Synthesis of coumarins via a Pechmann condensation using heterogeneous catalysts[1]

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The synthesis of coumarins via a Pechmann condensation involving the reaction between phenols and ethyl acetoacetate has been carried out using two heterogeneous catalysts, $NaHSO_4.SiO_2$ and silica chloride under solvent free conditions, thus avoiding acidic waste

Keywords: phenols, ethyl acetoacetate, coumarins, silica chloride, $NaHSO_4.SiO_2$

Coumarins are ubiquitous in nature and have an important place in both natural and synthetic organic chemistry.[2] They are mainly used as fragrances, pharmaceuticals and agrochemicals.[3] Coumarins are synthesised by several methods such as Pechmann,[4a,b] Perkin,[4c] Knoevenagel,[4b] Reformatsky[4d] and Wittig reactions.[4e,f]

Pechmann condensation is one of the most common procedure for the preparation of coumarin and its derivatives. This method involves the reaction between a phenol and a β-keto ester in the presence of an acidic catalyst. Simple starting materials are required here to produce coumarins in good yields. Different acid catalysts such as sulfuric acid,[4a] phosphorus pentoxide,[5a] aluminium chloride,[5b] and trifluoroacetic acid[5c] have been used for the Pechmann condensation. The mixture of reagents and catalyst are allowed to stand overnight or for a number of days or are heated above 150°C. The catalysts are also used in excess for example, H_2SO_4 is used in 10–12 equiv. and TFA 3–4 equiv.). The classical catalysts work under homogeneous conditions and so their recovery is difficult. Thus the main problem using the conventional acids is associated with the environment pollution.

Heterogeneous catalysts have attracted interest due to enviro-economic factors. These catalysts are generally less costly and can easily be handled and removed. Thus there will be no undesired waste for environmental pollution. Some methods[6] have recently used solid acids as heterogeneous catalysts for synthesis of coumarins. However, most of these methods require quite high temperatures, longer reaction times and give products in unsatisfactory yields.

In continuation of our work[7] on the development of novel synthetic methodologies using heterogeneous catalysts we recently observed that the synthesis of coumarin via Pechmann condensation can easily be carried out with the heterogeneous catalysts, silica supported sodium hydrogen sulfate ($NaHSO_4.SiO_2$)[8] and silica chloride.[9] A phenol and ethyl acetoacetate underwent condensation in the presence of a catalyst under solvent free conditions to produce the coumarin conveniently (Scheme 1).

Several coumarins were successfully synthesised (Table 1) in high yields by following the above method. The reaction mixture was heated at 85°C. However, resorcinol gave the product (7-hydroxy-4-methyl coumarin) (yield 72%) even at room temperature (reaction time: 7h). Both of the catalysts, $NaHSO_4.SiO_2$ and silica chloride worked efficiently. The yields of the products using these catalysts are comparable. The first catalyst can easily be prepared[8] from the readily available ingredients, $NaHSO_4$ and silica gel (finer than 200 mesh) while the other catalyst is prepared from silica gel and thionyl chloride.[9] The experimental procedure with these two catalysts is very simple. The catalysts can easily be removed by simple filtration. Thus there is no unnecessary acidic waste streams to create environmental pollution.

In conclusion, we have developed a simple and efficient synthesis of coumarins via Pechmann condensation using $NaHSO_4.SiO_2$ and silica chloride[9] as catalysts under solvent free conditions. The experimental simplicity, high yields, application of less costly heterogeneous catalysts and absence of solvent are the advantages of the present procedure. The method is environmentally benign.

Experimental

The spectra were recorded with the following instruments: IR: Nicolet 740 FT IR, ^{1}H NMR: Varian Gemini 200 MHz and EIMS: VG Micromass 7070H (70eV). The phenols and ethyl acetoacetate were obtained commercially.

