

# Synthesis of 7-hydroxy-4-methylcoumarin via the Pechmann reaction with Amberlyst ion-exchange resins as catalysts

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Received 9 December 2004; revised 31 January 2005; accepted 1 February 2005

Available online 7 April 2005

## Abstract

The Pechmann reaction of resorcinol with ethyl acetoacetate over various Amberlyst-type catalysts under mild reaction conditions in short reaction times resulted in high yields of 7-hydroxy-4-methylcoumarin. For purposes of comparison, other solid acid catalysts were also investigated. The best-performing material was Amberlyst-S, with 95% conversion and 98% selectivity in refluxing toluene after 2 h of reaction time at 120 °C. The materials could be regenerated and recycled.

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**Keywords:** Pechmann reaction; Solid acid catalyst; Amberlyst; Coumarin derivatives

## 1. Introduction

Coumarin and its derivatives have been attracting great interest because of their importance in synthetic organic chemistry. Many products that contain the coumarin subunit exhibit useful and diverse biological activity and find their application in pharmaceuticals, fragrances, agrochemicals, and insecticides [1–4].

A method for the coumarin synthesis is the Pechmann reaction, starting from phenols. In the conventional production concentrated sulphuric acid is used as a catalyst [5]; this process requires long reaction times, presents corrosion problems, and creates by-products and salt waste due to the neutralisation of the sulphuric acid. Therefore, attempts have been made to develop alternative, environmentally benign and heterogeneously catalysed synthesis routes. The use of heterogeneous acid catalysts presents advantages, such as ease of operation, reduced equipment corrosion, and minimised waste stream contamination, combined with catalyst reusability. Among others, the use of Nafion-H [6],

Nafion/silica composites [7], zeolite H-BEA [1], Amberlyst-15 [8], and other solid acids [9,10], has been investigated (see Table 1), and 7-hydroxy-4-methylcoumarin could be obtained in yields up to 96% yield over SAC80 (80% Nafion in the composite) [7].

Compared with Amberlyst-15, H-BEA could be regenerated easily and showed higher turnover numbers. However, an efficient Pechmann reaction over the solid acids investigated required long reaction times and large amounts of catalyst. For the case of Amberlyst 15, even special equip-

Table 1  
Synthesis of 7-hydroxy-4-methylcoumarin over different heterogeneous catalysts

Catalyst	Conversion (%)	Selectivity (%)	Yield (%)
SAC13	70	98	69
SAC40	81	98	79
SAC80	98	98	96
NR50	74	82	61
Amberlyst-15	70	93	65
H-BEA	31	89	28 (79 [1])
H-Y(US)	11	98	11
H-ZSM5	5	98	5

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Table 2  
Physico-chemical properties of various Amberlyst type catalysts

Amberlyst	$T_{\max}$ (°C)	Exchange capacity (meq g <sup>-1</sup> )	BET surface area (m <sup>2</sup> g <sup>-1</sup> )	BJH pore volume (cm <sup>3</sup> g <sup>-1</sup> )
-15	120	4.9	52	0.8
-35	120	5.4	50	0.4
-36	140	5.5	35	0.2
A-Cl	150	3.2	53	0.3
A-S	150	1.0	56	0.3

ment for accelerating the reaction by microwave irradiation had to be used [11].

Alternative catalysts for the Pechmann reaction could be the newly developed Amberlyst-type catalysts, such as Amberlyst-15, -35, -36, chlorinated Amberlyst (A-Cl), and surface-sulfonated Amberlyst (A-S), which have a polymeric structure similar to that of Amberlyst-15 [12]. The main differences compared with Amberlyst-15 are that the Amberlyst-35 and -36 resins are polysulfonated resins with a high concentration of acid sites, whereas A-Cl- and A-S-type resins have smaller average pore sizes and lower acid site concentrations (see Table 2).

## 2. Experimental

Resorcinol (98%), ethyl acetoacetate (99%), toluene, and acetone (Sigma-Aldrich) were purified by distillation; other chemicals were of p.a. quality and were used as such. Amberlyst ion-exchange resins were kindly provided by Rohm and Haas Company. For the first catalytic tests the catalysts were used in their initial fresh form; before the second catalytic cycle the materials were washed with water, dried in vacuum at 110 °C for 8 h, and stored under argon.

