Available online at www.sciencedirect.com

Journal of Catalysis 218 (2003) 315–320

JOURNAL OF CATALYSIS

www.elsevier.com/locate/jcat

Synthesis of 7-hydroxycoumarins by Pechmann reaction using Nafion resin/silica nanocomposites as catalysts

M.C. Laufer, H. Hausmann, and W.F. Hölderich *

Department of Chemical Technology and Heterogeneous Catalysis, University of Technology RWTH-Aachen, Worringerweg 1, 52074 Aachen, Germany

Received 31 October 2002; revised 14 February 2003; accepted 17 February 2003

Abstract

The reaction of resorcinol with ethyl acetoacetate (Pechmann reaction) or with acrylic acid over novel Nafion resin/silica composite materials with 40 and 80 wt% of Nafion in silica produces 7-hydroxycoumarins in high yields, under mild reaction conditions in short reaction time. Other solid acid catalysts were tested for comparison reasons.

Keywords: Pechmann reaction; Solid acid catalyst; Nafion resin/silica nanocomposite; Coumarin derivatives

1. Introduction

Coumarin and its derivatives have been attracting great interest because of their importance in synthetic organic chemistry. Many products which contain the subunit of coumarin exhibit useful and diverse biological activity [1]. These compounds find their application in pharmaceuticals, fragrances, agrochemicals, and insecticides [2–4].

A very valuable method for the synthesis of coumarins is the Pechmann reaction, which starts from phenols. In the conventional production of coumarins by Pechmann, concentrated sulfuric acid is used as the catalyst [5]. This process causes formation of by-products, needs long reaction time, and introduces corrosion problems. For these reasons, there have been some attempts to find alternative environmentally benign and heterogeneously catalyzed synthesis routes. The use of heterogeneous acid catalysts assumes advantages like ease of operation conditions, reduced equipment corrosion, and minimized contamination of the waste streams combined with reusability of the catalyst. Nafion-H [6], zeolite H-BEA, Amberlyst 15 [7], and other solid acids [8,9] have been employed for this purpose in the Pechmann reaction.

For example, the Pechmann reaction from resorcinol **1** and ethyl acetoacetate **2** to 7-hydroxy-4-methylcoumarin **3** (Scheme 1) over the regenerable zeolite H-BEA in toluene was first reported by van Bekkum and co-workers [2,7].

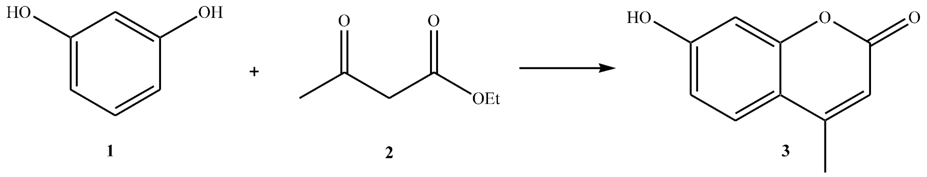
Compared with Amberlyst 15, H-BEA could easily be regenerated and showed higher turnover numbers. Nevertheless, an efficient Pechmann reaction with all these studied solid acids requires long reaction time and high amounts of catalyst. In the case of Amberlyst 15, special equipment for accelerating the reaction by microwave irradiation had to be used [10].

An alternative catalyst for the Pechmann reaction in toluene could be the newly developed Nafion resin/silica nanocomposites. The pure Nafion is an ionomer with a chemically resistant polymeric backbone with highly acidic sulfonic groups and possesses hydrophobic (–CF_2CF_2–) as well as hydrophilic regions (–SO_3H) [11,12]. The activity of this material in nonswelling solvents or in the gas phase is very low due to the very low surface area. This fact has limited the use of pure Nafion as a catalyst. To increase the acid site accessibility, Nafion resin/silica nanocomposites were produced by entrapment of nanometer-sized Nafion resin in a highly porous silica network [13,14]. The developed Nafion resin/silica nanocomposites have opened up a large number of applications due to the increase in the catalytic activity and selectivity [15–20].

---

* Corresponding author.
E-mail address: hoelderich@rwth-aachen.de (W.F. Hölderich).

0021-9517/03/$ – see front matter © 2003 Elsevier Inc. All rights reserved.
doi:10.1016/S0021-9517(03)00073-3



Scheme 1. Reaction of resorcinol and ethyl acetoacetate.

