Synthesis of 7-Hydroxycoumarins catalysed by Solid Acid Catalysts

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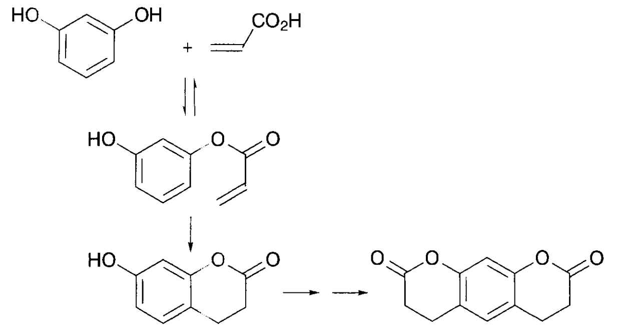
Syntheses of substituted 7-hydroxycoumarins *via* reactions of 1,3-dihydroxybenzene with ethyl acetoacetate (Pechmann reaction) and with propenoic acid and propynoic acids are reported, in which the production of environmentally harmful waste streams is minimized by the use of solid acid catalysts.

In electrophilic aromatic substitutions, non-regenerable catalysts such as metal chlorides and mineral acids are generally applied. Substitution of these by solid acid catalysts[1] such as zeolites, clays and sulfonic acid resins would result in simplified product recovery and reduction of undesirable waste streams. For this purpose, zeolites are good candidates,[2] as they are available in a range of pore sizes and have tunable hydrophobicity; moreover they can be modified in many ways and can be easily regenerated.

Indeed, in aromatic alkylation, zeolite catalysis has already achieved a strong and still expanding position. In aromatic acylation, however, progress—following the first successful attempts[3]—has been slower. Recently we have reported on the direct solid-acid catalyzed acylation of phenols.[4] Here esterification takes place first followed by the Fries rearrangement. By using zeolite H-beta as the catalyst, a high yield (88%) of 2,4-dihydroxybenzophenone was obtained from resorcinol and benzoic acid, with no production of soluble acid waste.

In the present paper we report on the solid-acid catalysed reaction of phenols with carboxylic acids (or their esters) possessing an additional function able to alkylate the benzene nucleus.

Acrylic (propenoic) acid was found to react under mild conditions (toluene, reflux with azeotropic removal of water, zeolite H-beta [Si/Al = 14] or Amberlyst-15 as the catalyst) with resorcinol to 7-hydroxy-3,4-dihydrocoumarin. The reaction of equimolar amounts of resorcinol and acrylic acid was found to involve esterification followed by ring closure (Scheme 1). Apparently ring closure is faster than the Fries rearrangement.

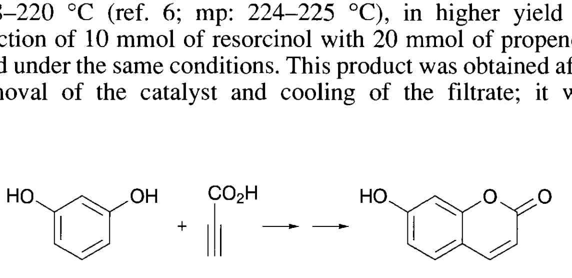


1 **2**

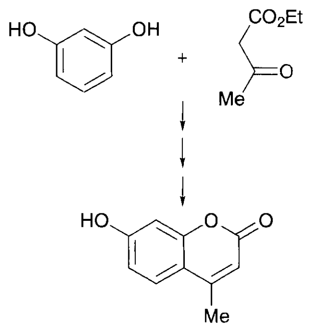
Scheme 1

Both the initial rate and the yield of 7-hydroxy-3,4-dihydrocoumarin **1** are slightly higher for the Amberlyst-15 catalyst. After filtration of the hot reaction mixture to remove the catalyst, **1** precipitated from the filtrate. After work-up 1.08 g (66%) of **1** was obtained.

The formation of a small percentage of a consecutive product, 3,4,6,7-tetrahydrobenzo[1,2-*b* : 5,4-*b*′]dipyran-2,8-dione **2**, is also observed. It proved possible to obtain this product, mp: 218–220 °C (ref. 6; mp: 224–225 °C), in higher yield by reaction of 10 mmol of resorcinol with 20 mmol of propenoic acid under the same conditions. This product was obtained after removal of the catalyst and cooling of the filtrate; it was



Scheme 2



Scheme 3

Table 1 Synthesis of 7-hydroxycoumarin derivatives starting from resorcinol[a]

Entry	Reactant	Catalyst	t/h	Solvent	T/°C	Yield (%)	Substituents
1	Ethyl acetoacetate	Amberlyst-15	4	Toluene	Reflux	81[b]	4-Me
2	Ethyl acetoacetate	H-Beta	4	Toluene	Reflux	71[b]	4-Me
3	Ethyl acetoacetate	Filtrol[c]	4	Toluene	Reflux	5[b]	4-Me
4	Ethyl acetoacetate	Amberlyst-15	2	None	150	72[b]	4-Me
5	Ethyl acetoacetate	H-Beta	2	None	150	78[b]	4-Me
6	Ethyl acetoacetate	Filtrol[c]	2	None	150	55[b]	4-Me
7	Propenoic acid	Amberlyst-15	4	Toluene	Reflux	73	3,4-di-H
8	Propenoic acid	H-Beta	4	Toluene	Reflux	70	3,4-di-H
9	Propynoic acid	Amberlyst-15	20	*p*-Cl-toluene	150	40	—
10	Propynoic acid	H-Beta	20	*p*-Cl-toluene	150	60	—

[a] Reaction conditions (entries 1–3 and 7–10): 10 mmol resorcinol, 10 mmol reactant, 40 ml of solvent, 1.0 g catalyst; heating with stirring and azeotropic removal of water, entries 4–6: without solvent. [b] Hydrolysis of ethyl acetoacetate decreases the yield; % yield after recrystallization from aqueous methanol. [c] Acid clay: Filtrol grade 105 (Engelhard).

characterised by ^{1}H NMR spectroscopy [δ 7.03(s), 6.73(s), 2.80(m)].

Previously reported routes to 7-hydroxy-3,4-dihydrocoumarin *via* the reaction of resorcinol with β-chloropropionitrile[5] or with methyl acrylate and a stoichiometric amount of aluminium chloride[6] both gave the product in 56% yield.

In an analogous way the reaction of resorcinol and propynoic acid (acetylenecarboxylic acid) was found to be a direct route to 7-hydroxycoumarin.

For this reaction a higher temperature (150 °C) and longer reaction times are required and zeolite H-beta is found to be the preferred catalyst.

In another approach to 7-hydroxycoumarins ethyl acetoacetate was allowed to react with resorcinol (Pechmann reaction). Here three steps (Scheme 3): hydroxyalkylation/transesterification/dehydration are involved.[14]

7-Hydroxy-4-methylcoumarin which is useful as a starting material for the preparation of an insecticide (Hymecromone) is obtained in this reaction in yields (after recrystallization) of about 80% by applying zeolite H-beta or Amberlyst-15.

Reported procedures for the Pechmann reaction include conventional reagents,[6–13] often applied in excess, and cation resins.[14,15] Recently, the formation of 4-methylcoumarin by cycloacylation of phenol with acetic anhydride over CeNaY zeolite[16] has been described.

Table 1 summarizes our results on solid-acid catalysed cyclization reactions of resorcinol yielding coumarin systems.

It is concluded that an entree into the coumarin and dihydrocoumarin systems from a broad range of starting materials is made possible by a suitable choice of solid-acid catalysts.

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