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Sulfated zirconia, a mild alternative to mineral acids in the synthesis of hydroxycoumarins

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Abstract—Sulfated zirconia (1%) was employed as Pechmann's catalyst without solvent or in some cases using a small amount of ethanol to obtain coumarins in moderate to good yields. With this procedure, no significant acidic waste was obtained and an environmental friendly alternative to obtain coumarins is provided.

1. Introduction

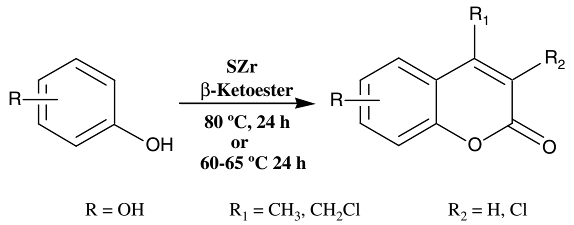
Pechmann's[1] reaction is a simple and easy procedure to synthesize coumarins in good yields by reacting phenols and β-ketoesters in the presence of acidic catalysts. The classical procedure employs large amounts of sulfuric acid as a catalyst, and therefore, produces a large amount of strongly acidic waste that has to be treated causing inconvenience for industry and environment. Other catalysts such as Lewis acids,[2] ionic liquids,[3] and recently, zirconium tetrachloride[4] have been employed, but these methods also generate strongly acidic waste.

In efforts to solve this problem resin[5] and zeolite[6] bared catalysts have been used, but the yields obtained were not satisfactory. Sulfated zirconia (SZr) is an acidic catalyst, which is not as strong as inorganic acids. It has been employed in the nitration of chlorobenzene,[7] dehydration of alcohols,[8] synthesis of benzodiazepine derivatives,[9] alkane isomerizations[10] and acylation of aromatic rings.[11]

In order to obtain coumarins in an environmental friendly procedure and taking as reference a previous work with zirconyl chloride octahydrate,[12] we found that substitution of strong acidic catalysts by sulfated zirconia (1% w/w) neat or in alcoholic media, allows the coumarins to be obtained in good yields (Scheme 1).

In general, reactions take place with 1% sulfated zirconia in neat (or small amount of ethanol) conditions by heating at 80 °C for 24 h giving high yields (Table 1). When working with ethyl 2- or 4-chloroacetoacetate, the reaction should be carried out at temperatures between 60 and 65 °C in order to avoid resinification of the material. Yields are not affected by longer reaction time or increases in the amount of catalyst. Only for obtaining 3-chloro-7-hydroxy 4-methyl coumarin and 7,8-dihydroxy 4-methyl coumarin (see Table 1), a greater amount of SZr (10% w/w) has to be used. We have focused our attention on hydroxycoumarins because they are useful intermediates with potential biological activity.

We have found that sulfated zirconia is a useful catalyst for obtaining hydroxy coumarins in good yields through an environmentally safe procedure that does not produce acidic (or toxic) waste. The spectral data and



Scheme 1.

Keywords: Coumarins; Pechmann's reaction.

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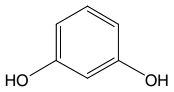
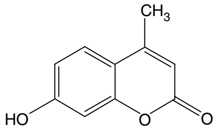
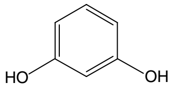
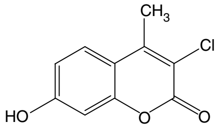
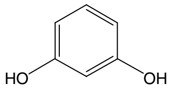
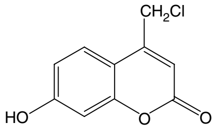
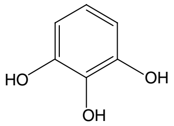
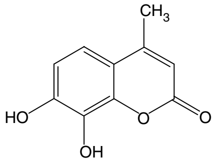
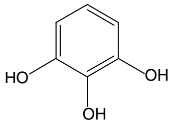
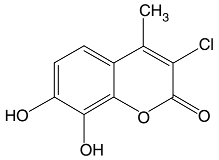
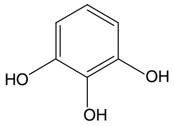
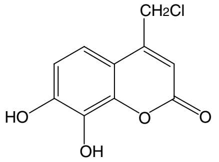
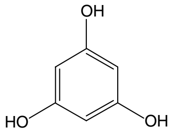
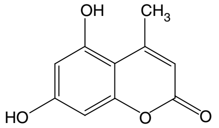
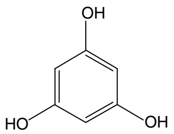
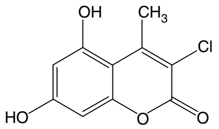
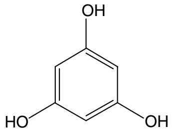
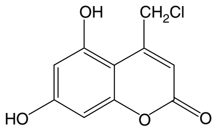
Table 1. Coumarins prepared and yields obtained

Phenols	Product	Yield (%), Mp$_{obt}$ (°C), Mp$_{lit}$ (°C)
		91, 186–189, 188[14]
		87,[a,b,c] 236–240, 236,[15a] 240[15b]
		91,[b,c] 190–191, 185[16]
		92,[a] 242–244, 241–243[4]
		84,[b,c] 267–268, 265[17]
		85,[b,c] 200–201, 198–199[18]
		52, 289–290, 292–293[19]
		74,[b,c] 317–319, 306–308[17]
		93,[b,c] 246–248, 243–245[20]

[a] 10% of SZr was employed.

[b] The reaction was carried out at 60–65 °C and 1 mL of ethanol/g of phenol was added after 2 h.

[c] To enable workup of the reaction, the mixture was diluted with 1 mL of ethanol/g of phenol before pouring it into water.

melting points of the synthesized coumarins match those reported in the literature.

2. Experimental

Reagents were purchased from ACROS Organics. Thin layer chromatography (TLC) was performed by using silica gel plates ALUGRAM Sil G/UV 254 and chloroform–ethyl acetate–acetic acid (8:6:1) was used as an eluent. The ^{1}H and ^{13}C NMR spectra were recorded on a AC Bruker 250 MHz spectrometer using DMSO-d_6 as a solvent. The chemical shifts are reported in ppm and coupling constants (J) in Hz. Melting points were determined on a Stuart Scientific SMP 3 capillary melting point apparatus and are uncorrected.

Sulfated zirconia was prepared as described by Sun et al.[13]

3. Typical procedure

Sulfated zirconia (1% weight of the phenol) was added to a mixture of equimolar quantities of phenols and acetoacetyl esters and left at 80 °C or 60–65 °C (see 'b' in Table 1) with rapid stirring for 24 h. The reaction was monitored by TLC. When all the starting materials were consumed and while hot the mixture was poured into cold water (20 mL/g of starting phenol) with a rapid stirring (see 'c' in Table 1). The precipitate was filtered, washed with cold water and dried at 50 °C overnight, yielding the hydroxycoumarins.

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