2. Experimental

2.1. Catalysts and analytical methods

The pure Nafion resin NR 50 and the composite materials were kindly provided by DuPont de Nemours & Company, Wilmington. The Nafion resin/silica composites contain 13% (SAC 13), 40% (SAC 40), and 80% (SAC 80) Nafion on silica, respectively. Amberlyst 15 was purchased from Fluka. Before use, all resins were dried at 120–150 °C in vacuum for 4 h.

The zeolites used in this work are commercially available from Zeolyst International: H-Y(US), Na-BEA, and H-ZSM-5. The concentrations of Si and Al in the samples were determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES) (Spectroflame D, Spectro Analytic Instrument). The number of acid sites of the catalysts was determined by ionexchange of the protons with a fivefold excess of $CuSO_4$ and $ZnSO_4$ solutions at 80 °C for 24 h. After washing with distilled water, the samples were dried at 120–150 °C in vacuum for 4 h. Then, the concentrations of Cu(II) and Zn(II) were measured by ICP-AES.

Na-BEA was converted to the acid form by a double ionexchange with a tenfold excess of 2 N NH_4NO_3 (aqueous) at 80 °C and all the zeolites have been calcined at 550 °C for 8 h before use.

The solid state ^{13}C NMR spectra were recorded on a Bruker DSX 500 spectrometer equipped with a wide-bore super-conducting magnet operating fieldstrength of 11.744 T and a resonance frequency for ^{13}C nuclei of 125.85 MHz. All spectra were recorded with a 7-mm multinuclear (50–161 MHz) double-bearing CP/MAS probehead at room temperature. Magic angle spinning (MAS) with a rotational speed of 5 kHz was applied for all spectra and controlled with a MAS-Remote-Control-Unit (Type H 2620, stability ± 2 Hz). The ^{13}C NMR spectra were referred to external TMS. For the NMR measurements, 7-mm ZrO_2 rotors were filled with 200–300 mg of the compounds and tightly locked with Kel-F caps.

The materials were also analysed with nitrogen sorption at -196 °C (Micromeritics ASAP 2010) using the BET method to determine the surface area. Prior to the measurements, the samples were degassed at 100 °C and high vacuum.

All chromatographic measurements were performed on a HP 6890 gas chromatograph equipped with a flame ionisation detector and using a FS-SE54 capillary column ($50\ \mathrm{m} \times 0.25\ \mu\mathrm{m}$) operated between 50 and 270 °C with a ramp of $12\ ^{\circ}\mathrm{C\,min^{-1}}$. Nitrogen was used as the carrier gas. The detector temperature was at 300 °C and a 1-µl volume sample was injected. Identification of the compounds by GC-MS was performed on Varian Satum 3 equipment.

2.2. Reaction procedure

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 were added to dissolve all products. Liquid samples were taken out of the reactor and analyzed by GC. Acetic acid phenyl ester was used as the internal standard. For recycle experiments, the catalysts were filtered off, washed with acetone, and then reused without further treatment.

2.3. Regeneration of the catalyst

Catalyst (0.5 g) was stirred in 20 ml of 15 wt% aqueous H_2O_2 at 80 °C for at least 2 h to recover its original appearance. Then, the catalyst was filtered off, washed with distilled water, and dried at 120–150 °C in vacuum for 4 h.

3. Results and discussion

3.1. Synthesis of 7-hydroxy-4-methylcoumarin via the Pechmann reaction

For the Pechmann reaction of resorcinol (**1**) and ethyl acetoacetate (**2**) to produce 7-hydroxy-4-methylcoumarin (**3**) (Scheme 1) in toluene, Amberlyst 15 and zeolites were compared with the pure Nafion and with Nafion resin/silica composites. Fig. 1 illustrates the performance of the different heterogeneous catalysts in the Pechmann reaction in toluene. The reaction proceeds through transesterification and intramolecular hydroxyalkylation, followed by dehydration [2,7].

