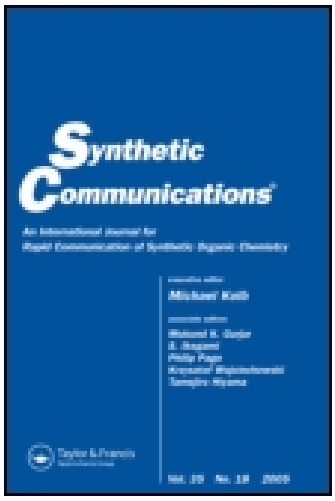

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SYNTHETIC COMMUNICATIONS, 31(24), 3729–3733 (2001)

A CONVENIENT SYNTHESIS OF 4-ARYL-7,7-DIMETHYL-5-OXO-3,4,5,6,7,8-HEXAHYDROCOUMARIN UNDER MICROWAVE IRRADIATION WITHOUT CATALYST

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ABSTRACT

A series of hexahydrocoumarins **4** were synthesized by the reaction of aromatic aldehyde, 5,5-dimethyl-1,3-cyclohexandione and meldiums acid under microwave irradiation without catalyst. The structure of **4a** was determined by x-ray analysis.

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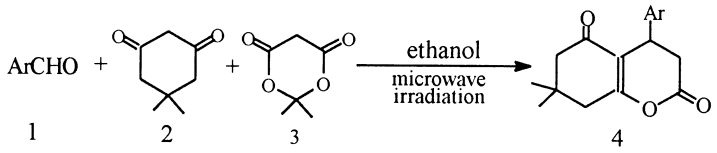
Organic synthesis under microwave irradiation is a topic that is drawing much recent research interest.[1] In our laboratory, we have been continually working on developing new synthetic methods for the synthesis of polyhydrocoumarins by taking advantage of microwave irradiation. Coumarin is one of the most important aroma chemicals having unique characteristics.[2] It is widely used in hand soaps, detergents, lotions, and perfumes. Coumarin has significant use in the electroplating industry, mostly in the automotive area, to provide high polished quality to chromeplated steel. Coumarin and some of its derivatives have been tested in pharmacology for treatment of schizophrenia,[3] or of microcirculation disorders and angiopathic ulcer[4] etc. The synthesis of coumarins usually involves the method of Rasching[2] discovered in 1909, i.e., starting with *o*-cresol, or the Von Pechmann method,[2] i.e., reaction of phenol with malic, maleic, or fumaric acids in the presence of concentrated sulfuric acid, or from salicylaldehyde by Perkin reaction, Knoevenagel reaction[2] etc. Recently, Bogdal[5] reported that the salicylaldehyde or its derivative react with various derivative of ethyl acetoacetate in the presence of piperidine to give coumarins by a solvent free reaction under microwave irradiation. Zhang et al.[6] reported the synthesis of coumarin under triphase catalysis of polystyrene-supported poly-ethylene glycol. In our previous paper,[7] we reported that aromatic aldehydes (1), dimedone (2) and meldrums acid (3) when treated with KF-alumina in alcohols at refluxing temperature, produce 3-aryl-3-(5,5-dimethyl-3-hydroxy-2-cyclohexene-1-one-2-yl) propanic esters. However, when aromatic aldehydes (1), dimedone (2) and meldrums acid (3) were treated with ethanol under microwave irradiation without catalyst, the product was hexahydrocoumarin (**4**) (scheme).

All the compounds obtained gave elemental analysis for C, H, N in good agreement to calculated values. The structures were established on the basis of spectroscopic data and confirmed by X-ray diffraction studies for **4a**.[8]

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX instrument.



Scheme.

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Table 1. The Synthesis of Compound **4**

Entry	Ar	Time (min)	Yield (%)
4a	*p*-$(CH_3)_2NC_6H_4$	4	66
4b	*p*-ClC_6H_4	3	82
4c	*p*-$CH_3OC_6H_4$	5	68
4d	3,4-$(OCH_2O)C_6H_3$	5	85
4e	4-HO-3-$CH_3OC_6H_3$	4	75

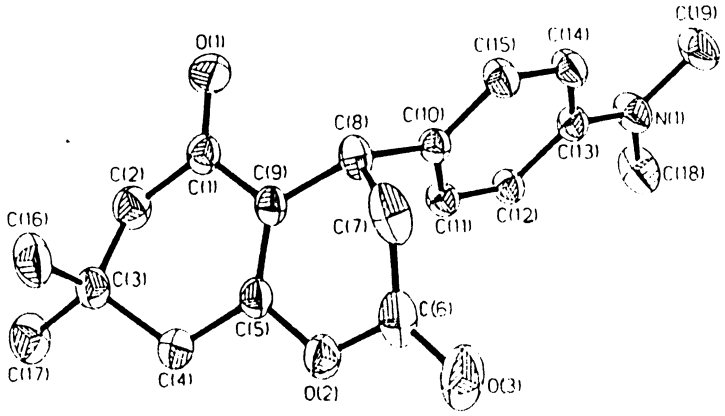

Figure 1. X-ray crystal structure of **4a**.