The reactions were carried out in batch reactors, partially under argon. Typically, 10 mmol of each reactant and 0.5 g of catalyst were stirred in 10 ml of toluene under reflux for 2 h. Subsequently, 10 ml of acetone was added to dissolve all products. Samples were analysed by gas chromatography (HP 6890, 50 m FS-SE 54 capillary column, 50–270 °C, heating rate 12 °C/min) and GC-MS (Varian Saturn 3). Experiments using solvents such as cumene, THF, petroleum ether, and dichloromethane were performed under reflux conditions.

For recycle experiments, the catalysts were filtered off, washed with 10 ml of acetone, and then reused without further treatment. The catalysts were regenerated by Soxhlet extraction in 30 ml of toluene for 12 h at 80 °C.

## 3. Results and discussion

For the Pechmann reaction of resorcinol and ethyl acetoacetate to 7-hydroxy-4-methylcoumarin in refluxing toluene, the activity of the different Amberlyst-type catalysts

Table 3  
Resorcinol conversion and selectivity to 7-hydroxy-4-methylcoumarin over various fresh and under vacuum dried Amberlyst type catalysts at 100 and 120 °C after 2 h reaction time

Amberlyst	Fresh catalyst				Vacuum dried at 120 °C			
	Conversion (%)		Selectivity (%)		Conversion (%)		Selectivity (%)	
	100 °C	120 °C	100 °C	120 °C	100 °C	120 °C	100 °C	120 °C
-Cl	91	92	57	70	85	97	83	97
-15	87	87	63	69	95	95	68	92
-35	87	87	54	56	98	98	73	80
-36	86	86	58	67	92	93	67	74
-S	90	90	66	76	93	95	83	98

as described in Table 2 at 100 and 120 °C was investigated (see Table 3). After a contact time of 2 h, 7-hydroxy-4-methylcoumarin was obtained in yields of up to 64% over the A-Cl and 68% over the A-S catalyst. The highest conversion of 92% was obtained over the A-Cl catalyst at 120 °C, whereas the highest 7-hydroxy-4-methylcoumarin selectivity of 76% could be obtained over the A-S catalyst at 120 °C.

Furthermore, in Table 3 the influence of pre-drying the various Amberlyst type catalysts at 110 °C in vacuum is presented. Again, A-Cl and A-S showed the best performance. Compared with the fresh, undried materials, the coumarin yield increased from 68% to 93% over A-S and from 64 to 94% over the A-Cl material. This illustrates the importance of pretreatment.

Compared with the Amberlyst-15, -35, and -36 catalysts, the A-Cl and A-S materials contain fewer acid sites per gram of dry resin (see Table 1). However, the conversions over A-Cl and A-S are still very high. This might indicate that not all sites in the interior of the gel phase are accessible to the reactants, which is confirmed by the fact that the surface sulfonated A-S also showed high conversion. A slightly higher conversion over Amberlyst-35, with the dried catalyst, can be explained by a higher number of active sites (even though the BET surface area is lower). At the same time, lower 7-hydroxy-4-methylcoumarin selectivities were observed over Amberlyst-35 and -36.

The 7-hydroxy-4-methylcoumarin formation increased with increasing temperature; the highest 7-hydroxy-4-methylcoumarin formation was found over A-Cl (94% yield) and A-S (93% yield) at 120 °C. At this temperature A-Cl showed higher conversions (97%), whereas A-S showed higher 7-hydroxy-4-methylcoumarin selectivities (98%). This higher conversion over A-Cl might be caused by the higher number of active sites, whereas the higher 7-hydroxy-4-methylcoumarin selectivities over the surface sulfonated A-S showed that the reaction that proceeded on the surface was more selective for the desired coumarin, with more by-products being formed in the interior of the resin gel phase.

There was essentially no influence by the amount of A-Cl and A-S on the conversions; when the amount of catalyst was doubled from 0.5 to 1.0 g, the conversion over A-Cl remained at 97%, whereas over the A-S the conversion increased from 95 to 96%. However, the selectivities

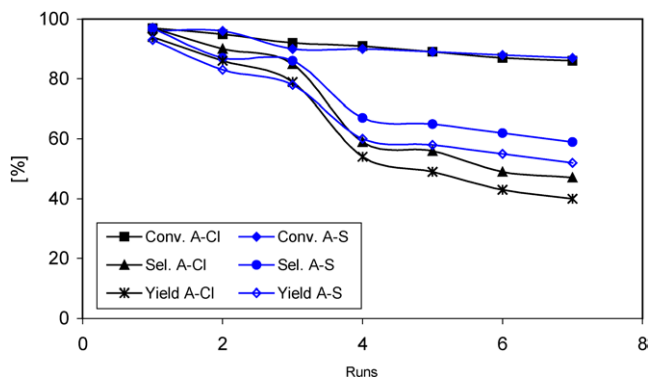


Fig. 1. Synthesis of 7-hydroxy-4-methylcoumarin with reused, non-regenerated dry Amberlyst-Cl and Amberlyst-S after 2 h reaction time at 120 °C.

dropped from 97 to 85% over A-Cl, and from 98 to 92% over A-S.