7-Hydroxy-4-methylcoumarin was obtained in very high yields up to 81% over SAC 40 (containing 40% Nafion on silica) and 96% yield over the SAC 80 (80% of Nafion in composite) in refluxing toluene after 2 h of contact time. In contrast to the reaction conditions of the Pechmann reaction in toluene studied by van Bekkum and co-workers [2,7], the use of the Nafion resin/silica composite materials led to two

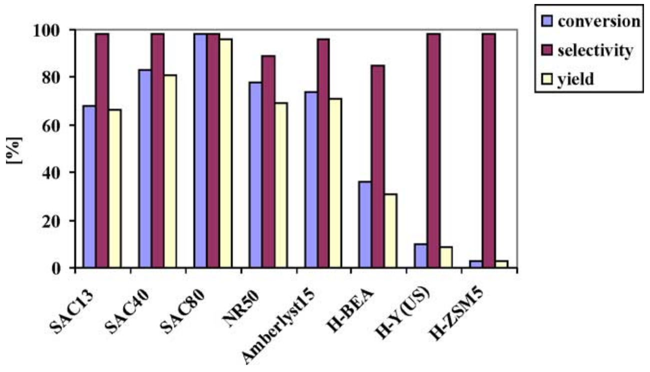


Fig. 1. Synthesis of 7-hydroxy-4-methylcoumarin with different heterogeneous catalysts.

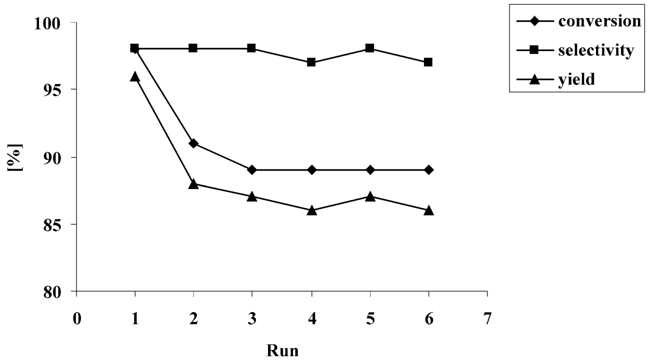


Fig. 2. Synthesis of 7-hydroxy-4-methylcoumarin with reused, nonregenerated SAC 80.

remarkable effects. First, the amount of catalyst was reduced up to 50% and, second, the reaction time was divided in half.

The activity of the composites correlates with the amount of Nafion on silica. Therefore, the conversion of resorcinol raises from 68% for 13 wt% Nafion containing material (SAC 13) to 83% for the 40 wt% containing composite (SAC 40). The better activity of SAC 40 and SAC 80 compared with that of SAC 13 cannot be explained by higher BET surface area or cumulative pore volume. N_2-sorption data show that the BET surface area and the pore volume of SAC 40 (71.40 $\mathrm{m^2\,g^{-1}}$; 17.48×10^{-2} $\mathrm{cm^3\,g^{-1}}$) and of SAC 80 (16.89 $\mathrm{m^2\,g^{-1}}$; 4.16×10^{-2} $\mathrm{cm^3\,g^{-1}}$) were lower than those of SAC 13 (94.92 $\mathrm{m^2\,g^{-1}}$; 22.32×10^{-2} $\mathrm{cm^3\,g^{-1}}$). Therefore, it can be concluded that the higher catalytic performance of SAC 40 and particularly of SAC 80 is due to the higher amount of strong acid centers related to the increased amount of Nafion on silica (Table 1).

However, in the case of the pure Nafion resin NR 50, the surface area is too low (< 0.02 $\mathrm{m^2\,g^{-1}}$) [13] and seems to influence negatively the accessibility to these acid centers. As a result, despite its higher acidic capacity, the conversion of resorcinol by using the pure Nafion NR 50 reaches only 78%.

In the case of Amberlyst 15, a conversion of resorcinol of 74% can be observed. Although the number of acid sites is high (Table 1), it is generally accepted that Amberlyst 15 is not such a strong acid like the perfluorinated sulfonic acid resin [20]. The value of the Hammett acidity function (H_0) ranges from -11 to -13 for Nafion compared to about -2.2 for Amberlyst 15.

