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Communications

One-Pot Synthesis of (*E*)-2-Arylideneindan-1-ones from the Baylis-Hillman Adducts *via* the Successive Inter- and Intramolecular Friedel-Crafts Reactions

Hong Jung Lee, Taek Hyeon Kim,[†] and Jae Nyoung Kim[*]

Department of Chemistry and Institute of Basic Science, Chonnam National University, Kwangju 500-757, Korea
[†]Faculty of Applied Chemistry, Chonnam National University, Kwangju 500-757, Korea
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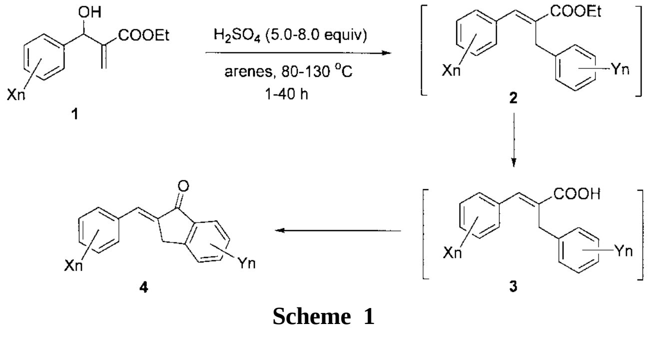
The Baylis-Hillman reaction is well known as a coupling reaction of aldehydes and activated alkenes catalyzed by tertiary amines or tertiary phosphines.[1] The reaction with ethyl acrylate serves α-methylene-β-hydroxy esters, which have been transformed to various useful compounds.[2]

Friedel-Crafts reaction of the Baylis-Hillman adducts is well documented in the literature.[3] Recently, we described on the Friedel-Crafts reaction of the Baylis-Hillman adducts of *N*-tosylimines with arenes under the catalytic influence of sulfuric acid providing a facile stereoselective synthesis of ethyl 3-aryl-2-benzylprop-2-enoates.[3a] We felt that the synthesis of 2-arylideneindan-1-one derivatives would be possible from ethyl 3-aryl-2-benzylprop-2-enoates (**2** in Scheme 1) via the intramolecular Friedel-Crafts acylation by using excess amounts of sulfuric acid. 2-Arylideneindan-1-one derivatives are useful for the synthesis of various biologically important compounds.[4] These compounds can be synthesized by a Claisen-Schmidt condensation between appropriate aryl aldehydes and 1-indanones.[5,6] However, synthesis of 1-indanone derivatives must be preceded in order to synthesize 2-arylideneindan-1-ones.

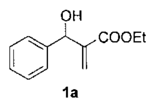
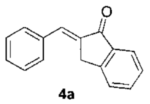
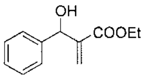
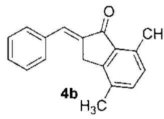
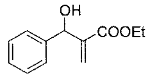
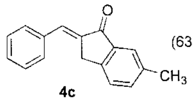
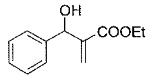
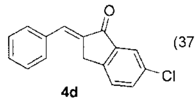
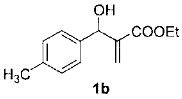
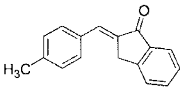
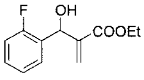
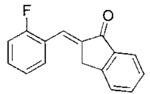
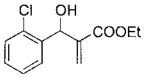
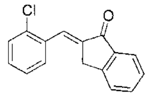
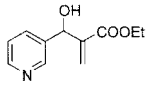
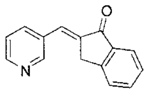


Scheme 1

Thus, we examined the reaction of the Baylis-Hillman adduct and benzene in the presence of sulfuric acid. A mixture of **1a** (412 mg, 2 mmol) and H_2SO_4 (980 mg, 10 mmol, 5 equiv) in dry benzene (5 mL) was stirred during reflux for 3 h. After the usual work-up and column chromatography (hexane/ether, 9 : 1), we could obtain the desired (*E*)-2-benzylideneindan-1-one (**4a**) in 65% yield as a pale yellow solid.[7]

