One-Pot Synthesis of Naphthalenes from Baylis-Hillman Adducts *via* Pd-Mediated Successive Allylation and Arylation

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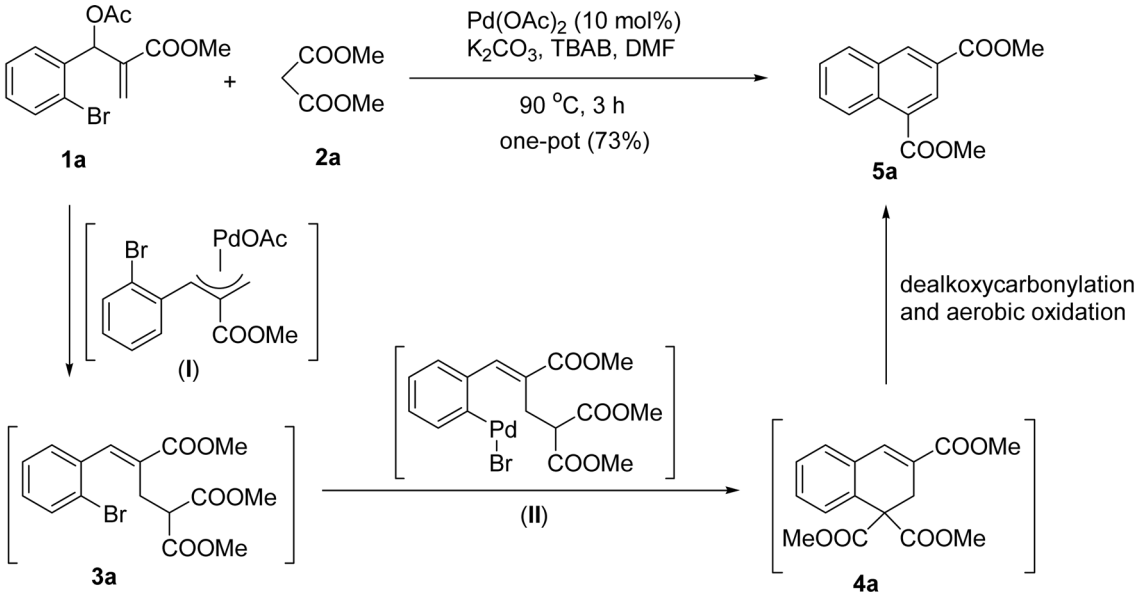
Introduction of nucleophiles at the primary position of Baylis-Hillman adducts has been carried out by the nucleophilic substitution reaction from the acetate or primary bromide derivative of Baylis-Hillman adduct.[1] Palladium-assisted introduction of nucleophiles has also been reported in the Baylis-Hillman chemistry *via* the corresponding π-allylpalladium intermediate.[2]

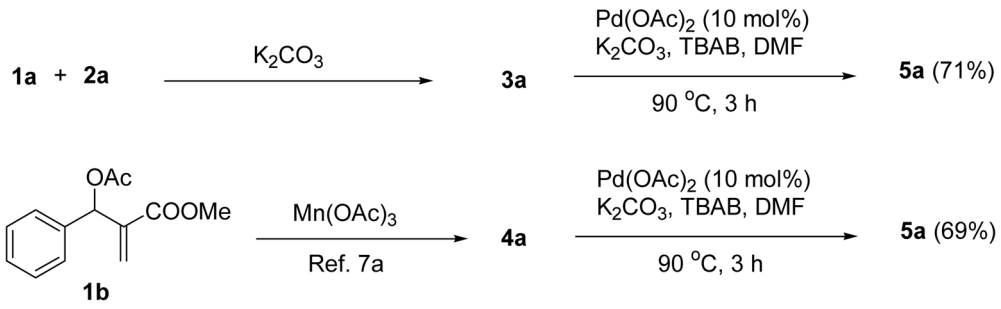
Thus we reasoned that one-pot synthesis of dihydronaphthalene could be carried out by Pd-mediated successive allylation and arylation protocol from the reaction of **1a**, the acetate of Baylis-Hillman adduct of 2-bromobenzaldehyde, and dimethyl malonate (**2a**) as in Scheme 1.[3-6] The reaction between **1a** and **2a** produced naphthalene derivative **5a** (73%) in a one-pot, under the influence of $Pd(OAc)_2$/TBAB/K_2CO_3 in DMF at 90 °C (3 h), instead of the expected dihydronaphthalene **4a**.

