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Structure of Methyl (1S, 6S) 6-(4-chlorophenyl)-4-(4-methylphenyl) cyclohex-3-en-2-one-1-carboxylate

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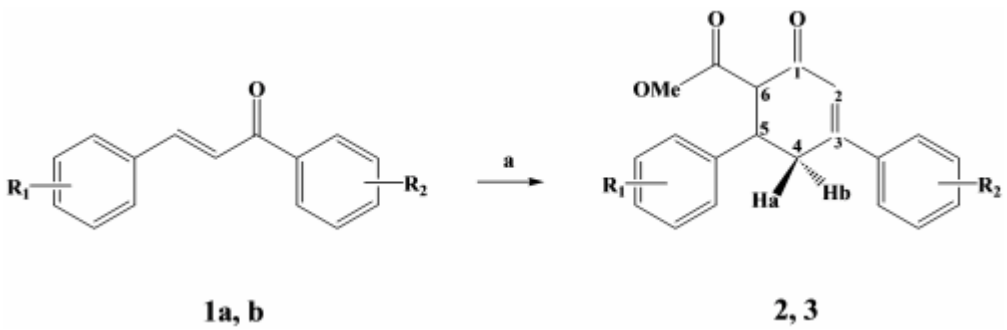
Introduction

The exploration of a simple molecule with different functionalities for the synthesis of heterocycles is a worthwhile contribution in the chemistry of heterocycles. In fact, the 6-carbetoxy-3,5-diarylcyclohexenone has been used as an effective synthon in some projected synthesis of benzoselenadiazoles/thiadiazoles[1], spirocyclohexanones[2], carbazol derivatives[3], fused isoxazoles and pyrazoles[4,5]. The intermediates present in this communication has been chosen by us as a promising starting material to develop pyrazole rings with antimalarial and antibacterial activities[6].

New compounds were synthesised by a base catalysed Claisen-Schmidt condensation of the 4-chloro benzaldehyde with their appropriate acetophenone. These ketones on treatment with methyl acetoacetato in presence of sodium methoxide yield Methyl (1S, 6S) 6-(4-chlorophenyl)-4-(4-methylphenyl) cyclohex-3-en-2-one-1-carboxylate **2** or Methyl (1S, 6S) 4,6-diphenylcyclohex-3-en-2-one-1-carboxylate **3** (see Scheme 1 and http://www.mdpi.org/molbank/molbank2007/m559.htmFig. 1). In the present job we report the formation of **2** by analysis elemental as well IR, ^{1}H NMR, ^{13}C NMR, COSY, and HETCOR spectral and crystallographic studies. The analyses of **3** will be the focus of discussion in a future paper.



1a, b **2, 3**

Scheme 1. Chemical synthesis of Methyl (1S, 6S) 6-(4-chlorophenyl)-4-(4-methylphenyl) cyclohex-3-en-2-one-1-carboxylate **2**.There, **a** represents to $CH_3COCH_2CO_2CH_3$, NaOMe, MeOH, rt. **2** (R_1: 4-Cl; R_2: 4-Me); **3** (R_1= R_2: H).

The IR spectra of **2** showed bands around 1718, 1654 and 1603 cm^{-1} corresponding to carbonyl

a,b-unsaturated, carbonyl ester and C=C bonds, respectively. The ^{1}H NMR spectra of **2** exhibited a doublet and doublet of triplet at 3.06 and 3.07, respectively for H_{4a} and H_{4b}. Proton 4a or 4b is coupling with proton in position 2. The absence of doublet corresponding to a,b-unsaturated of starter material indicates that addition reaction has indeed taken place. ^{13}C NMR confirm the presence of carbonyl of ketone and ester at 194 and 170 ppm. In addition, COSY and HETCOR confirmed the assignments. The X-Ray structure is shown in Figure 1.

