

# Microwave-assisted solventless Pechmann condensation<sup>†‡</sup>

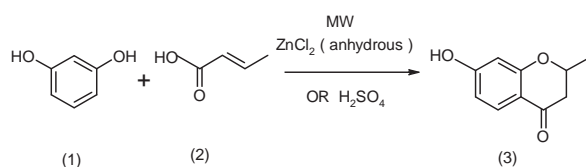
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Solventless Pechmann condensation of various phenols with crotonic acid, malic acid, fumaric acid or maleic acid, using sulfuric acid or anhydrous zinc chloride under microwave irradiation yielded coumarins and chromanones.

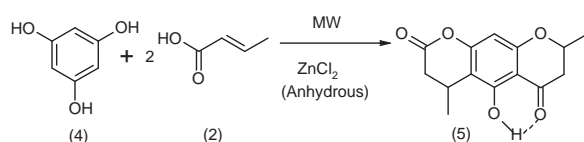
**Key words:** Pechmann condensation, phenols

Coumarins and chromanones are important natural products exhibiting biological activity.<sup>1,2</sup> Microwave (MW) heating has attracted considerable attention recently as it provides the means to achieve organic reactions in a short time and with greater efficiency.<sup>3a-i</sup> We report here a number of interesting Pechmann condensation reactions of various phenols with crotonic acid, malic acid, fumaric acid and maleic acid using sulfuric acid and anhydrous zinc chloride under MW irradiation. Condensation of resorcinol under MW irradiation with crotonic acid using anhydrous zinc chloride or sulfuric acid yielded 7-hydroxy-2-methylchroman-4-one (**3**) in 72 and 76% yield respectively (Scheme-1). The earlier work under thermal conditions reports the synthesis of this compound using polyphosphoric acid (PPA) in 23% yield.<sup>4</sup>



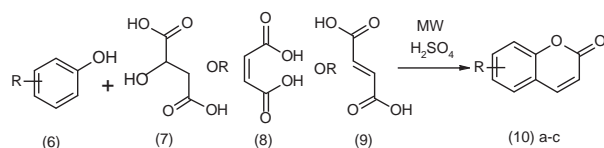
**Scheme 1**

Condensation of phloroglucinol with crotonic acid using anhydrous zinc chloride under MW irradiation gave linear pyranodihydrocoumarin (**5**, Scheme 2) in 80% yield, the structure of which has been established by spectroscopic methods.



**Scheme 2**

The Pechmann condensation of various phenols and malic acid, maleic acid or fumaric acid using sulfuric acid under MW irradiation yielded coumarins in good yield (Scheme 3, Table 1). The method reported here is much superior to conventional heating.



**Scheme 3**

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

<sup>‡</sup> Dedicated to the memory of the late Dr Nitiraj R. Mane.

**Table 1**

Substrate	Acid used	Product (10a-c)	MW irradiation Sec X Pulse = Min	Yield %	m.p. <sup>o</sup> (lit.)/ <sup>o</sup> C
Phenol	7	<b>10a</b> ; R = H	60 × 4 = 4 Min.	15	70(70) <sup>6</sup>
Phenol	8	<b>10a</b> ; R = H	40 × 6 = 4 Min.	18	68(70) <sup>6</sup>
Resorcinol	7	<b>10b</b> ; R = 7-OH	60 × 4 = 4 Min.	57	228(228) <sup>7</sup>
<i>p</i> -Cresol	8	<b>10c</b> ; R = 6-CH <sub>3</sub>	30 × 4 = 4 Min.	67	75(75) <sup>8</sup>
<i>p</i> -Cresol	9	<b>10c</b> ; R = 6-CH <sub>3</sub>	30 × 10 = 5 Min.	82	75(75) <sup>8</sup>

## Experimental

Reactions were carried out in a microwave oven model BPL-Sanyo-BMO-700T. NMR spectra were recorded on a Bruker AC 300 FNMR Spectrometer and chemical shifts are in  $\delta$  units. The IR spectra were recorded on a Perkin Elmer FI-spectrometer and peak positions are in wavenumbers (cm<sup>-1</sup>). Melting points are uncorrected.

**7-Hydroxy-2-methylchroman-4-one (3):** A mixture of crotonic acid (0.01mol, 0.860g), resorcinol (0.01mol, 1.1g) and anhydrous zinc chloride (2.5g) or conc. sulfuric acid (0.5ml) was stirred well with a Teflon coated magnetic needle using a magnetic stirrer in a 100 ml R.B. flask and exposed to MW irradiation for 60 seconds at 30HI power. The MW irradiation was stopped and the reaction mixture was stirred well and cooled. The application of MW irradiation pulses and cooling was repeated (five times for zinc chloride and four for sulfuric acid).

The reaction mixture was diluted with water and the product was extracted with ether. The ether layer was washed with water and sodium bicarbonate and dried over anhydrous sodium sulfate. Removal of ether gave the crude product, which was purified by recrystallisation. m.p. 182<sup>o</sup>C (lit.<sup>6</sup> 177<sup>o</sup>C) IR: 3100(broad), 1650, 1580, 1493cm<sup>-1</sup>, PMR (CDCl<sub>3</sub>): 1.49 (3H, *d*, *J* = 7 Hz, methyl group), 2.60 (2H, *m*, methylene-H), 4.57 (1H, *m*, methine-H), 6.40 (1H, *d*, *J* = 2 Hz, Ar-H), 6.51 (1H, *dd*, *J* = 8 and 2Hz, Ar-H), 7.81 (1H, *d*, *J* = 8 Hz, Ar-H *ortho* to keto group).

