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Palladium catalyzed atom-economic synthesis of functionalized 9-(diarylmethylene)-9*H*-fluorenes using triarylbismuths in one-pot bis-coupling process

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ABSTRACT

An efficient palladium catalyzed atom-economic synthesis of functionalized 9-(diarylmethylene)-9*H*-fluorenes has been accomplished in one-pot bis-coupling process using triarylbismuths as organometallic reagents. These bis-couplings in 1 hour short reaction time afforded various 9-(diarylmethylene)-9*H*-fluorenes in good to high yields.

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9-(Diarylmethylene)-9*H*-fluorenes or diarylmethylidenefluorenes are novel structural components useful in various material applications.[1] Metal catalyzed reactions are indispensable for facile synthesis of organic skeletons useful in materials chemistry.[2] Various synthetic methods are reported recently for the synthesis of 9-(diarylmethylene)-9*H*-fluorenes under palladium catalyzed conditions.[3] These reactions include: (i) couplings of oxime ether with aryl iodide involving long hours heating,[3a] (ii) 5-*exo*-dig cyclization of 2-bromo-2′-(phenylethynyl)biphenyl with arylboronic acids,[3b] (iii) double cross-coupling reaction of 9-stannafluorenes with 1,1-dibromoalkenes,[3c] (iv) 5-*exo*-dig annulations of *o*-alkynylbiaryls with aryl halides,[3d] and (v) double cross-couplings of 9-(dibromomethylene)-9*H*-fluorene with arylboronic acids[3e] reported by Ramana et al. A few other synthetic methods are also available.[4] For example, the 9-(diphenylmethylene)-9*H*-fluorene was also prepared through the addition–elimination protocol involving fluorenyl lithium addition to diphenyl ketone[4a] or diphenylmethyl lithium addition to 9-fluorenone.[5] However, some of these methods involve cumbersome procedures.

The double Suzuki coupling process[3e] is of special interest as this provides the desired flexibility in the synthesis of various functionalized diarylmethylidenefluorenes.

The required 9-(dibromomethylene)-9*H*-fluorenes[6] and several aryl organometallic reagents are readily available and these factors bestow this process an edge over other methods. However, only one palladium catalyzed protocol involving double bis-couplings of 9-(dibromomethylene)-9*H*-fluorene with aryl boronic acids was reported so far.[3e] This prompted us to expand the scope and general utility of this bis-couplings with triarylbismuths, as these reagents demonstrated an excellent multi-coupling ability as organometallic nucleophiles under palladium catalysis.[7] Advantage of using $BiAr_3$ reagents is that they serve three aryl groups efficiently in an atom-economic manner and this reduces the organometallic loadings to one third in such couplings.[8] In tune with the growing importance of the utility of diarylmethylidenefluorenes, we report here a facile palladium catalyzed atom-economic synthesis of functionalized 9-(diarylmethylene)-9*H*-fluorenes in one-pot bis-coupling process using triarylbismuth reagents.

Synthesis of 9-(dibromomethylene)-9*H*-fluorene (**1**) was carried out using Ramirez *gem*-dibromoolefination with Horner–Wadsworth–Emmons modification reported for aldehydes and ketones.[9] This reaction using 9-fluorenone in combination with tetrabromomethane and triethylphosphite afforded the desired 9-(dibromomethylene)-9*H*-fluorene in an 86% yield after treating with mixture of acids under reflux condition (Scheme 1).[10]

As three aryl groups are available, 1 equiv of triarylbismuths was chosen to couple with 1.5 equiv of 9-(dibromomethylene)-9*H*-fluorene to afford 1.5 equiv of 9-(diarylmethylene)-9*H*-fluorenes (Scheme 2).

To establish a viable palladium catalyzed protocol for efficient bis-couplings, a systematic screening was carried out using 9-(dibromomethylene)-9*H*-fluorene (**1**) and $BiPh_3$ as model substrates to obtain 9-(diphenylmethylene)-9*H*-fluorene (**1a**) product.

