Communications

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

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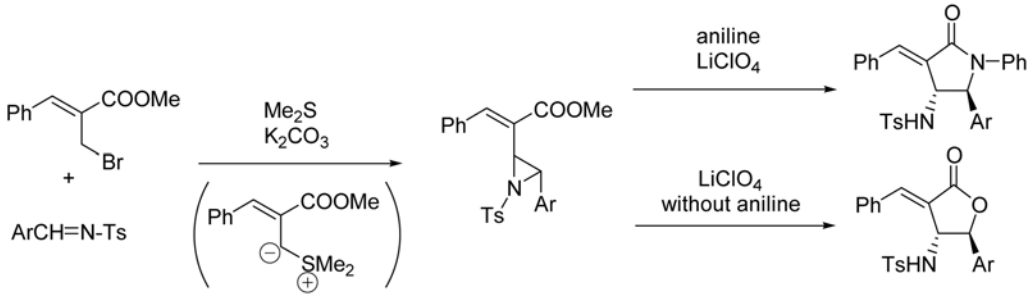
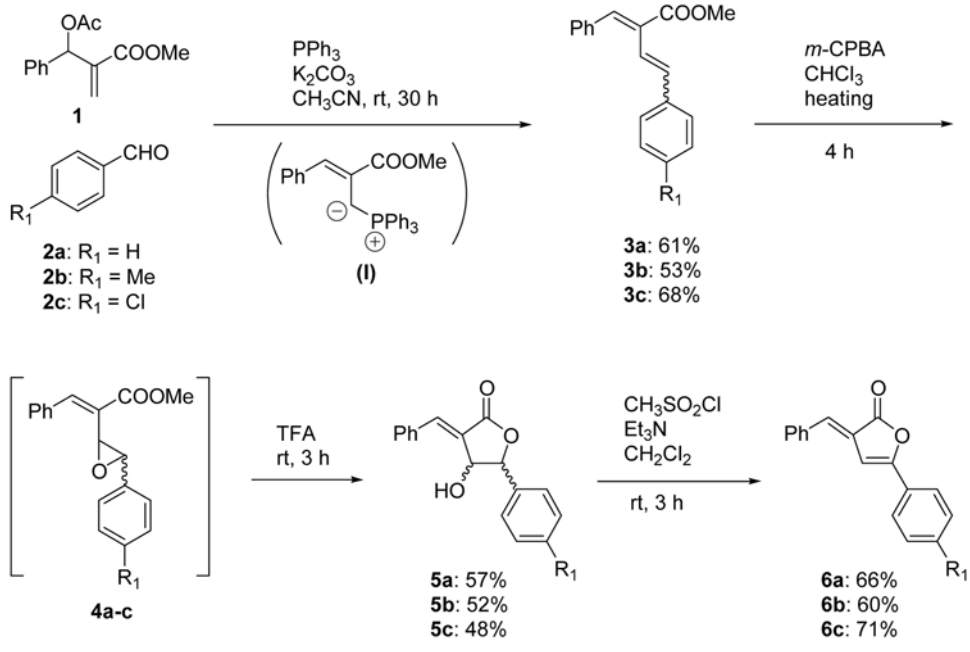
Recently we reported the synthesis of 3-arylidenelactams and 3-arylidenelactones starting from the Baylis-Hillman adducts *via* the following sequences: (i) preparation of cinnamyl bromide from the Baylis-Hillman adducts, (ii) generation of sulfur ylide (Me_2S/K_2CO_3) and the following reaction with *N*-tosylimine to produce *N*-tosylaziridine, (iii) $LiClO_4$-assisted ring-opening reaction with aniline and the cyclization to 3-arylidenelactam or $LiClO_4$-assisted intramolecular lactonization and concomitant aziridine-opening reaction to 3-arylidenelactone.[1] The reaction sequence is depicted in Scheme 1.

In this communication, we wish to report another expeditious route for the synthesis of 3-benzylidenelactone 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 ylide[1] and epoxide intermediate **4** instead of *N*-tosylaziridine intermediate[1] as shown in Scheme 2. The reaction of Baylis-Hillman acetates **1** and benzaldehyde (**2a**) in the presence of triphenylphosphine (2 equiv) and K_2CO_3 (2 equiv) in CH_3CN (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* mixture[2] and used without further purification. The epoxidation of diene **3a** with *m*-CPBA (1.5 equiv, $CHCl_3$, 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 CH_3SO_2Cl (1.5 equiv) and Et_3N (2.5 equiv) in CH_2Cl_2 (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.

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References and Notes

1. 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.
2. 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.
3. For the examples of cyclization involving the ester moiety, see: (a) Alvernhe, 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) Wawrzenczyk, C.; Grabarczyk, M.; Bialonska, A.; Ciunik, Z. *Tetrahedron* **2003**, *59*, 6595. (d) Mead, K. T.; Yang, H.-L. *J. Org. Chem*. **1990**, *55*, 2991.
4. The synthesis of 3-benzylidene-4-hydroxylactone derivative **5a** was reported by using different route, please see: Rhee, J. U.; Krische, M. J. *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*): ^{1}H NMR ($CDCl_3$, 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] ^{1}H NMR ($CDCl_3$, 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).
5. 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.
6. 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; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.92 (d, J = 0.9 Hz, 1H), 7.38-7.50 (m, 7H), 7.60-7.77 (m, 4H); ^{13}C NMR ($CDCl_3$, 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; ^{1}H NMR ($CDCl_3$, 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; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.93 (d, J = 0.9 Hz, 1H), 7.40-7.51 (m, 6H), 7.60-7.71 (m, 4H); ^{13}C NMR ($CDCl_3$, 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.
7. 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.