The reaction mechanism for the one-pot formation of **5a** can be postulated as the following successive processes: (i) allylation of **2a** *via* the π-allylpalladium intermediate (**I**) to produce the substitution product **3a**, (ii) Pd-mediated arylation of **3a** to dihydronaphthalene **4a** *via* the intermediate (**II**), and (iii) dealkoxycarbonylation and concomitant aerobic oxidation process to give the final product **5a**.[7a,8] In order to clarify the last step of the concomitant dealkoxycarbonylation and aerobic oxidation, we examined the reaction in more detail as in Scheme 2. The reaction of compound **3a**, prepared by nucleophilic substitution reaction from **1a** and **2a** (K_2CO_3, CH_3CN, rt, 3 h, 78%),[1,7,9] under the same conditions produced compound **5a** (71%).[10] The reaction of compound **4a**, prepared from Baylis-Hillman adduct **1b** according to the reported method using $Mn(OAc)_3$,[7a] showed also the formation of **5a** (69%).[11] Thus the mechanism for the formation of **5a** can be regarded as the combination of Pd-mediated successive allylation-arylation and the following base-assisted dealkoxycarbonylation-oxidation.[11]

Encouraged by the results we examined various active methylene compounds **2b-g** under similar conditions with **1a**, as the representative example. The results are summarized in Table 1. The reaction of 2,4-pentanedione (**2b**) produced **5b** in 78% yield, similarly (entry 2). As in entry 3, we obtained a mixture of **5a** (13%) and **5b** (54%) when we used methyl acetoacetate (**2c**). The reaction of primary nitroalkanes **2d** and **2e** showed clean reaction and high yields of products **5d** and **5e**. The last step in these cases would be base-assisted elimination of nitrous acid.[7c] When we use 1,3-

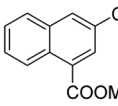
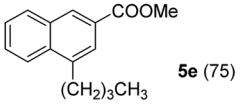
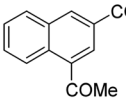
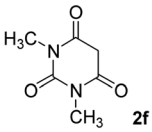
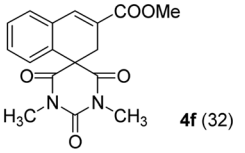
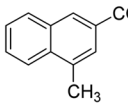
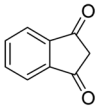
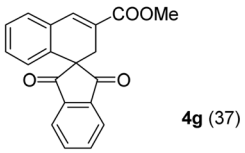


Scheme 1



Scheme 2

Table 1. Synthesis of naphthalenes and spiro dihydronaphthalenes from **1a** and **2a-g**[a]

Entry	2	Time (h)	Product (%)	Entry	2	Time (h)	Product (%)
1	 **2a**	3	 **5a** (73)	5	$CH_3(CH_2)_4NO_2$ **2e**	4	 **5e** (75)
2	 **2b**	3	 **5b** (78)	6	 **2f**	4	 **4f** (32)
3	 **2c**	2	**5a** (13) + **5b** (54)				
4	$CH_3CH_2NO_2$ **2d**	3	 **5d** (80)	7	 **2g**	3	 **4g** (37)

[a]Conditions: Substrate **1a** (1.0 mmol), **2a-g** (1.0 mmol), $Pd(OAc)_2$ (10 mol%), K_2CO_3 (2.0 mmol), TBAB (1.0 mmol), DMF, 90 °C.

dimethyl barbituric acid (**2f**) and 1,3-indandione (**2g**) as the nucleophile, we could obtain spiro dihydronaphthalene derivatives **4f** and **4g**, albeit in low yields (32-37%). We could not isolate the other compound like naphthalene derivative due to the formation of many intractable side products.

In summary, various naphthalenes and spiro dihydronaphthalenes were prepared by the Pd-mediated one-pot reaction involving consecutive allylation and arylation reaction from Baylis-Hillman acetate and activated methylene compounds.