The reaction mechanism is depicted in Scheme 1. The reaction of the Baylis-Hillman adduct **1** and arene gave ethyl (2*E*)-3-aryl-2-arylmethylprop-2-enoate **2** regioselectively *via* the intermolecular Friedel-Crafts reaction as reported.[3] Successive intramolecular Friedel-Crafts acylation of **2** gave the desired product (*E*)-2-arylideneindan-1-ones **4**. To a certain extent, hydrolysis of **2** to the corresponding carboxylic acid **3** would occur in the reaction conditions. As shown in Table 1, various Baylis-Hillman adducts **1a-e** in the reaction with some arenes (benzene, toluene, xylene, chlorobenzene) gave similar results. Unexpectedly, we obtained one regioisomer in the cases of mono-substituted arenes such as toluene (**4c** in entry 3) and chlorobenzene (**4d** in entry 4). The other possible regioisomer can not be isolated.[8] The structures of **4c** and **4d** were identified by NOE experiment (Figure 1). Irradiation of the methylene protons (δ = 4.02 ppm) at the 3-position of **4c** showed an increase of aromatic protons at the benzylidene portion (δ = 7.66-7.70 ppm, 3%) and at the indanone ring (H_4, δ = 7.40-7.50 ppm, 0.5%). Irradiation of the methyl protons (δ = 2.44 ppm) at the 6-position of **4c** showed an increase of H_7 (δ = 7.72 ppm, 0.6%) and H_5 (δ = 7.40-7.50 ppm, 0.5%) at the indanone ring. Similar NOE results were observed in the case of **4d** as shown in Figure 1.

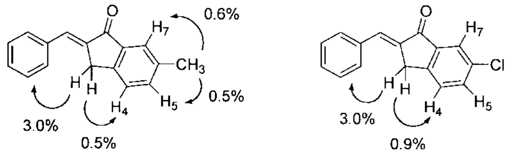
Table 1. Synthesis of (*E*)-2-arylideneindan-1-ones **4**

Entry	B-H adduct (**1**)	Conditions	Product (% yield)
1	 **1a**	benzene H$_2$SO$_4$ (5 equiv) reflux 3 h	 **4a** (65)
2	 **1a**	*p*-xylene H$_2$SO$_4$ (5 equiv) 110-120 °C 1 h	 **4b** (79)
3	 **1a**	toluene H$_2$SO$_4$ (8 equiv) reflux 36 h	 **4c** (63)
4	 **1a**	chlorobenzene H$_2$SO$_4$ (6 equiv) 120-130 °C 5 h	 **4d** (37)
5	 **1b**	benzene H$_2$SO$_4$ (6 equiv) reflux 5 h	 **4e** (81)
6	 **1c**	benzene H$_2$SO$_4$ (8 equiv) reflux 12 h	 **4f** (77)
7	 **1d**	benzene H$_2$SO$_4$ (6 equiv) reflux 40 h	 **4g** (60)
8	 **1e**	benzene H$_2$SO$_4$ (6 equiv) reflux 20 h	 **4h** (42)

From the NOE experiment, we could confirm the structure as well as the stereochemistry (*E*) of the double bond.

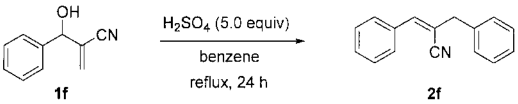
As expected from the previous reports,[3] for nitrile substituted Baylis-Hillman adduct such as **1f**, the first intermolecular Friedel-Crafts reaction with benzene gave the corresponding *Z*-form olefin **2f**,[3a] which did not undergo the next intramolecular Friedel-Crafts acylation in the reaction conditions.

The use of trifluoromethanesulfonic acid (5 equiv) instead of sulfuric acid in the reaction of **1a** and benzene (reflux, 2 h) gave increased yield of **4a** (87%). However, when we use trifluoromethanesulfonic acid or sulfuric acid lesser than 5.0 equivalents low yields of **4** were obtained. Instead, **2** and **3** were isolated as the major products.



4c **4d**

Figure 1



Scheme 2

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6. Recently, Basavaiah and Reddy have reported the synthesis of 2-arylideneindan-1-ones from the Baylis-Hillman adducts obtained from *tert*-butyl acrylate. Basavaiah, D.; Reddy, R. M. *Tetrahedron Lett.* **2001**, *42*, 3025.
7. The structure of **4** was confirmed by comparison with the reported data (mp or ^{1}H NMR spectrum).[4-6] As an example, spectral data of **4a** is as follows: mp 109-110 °C (lit,[6] 109-110 °C); IR (KBr) 1693, 1624 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.06 (s, 2H), 7.37-7.70 (m, 9H), 7.92 (d, J = 7.8 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 32.43, 124.44, 126.14, 127.66, 128.90, 129.61, 130.68, 133.89, 134.57, 134.76, 135.44, 138.05, 149.62, 194.26.
8. It is interesting to note that the possible regioisomers, 4-methyl-2-benzylideneindan-1-one or 4-chloro-2-benzylideneindan-1-one, was not isolated nor detected on tlc.