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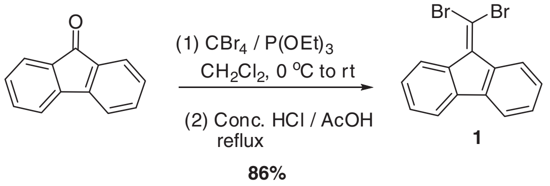
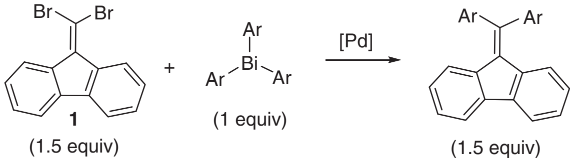


Scheme 1. Synthesis of 9-(dibromomethylene)-9*H*-fluorene.[10]

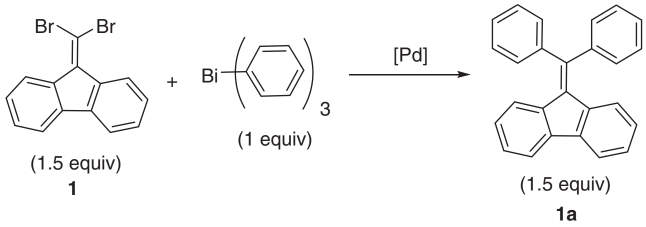


Scheme 2. Bis-couplings with dibromide and $BiAr_3$.

The coupling reaction carried out using $Pd(PPh_3)_4$ catalyst and K_3PO_4 base in *N*,*N*-dimethylformamide (DMF) at 90 °C afforded bis-coupled product **1a** in a 36% yield (entry 1, Table 1). This reaction at 110 °C afforded a marginal change in yield up to 45% (entry 2, Table 1). Other solvents such as *N*,*N*-dimethylacetamide (DMA), *N*-methylpyrrolidinone (NMP) did not improve the yield under similar coupling conditions (entries 3 and 4, Table 1). The effect of various bases was studied to check their efficacy. For example, Cs_2CO_3 and Na_2CO_3 bases furnished 41% and 54% yields (entries 5 and 7, Table 1), whereas K_2CO_3 and KOAc proved to be more efficient with 78–79% yields (entries 6 and 8, Table 1). Reaction with $PdCl_2(PPh_3)_2$ as catalyst precursor furnished a 76% yield of the desired product (entry 9, Table 1). Thus, additional scrutiny was carried out with low catalyst loadings of $Pd(PPh_3)_4$ using 0.04 and 0.02 equiv and KOAc base. These reactions provided 82% and 77% yields, respectively (entries 10 and 11, Table 1). Different KOAc loadings using 1–4 equiv revealed that bis-coupling process is more effective with either 4 or 3 equiv (entries 12 and 13, Table 1). However, moderate yields were obtained with 2 and 1 equiv of base (entries 14 and 15, Table 1). Reaction checked for optimum reaction time with 3 and 1 h revealed a marginal improvement in yield with longer reaction time (entries 16 and 17, Table 1). Two control reactions carried out without base and catalyst (entries 18 and 19, Table 1) amply indicated their importance for effective bis-couplings. Triarylbismuths are thermally labile to give biaryls in the presence of palladium catalyst.[11] This resulted in the formation of biphenyl as a minor side product in all screening reactions. In some cases, the mono phenylated product 9-benzylidene-9*H*-fluorene was also formed in minor amounts.[3d] From this study, it was realized that $Pd(PPh_3)_4$ (0.02 equiv), KOAc (4 equiv) in DMF at 110 °C and 1 hour reaction time as an optimum condition to obtain high coupling yield (entry 17, Table 1).

