

Short Note

Methyl (6-Ethyldibenzo[*d,f*][1,3]dioxepin-6-yl)acetate

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Abstract: Starting from 2,2'-dihydroxybiphenyl and an allenic ester, the title dibenzo-condensed dioxepine derivative was synthesized using a one-pot procedure.

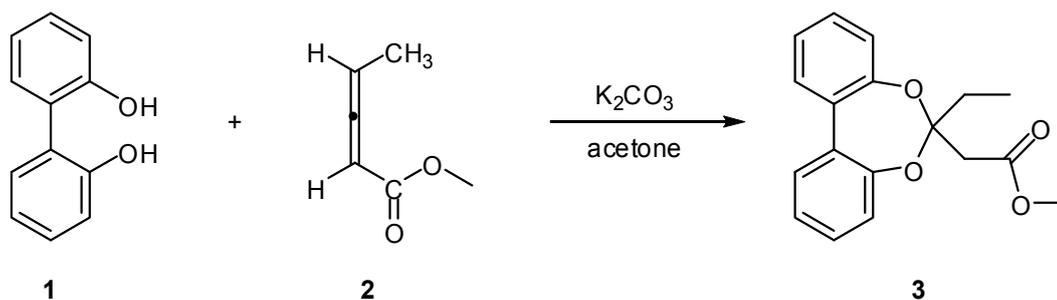
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1. Introduction

Allenes are versatile reagents in organic synthesis [1]. The reaction of allenic esters with 1,2-dihydroxy-, 1,2-disulfanyl-, 1-hydroxy-2-sulfanyl-benzenes to yield benzocondensed five-membered heterocycles has been reported [2]. In the presence of K_2CO_3 , one of the nucleophilic group on the aromatic ring reacts with the central carbon atom of the allene. The second nucleophilic group attacks the same carbon in an intramolecular Michael-type reaction leading to ring closure. This simple, one-pot procedure was applied for the synthesis of a seven-membered ring, using the same allenic derivative as starting material.

2. Results and Discussion

Allenic esters have proved to be efficiently attacked by nucleophilic reagents to the central carbon atom. An interesting extension of the above mentioned synthetic strategy is the use of a structure bearing two nucleophilic moieties on two different aromatic rings such as a biphenyl derivative. In this case, 2,2'-dihydroxybiphenyl **1** was treated with an equimolar amount of the allenic ester **2**. In order to enhance the nucleophilicity of hydroxyl groups, the reaction was performed in a basic K_2CO_3 /acetone medium.



Scheme 1. Synthesis of methyl (6-ethylidibenzo[*d,f*][1,3]dioxepin-6-yl)acetate **3**.

The two consecutive attacks of the hydroxyl groups on the allenic central carbon atom led to a ring closure with the formation of a seven-membered heterocyclic ring, namely a 1,3-dioxepine. The product **3** was easily isolated from the reaction mixture and purified by flash-chromatography. Further purification by crystallization from ethanol afforded the product **3** with an overall yield of 12%. As reported in a previous work [2], this low value may be explained by the formation of open-chain products derived from the addition of one or two molecules of allene. Although such compounds could be responsible for allene consumption, in this case it was not possible to isolate and characterize any by-product. Recently, Szeto [3] reported a similar procedure to prepare benzocondensed five-membered heterocycles obtaining higher yields, but employing less “eco-friendly” reagents and solvents, and using a more complicated experimental procedure.

3. Experimental Section

3.1. General Information

Reagent-grade, commercially available reagents and solvents were used. Methyl 2,3-pentadienoate (**2**) was prepared by literature method [4]. Flash chromatography was performed on silica gel 60, 0.04–0.063 mm (Fluka, Buchs, Switzerland). Melting points were determined with a Kofler hot stage microscope and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Varian VXR-400 and VXR-500 spectrometers (Agilent Technologies, Santa Clara, CA, USA). Chemical shifts are given as δ values (ppm) from internal TMS. Mass spectra were obtained at 70 eV with a Agilent 5973 mass spectrometer interfaced to the GC 6890N equipped with a DB-5ms column (J&W, Agilent Technologies, Santa Clara, CA, USA). Elemental analysis was performed on a PerkinElmer 2400 Series II Elemental analyser (PerkinElmer, Inc. Waltham, MA, USA).

3.2. Methyl (6-Ethylidibenzo[*d,f*][1,3]dioxepin-6-yl)acetate (**3**)

A mixture of **1** (6.64 g, 35.6 mmol), anhydrous potassium carbonate (7 g, 72 mmol), and dry acetone (40 mL) was stirred and refluxed for 2 h at room temperature. A solution of **2** (4 g, 35.6 mmol) in acetone (10 mL) was added dropwise and stirring was continued for 24 hours. The mixture was poured into water and then extracted with diethyl ether. The organic layer was washed with 10% aqueous sodium hydroxide and then dried over anhydrous sodium sulphate. Solvent evaporation *in vacuo* furnished a residue that was purified by flash-chromatography. On elution with hexane–ethyl acetate (5:1), methyl

(6-ethylidibenzo[*d,f*][1,3]dioxepin-6-yl)acetate **3** was obtained as a white solid, that was purified by crystallization from ethanol.

Yield 1.27 g (12%), colorless crystals, mp 82–84 °C. ¹H-NMR (500 MHz, CDCl₃): δ (ppm) 1.21 (t, *J* = 7.5 Hz, 3H, CH₃CH₂), 2.14 (q, *J* = 7.5 Hz, 2H, CH₃CH₂), 3.00 (s, 2H, CH₂), 3.78 (s, 3H, OCH₃), 7.21 (dd, *J* = 7.5, 1.5 Hz, 2H, Ar-H), 7.30 (td, *J* = 7.5, 1.5 Hz, 2H, Ar-H), 7.35 (td, *J* = 7.5, 1.5 Hz, 2H, Ar-H), 7.52 (dd, *J* = 7.5, 1.5 Hz, 2H, Ar-H). ¹³C-NMR (100 MHz, CDCl₃): δ (ppm) 8.7 (CH₃CH₂), 28.4 (CH₃CH₂), 39.3 (CH₂), 51.8 (OCH₃), 117.1 (C(6)), 123.4 (2CH), 125.3 (2CH), 128.4 (2CH), 128.7 (2CH), 133.1 (2C), 151.1 (2C), 169.4 (C=O). MS-EI (C₁₈H₁₈O₄) *m/z*: 298 (52, M⁺), 266 (100), 237 (21), 225 (36), 186 (58), 168 (77), 139 (36%). Anal. Calcd for C₁₈H₁₈O₄: C, 72.47; H, 6.08; Found: C, 73.38; H, 6.11% (Figure S1–S5 in the supplementary materials).

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Author Contributions

C.F. performed the synthesis and the instrumental analysis, F.P. wrote the paper.

Conflicts of Interest

The authors declare no conflict of interest.

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