SHORT PAPER

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Microwave-induced *in situ* Wittig reaction of salicylaldehydes with ethyl chloroacetate and triphenylphosphine in solventless system†

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A variety of coumarins was prepared by an *in situ* Wittig reaction of salicylaldehydes, triphenylphosphine and ethyl chloroacetate using sodium methoxide/molecular sieves (3Å) under solvent-free conditions.

Keywords: coumarin, Wittig reaction, solventless system

Coumarins are very well known natural products and many such compounds exhibit high level of biological activity.[1] Coumarins are common in nature and used as intermediates in the synthesis of pharmaceuticals,[2] insecticides,[3] fluorescent brighteners[4] and anticoagulant agents.[5]

Coumarins can be synthesised by one of several methods such as the Claisen rearrangement, Perkin reaction, Knoevenagel condensation and Wittig reaction.[6] These methods have their own merits and drawbacks. Therefore introduction of new methods based on green methodology is still desirable.

Takashi *et al*. have reported the synthesis of coumarins via the Wittig reaction of salicylaldehydes and carbethoxymethylenetriphenylphosphorane in *N,N*-diethylaniline under reflux conditions.[7] It is well documented in the literature that Wittig reactions of the stable ylids with aldehydes are much slower, especially in non polar solvents.[8]

Microwave-enhanced chemical reactions in solventless systems have gained popularity[9] as they can be conducted efficiently and rapidly to afford pure products in quantitative yields.

In this communication we wish to report the synthesis of simple coumarins via a one-pot Wittig reaction of salicylaldehydes, ethyl chloroacetate and triphenylphosphine using NaOMe/molecular sieves (3 Å) under microwave irradiation under solvent-free conditions.

In view of the current emphasis on solid state synthesis[10] and on green chemistry[11] there is a merit in developing a solventless preparation of coumarins using an inexpensive and non-polluting catalyst. We recently used molecular sieves (3 Å) as a promoting agent in the synthesis of 4-substituted coumarins[12] and in continuation of our interest in organic synthesis in solventless systems under microwave irradiation,[13] we now report an alternative method for the preparation of simple coumarins **2** using NaOMe supported onto molecular sieves (3 Å) under microwave irradiation (Scheme 1).

In this reaction, in addition to coumarins, *trans*-cinnamates **3** were also isolated as minor products and no Darzens products were isolated. The presence of electron-donating groups at C_4 on salicylaldehydes **1** such as methoxyl and hydroxyl accelerated the formation of the coumarin and no *trans*-cinnamate products were detected in these cases.

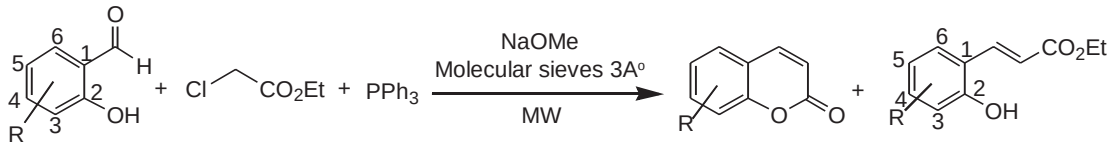
The reaction is conducted by exposure of a mixture of the salicylaldehyde, ethyl chloroacetate, triphenylphosphine, NaOMe and molecular sieves (3 Å) to microwave irradiation. Most of salicylaldehyde disappeared within first 3 minutes, determined by TLC. Other types of solid supports were also utilised with this procedure but molecular sieves (3 Å) were found to give the best yields.

In conclusion, we have developed an alternative chemoselective procedure for the fast and microwave-assisted preparation of coumarins. Our method features mild reaction conditions, good yields and a facile work up procedure. We believe this method should find utility in organic synthesis.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were recorded on a Bruker 843 instrument and ^{1}H NMR spectra on a Bruker (60 MHz) spectrometer. Column chromatography was carried out on silica gel (Merck, No 10180). The products were identified by comparison of their spectral (^{1}H NMR, IR) data with those of either commerical or synthetic authentic samples or by comparison with physical data in the cited references (Table 1).

General procedure: The salicylaldehyde derivative (14.5 mmol), ethyl chloroacetate (1.83g, 15 mmol), triphenylphosphine (3.8g, 14.5 mmol), NaOMe(0.88g, 14.5 mmol) and molecular sieves (3 Å) (2.5g) (as powder) were mixed thoroughly using a spatula in a beaker. The beaker was placed in an household microwave oven and the progress of reaction was monitored by TLC. The intimate mixture was then taken up in aqueous and extracted with ether. The ether was evaporated and the residue was directly subjected to column



1 **2** **3**

Scheme 1

3a R=H
3c R=5-No_2
3d R=5-Br
3e R=3-NO_2

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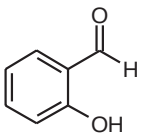
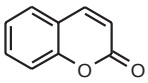
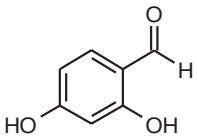
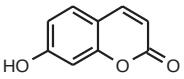
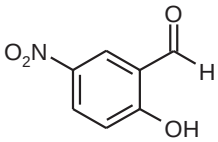
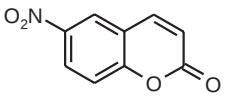
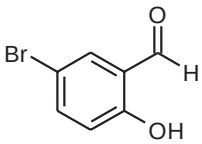
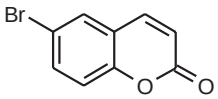
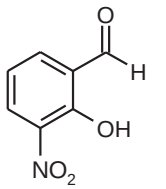
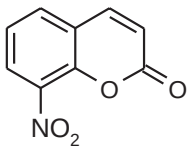
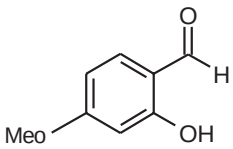
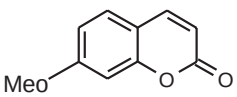
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Preparation of simple coumarins under microwave irradiation in a solventless system

