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Synthesis, Characterization and Crystal Structure of 4,7-Dioxo-7-phenylheptanoic Acid

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4,7-Dioxo-7-phenylheptanoic acid was synthesized from acetophenone and furfural. Firstly, acetophenone reacted with furfural in the presence of sodium hydroxide at room temperature, then the product of the first step was transformed into 4,7-dioxo-7-phenylheptanoic by the process of hydrolyzation by using acetic acid and hydrochloric acid. The product was characterized by ^{1}H NMR and LC-MS. The crystal structure of compound **1** was investigated using X-ray diffraction and SHELXTL-97 software and it was first reported here. The result indicated that compound **1** crystallized in the monoclinic system, space group P2(1)/c with a = 5.3007 (14), b = 28.405 (8), c = 7.679(2) Å, V = 1130.4 (5) Å^3; Z 4.

Keywords: 4,7-Dioxo-7-phenylheptanoic, Synthesis, Characterization, Crystal structure.

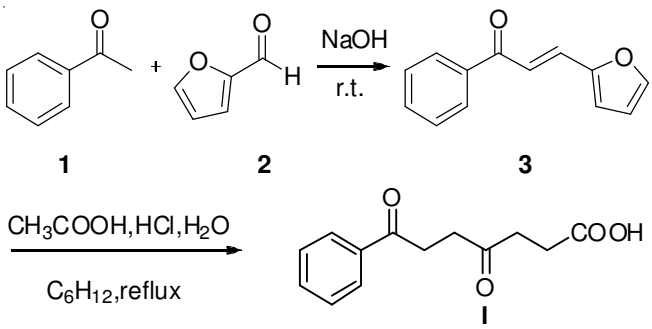
INTRODUCTION

The photochromism is an interesting phenomenon that has been attracted attention for several decades. Various photochromic compounds were synthesized and used in ophthalmic lenses[1], information storage[2] and smart windows[3]. Compared to other photochromic families, the naphthopyran compounds have the advantages of the low initial color, low solvachromism, high color density and large color gamut provided by the ring open form when substituted with various electron donating and withdrawing groups[4,5]. Furthermore, many naphthopyran derivatives have good biological activities and pharmacological activities[6], such as dysplasia resistance[7], tracheitis resisitance[8], antibacterial property and anticancer.

Naphthol derivatives are widely concerned as the most important intermediates to synthesize naphthopyran compounds[9,10]. 4,7-Dioxo-7-phenylheptanoic acid (**1**) can be utilized to synthesize the compound 5-hydroxy-1*H*-cyclopenta[a]-naphthalen-3(2H)-one through a two-step reaction. Herein, we introduce a new synthetic method of compound **1** from acetophenone (**1**) and furfural (**2**) with an overall yield of about 52.9 %. Meanwhile, the crystal structure of **1** was also investigated. The synthetic route of compound I was presented as **Scheme-I**.

EXPERIMENTAL

Furfural was supplied by Well Chemical Co. Ltd of Jiangsu (Yancheng, People's Republic of China), its mass content is



Scheme-I: Route for the synthesis of compound **1**

99 % determined by GC. Acetophenone was purchased from Sinopharm Chemical Reagent Co. Ltd of China. All other chemicals were of reagent grade and used without purification as received.

^{1}H NMR spectrum was obtained with Bruker AV-500 spectrometer at 500.13 MHz and measured in $CDCl_3$ solution at 30 ± 0.5 °C. The sample was dissolved in a 5 mm diameter tube at a concentration of 20 mg/mL. X-ray diffraction was performed on a Bruker APEXII CCD diffractometer. Mass spectrum of **1** was analyzed using Trace DSQ LC/MS (Thermo Electron Co., USA).

