

Short Note

(2E)-3-[4-(1H-Benzimidazol-2-ylmethoxy)-3-methoxyphenyl]-1-(4,4''-difluoro-5'-methoxy-1,1':3',1''-terphenyl-4'-yl)prop-2-en-1-one

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Abstract: Novel terphenyl chalcone containing benzimidazole moiety (**3**) is synthesized by the base-catalyzed Claisen–Schmidt condensation of acetyl terphenyl derivative (**1**) with 4-(1H-benzimidazol-2-ylmethoxy)-3-methoxybenzaldehyde (**2**). Newly prepared chalcone derivative (**3**) is characterized by IR, NMR and mass spectral data.

Keywords: acetyl terphenyl; chalcone; benzimidazole

Introduction

Terphenyl is a common structural motif found in various natural products, largely isolated from microbes and mushrooms [1]. In recent years, it has been reported that some terphenyls exhibit significant biological activities, e.g., potent anticoagulant, immunosuppressants, antithrombotic, neuroprotective, specific 5-lipoxygenase inhibitory and cytotoxic activities [2]. Because of their promising biological activities and important properties, terphenyls have produced increasing research interest. Also, the pharmacological and toxicological properties of benzimidazole derivatives are well documented [3].

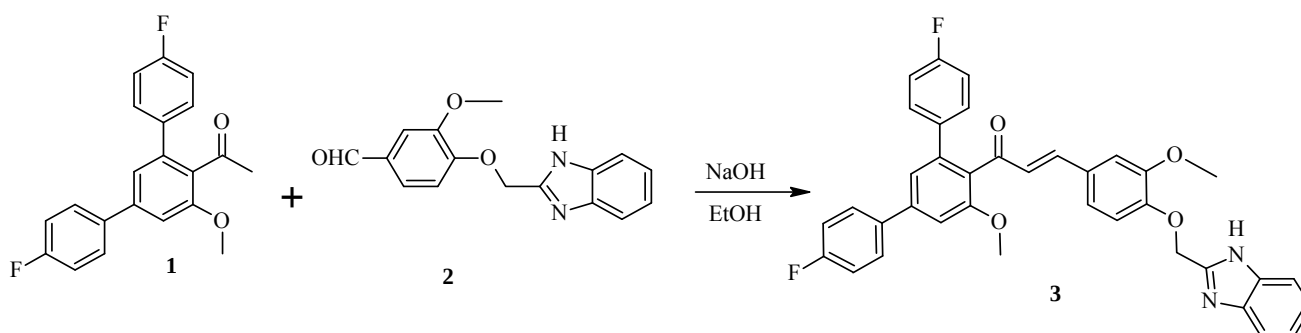
Recently we have reported the synthesis of many functionalized derivatives using 4,4'-difluoro chalcone as a powerful synthon [4–12]. In continuation of our ongoing efforts on the synthesis of large range of new compounds from a single precursor 4,4'-difluoro chalcone and in view of the importance

of terphenyls and benzimidazoles, we converted the 4,4'-difluoro chalcone into acetyl terphenyl derivative and condensed with an aldehyde containing benzimidazole moiety to yield title compound.

Results and Discussion

The title compound, (2*E*)-3-[4-(1*H*-benzimidazol-2-ylmethoxy)-3-methoxyphenyl]-1-(4,4''-difluoro-5'-methoxy-1,1':3',1''-terphenyl-4'-yl)prop-2-en-1-one (**3**), was prepared by the base-catalyzed Claisen–Schmidt condensation of acetyl terphenyl derivative (**1**) with 4-(1*H*-benzimidazol-2-ylmethoxy)-3-methoxybenzaldehyde (**2**) (Scheme 1). The starting material **1**, in turn prepared by the condensation of acetylacetone with the 4,4'-difluoro chalcone followed by the aromatization using iodine in methanol as described in our earlier work [13]. Also, the other starting material **2** was prepared according to the method reported by our group [14]. The product **3** was well characterized by using NMR, IR and mass spectral data.

Scheme 1. Synthesis of (2*E*)-3-[4-(1*H*-benzimidazol-2-ylmethoxy)-3-methoxyphenyl]-1-(4,4''-difluoro-5'-methoxy-1,1':3',1''-terphenyl-4'-yl)prop-2-en-1-one.