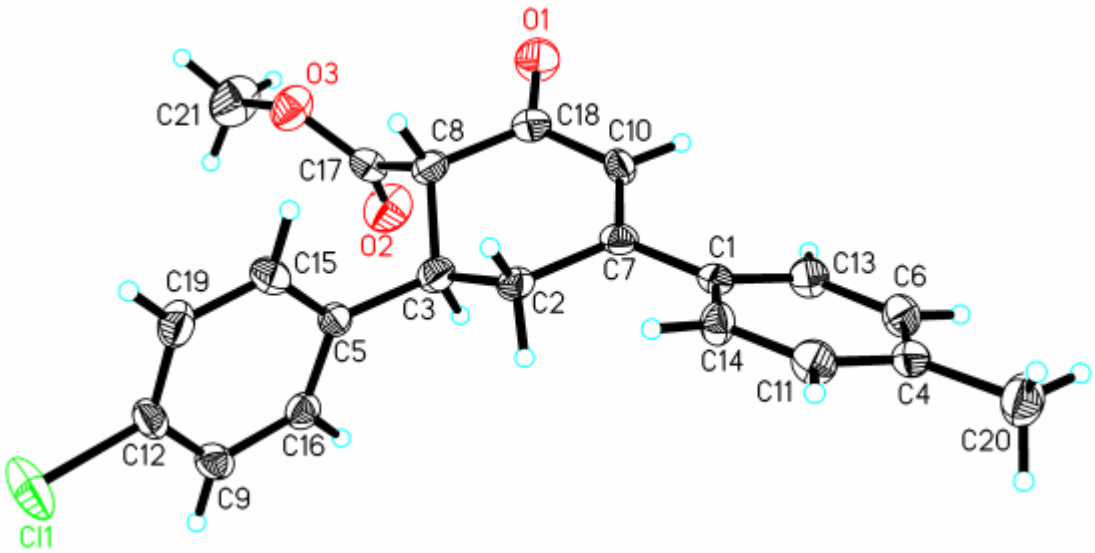


Figure 1. View of the structure of **2** with the atom numbering, showing displacement ellipsoids at the 50% probability level.

Experimental

Melting points were determined on a Thomas micro hot stage apparatus and are uncorrected. Infrared spectra were determined as KBr pellets on a Shimadzu model 470 spectrophotometer. The ^{1}H NMR, ^{13}C NMR, COSY and HETCOR spectra were recorded using a Jeol Eclipse 270 MHz spectrometer. Chemical shifts are expressed relative to residual chloroform. Central Service of Universidad de Málaga, Málaga, España performed elemental analyses, results were within ± 0.4% of predicted values for all compounds. Chemical reagents were obtained from Aldrich Chemical Co., USA. All solvents were distilled and dried with the usual desiccant.

X-ray Crystallographic Data Collection and Structural Determination.

Single-crystal X-ray diffraction measurement of the compound carried out with a Bruker Smart 1000 CCD diffractometer equipped with a graphite crystal monochromator situated in the incident beam for data collection at 298(2) K. The lattice parameters were obtained by least-squares refinement of the diffraction data of 9336 reflections, and data collections were performed with Mo Kαradiation (λ= 0.71073 Å) by ω scan mode in the range of $1.96 < \theta < 25.10°$. All of the measured independent reflections were used in the structural analysis, and semiempirical absorption corrections were applied using the SADABS program. The maximum and minimum transmission factors were 0.980 and 0.961. The program SAINT14 was used for integration of the diffraction profiles.

Table 1. Crystallographic data for compound **2**

Parameter	Compound **2**	Parameter	Compound **2**
formula	C_{21} H_{19} Cl O_3	ρ(calcd), g cm^{-3}	1.308
fw	354.81	*F*(000)	744
lattice	Monoclinic	μ(Mo KR), cm^{-1}	2.28
a, Å	10.949(2)	diffractometer	APEX

b, Å	14.047(3)	radiatn λ, Å	0.71073
c, Å	12.343(2)	temp, ○C	25
β, deg	108.392(4)	R ($I > 2.00\sigma(I)$)*a*	0.1331
V, Å^3	1801.4(6)	*R*w (all data)*b*	0.2143
space group	P2(1)/c	no. of observs	3212 (all data)
Z	4	no. of variables	228

The structure was solved by direct methods using the SHELXS97 program of the SHELXTL package and refined with SHELXL9715. The non-hydrogen atoms were located in successive difference Fourier syntheses. The final refinement was performed by full-matrix least-squares methods with anisotropic thermal parameters for all of the non-hydrogen atoms on *F2*. All of the hydrogen atoms were generated theoretically onto the specific atoms and refined isotropically with fixed thermal factors. A summary of the crystallographic data and structure refinement is listed in Table 1. Selected bond lengths as well as bond angles of **2** are listed in Table 2.