As described in the literature [6,8], the Pechmann reaction was carried out with toluene as a solvent. The use of other aromatic and nonaromatic solvents with other boiling points did not improve the yield of the desired 7-hydroxy-4-methylcoumarin. Over dry A-S at 120 °C the yield in toluene ( $T_b = 110.6^\circ\text{C}$ ) was 89%, whereas the yield decreased to 55% in cumene ( $T_b = 152.4^\circ\text{C}$ ), to 48% in THF ( $T_b = 67^\circ\text{C}$ ), to 49% in petroleum ether ( $T_b = 50\text{--}70^\circ\text{C}$ ), and to 62% in dichloromethane ( $T_b = 40^\circ\text{C}$ ). Based on earlier experience [7] and because in the literature mostly apolar solvents have been used [1,6–10], the use of polar solvents such as ether was not considered, as such polar solvents suffer cleavage.

To investigate the recyclability of the catalysts, the Amberlyst-type materials were filtered off, washed with acetone, and dried under ambient conditions for 1 h after each experiment. After the first cycle the resorcinol conversion decreased from 97 to 95% (see Fig. 1). After a second recycle, the conversion decreased a further 2% to ca. 93%. In the following four reaction cycles the conversion remained constant at ca. 88% over both A-Cl and A-S catalysts. However, in the first three cycles the selectivity to 7-hydroxy-4-methylcoumarin decreased with 5%, followed by a further drop from 70% to 60% over A-S catalyst, and from 65 to 58% over A-Cl catalyst in the next four reaction cycles. The catalyst deactivation was low, although coke formation by aromatic resorcinol was expected to occur. Apart from a rapid and high conversion (>97%) of resorcinol with ethyl acetoacetate, the coumarin formed precipitates in refluxing toluene in high selectivities (98%). Therefore, the observed adsorption/deposition of the solid product on the solid catalyst is weak, which might be an explanation for the low catalyst deactivation.

Finally, the catalysts were regenerated after each run via Soxhlet extraction in toluene and reused (see Table 4). Upon regeneration both catalysts were more stable and retained their activity; after three runs, the conversion was 97% for both catalysts, whereas the selectivity decreased by 1–2%

Table 4

Synthesis of 7-hydroxy-4-methylcoumarin over regenerated (via Soxhlet extraction in toluene after each run) dry A-Cl and A-S, after 2 h reaction time, at 120 °C

		1	2	3	4	5	6	7	8
A-Cl	Conversion (%)	97	97	97	96	94	92	90	88
	Selectivity (%)	97	96	94	92	88	83	79	74
A-S	Conversion (%)	97	97	97	96	96	94	94	93
	Selectivity (%)	97	97	95	93	89	88	85	82

after each run. Clearly, the catalysts' activity decreased very slowly upon regeneration.

#### 4. Conclusions

The synthesis of 7-hydroxy-4-methylcoumarin via the Pechmann reaction of resorcinol and ethyl acetoacetate over various Amberlyst-type catalysts was investigated. The highest formation of 7-hydroxy-4-methylcoumarin was found over dry Amberlyst-S with 95% conversion and 98% selectivity in refluxing toluene after 2 h of reaction time at 120 °C. Catalysts with fewer acid sites, such as A-Cl and A-S, showed the best catalytic performance. Furthermore, the new Amberlyst-Cl and Amberlyst-S materials showed better activities and were more stable than Amberlyst-15. At the same time, the Amberlyst catalysts are not as expensive as Nafion silica and BEA zeolite catalysts.

The selectivity for 7-hydroxy-4-methylcoumarin dropped with increasing amount of catalyst over both A-Cl and A-S. Upon recycling without regeneration, Amberlyst-S showed a decrease in conversion from 97 to 88% and a decrease in selectivity to 7-hydroxy-4 methylcoumarin from 98 to 65% after seven runs. However, upon regeneration in refluxing toluene, the catalyst activity decreased only very slowly by 1–2% after each run.

#### Acknowledgments

The authors (R.S. and W.F.H.) are grateful to the Rohm and Haas Company for providing the Amberlyst ion-exchange resins and for their generous financial support, as well as for allowing us to publish these results.

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