Synthesis of compound 1: A 250-mL, round-bottomed flask with a stirring bar and a pressure-equalizing addition funnel was charged with 1 (4 g, 0.0333 mol), 2 (3.36 g, 0.0350 mol) and ethanol (40 mL). Sodium hydroxide (0.667 g, 0.0166 mol) in water (20 mL) was added through the dropping funnel

to the solution. The reaction mixture was stirred magnetically for 4 h at room temperature. After the reaction was completed, the solvents were removed on a rotary evaporator. The resulting dark brown residue was dissolved in ethyl acetate. The organic layer was washed with 5 % sodium hydrogen sulfite solution (3 × 40 mL) and saturated sodium chloride solution (3 × 40 mL) and dried over anhydrous sodium sulfate. Filtration and removal of the solvent gave the product as a dark brown viscous liquid. The crude product was subjected to silica gel column chromatography, using a gradient elution with petroleum ether-ethyl acetate to obtain **3** (6.27 g, 0.0316 mol).

Compound **3** (6.27 g, 0.0316 mol) was dissolved in cyclohexane (75 mL) and was added to a mixture of acetic acid (30 mL), hydrochloric acid (22 mL), ethanol (22 mL) and water (30 mL). The reaction mixture was heated on an oil bath under reflux, while stirring mechanically for 24 h. After the reaction was completed, the solvent and acids were removed under reduced pressure. The resultant dark brown product was treated with saturated aqueous sodium hydrogen carbonate until there was no further evolution of carbon dioxide and then extracted with diethyl ether to remove the unreacted compound **3**. The aqueous layer was acidified with 20 % sulphuric acid and extracted into ethyl acetate. The ethyl acetate extract was dried over anhydrous sodium sulphate and concentrated under reduced pressure. By that means, 4.13 g (52.9 %, m.p. 117-118 °C) of the compound (**1**) can be obtained in the form of a brown grainy crystal.

Crystals of **1** that suitable for X-ray diffraction were obtained by slow evaporation of dichloromethane solution of **1**.

X-ray crystallography: A colorless block-like crystal of compound **1** grown in dichloromethane with dimensions of 1.00 mm × 0.50 mm × 0.15 mm was used for structural determination. Diffraction data were collected on a Bruker APEXII CCD diffractometer by using graphite monochromated MoK_α radiation (λ = 0.71073 Å). The structure was solved by direct methods with SHELXS-97 and refined on the F^2 by full-matrix least-squares method with SHELXL-97. All non-hydrogen atoms were refined anisotropically.

RESULTS AND DISCUSSION

In the ^{1}H NMR of compound **1**, the peak at 3.30-3.32 ppm was ascribed to the proton of methylene which was substituted by benzoyl group. The other data was described as below, ^{1}H NMR ($CDCl_3$): δ 2.68-2.70 (2H, t), 2.86-2.91 (4H, m), 3.30-3.32 (2H, t), 7.44-7.49 (2H, m), 7.54-7.57 (1H, m), 7.96-7.99 (2H, m).

In the LC spectrum peak at 2.626 minute ascribed to the compound **1**. In the MS spectrum, the existence of the peaks at right end showed the compound **1**, *m/z* 234.90 was ascribed to molecular ion peak (M^+), *m/z* 256.85 was ascribed to M + Na peak.

The crystal configuration of compound **1** was confirmed by X-ray structural analysis. Experimental details for X-ray data collection were presented in Table-1 and the geometric parameters for compound **1** were listed in Table-2. Molecular structure and packing plot of compound **1** were showed in Figs. 1 and 2, respectively.

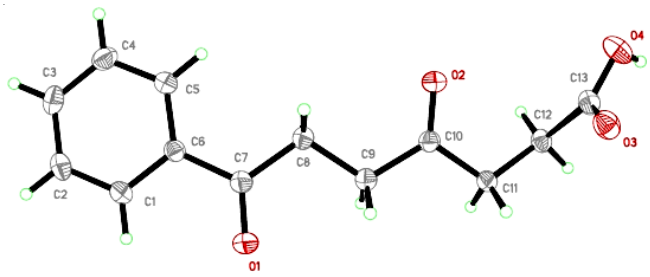


Fig. 1. General appearance of compound **1** with the atoms represented by thermal vibration ellipsoids of 50 % probability