With optimized condition in hand, generality of this one-pot bis-coupling process was checked using electronically different $BiAr_3$ reagents[12] (Table 2). It is fascinating to see that the bis-couplings using various $BiAr_3$ reagents are facile to furnish a variety of functionalized 9-(diarylmethylene)-9*H*-fluorenes in good to high yields. For example, $BiAr_3$ reagents substituted with various alkoxy and methyl substituents furnished high product yields in short

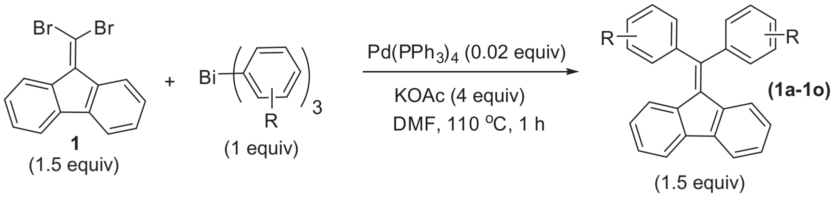
Table 1
Screening conditions[a,b,c,d]

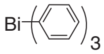
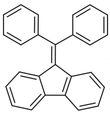
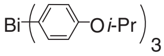
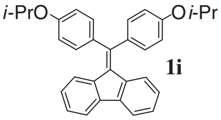
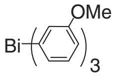
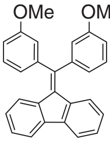
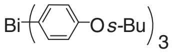
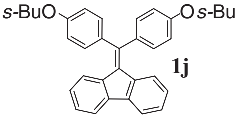
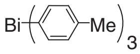
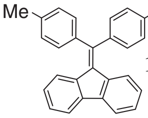
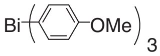
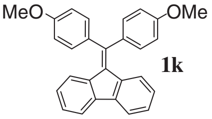
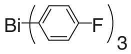
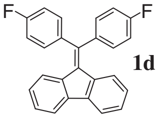
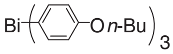
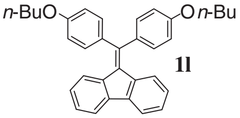
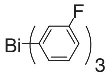
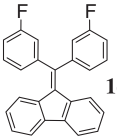
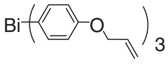
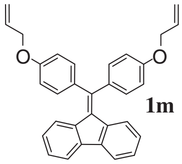
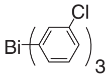
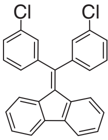
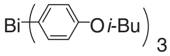
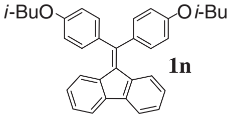
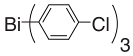
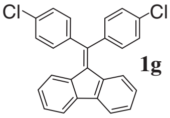
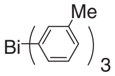
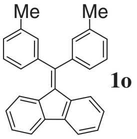
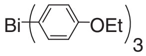
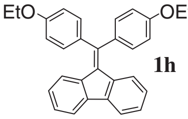


Entry	Catalyst (equiv)	Base (equiv)	Solvent	Time (h)	Yield (%)
1	$Pd(PPh_3)_4$ (0.09)	K_3PO_4 (6)	DMF	4	36[e]
2	$Pd(PPh_3)_4$ (0.09)	K_3PO_4 (6)	DMF	4	45
3	$Pd(PPh_3)_4$ (0.09)	K_3PO_4 (6)	DMA	4	35
4	$Pd(PPh_3)_4$ (0.09)	K_3PO_4 (6)	NMP	4	34
5	$Pd(PPh_3)_4$ (0.09)	Cs_2CO_3 (6)	DMF	4	41
6	$Pd(PPh_3)_4$ (0.09)	K_2CO_3 (6)	DMF	4	78
7	$Pd(PPh_3)_4$ (0.09)	Na_2CO_3 (6)	DMF	4	54
8	$Pd(PPh_3)_4$ (0.09)	KOAc (6)	DMF	4	79
9	$PdCl_2(PPh_3)_2$ (0.09)	KOAc (6)	DMF	4	76
10	$Pd(PPh_3)_4$ (0.04)	KOAc (6)	DMF	4	82
11	$Pd(PPh_3)_4$ (0.02)	KOAc (6)	DMF	4	77
12	$Pd(PPh_3)_4$ (0.02)	KOAc (4)	DMF	4	82
13	$Pd(PPh_3)_4$ (0.02)	KOAc (3)	DMF	4	81
14	$Pd(PPh_3)_4$ (0.02)	KOAc (2)	DMF	4	55
15	$Pd(PPh_3)_4$ (0.02)	KOAc (1)	DMF	4	52
16	$Pd(PPh_3)_4$ (0.02)	KOAc (4)	DMF	3	81
17	$Pd(PPh_3)_4$ (0.02)	KOAc (4)	DMF	1	79
18	$Pd(PPh_3)_4$	none	DMF	1	35
19	none	KOAc	DMF	1	–

