Communications

Facile Synthesis of 3-Benzylidene-5-aryl-3H-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 ylides (Me₂S/K₂CO₃) and the following reaction with N-tosylimine to produce N-tosylaziridine, (iii) LiClO₄-assisted ring-opening reaction with aniline and the cyclization to 3-arylidenelactam or LiClO₄-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-benzylidene lactone compounds 5 and 3-benzylidene-5-aryl-3H-furan-2-ones 6.
We used phosphorous ylide (I) instead of the sulfur ylide and epoxide intermediate 4 instead of N-tert-butylaziridine intermediate as shown in Scheme 2. The reaction of Baylis-Hillman acetates 1 and benzaldehyde (2a) in the presence of triphenylphosphine (2 equiv) and K3CO3 (2 equiv) in CH2CN (rt, 30 h) afforded the corresponding diene derivative 3a in 61% via the corresponding phosphorous ylide intermediate as reported. The diene 3a was isolated as a cis/trans mixture 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-hydroxy lactone 5a in a one-pot procedure from 3a under acidic conditions. When we added trifluoroacetic acid (0.5 equiv, rt, 3 h) after the formation of epoxide, the epoxide 4a was converted into the desired 3-benzylidene-4-hydroxy lactone 5a in 57% yield. The lactone 5a could be converted into butenolide derivative 6a under the influence of CH2SO2Cl (1.5 equiv) and Et2N (2.5 equiv) in CH2Cl2 (rt, 3 h) in moderate yield (66%). 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-hydroxy lactones and 3-benzylidene-5-aryl-3H-furan-2-ones starting from the Baylis-Hillman adducts. Further extensions of our findings are currently underway.

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References and Notes


4. The synthesis of 3-benzylidene-4-hydroxy lactone derivative 5a was reported by using different route, please see Rhee, J. U.; Kischince, 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 not 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), 6.56 (s, 1H), 7.38-7.46 (m, 2H), 7.83 (s, 1H), Reported compound 5a (E)-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).


6. Selected spectroscopic data of 3-benzylidene-5-aryl-3H-furan-2-ones were as follows.

-compound 6a (E)-1H-NMR (CDCl3, 300 MHz), δ 2.48 (d, J = 7.8 Hz, 1H), 6.93 (d, J = 9.2 Hz, 1H), 7.38-7.50 (m, 2H), 7.69-7.77 (m, 4H), 7.99-8.01 (m, 2H). 13C-NMR (CDCl3, 75 MHz) δ 39.79, 125.29, 129.57, 128.01, 128.62, 129.06, 130.06, 130.42, 130.90, 135.58, 135.86, 136.91, 169.29.

-compound 6a (Z)-1H-NMR (CDCl3, 300 MHz), δ 2.36 (d, J = 1.2 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.36-7.47 (m, 4H), 7.53-7.65 (m, 4H). 13C-NMR (CDCl3, 75 MHz) δ 39.79, 125.81, 125.67, 129.14, 129.23, 130.11, 130.43, 130.06, 130.47, 135.54, 135.04, 169.04.