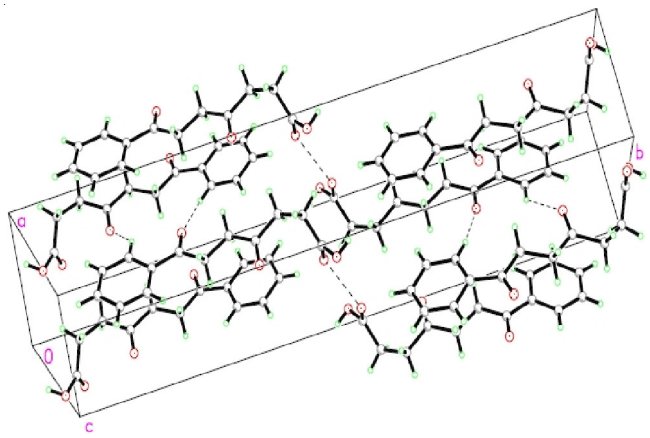


Fig. 2. Packing diagram for compound **1**

TABLE-1
CRYSTALLOGRAPHIC DATA FOR COMPOUND **1**

Properties	Data
Molecular formula	$C_{13}H_{14}O_4$
Molecular weight	234.24
Temperature (K)	293 (2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	P2(1)/c
a (Å)	5.3007 (14)
b (Å)	28.405 (8)
c (Å)	7.679 (2)
Volume (Å^3)	1130.4 (5)
Z	4
Calculated density (g/cm^3)	1.376
Absorption coefficient (mm^{-1})	0.10
F (000)	496.0
Crystal size (mm)	1.00 × 0.50 × 0.15
Theta range for data collection (°)	1.4 to 26.0
Reflections collected/unique	2226/1971 [R(int) = 0.044]
Completeness to theta = 25.38 (%)	99.7
Max. and min. transmission	0.905 and 0.985
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	2226/15/155
Goodness-of-fit on F^2	1.081
Final R indices [I>2σ (I)]	R1 = 0.0564, wR2 = 0.1269
R indices (all data)	R1 = 0.0486, wR2 = 0.1228
Largest diff. peak and hole (e. Å^{-3})	0.29 and -0.48

According to the data from X-ray crystallographic analysis, compound **1** crystallized in a P2(1)/c space group of the triclinic system. All H atoms were positioned geometrically and constrained to ride on their parent atoms, with C-H = 0.93 Å for aromatic H. Other H atoms were positioned geometrically and refined using a riding model, with C-H = 0.96 Å for alkyl H, with Uiso(H) =1.2 Ueq(C) for aromatic H and Uiso(H)