[a] Coupling conditions: 9-(dibromomethylene)-9*H*-fluorene (0.375 mmol, 1.5 equiv), $BiPh_3$ (0.25 mmol, 1 equiv), base, catalyst, solvent (3 mL), 110 °C.
[b] Isolated yields.
[c] Biphenyl as a minor side homo-coupling product was formed in all the reactions.
[d] Mono phenylated product 9-benzylidene-9*H*-fluorene was also formed in some reactions in minor amounts.
[e] At 90 °C.

Table 2
One-pot bis-couplings with different triarylbismuths[a,b,c,d,e]



Entry	Triarylbismuth	Product	Yield (%)	Entry	Triarylbismuth	Product	Yield (%)
1		 **1a**	79	9		 **1i**	84
2		 **1b**	69	10		 **1j**	62
3		 **1c**	93	11		 **1k**	87
4		 **1d**	66	12		 **1l**	76
5		 **1e**	59	13		 **1m**	73
6		 **1f**	44	14		 **1n**	84
7		 **1g**	51	15		 **1o**	71
8		 **1h**	79				

[a] Coupling conditions: 9-(dibromomethylene)-9*H*-fluorene (0.375 mmol, 1.5 equiv), $BiAr_3$ (0.25 mmol, 1 equiv), KOAc (1 mmol, 4 equiv), $Pd(PPh_3)_4$ (0.005 mmol, 0.02 equiv), DMF (3 mL), 110 °C, 1 h.

[b] Isolated yields.

[c] Biaryls as a minor side homo-coupling products were formed in all the reactions.

[d] Mono arylated product 9-benzylidene-9*H*-fluorene was formed in some reactions in minor amounts.

[e] All the product were identified by ^{1}H NMR, ^{13}C NMR, EI-HRMS and IR spectroscopic analyses.

reaction time. Triarylbismuths substituted with electron-withdrawing halo substituents provided moderate yields. It is important to note that electronically rich aryl boronic acids did not fare well in the reported double Suzuki coupling process.[3e] However, it is highly satisfying to note that similar couplings with $BiAr_3$ afforded good yields in an atom-efficient manner under present conditions.

In summary, we have demonstrated a facile palladium catalyzed protocol for an efficient synthesis of various functionalized 9-(diarylmethylene)-9*H*-fluorenes using triarylbismuths as multi-coupling organometallic nucleophiles under palladium catalyzed condition. These one-pot bis-couplings are fast and completed in 1 hour reaction time furnishing good to high yields. Given the importance of 9-(diarylmethylene)-9*H*-fluorenes, this method is expected to provide an easy access to a plethora of these molecular entities in a facile manner.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.10.156.

