

Communications

Facile Synthesis of 3-Benzylidene-5-aryl-3*H*-furan-2-ones Starting from the Baylis-Hillman Adducts

Chang Gon Lee, Ka Young Lee, Seong Jin Kim, and Jae Nyong Kim*

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

*E-mail: kimjn@chonnam.ac.kr

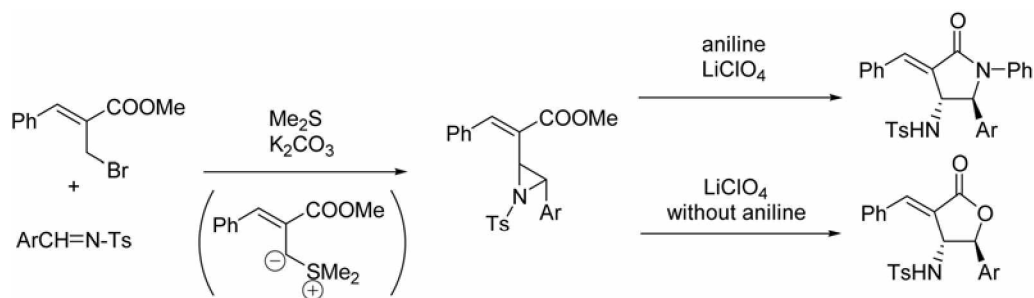
Received February 20, 2007

Key Words : Baylis-Hillman adducts. 3*H*-Furan-2-ones. Lactones

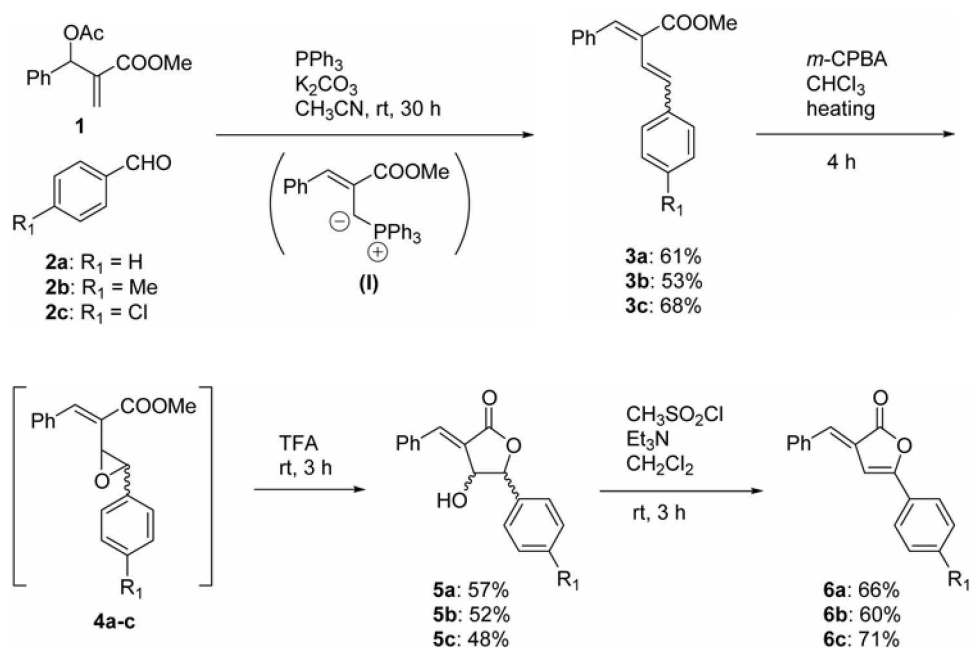
Recently we reported the synthesis of 3-arylidene lactams and 3-arylidene lactones starting from the Baylis-Hillman adducts *via* the following sequences: (i) preparation of cinnamyl bromide from the Baylis-Hillman adducts, (ii) generation of sulfur ylide ($\text{Me}_2\text{S}/\text{K}_2\text{CO}_3$) and the following reaction with *N*-tosylimine to produce *N*-tosylaziridine. (iii) LiClO_4 -assisted ring-opening reaction with aniline and the

cyclization to 3-arylidene lactam or LiClO_4 -assisted intramolecular lactonization and concomitant aziridine-opening reaction to 3-arylidene lactone.¹ The reaction sequence is depicted in Scheme 1.