TABLE-2
GEOMETRIC PARAMETERS FOR COMPOUND **1**

Bond	Dist. (Å)	Bond	Dist. (Å)
C1—C2	1.382(3)	C8—H8B	0.9700
C1—C6	1.390(3)	C9—C10	1.498(2)
C1—H1	0.9300	C9—H9A	0.9700
C2—C3	1.371(3)	C9—H9B	0.9700
C2—H2	0.9300	C10—O2	1.205(2)
C3—C4	1.373(3)	C10—C11	1.504(2)
C3—H3	0.9300	C11—C12	1.514(2)
C4—C5	1.384(3)	C11—H11A	0.9700
C4—H4	0.9300	C11—H11B	0.9700
C5—C6	1.383(3)	C12—C13	1.490(2)
C5—H5	0.9300	C12—H12A	0.9700
C6—C7	1.492(3)	C12—H12B	0.9700
C7—O1	1.207(2)	C13—O3	1.255(2)
C7—C8	1.507(2)	C13—O4	1.260(2)
C8—C9	1.513(2)	O4—H4A	0.8501
C8—H8A	0.9700	–	–
Angle	**Data (°)**	**Angle**	**Data (°)**
C2—C1—C6	120.22(18)	H8A—C8—H8B	108.0
C2—C1—H1	119.9	C10—C9—C8	115.67(15)
C6—C1—H1	119.9	C10—C9—H9A	108.4
C3—C2—C1	120.17(18)	C8—C9—H9A	108.4
C3—C2—H2	119.9	C10—C9—H9B	108.4
C1—C2—H2	119.9	C8—C9—H9B	108.4
C2—C3—C4	119.96(19)	H9A—C9—H9B	107.4
C2—C3—H3	120.0	O2—C10—C9	123.54(16)
C4—C3—H3	120.0	O2—C10—C11	121.31(16)
C3—C4—C5	120.54(19)	C9—C10—C11	115.14(15)
C3—C4—H4	119.7	C10—C11—C12	113.52(15)
C5—C4—H4	119.7	C10—C11—H11A	108.9
C6—C5—C4	119.88(18)	C12—C11—H11A	108.9
C6—C5—H5	120.1	C10—C11—H11B	108.9
C4—C5—H5	120.1	C12—C11—H11B	108.9
C5—C6—C1	119.22(17)	H11A—C11—H11B	107.7
C5—C6—C7	122.82(16)	C13—C12—C11	115.92(15)
C1—C6—C7	117.96(16)	C13—C12—H12A	108.3
O1—C7—C6	119.68(17)	C11—C12—H12A	108.3
O1—C7—C8	120.57(17)	C13—C12—H12B	108.3
C6—C7—C8	119.76(15)	C11—C12—H12B	108.3
C7—C8—C9	111.20(15)	H12A—C12—H12B	107.4
C7—C8—H8A	109.4	O3—C13—O4	120.48(17)
C9—C8—H8A	109.4	O3—C13—C12	119.13(17)
C7—C8—H8B	109.4	O4—C13—C12	120.33(17)
C9—C8—H8B	109.4	C13—O4—H4A	109.1
C6—C1—C2—C3	-0.1(3)	C1—C6—C7—C8	173.66(17)
C1—C2—C3—C4	-0.6(3)	O1—C7—C8—C9	10.4 (3)
C2—C3—C4—C5	0.7(3)	C6—C7—C8—C9	-169.45(16)
C3—C4—C5—C6	-0.1(3)	C7—C8—C9—C10	179.36(15)
C4—C5—C6—C1	-0.7(3)	C8—C9—C10—O2	8.6 (3)
C4—C5—C6—C7	178.25(18)	C8—C9—C10—C11	-172.37(16)
C2—C1—C6—C5	0.8(3)	O2—C10—C11—C12	-13.0 (2)
C2—C1—C6—C7	-178.20(17)	C9—C10—C11—C12	167.92(15)
C5—C6—C7—O1	174.9(2)	C10—C11—C12—C13	71.2 (2)
C1—C6—C7—O1	-6.2(3)	C11—C12—C13—O3	29.3 (3)
C5—C6—C7—C8	-5.3(3)	C11—C12—C13—O4	-153.45(18)

Symmetry code: (i) *x*, *y* ,z (ii)-x, 1/2 + y, 1/2-z.

TABLE-3
HYDROGEN-BOND GEOMETRY FOR COMPOUND **1**

D–H···A	D–H	H···A	D···A	D–H···A
O4–H4A···O4	0.85 Å	2.31 Å	2.647 (2) Å	104?
C1–H1···O2	0.93Å	2.56Å	3.289 (3) Å	136?
C5–H5···O1	0.93Å	2.46Å	3.324 (3) Å	155?
C12–H12A···O4	0.97Å	2.58Å	3.394 (3) Å	140?

= 1.5 Ueq(C) for other H. There are no intramolecular hydrogen bonds in the structure. There are 4 intermolecular hydrogen bonds in the structure and the hydrogen-bond geometry for compound **1** was listed in Table-3. Unit cell parameters: a = 5.3007 (14), b = 28.405 (8), c = 7.679 (2) Å, V = 1130.4 (5) $Å^3$; Z = 4.

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