BULLETIN

OF THE

KOREAN CHEMICAL SOCIETY

ISSN 0253-2964 BKCSDE 23(6) 783-924
Volume 23, Number 6 June 20, 2002

Synthesis of Naphthalenes from the Reaction of Baylis-Hillman Acetates and Sulfonyl Group-containing Active Methylene Compounds

Yang Jin Im, Yun Mi Chung, Ji Hyeon Gong, and Jae Nyoung Kim*

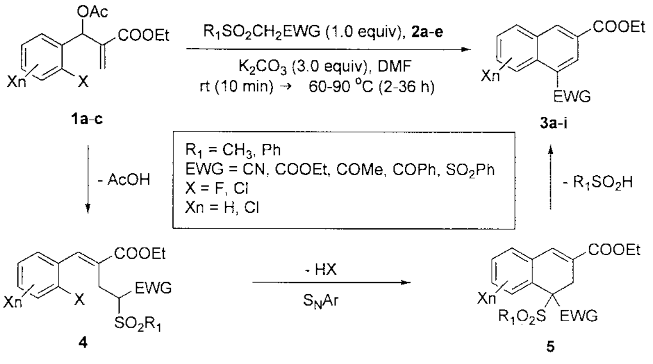
Department of Chemistry and Institute of Basic Science, Chonnam National University, Kwangju 500-757, Korea

Received February 8, 2002

Keywords : Naphthalenes, Baylis-Hillman acetates, Sulfonyl group, Active methylene compounds.

Regioselective synthesis of naphthalene derivatives has been and continues to be of great interest in organic synthesis.[1,2] New synthetic procedure is still highly desired due to the abundance of the skeleton in many biologically important natural products.[1,2] Recently we have reported on the synthesis of naphthalenes from the reaction of the Baylis-Hillman acetates derived from *o*-halobenzaldehydes and primary nitro alkanes *via* the successive S_N2'-S_NAr-elimination strategy.[2]

As an extension of the reaction we examined the reaction with sulfonyl group-containing active methylene compounds **2a-e** as the surrogates of primary nitro alkanes and the Baylis-Hillman acetates **1**. Our rationale was based on the followings: (1) The first S_N2' reaction of **2a-e** in *N,N*-dimethylformamide in the presence of K_2CO_3 would proceed without any problem due to the fact that primary nitro alkanes and active methylene compounds **2** have similar pK_a values.[3] (2) By the same reason, the second S_NAr step would give good results. (3) In the final elimination step, elimination of *p*-toluenesulfinic acid or methanesulfinic acid could proceed well as in the case of nitrous acid in our previous paper.[2] And finally, (4) many sulfonyl group-containing active methylene compounds are commercially available.



Scheme 1

As expected, a variety of 1,3-disubstituted naphthalenes **3a-i** were synthesized in good to moderate yields in a one-pot reaction as shown in Scheme 1. We used three Baylis-Hillman acetates **1a-c** as the representative examples. As the sulfonyl group-containing active methylene compounds we chose (phenylsulfonyl)acetonitrile (**2a**), ethyl methanesulfonylacetate (**2b**), methanesulfonylacetone (**2c**), α-(phenylsulfonyl)-acetophenone (**2d**) and bis(phenylsulfonyl)methane (**2e**). The results are summarized in Table 1.

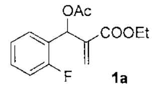
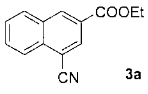
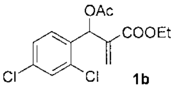
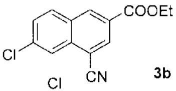
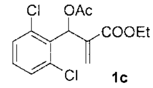
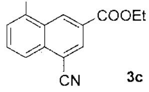
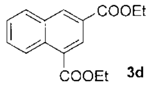
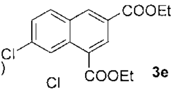
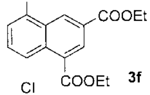
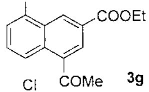
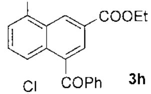
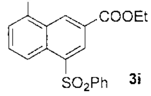
When we used **2a** and **2b**, the corresponding naphthalene derivatives **3a-f** were obtained in good to moderate yields (60-92%, Table 1).[4] However, in the cases of **2c-e** low yields of products **3g-i** were obtained (23-55%). Low yield of **3g** might be arisen because of the labile acetyl group in the reaction conditions. In the cases of **3h** and **3i**, steric hindrance in the S_NAr step seemed the major reason for low yields.

The reaction mechanism for the formation of **3** was depicted in Scheme 1. The S_N2' type reaction of the *in situ* generated potassium salt of **2** to the Baylis-Hillman acetates **1** gave the *E*-form of cinnamate derivatives **4** as in our previous paper.[2,5] Under the reaction conditions **4** readily underwent the next S_NAr reaction to give **5**. Trace amounts of the corresponding *Z*-form of **4** cannot undergo the next S_NAr reaction. Finally, a rapid elimination of *p*-toluenesulfinic acid or methanesulfinic acid from **5** gave the naphthalenes **3**.