Table 2. Selected bond distances (Å), angles (deg) and torsion angles (deg) for compound **2** at 298 K

Distances	
Cl(1)-C(12)	1.748(6)
O(1)-C(18)	1.217(6)
O(2)-C(17)	1.189(7)
O(3)-C(17)	1.320(7)
O(3)-C(21)	1.454(7)
C(1)-C(7)	1.472(7)
C(2)-C(7)	1.507(7)
C(2)-C(3)	1.508(7)
C(3)-C(5)	1.503(7)
C(3)-C(8)	1.532(7)
C(4)-C(20)	1.509(8)
C(7)-C(10)	1.337(7)
C(8)-C(17)	1.512(8)
C(8)-C(18)	1.520(8)
C(10)-C(18)	1.462(8)
angles	
C(7)-C(2)-C(3)	114.2(4)
C(2)-C(3)-C(8)	111.0(5)
C(10)-C(7)-C(2)	118.9(5)
C(18)-C(8)-C(3)	112.1(5)
C(7)-C(10)-C(18)	124.2(5)
C(10)-C(18)-C(8)	118.0(5)
torsion angles	
C(7)-C(2)-C(3)-C(5)	-179.6(4)
C(7)-C(2)-C(3)-C(8)	-51.3(6)
C(2)-C(3)-C(5)-C(16)	-106.7(6)
C(8)-C(3)-C(5)-C(16)	126.9(5)
C(2)-C(3)-C(5)-C(15)	66.7(7)
C(8)-C(3)-C(5)-C(15)	-59.7(7)
C(14)-C(1)-C(7)-C(10)	151.8(5)
C(13)-C(1)-C(7)-C(10)	-28.9(8)
C(14)-C(1)-C(7)-C(2)	-26.5(7)
C(13)-C(1)-C(7)-C(2)	152.8(5)
C(3)-C(2)-C(7)-C(10)	26.4(7)
C(3)-C(2)-C(7)-C(1)	-155.1(5)
C(5)-C(3)-C(8)-C(17)	-62.5(6)
C(2)-C(3)-C(8)-C(17)	171.2(5)

C(5)-C(3)-C(8)-C(18)	175.1(5)
C(2)-C(3)-C(8)-C(18)	48.8(6)
C(1)-C(7)-C(10)-C(18)	-176.8(5)
C(2)-C(7)-C(10)-C(18)	1.5(8)
C(21)-O(3)-C(17)-O(2)	-1.0(9)
C(21)-O(3)-C(17)-C(8)	178.7(5)
C(18)-C(8)-C(17)-O(2)	62.7(7)
C(3)-C(8)-C(17)-O(2)	-61.4(7)
C(18)-C(8)-C(17)-O(3)	-117.0(5)
C(3)-C(8)-C(17)-O(3)	119.0(5)

General procedure for the synthesis

A mixture of sodium methoxide (catalytic), freshly distilled methyl or methyl acetoacetate (0.01 mol) and chalcone **1a,b** (0.01 mol) in absolute methanol 20 ml was stirred at room temperature over night. The resulting precipitate was collected off by filtration, washed with methanol, and then the crystals were washed with bidistilled water. Crystallisation from methanol solutions yields crystals suitable for single-crystal X-ray diffraction.

Methyl (1S, 6S) 6-(4-chlorophenyl)-4-(4-methylphenyl)cyclohex-3-en-2-one-1-carboxylate

Yield 83%; m.p. 148-150 ^{o}C; IR (cm^{-1}, KBr): 1718 (CO), 1654 (CO), 1603 (C=C). ^{1}H NMR $CDCl_3$: d 2.37 (s, 3H, CH_3), 3.06 (d, 1H, H_{4a}, J:12 Hz), 3.07 (dt, 1H, H_{4b}, J:12, 3.7, 2.0 Hz), 3.59 (s, 3H, OCH_3), 3.75 (m, 2H, $H_{5,6}$), 6.54 (d, 1H, H_2, J:1.9 Hz), 7.21 (m, 4H, Ar), 7.31 (d, 2H, Ar, J:8.4 Hz), 7.43 (d, 2H, Ar, J:8.2 Hz). ^{13}C NMR: 21,01, 35.49, 43.13, 52.02, 59.21, 123.36, 126.36, 128.83, 129.32, 129.91, 133.54, 134.74, 139.92, 141.55, 158.79, 170.12, 194.13. Anal. Calcd. For $C_{21}H_{19}O_3Cl$: C, 71.02; H, 5.39. Found. C, 71.28; H, 5.

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