^{1}H-NMR were measured on a Bruker 300 MHz spectrometer in $CDCl_3$ with TMS as internal standard. Elemental analyzer were determined using Perkin-Elmer 240C elemental analyzer. X-ray diffraction were measured on a Nonius Kapph CCD diffractometer. The reactions were carried out with a modified commercial microwave oven (Sanle WP650D 650w) under atmospheric pressure.

GENERAL PROCEDURE

A mixture of aromatic aldehydes **1** (5 mmol), dimetone **2** (0.70 g, 5 mmol), meldrums acid **3** (0.72 g, 5 mmol) and 5 mL of ethanol was transferred into a dry flask connected with refluxing equipment. After microwave irradiation for 3–5 min, the reaction mixture was cooled with ice–water. The precipitated product was filtered and washed with ethanol.

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The crude product was collected by filtration and recrystallised from ethanol to give compound **4a–e**.

4a: M.p. 136–138°C; IR (KBr, ν, cm^{-1}): 1791, 1703. ^1H NMR ($CDCl_3$): δ: 0.91 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 2.10 (s, 2H, CH_2), 2.38 (s, 2H, $COCH_2$), 2.64 (m, 2H, $OCOCH_2$), 2.91 (s, 6H, $2NCH_3$), 4.06–4.34 (m, 1H, CH), 6.50–7.15 (m, 4H, ArH) ppm. Anal. Calcd. (%) for $C_{19}H_{23}NO_3$: C, 72.81; H, 7.33; N, 4.46. Found: C, 72.90; H, 7.28; N, 4.31.

4b: M.p. 156–158°C; IR (KBr, ν, cm^{-1}): 1773, 1658. ^1H NMR ($CDCl_3$): δ: 0.88 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 2.10 (s, 2H, CH_2), 2.31 (s, 2H, $COCH_2$), 2.65–2.72 (m, 2H, $OCOCH_2$), 4.05 (m, 1H, CH), 6.86–7.03 (m, 4H, ArH) ppm. Anal. Calcd. (%) for $C_{17}H_{17}ClO_3$: C, 66.99; H, 5.62. Found: C, 66.89; H, 5.53.

4c: M.p. 128–130°C; IR (KBr, ν, cm^{-1}): 1771, 1650. ^1H NMR ($CDCl_3$): δ: 1.11 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 2.32 (s, 2H, CH_2), 2.53 (s, 2H, $COCH_2$), 2.90–2.92 (m, 2H, $OCOCH_2$), 3.77 (s, 3H, OCH_3), 4.25–4.27 (m, 1H, CH), 6.68–7.06 (m, 4H, ArH) ppm. Anal. Calcd. (%) for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.04; H, 6.67.

4d: M.p. 130–132°C; IR (KBr, ν, cm^{-1}): 1780, 1650. ^1H NMR ($CDCl_3$): δ: 1.13 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.33 (s, 2H, CH_2), 2.54 (s, 2H, $COCH_2$), 2.90–2.91 (m, 2H, $OCOCH_2$), 4.21–4.24 (m, 1H, CH), 5.93 (s, 2H, OCH_2O), 6.11–6.64 (m, 3H, ArH) ppm. Anal. Calcd. (%) for $C_{18}H_{18}O_5$: C, 68.77; H, 5.77. Found: C, 68.83; H, 5.61.

4e: M.p. 158–160°C; IR (KBr, ν, cm^{-1}): 1789, 1630. ^1H NMR ($CDCl_3$): δ: 1.11 (s, 3H, CH_3), 1.16 (s, 3H, CH_3), 2.33 (s, 2H, CH_2), 2.53 (s, 2H, $COCH_2$), 2.91–2.93 (m, 2H, $OCOCH_2$), 3.85 (s, 3H, OCH_3), 4.22–4.25 (m, 1H, CH), 6.60–6.82 (m, 3H, ArH), 10.91 (s, 1H, OH) ppm. Anal. Calcd. (%) for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.26; H, 6.45.

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8. X-ray analysis of **4a:** Empirical formula $C_{23}H_{30}NO_4$, F.W. 384.48, $T = 293(2)$ K, monoclinic, space group $P2_1$, $a = 9.3639(19)$ Å, $b = 5.9740(12)$ Å, $c = 15.731(3)$ Å, $\alpha = 90^\circ$, $\beta = 102.87(3)^\circ$, $\gamma = 90^\circ$, $V = 857.9(3)$ Å^3, $Z = 2$, $Dc = 1.488$ Mg/cm^3, $\lambda(M_0K_\alpha) = 0.71073$ Å, $\mu = 0.101$ mm^{-1}, $F(000) = 414$. $3.83 < \sigma < 27.87$, $R = 0.0805$, $R_w =$ 02441. Largest diff. Peak and hole: 0.469 and -0.235 e Å^{-3}.

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