylketones, see: (a) G. Qabaja, G. B. Jones, *Tetrahedron Lett*. 2000, **41**, 5317; (b) J. Chang, L. Sun, J. Dong, Z. Shen, Y. Zhang, J. Wu, R. Wang, J. Wang, C. Song, *Synlett* 2012, **23**, 2704; (c) C. C. Silveira, E. L. Larghi, S. R. Mendes, A. B. J. Bracca, F. Rinaldi, T. S. Kaufman, *Eur. J. Org. Chem*. **2009**, 4637; (d) S. Wang, Q. Yang, J. Dong, C. Li, L. Sun, C. Song, J. Chang, *Eur. J. Org. Chem*. **2013**, 7631; (e) R. A. Haggam, *Tetrahedron* 2013, **69**, 6488; (f) N. Marquise, P. J. Harford, F. Chevallier, T. Roisnel, V. Dorcet, A.-L. Gagez, S. Sablé, L. Picot, V. Thiéry, A. E. H. Wheatley, P. C. Gros, F. Mongin, *Tetrahedron* 2013, **69**, 10123.

12 For selcted examples of C(CO)–C bond cleavage caused by the nucleophilic attack of –O^{t}Bu to ketone group, see: (a) H.Serizawa, K. Aikawa, K. Mikami, *Chem. Eur. J.* 2013, **19**, 17692; (b) Y. Nakaike, N. Taba, S. Itoh, Y. Tobe, N. Nishiwaki, M. Ariga, *Bull. Chem. Soc. Jpn*. 2007, **80**, 2413; (c) T. Shimizu, K. Murakoshi, K. Yasui, M. Sodeoka, *Synthesis* 2008, **20**, 3209; (d) H. Serizawa, K. Aikawa, K. Mikami, *Org. Lett.* 2014, **16**, 3456; (e) Y. L. Tnay, S. Chiba, *Chem. Asia J.* 2015, **10**, 873.