

Pd-Catalyzed/Iodide-Promoted α -Arylation of Ketones for the Regioselective Synthesis of Isocoumarins

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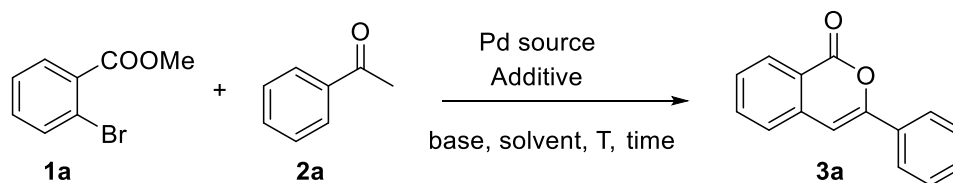
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Supporting Information

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Table S1. Optimization study for the palladium-catalyzed synthesis of isocoumarin **3a** from methyl 2-bromobenzoate **1a** and acetophenone **2a**^a



Entry	Pd source	Base	Additive (equiv)	Solvent	T (°C)	Time (h)	Conv 1a (%) ^b	Yield 3a (%) ^b
1	-	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
2	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	-	DMF	105	24	45	34
3	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	-	DMF	120	24	51	39
4	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	-	DMF	130	24	96	50
5	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.025)	DMF	130	24	96	53
6	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.05)	DMF	130	24	97	56
7	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.075)	DMF	130	24	>98	59
8	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.1)	DMF	130	24	>98	61
9	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.2)	DMF	130	24	>98	66
10	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (0.5)	DMF	130	24	100	70
11	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (1)	DMF	130	24	>98	73
12	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	130	4	100	77
13	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	4	100	84 ^c
14	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	80	24	37	31
15	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (4)	DMF	105	4	62	39
16	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	<i>n</i> -Bu ₄ NI (2)	DMF	105	4	100	67
17	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	NaI (2)	DMF	105	4	35	27
18	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.1)	KI (2)	DMF	105	4	100	79
19	1% Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.1)	KI (2)	DMF	105	24	82	67
20	1% Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
21	5% Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	4	100	71

22	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.4)	KI (2)	DMF	105	8	100	64
23	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.5)	KI (2)	DMF	105	24	0	0
24	Pd(OAc) ₂	K ₂ CO ₃	KI (2)	DMF	105	8	100	51
25	Pd(OAc) ₂	Na ₂ CO ₃	KI (2)	DMF	105	24	100	36
26	Pd(OAc) ₂	K ₃ PO ₄	KI (2)	DMF	105	24	100	62
27	Pd(OAc) ₂	<i>t</i> -BuOK	KI (2)	DMF	105	24	80	12
28	Pd(OAc) ₂	PhOK	KI (2)	DMF	105	24	100	9
29 ^d	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
30	Pd(OAc) ₂ + PPh ₃ (5%)	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	57	25
31	PdCl ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	4	100	73
32	PdCl ₂ (MeCN) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	4	100	76
33	PdCl ₂ (PPh ₃) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	26	17
34	Pd(PPh ₃) ₄	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	14	9
35	Pd/C	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
36	Pd/CaCO ₃	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
37	Pd(dba) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DMF	105	24	0	0
38	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	MeCN	80	24	0	0
39	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	DME	105	24	78	56
40	Pd(OAc) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	toluene	105	24	0	0
41	Pd(dba) ₂	K ₂ CO ₃ /PhOK (1/0.3)	KI (2)	toluene	105	24	0	0

^a Reaction conditions (*General procedure A*): Pd source (2.5% mol), **1a** (0.4 mmol, 1 equiv), **2a** (5 equiv), base, additive, solvent (4 mL). ^b Yields determined by GC using C12 as internal standard. ^c Isolated yield. ^d 20 µL of H₂O were added.

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