As a conclusion we disclosed a facile methodology for the synthesis of 1,3-disubstituted naphthalenes from the reaction of Baylis-Hillman acetates and sulfonyl group-containing active methylene compounds *via* the successive S_N2'-S_NAr-elimination strategy.

Acknowledgment. This work was supported by a Korea

Table 1. Synthesis of 1,3-disubstituted naphthalene derivatives **3a-i**

Entry	B-H acetate **1**	Conditions	Product **3**	Yield (%)[a]
1	 **1a**	$PhSO_2CH_2CN$ (**2a**) K_2CO_3, DMF rt (10 min) → 60 °C (5 h)	 **3a**	92 (97-98)
2	 **1b**	$PhSO_2CH_2CN$ K_2CO_3, DMF rt (10 min) → 60 °C (3 h)	 **3b**	90 (132-133)
3	 **1c**	$PhSO_2CH_2CN$ K_2CO_3, DMF rt (10 min) → 60 °C (2 h)	 **3c**	88 (154-155)
4	**1a**	$CH_3SO_2CH_2COOEt$ (**2b**) K_2CO_3, DMF rt (10 min) → 70 °C (36 h)	 **3d**	77 (38-39)
5	**1b**	$CH_3SO_2CH_2COOEt$ K_2CO_3, DMF rt (10 min) → 70 °C (36 h)	 **3e**	60 (87-88)
6	**1c**	$CH_3SO_2CH_2COOEt$ K_2CO_3, DMF rt (10 min) → 70 °C (18 h)	 **3f**	69 (77-78)
7	**1c**	$CH_3SO_2CH_2COMe$ (**2c**) K_2CO_3, DMF rt (10 min) → 70 °C (12 h)	 **3g**	26 (89-90)
8	**1c**	$PhSO_2CH_2COPh$ (**2d**) K_2CO_3, DMF rt (10 min) → 90 °C (36 h)	 **3h**	55[b] (139-140)
9	**1c**	$PhSO_2CH_2SO_2Ph$ (**2e**) K_2CO_3, DMF rt (10 min) → 90 °C (36 h)	 **3i**	23[c] (170-171)

[a]Mp was written in parenthesis. [b]The yield of **3h** was improved up to 70% when we used 2.0 equiv. of **1c**. [c]The yield of **3i** was improved to 39% when we used 2.0 equiv. of **1c**.

Research Foundation Grant (KRF-2001-015-DP0326).

References and Notes

1. (a) Seong, M. R.; Song, H. N.; Kim, J. N. *Tetrahedron Lett.* **1998**, *39*, 7101 and further references cited therein. (b) Rucker, M.; Bruckner, R. *Synlett* **1997**, 1187.
2. Kim, J. N.; Im, Y. J.; Gong, J. H.; Lee, K. Y. *Tetrahedron Lett.* **2001**, *42*, 4195 and further references cited therein.
3. Smith, M. B.; March, J. *Advanced Organic Chemistry*, Fifth ed.; Wiley-Interscience: New York, 2001; pp 327-362.
4. Typical procedure for the preparation of 6-chloro-4-cyanonaphthalene-2-carboxylic acid ethyl ester (**3b**): To a stirred suspension of (phenylsulfonyl)acetonitrile (**2a**, 182 mg, 1.0 mmol) and potassium carbonate (415 mg, 3 mmol) in DMF (3 mL) was added dropwise the Baylis-Hillman acetate **1b** (317 mg, 1 mmol in 1 mL of DMF, 10 min) and stirred at 60 °C for 3 h. After the usual workup process and column chromatographic purification (hexane: CH_2Cl_2, 1 : 3) analytically pure product **3b** was isolated 234 mg (90%): white solid, mp 132-133 °C; IR (KBr) 2224, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (t, J = 7.1 Hz, 3H), 4.48 (q, J = 7.1 Hz, 2H), 7.65 (d, J = 8.7 Hz, 1H), 8.00 (d, J = 8.7 Hz, 1H), 8.28 (s, 1H), 8.53 (s, 1H), 8.79 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.37, 62.04, 109.94, 116.59, 124.30, 127.68, 129.57, 130.49, 131.57, 133.07, 134.53, 135.27, 137.54, 164.53.
5. For our recent papers, see: (a) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Gong, J. H. *Synlett* **2002**, 173. (b) Gong, J. H.; Im, Y. J.; Lee, K. Y.; Kim, J. N. *Tetrahedron Lett.* **2002**, *43*, 1247. (c) Chung, Y. M.; Gong, J. H.; Kim, T. H.; Kim, J. N. *Tetrahedron Lett.* **2001**, *42*, 9023. (d) Kim, J. N.; Kim, H. S.; Gong, J. H.; Chung, Y. M. *Tetrahedron Lett.* **2001**, *42*, 8341. (e) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Kim, H. S. *Tetrahedron Lett.* **2001**, *42*, 3737. (f) Kim, H. S.; Kim, T. Y.; Lee, K. Y.; Chung, Y. M.; Lee, H. J.; Kim, J. N. *Tetrahedron Lett.* **2000**, *41*, 2613. (g) Kim, J. N.; Lee, K. Y.; Kim, H. S.; Kim, T. Y. *Org. Lett.* **2000**, *2*, 343.