References and notes

1. (a) Heeney, M.; Bailey, C.; Giles, M.; Shkunov, M.; Sparrowe, D.; Tierny, S.; Zhang, W.; McCulloch, I. *Macromolecules* **2004**, *37*, 5250–5256; (b) Mills, N. S.; Benish, M. A.; Ybarra, C. *J. Org. Chem.* **2002**, *67*, 2003–2012; (c) Mladenova, G.; Chen, L.; Rodriquez, C. F.; Siu, K. W. M.; Johnston, L. J.; Hopkinson, A. C.; Lee-Ruff, E. *J. Org. Chem.* **2001**, *66*, 1109–1114; (d) Mills, N. S.; Malinky, T.; Malandra, J. L.; Burns, E. E.; Crossno, P. *J. Org. Chem.* **1999**, *64*, 511–517.
2. (a) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174–238; (b) McGlacken, G. P.; Fairlamb, I. J. S. *Eur. J. Org. Chem.* **2009**, 4011–4029; (c) Corbet, J.-P.; Mignani, G. *Chem. Rev.* **2006**, *106*, 2651–2710.
3. (a) Thirunavukkarasu, V. S.; Parthasarathy, K.; Cheng, C.-H. *Chem. Eur. J.* **2010**, *16*, 1436–1440; (b) Morishita, T.; Yoshida, H.; Ohshita, J. *Chem. Commun.* **2010**, *46*, 640–642; (c) Nagao, I.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 7573–7576; (d) Chernyak, N.; Gevorgyan, V. *Adv. Synth. Catal.* **2009**, *351*, 1101–1114; (e) Ramana, C. V.; Reddy, B. K. K.; Reddy, C. N.; Gonnade, R. G.; Gurjar, M. K. *Synlett* **2007**, 127–128.
4. (a) Luisa, M.; Franco, T. M. B.; Herold, B. J.; Evans, J. C.; Rowlands, C. C. *J. Chem. Soc., Perkin Trans. 2* **1988**, 443–449; (b) Other references cited in 3e
5. Banerjee, M.; Emond, S. J.; Lindeman, S. V.; Rathore, R. *J. Org. Chem.* **2007**, *72*, 8054–8061.
6. (a) Donovan, P. M.; Scott, L. T. *J. Am. Chem. Soc.* **2004**, *126*, 3108–3112; (b) Paul, G. C.; Gajewski, J. J. *Synthesis* **1997**, 524–526.
7. Rao, M. L. N.; Jadhav, D. N.; Dasgupta, P. *Org. Lett.* **2010**, *12*, 2048–2051. and references cited therein.
8. (a) Rao, M. L. N.; Venkatesh, V.; Banerjee, D. *Synfacts* **2008**, *4*, 406; (b) Rao, M. L. N.; Banerjee, D.; Dhanorkar, R. J. *Synfacts* **2010**, *8*, 928.
9. Fang, Y.-Q.; Lifchits, O.; Lautens, M. *Synlett* **2008**, 413–417.
10. Synthesis of 9-(dibromomethylene)-9*H*-fluorene, **1**: to a solution of 9-fluorenone (2.0 g, 11.1 mmol) and CBr_4 (5.5 g, 16.7 mmol) in CH_2Cl_2 (20 mL) was added dropwise $P(OEt)_3$ (5.6 mL, 33.3 mmol) in CH_2Cl_2 (10 mL) at 0 °C under nitrogen atmosphere. The reaction was continued at 0 °C for 1 h followed by rt, stirring for 3 h. The reaction mixture was diluted with CH_2Cl_2 (20 mL) and washed with water and extracted with CH_2Cl_2 (2 × 15 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The crude product thus obtained was treated with conc. HCl (8 mL) and glacial acetic acid (8 mL) at 100 °C for 12 h. Reaction mixture was cooled to rt, and quenched with saturated ice cold Na_2CO_3 solution. After neutralization, the reaction mixture was extracted following usual procedure. The crude product was purified by silica gel column chromatography with pet ether as eluent to afford product as pure yellow crystalline solid (3.2 g, 86%).
11. Barton, D. H. R.; Ozbalik, N.; Ramesh, M. *Tetrahedron* **1988**, *44*, 5661–5668.
12. Representative procedure: to an oven-dried 50 mL Schlenk tube, 9-(dibromomethylene)-9*H*-fluorene (0.126 g, 0.375 mmol, 1.5 equiv), $BiPh_3$ (0.110 g, 0.25 mmol, 1.0 equiv), KOAc (0.098 g, 1.0 mmol, 4.0 equiv), $Pd(PPh_3)_4$ (0.0058 g, 0.005 mmol, 0.02 equiv) and DMF (3 mL) were added under nitrogen atmosphere. The reaction mixture was stirred in a pre-heated oil bath at 110 °C for 1 h. The contents were cooled to rt, and extracted with ethyl acetate (15 mL × 3). The combined extract was treated with water, brine and dried over anhydrous $MgSO_4$ and concentrated. The crude mixture was purified by silica gel column chromatography using petroleum ether as an eluent to obtain pure 9-(diphenylmethylene)-9*H*-fluorene in a 79% yield (0.098 g). The product was identified by ^1H NMR, ^{13}C NMR, EI-HRMS and IR spectroscopic methods. In all the cases, isolated yields are calculated considering 0.375 mmol of product as a 100% yield.