Entry	Substrate	Product (**2**)	Product(s) M.p/°C **2** Found(Reported)[ref]	**3** Found(Reported)[ref]	Ratio **2** to **3**	Yield
a			67–8(68–70)[14]	86–7(87)[15]	75:25	85
b			230–2(234–5)[16]	_	100:0	88
c			178–9(181–2)	168–170(170–172)[18]	70:30	92
d			161–3(161–3)[19]	118–20	73:27	89
e			187–9(190–1)[7b]	81–83(82–3)[7b]	75:25	90
f			115–7(118–9)[20]	_	100:0	89

Reported yields are sum of the yields of compounds **2** and **3**.
Structure of compound **3d** was supported by elemental analysis and mass spectrometry (see text).

Caution : Although we did not have any problem with this procedure in a microwave oven, it is recommended that the reaction is conducted with care in an efficient fume hood.

chromatography using hexane and ethylacetate (7:1) as solvent to obtain the products.

Typical ^1H NMR data of products (δ relative to TMS): *Compounds* **2a**: ($CDCl_3$):6.48(d, *J* = 9.5, C_3-H), 7.3–7.65(m, 4H, aromatic protons), 7.8(d, *J* = 9.5, C_4-H); IR, ν (KBr disc): 1710, 1610, 1450, 1400 cm^{-1}. **2b**: (acetone d_6): 6.25(d, *J* = 9.45, C_3-H), 6.9–7.8(m, 3H, aromatic protons), 7.9(d, *J* = 9.45, C_4-H), 9.4(s, OH); IR, ν (KBr disc): 3220(OH broad), 1720, 1680, 1620cm^{-1}. **2c**: (acetone d_6): 6.3(d, *J* = 9.4, C_3-H), 7–7.7(m, 3H, aromatic protons), 7.85(d, *J* = 9.4, C_4-H), IR, ν (KBr disc): 1715, 1620, 1550, 1360 cm^{-1} . **2d**: (acetone d_6): 6.35(d, *J* = 9.5, C_3-H), 7.1–7.75(m, 3H, aromatic protons), 7.8 (d, *J* = 9.5, C_4-H), IR, ν (KBr disc): 1720, 1620 cm^{-1}. **2e**: (acetone d_6): 6.3(d, *J* = 9.45, C_3-H), 7.2–7.75(m, 3H, aromatic protons), 7.85(d, *J* = 9.45, C_4-H), IR, ν (KBr disc): 1720, 1630, 1555, 1360 cm^{-1}. **2f**: ($CDCl_3$): 4.25 (s, 3H, OMe), 6.4(d, *J* = 9.4, C_3-H), 7.1–7.8(m, 3H, aromatic protons), 7.9(d, *J* = 9.4, C_4-H), IR, ν (KBr disc): 1715, 1620 cm^{-1}. **3a**: ($CDCl_3$): 1.34(t, *J* = 7, $-CO_2CH_2C\underline{H}_3$), 4.25(q, *J* = 7, $-CO_2C\underline{H}_2CH_3$), 6.6(d, *J* = 16.4, $-CH=C\underline{H}-CO_2Et$), 7–8.1 (m, 5H, $-C\underline{H}=CHCO_2Et$ and aromatic protons), OH is unobserved; IR, ν (KBr disc): 3350 (OH broad), 1720, 1615 cm^{-1}. **3c**: (acetone d_6): 1.35(t, *J* = 7, $-CO_2CH_2C\underline{H}_3$), 4.25(q, *J* = 7, $-CO_2C\underline{H}_2CH_3$), 6.6 (d, *J* = 16.35, $-CH=C\underline{H}CO_2Et$), 7–8.2 (m, 4H, $-C\underline{H}=CHCO_2Et$ and aromatic protons), OH is unobserved; IR, ν (KBr disc): 3345 (OH broad), 1720, 1615, 1540, 1330 cm^{-1} . **3d**: (acetone d_6):1.34(t, *J* = 7, $-CO_2CH_2\ C\underline{H}_3$), 4.25(q, *J* = 7, $-CO_2C\underline{H}_2CH_3$), 6.7(d, *J* = 16.2, $-CH=C\underline{H}\ CO_2Et$), 7.2–8.3 (m, 4H, $-C\underline{H}=CH\ CO_2Et$ and aromatic protons), OH is unobserved; IR, ν (KBr disc): 3360 (OH broad), 1720,1615 cm^{-1}. EIMS (70ev) *m/z*: (M^+ 271), Anal.Calcd. for $C_{11}H_{11}BrO_3$: C, 48.7%; H, 4.06%; found C, 48.82%; H, 4.07%. 3e: (acetone d_6):1.34(t, *J* = 7, $-CO_2CH_2C\underline{H}_3$), 4.25(q, *J* = 7, $-CO_2-C\underline{H}_2CH_3$), 6.5 (d, *J* = 16.4, $-CH=C\underline{H}CO_2Et$), 7.1-8.2 (m,4H,$-C\underline{H}=CHCO_2Et$ and aromatic protons), OH is unobserved; IR, ν (KBr disc):3350 (OH broad), 1720,1615, 1540, 1335cm^{-1}.

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