In contrast to our newly founded better activity under milder reaction conditions with reduced amount of catalyst, the low conversion of resorcinol (36%) in the presence of H-BEA {16} (in braces, the silica alumina ratios) are not comparable with the better results of van Bekkum [2,7]. Furthermore, the activities of other zeolites like H-Y(US) {40} or H-ZSM 5 {28} are remarkably low with conversions of resorcinol of 10 and 3%, respectively. Probably, resorcinol is not able to optimally enter the pores of the zeolites. Not only in the phenol alkylation with methanol to cresol using H-Y, H-Y(US), or H-ZSM-5 but also in the hydroxylation of phenol with H-ZSM-5, the formation of *ortho*/*para* products was favored [21]. In contrast, resorcinol is a *meta* hydroxy substituted phenol and perhaps hindered from diffusing through the zeolitic channels.

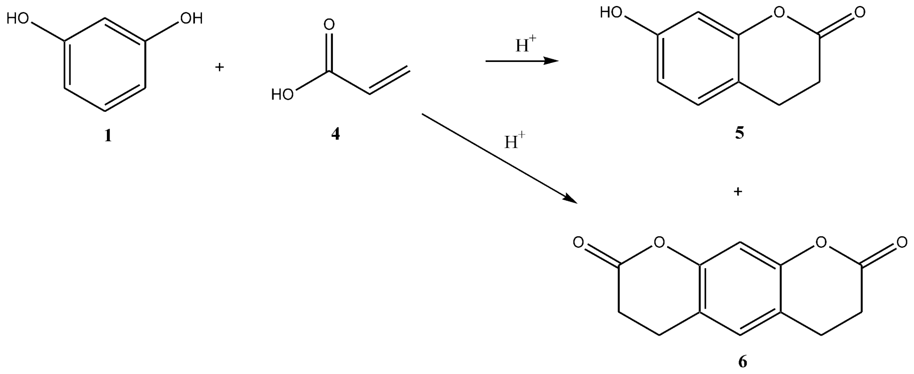
As described in the literature [6–9], we also carried out the Pechmann reaction preferably in toluene as solvent. Other aromatic solvents with higher boiling point like cumene or the more toxic *p*-Cl-toluene did not improve the obtained yield of the desired coumarin. Besides, with those last mentioned solvents, rapid deactivation of the Nafion resin/silica composites was observed. The use of nonaromatic solvents like tetrahydrofuran, petroleum ether, and dichloromethane, which is connected with lower reaction temperatures, did not show competitive results.

To investigate whether the catalyst could be recycled, the most active Nafion resin composite SAC 80 was filtered off, rinsed with acetone, and dried under ambient conditions for 2 h after each experiment. As presented in Fig. 2, there is a decrease in the conversion of resorcinol from 98 to 91% after the first recycle.

After a second reaction cycle, the conversion decreased another 2%. In the following four reaction cycles, however, the conversion remained constant at ca. 89%. Nevertheless, the selectivity to 7-hydroxy-4-methylcoumarin did not change; it remained constant at ca. 98% for all six cycles. The deactivation of the catalyst is low, although coke formation by aromatic resorcinol or coumarin was expected [15–19]. Apart from a rapid and high conversion ($> 98\%$) of resorcinol with the ethyl acetoacetate, the formed coumarin precipitates in refluxing toluene in high selectivity (98%). Therefore, a strong adsorption/deposition of

Table 1
Acidic capacity of the catalysts

Catalyst	SAC 13	SAC 40	SAC 80	NR 50	Amb. 15	H-BEA	H-Y(US)	H-ZSM-5
Capacity (mequiv of H^+/g)	0.08	0.25	0.43	0.89	4.30	0.49	0.14	0.19



Scheme 2. Reaction of resorcinol and acrylic acid.

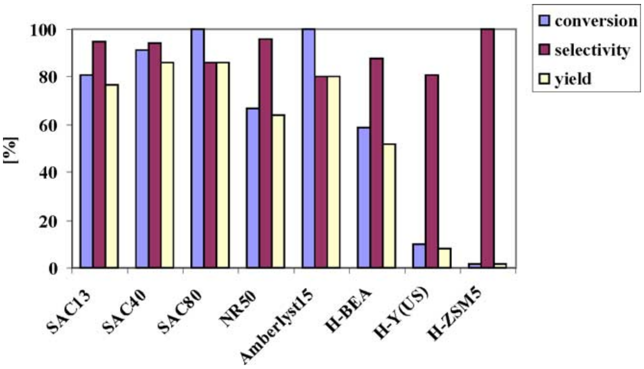


Fig. 3. Synthesis of 7-hydroxy-3,4-dihydrocoumarin with different heterogeneous catalysts.