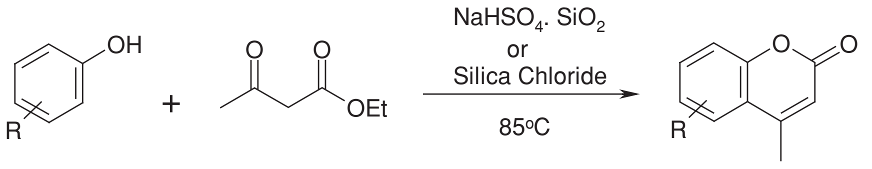
General procedure: A mixture of a phenol (1mmol), ethyl acetoacetate (1.2 mmol) and $NaHSO_4.SiO_2$ ($NaHSO_4.SiO_2$, 0.41:1) or silica chloride ($SOC1_2:SiO_2$, 6.56:1)[9] (100 mg) was heated at 85°C. The reaction was monitored by TLC. After completion the reaction mixture was filtered and the residue was washed with EtOAc. The total organic portion was concentrated and subjected to purification by column chromatography over silica gel.

All the products (except **3d**) are known compounds (references in the Table 1) and were characterised from their spectroscopic (IR, NMR and MS) properties. The spectral data of the compound **3d** are given below.

Compound **3d** (6-n-propoxy-4-methyl coumarin): IR (KBr): 1725, 1612, 1482, 1434 cm^{-1}. ^{1}H NMR: ($CDCl_3$, 200 MHz) δ 7.28 (1H, d, *J*=8.0 Hz), 7.06 (1H, dd, *J*=8.0 Hz), 6.88 (1H, d, *J*=2.0 Hz), 6.28 (1H, s), 3.83 (2H, t, *J*=7.0 Hz), 2.42 (3H, s), 1.88-1.74 (2H, m), 1.03 (3H, t, *J*=7.0 Hz). EIMS (*m/z*): 218 ($M^{+\cdot}$). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.56; H, 6.42; Found: C, 71.42; H, 6.51%.

The authors thank CSIR, New Delhi for financial assistance.

Received 18 August 2004; accepted 1 October 2004
Paper 04/2668



1 2 3

Scheme 1

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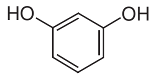
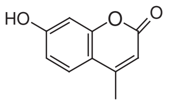
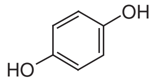
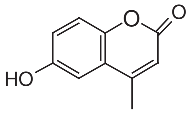
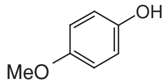
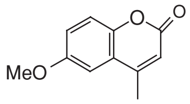
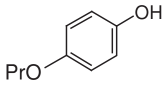
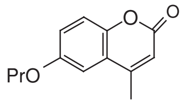
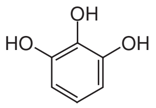
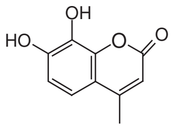
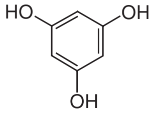
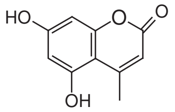
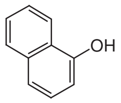
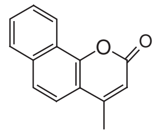
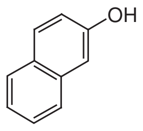
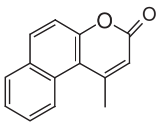
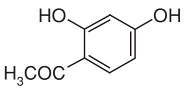
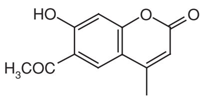
Table 1 Synthesis of coumarins using $NaHSO_4$. SiO_2 and silica chloride*

Entry	Substrate	Product	Catalyst⁺	Time /h	Isolated yeild /%	Ref	M.p. /°C (Lit.)
a			i ii	0.5 0.5	91 93	10a	183–184 (185)[10a]
b			i ii	3.5 3.5	81 82	10a, 10b	246–247 (243–247)[10b]
c			i ii	3.5 3.5	80 81	10c	169–170 (168)[10c]
d			i ii	3.5 3.5	79 79		81–82
e			i ii	1.0 1.0	90 91	10d, 10e	243–244 (243)[10e]
f			i ii	0.5 0.5	88 88	10a	281–282 (280)[10a]
g			i ii	2.0 2.0	86 87	10a, 10d	152–153 (155)[10a]
h			i ii	3.5 3.5	80 82	10f	181–182 (180.5–181)[10f]
i			i ii	3.0 3.0	45 45	10d, 10g	165–166 (164–165)[10g]

Calalyst i. $NaHSO_4$. Sio_2; ii. silica chloride
*The structures of the products were established from their physical and spectroscopic (IR, ^1H NMR and Ms) data.

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