In this communication, we wish to report another expeditious route for the synthesis of 3-benzylidene lactone compounds **5** and 3-benzylidene-5-aryl-3*H*-furan-2-ones **6**.



Scheme 1



Scheme 2

We used phosphorous ylide (**I**) instead of the sulfur ylide¹ and epoxide intermediate **4** instead of *N*-tosylaziridine intermediate¹ as shown in Scheme 2. The reaction of Baylis-Hillman acetates **1** and benzaldehyde (**2a**) in the presence of triphenylphosphine (2 equiv) and K₂CO₃ (2 equiv) in CH₃CN (rt, 30 h) afforded the corresponding diene derivative **3a** in 61% *via* the corresponding phosphorous ylide intermediate as reported.² The diene **3a** was isolated as a *cis/trans* mixture² and used without further purification. The epoxidation of diene **3a** with *m*-CPBA (1.5 equiv, CHCl₃, 40-50 °C, 4 h) proceeded in a highly regio-selective manner at the disubstituted alkene moiety to provide **4a**. However, the purification of **4a** in analytically pure state was difficult due to the contamination of unknown impurities. Thus we examined the synthesis of 3-benzylidene-4-hydroxylactone **5a** in a one-pot procedure from **3a** under acidic conditions.³ When we added trifluoroacetic acid (0.3 equiv, rt, 3 h) after the formation of epoxide, the epoxide **4a** was converted into the desired 3-benzylidene-4-hydroxylactone **5a** in 57%.^{1,4} The lactone **5a** could be converted into butenolide derivative **6a** under the influence of CH₃SO₂Cl (1.5 equiv) and Et₃N (2.5 equiv) in CH₂Cl₂ (rt, 3 h) in moderate yield (66%).^{5,6} The reactions of *p*-tolualdehyde (**2b**) and *p*-chlorobenzaldehyde (**2c**) were carried out under the exactly same conditions and the results are also summarized in Scheme 2.

In conclusion, we disclosed an effective pathway for the synthesis of 3-benzylidene-4-hydroxylactones and 3-benzylidene-5-aryl-3*H*-furan-2-ones starting from the Baylis-Hillman adducts.⁷ Further extensions of our findings are currently underway.

Acknowledgments. This work was supported by the Korea Research Foundation Grant funded by the Korean Government (MOEHRD, KRF-2006-311-C00384). Spectroscopic data was obtained from the Korea Basic Science Institute, Gwangju branch.