**Pyranodihydrocoumarin (5):** A mixture of crotonic acid (0.02mol, 1.720g), phloroglucinol (0.01mol, 1.260g) and anhydrous zinc chloride (2.5g) was stirred well with a Teflon coated magnetic needle using a magnetic stirrer and exposed to MW irradiation for 60 seconds at 30HI power. The MW irradiation was stopped and the reaction mixture was stirred and cooled. The application of MW irradiation pulses and cooling was repeated 4 times. Work-up as above furnished the product, yield 2.10 g [M.P. 195<sup>o</sup> C (lit.<sup>5</sup> 195–196<sup>o</sup> C)].

IR: 1768, 1637 (H-bonded C=O), 1589 cm<sup>-1</sup>, PMR (CDCl<sub>3</sub> + d<sub>6</sub>-DMSO): 1.23 (3H, *d*, *J* = 7 Hz, CH<sub>3</sub> of coumarin ring), 1.52 (3H, *d*, *J* = 7 Hz, CH<sub>3</sub> of chromanone ring), 2.71 (4H, *m*, methylene-H), 3.48 (1H, *m*, benzylic methine-H), 4.56 (1H, *m*, methine-H of chromanone ring), 6.15 (1H, *s*, Ar-H), 12.27 (1H, *s*, chelated phenolic-OH). Carbon-13 NMR (CDCl<sub>3</sub> + d<sub>6</sub>-DMSO): (14 signals) 19.00 and 19.99 (methyl groups), 22.89 (benzylic methine carbon), and 35.28 and 42.67 (methylene signals of coumarin and chromanone unit respectively), 73.47 (methine carbon of chromanone unit deshielded due to oxygen), 95.42 (shielded aromatic carbon bearing hydrogen), 104.09 and 107.10 (quaternary aromatic carbons not attached to oxygen), 157.32, 159.00 and 160.70 (quaternary aromatic carbons attached to oxygen), 166.10 (lactone carbonyl), and 196.72 (conjugated keto carbonyl). DEPT (Carbon-13 N.M.R) (CDCl<sub>3</sub> + d<sub>6</sub>-DMSO) 19.00 and 19.99 (methyl groups) 22.86 (methine carbon), 35.25 and 42.64 (methylene carbons), 73.44 and 95.42 (methine carbons).

*Synthesis of coumarins from substituted Phenols and malic acid, maleic or fumaric acid. general procedure:* A mixture of acid (0.01mol), phenol (0.01mol) and con. sulfuric acid (0.5 ml) was stirred well with teflon coated magnetic needle and exposed to MW irradiation for 60 seconds at 30HI power. The MW irradiation was stopped and the reaction mixture was stirred well and cooled. The application of MW irradiation pulses and cooling was repeated as required which is given in Table 1.

The reaction mixtures were diluted with water and the compounds extracted with ether. The ether layer was washed with water and sodium bicarbonate and dried over anhydrous sodium sulfate. Removal of ether gave crude products, which were purified by recrystallisation. The products were characterised by comparison of IR, PMR and physical constants with literature data.

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## References

- 1 O.S. Park and B.S.Jang *Arch, Pharm. Res.* 1995, **18**, 277.
- 2 D.R. Buckle, B.C.C. Cantello, H. Smith and B.A. Spicer, *J. Med. Chem.*, 1975, **18**, 726.
- 3 (a) S. Stinson Use of microwave heating to speed organic reactions continues to grow, *Chem. Eng. News*, 1996, **73**, 45; (b) D.M.P. Mingos and D.R. Baghurst, *Chem. Soc. Rev.*, 1991, **20**, 1; (c) A. Loupy, *Spectra Analyt.*, 1993, **22**, 175, 33; (d) C.R. Strauss and R.W. Trainor, *Aust. J. Chem.* 1995, **48**, 1665; (e) S. Caddick, *Tetrahedron*, 1995, **38**, 10403; (f) S.A. Galema, *Chem. Soc. Rev.*, 1997, **26**, 233; (g) R.S. Verma, *Green Chemistry*, February, 1999, **43**; (h) L. Perreux and A. Loupy, *Tetrahedron*, 2001, **57**, 9199; (i) P. Lidstrom, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, 2001, **57**, 9225.
- 4 H.D. Munro; O.C. Musgrave, R. Templeton *J. Chem. Soc. (C)*, 1971, 95.
- 5 R.K. Rane, Ph.D. thesis: Synthetic Studies in Natural Products, Shivaji University, Kolhapur, 1986.
- 6 (a) H.V. Pechmann, *Ber.*, 1884, **17**, 929; (b) P. May, *Perfum. Essent. Oil Record*, 1925, **16**, 45.
- 7 B.B. Dey, R.H.R. Rao and T.R. Sheshadri, *J. Chem. Soc. (C)*, 1969, 29.
- 8 (a) T. Yoshino and I. Kijima, *J. Soc. Org. Synthetic Chem, Jap.*, 1952, 10338; (b) J. Buckingham *Dictionary of Organic Compounds*, 5th edn., Vol. 4, Chapman and Hall, London, 1984.