Experimental Section

Typical procedure for the synthesis of 5a: A mixture of **1a** (313 mg, 1.0 mmol), **2a** (132 mg, 1.0 mmol), $Pd(OAc)_2$ (22.4 mg, 10 mol%), K_2CO_3 (276 mg, 2.0 mmol), and TBAB (322 mg, 1.0 mmol) in DMF (2 mL) was heated to 90 °C for 3 h. After aqueous extractive workup with ether and column chromatographic purification process (hexanes/EtOAc, 8:2) compound **5a** was obtained, 179 mg (73%). The structures of products were confirmed by their spectroscopic data, and the representative data are as follows.[7,12]

Compound 5a:[7,12b,d] 73%; colorless oil; IR (film) 2960, 1728, 1236 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.01 (s, 3H), 4.03 (s, 3H), 7.57-7.63 (m, 1H), 7.70-7.75 (m, 1H), 7.98-8.01 (m, 1H), 8.75 (s, 2H), 8.94-8.97 (m, 2H).

Compound 5b:[7,12c] 78%; white solid, mp 46-48 °C; IR (film) 2952, 1721 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.80 (s, 3H), 4.02 (s, 3H), 7.57-7.63 (m, 1H), 7.68-7.74 (m, 1H), 7.97-8.00 (m, 1H), 8.51-8.52 (m, 1H), 8.73 (s, 1H), 8.76-8.79 (m, 1H).

Compound 5d:[7,12a] 80%; colorless oil; IR (film) 2950, 2930, 1721 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.72 (s, 3H), 3.97 (s, 3H), 7.51-7.57 (m, 1H), 7.60-7.65 (m, 1H), 7.90-7.91 (m, 1H), 7.94-7.97 (m, 1H), 8.00-8.03 (m, 1H), 8.46 (s, 1H).

Compound 5e: 75%; colorless oil; IR (film) 1721, 1292, 1242 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.98 (t, J = 7.2 Hz, 3H), 1.41-1.53 (m, 2H), 1.70-1.80 (m 2H), 3.07-3.12 (m, 2H), 3.98 (s, 3H), 7.50-7.55 (m, 1H), 7.58-7.64 (m, 1H), 7.90 (s, 1H), 7.94-7.97 (m, 1H), 8.05-8.08 (m, 1H), 8.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.97, 22.85, 32.76, 32.85, 52.16, 123.92, 124.91, 126.11, 126.88, 128.00, 129.49, 130.24, 133.02, 134.15, 139.57, 167.47; ESIMS m/z 243 ($M^+ + 1$).

Compound 4f: 32%; yellow solid, mp 207-209 °C; IR (film) 1682, 1439, 1376 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.34 (d, J = 1.8 Hz, 2H), 3.36 (s, 6H), 3.83 (s, 3H), 6.93-6.96 (m, 1H), 7.28-7.36 (m, 3H), 7.55 (t, J = 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 29.19, 32.43, 52.08, 54.94, 124.80, 125.96, 129.51, 130.40, 130.58, 131.72, 132.70,

134.79, 150.91, 166.46, 170.24; ESIMS *m/z* 329 (M^+ + 1). Anal. Calcd for $C_{17}H_{16}N_2O_5$: C, 62.19; H, 4.91; N, 8.53. Found: C, 62.43; H, 5.03; N, 8.36.

Compound 4g: 37%; yellow solid, mp 161-163 °C; IR (film) 1746, 1708 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.06 (d, J = 1.5 Hz, 2H), 3.80 (s, 3H), 6.71-6.73 (m, 1H), 7.14-7.20 (m, 1H), 7.25-7.31 (m, 1H), 7.36-7.38 (m, 1H), 7.65 (t, J = 1.5 Hz, 1H), 7.89-7.94 (m, 2H), 8.05-8.09 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.92, 51.98, 57.21, 124.17, 124.63, 126.36, 128.63, 130.05, 130.19, 132.16, 133.22, 136.26, 136.36, 141.05, 166.75, 200.25; ESIMS *m/z* 319 (M^+ + 1). Anal. Calcd for $C_{20}H_{14}O_4$: C, 75.46; H, 4.43. Found: C, 75.26; H, 4.57.

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10. The reaction of **3a** also produced **5a** without Pd catalyst, however, the yield was lower (53%) and required long time (20 h) at higher temperature (110 °C).
11. Compound **5a** was also generated from **4a** without the influence of Pd catalyst in a similar yield (63%). The results state that the last step is a base-mediated process not Pd-mediated one, actually.
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