References and Notes

- Lee, K. Y.; Lee, H. S.; Kim, J. N. *Tetrahedron Lett.* **2007**, *48*, 2007 and further references on the synthesis of lactone derivatives were cited therein.
- For the synthesis of diene derivatives and their stereochemistry, see: (a) Crist, R. M.; Reddy, P. V.; Borhan, B. *Tetrahedron Lett.* **2001**, *42*, 619. (b) Janecki, T.; Bodalski, R. *Synthesis* **1989**, 506. (c) Minami, T.; Tokumasu, S.; Hirao, I. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 2139. (d) Muthiah, C.; Kumar, K. S.; Vittal, J. J.; Kumara Swamy, K. C. *Synlett* **2002**, 1787.
- For the examples of cyclization involving the ester moiety, see: (a) Alverne, G.; Lacombe, S.; Laurent, A.; Marquet, B. *J. Chem. Res.* **1980**, 54. (b) Yao, T.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 5936. (c) Wawrzencyk, C.; Grabarczyk, M.; Bialonska, A.; Ciunik, Z. *Tetrahedron* **2003**, *59*, 6595. (d) Mead, K. T.; Yang, H.-L. *J. Org. Chem.* **1990**, *55*, 2991.
- The synthesis of 3-benzylidene-4-hydroxylactone derivative **5a** was reported by using different route, please see: Rhee, J. U.; Kriische, M. *J. Am. Chem. Soc.* **2006**, *128*, 10674. However, in this paper the authors reported the compound having *Z* stereochemistry of double bond and *syn* relationships between hydroxyl and phenyl group. Instead our compound **5a** could be regarded as *E* (double bond) based on the spectroscopic data although the relative stereochemistry between the hydroxyl and the phenyl group was undetermined. Our compound **5a** (*E*): ¹H NMR (CDCl₃, 300 MHz) δ 2.46 (d, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 7.8 Hz, 1H), 5.56 (s, 1H), 7.28-7.46 (m, 8H), 7.71-7.74 (m, 2H), 7.83 (s, 1H); Reported compound **5a** (*Z, syn*):⁴ ¹H NMR (CDCl₃, 400 MHz) δ 2.71 (br s, 1H), 4.79 (d, *J* = 4.8 Hz, 1H), 5.25 (d, *J* = 5.2 Hz, 1H), 7.19 (d, *J* = 2.0 Hz, 1H), 7.36-7.42 (m, 8H), 7.99-8.01 (m, 2H).
- 3-Benzylidene-5-aryl-3*H*-furan-2-ones could be synthesized by different methods, see: (a) Rossi, R.; Bellina, F.; Bechini, C.; Mannina, L.; Vergamini, P. *Tetrahedron* **1998**, *54*, 135. (b) Filler, R.; Piasek, E. J.; Mark, L. H. *J. Org. Chem.* **1961**, *26*, 2659. (c) Raj, A. A.; Raghunathan, R. *Tetrahedron* **2003**, *59*, 2907. (d) Raj, A. A.; Raghunathan, R.; SrideviKumari, M. R.; Raman, N. *Bioorg. Med. Chem.* **2003**, *11*, 407. (e) Huang, Y.; Alper, H. *J. Org. Chem.* **1991**, *56*, 4534. (f) Bourotte, M.; Schmitt, M.; Follenius-Wund, A.; Pigault, C.; Haiech, J.; Bourguignon, J.-J. *Tetrahedron Lett.* **2004**, *45*, 6343. (g) Patil, S. N.; Liu, F. *Org. Lett.* **2007**, *9*, 195 and further references cited therein.
- Selected spectroscopic data of 3-benzylidene-5-aryl-3*H*-furan-2-ones are as follows.
Compound 6a:^{5b,c} 66%: pale yellow solid, mp 140-141 °C; ¹H NMR (CDCl₃, 300 MHz) δ 6.92 (d, *J* = 0.9 Hz, 1H), 7.38-7.50 (m, 7H), 7.60-7.77 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ 99.79, 125.29, 125.37, 128.01, 128.82, 129.06, 130.04, 130.22, 130.46, 135.10, 135.38, 156.91, 169.29.
Compound 6b:^{5e} 60%: pale yellow solid, mp 148-149 °C; ¹H NMR (CDCl₃, 300 MHz) δ 2.38 (s, 3H), 6.84 (d, *J* = 1.2 Hz, 1H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.36-7.47 (m, 4H), 7.53-7.65 (m, 4H).
Compound 6c:^{5e} 71%: pale yellow solid, mp 207-209 °C; ¹H NMR (CDCl₃, 300 MHz) δ 6.93 (d, *J* = 0.9 Hz, 1H), 7.40-7.51 (m, 6H), 7.60-7.71 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ 100.25, 125.21, 126.54, 126.57, 129.14, 129.23, 130.11, 130.43, 135.04, 136.05, 136.47, 155.85, 169.04.
- For our recent chemical transformations using epoxides and aziridines, see: (a) Lee, K. Y.; Kim, S. C.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 977. (b) Lee, K. Y.; Park, Y. J.; Kim, J. N. *Bull. Korean Chem. Soc.* **2007**, *28*, 143. (c) Kim, S. C.; Lee, H. S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2007**, *28*, 147. (d) Lee, K. Y.; Park, D. Y.; Kim, J. N. *Bull. Korean Chem. Soc.* **2006**, *27*, 1489.