The IR spectrum of (2*E*)-3-[4-(1*H*-benzimidazol-2-ylmethoxy)-3-methoxyphenyl]-1-(4,4''-difluoro-5'-methoxy-1,1':3',1''-terphenyl-4'-yl)prop-2-en-1-one **3** showed an absorption band at 3313 cm⁻¹ due to benzimidazole N-H group and bands at 2,937 & 2,858 cm⁻¹ attributed to aliphatic C-H groups. A band seen at 1,654 cm⁻¹ was due to keto group of the chalcone. The ¹H-NMR spectrum showed two singlets at δ 3.79 & 3.86 ppm integrating for three protons each due to two methoxy groups. Another singlet observed at δ 5.55 ppm integrating two protons of bridging methylene group. One more singlet at δ 7.93 ppm was due to NH proton. The resonances of H_α & H_β protons of chalcone moiety appeared as two doublets one at δ 6.85 ppm and other doublet merged with the aromatic proton signals. The coupling constant *J* = 16 Hz indicated the *E* configuration of the chalcone. The multiplets appeared in the region δ 7.11–7.89 ppm integrating for 17 protons were due to aromatic protons. Mass spectrum showed a molecular ion peak at *m/z* 603.2 (*M*⁺+1) corresponding to the molecular formula of C₃₇H₂₈F₂N₂O₄. Elemental analysis and ¹³C-NMR spectrum also gave satisfactory results for the title compound.

Experimental

Melting point was taken in open capillary tube and was uncorrected. The purity of the compound was confirmed by thin layer chromatography using Merck silica gel 60 F₂₅₄ coated aluminium plates.

IR spectrum was recorded on Shimadzu-FTIR Infrared spectrometer in KBr ($\nu_{\max}$ in cm^{-1}). ^1H -NMR (400 MHz) spectrum was recorded on a Bruker AMX 400 spectrometer, with 5 mm PABBO BB -1H TUBES and ^{13}C -NMR (100 MHz) spectrum was recorded for approximately 0.03 M solutions in $\text{DMSO}-d_6$ at 100 MHz with TMS as internal standard. LCMS was obtained using Agilent 1200 series LC and Micromass zQ spectrometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmbH).

A mixture of 1-(4,4''-difluoro-5'-methoxy-1,1':3',1''-terphenyl-4'-yl)ethanone **1** (0.005 mol) and 4-(1*H*-benzimidazol-2-ylmethoxy)-3-methoxybenzaldehyde **2** (0.005 mol) in 30 mL ethanolic sodium hydroxide was stirred at 5–10 °C for 3 h, then maintained at room temperature for 24 h. The precipitate formed after neutralization with dilute hydrochloric acid was collected by filtration and purified by recrystallization from 1:1 mixture of DMF and ethanol.

Melting point: 120–122 °C.

LCMS: $m/z = 603.2$ ($\text{M}^+ + 1$).

IR (KBr): $\nu_{\max}$ (cm^{-1}), 3313 (NH), 2937, 2858 (C-H), 1654 (C=O), 1355 (C-F).

^1H -NMR (400 MHz, $\text{DMSO}-d_6$): δ ppm, 3.79 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 5.55 (s, 2H, OCH_2), 6.89 (d, 1H, CH_α , $J = 16$ Hz), 7.11–7.89 (m, 17H+1H, Ar-H + CH_β), 7.93 (s, 1H, NH).

^{13}C -NMR (100 MHz, $\text{DMSO}-d_6$): δ ppm, 56.06 (OCH_3), 56.57 (OCH_3), 64.67 (OCH_2), 109.61, 111.36, 111.99, 113.63, 115.46 (d), 116.07 (d), 119.43, 120.95, 121.91, 123.05, 123.51, 127.42, 128.13 (d), 129.71, 131.18, 134.84, 136.37 (d), 140.24, 141.51, 143.20, 145.90, 149.62, 149.95 (d), 157.35, 160.8 (d) (C-F), 163.32 (d) (C-F), 196.23 (C=O).

Elemental analysis: Calculated for $\text{C}_{37}\text{H}_{28}\text{F}_2\text{N}_2\text{O}_4$, C, 73.74%; H, 4.68%; N, 4.65%; Found: C, 73.70%; H, 4.69%; N, 4.63%.

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