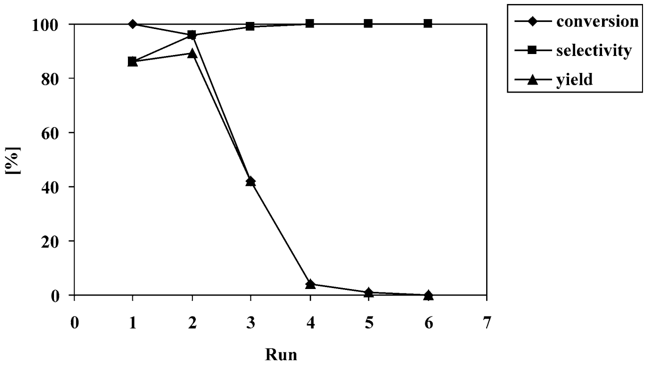


Fig. 4. Synthesis of 7-hydroxy-3,4-dihydrocoumarin with reused, nonregenerated SAC 80.

the solid product on the solid catalyst is more difficult. This may probably explain the low deactivation of the catalyst.

For the complete reactivation of SAC 80, a washing procedure with diluted nitric acid [14] or hydrogen peroxide solution can be applied. After this treatment, either with nitric acid or with hydrogen peroxide, the original activity of the catalyst with 98% conversion of resorcinol can be restored. Due to the possibility to regenerate the catalyst and the fact that the reaction did not continue after the catalyst was removed, Nafion leaching in nonpolar toluene can be excluded. As reported in the literature, the Nafion resin/silica composite materials produced by an in situ sol–gel technique exhibit for several reaction types excellent lifetime stability [14]. The Nafion particles are well entrapped in the silica network.

3.2. *Synthesis of 7-hydroxy-3,4-dihydrocoumarin*

A modification of the Pechmann reaction involves the use of an α,β-unsaturated carboxylic acid instead of β-ketoesters. The reaction of resorcinol (**1**) with acrylic acid (**4**) to 7-hydroxy-3,4-dihydrocoumarin (**5**) (Scheme 2) was found to involve esterification followed by ring closure.

As emphasized in the literature [7], ring closure is faster than the Fries rearrangement. The formation of the consecutive product [1,2-b:5,4-b]dipyran-2,8-dione (**6**) [7] is also observable by GC-MS. Fig. 3 shows the results of the synthesis of 7-hydroxy-3,4-dihydrocoumarin from resorcinol and acrylic acid with different heterogeneous catalysts in refluxing toluene.

Also in this reaction, SAC 40 and SAC 80 led to the best results. After the short contact time of only 2 h, the yield of the desired coumarin was enhanced from 78% up to 86% by increasing the amount of Nafion in silica from 13 to 40%, whereas with the pure Nafion NR 50 only 64% yield was achieved. Since the number of the acid sites is lower, Nafion/silica composites with 13 or 40% loading of Nafion show increasing selectivity up to 95 and 94%, respectively.

On account of the high yield of 80% obtained, Amberlyst 15 is here more competitive with the Nafion/silica composites than the pure Nafion NR 50. H-BEA demonstrated a high selectivity to **5** (88%) but still too low activity (59%). As in the case of the Pechmann reaction to 7-hydroxy-4-methylcoumarin, low activity of the acidic H-Y(US) or H-ZSM-5 zeolites could be confirmed.

In further experiments, the recycling of SAC 80 was examined. Fig. 4 describes the gradual decrease of the catalyst activity until its complete loss after four cycles.

As presented in Fig. 3 and Table 1, a decreased number of acid sites seems to be responsible for the observed increase in selectivity to **5**. Furthermore, contamination of the catalyst can also reduce the number of acid sites. Hence, the formation of the consecutive product **6** decreases with the deactivation grade of the catalyst. Experiments with SAC 80 in diluted reaction mixtures did not lead to substantial improvement of selectivity to **5** and to reduced coke formation on the catalyst. For example, the use of a twofold or threefold amount of toluene improves the selectivity to **5** around 2%.

It has to be pointed out that the formation of the side product **6** affords only 1 equiv of resorcinol and 2 equiv of acrylic acid. If the by-product **6** is formed, unchanged resorcinol is expected in the reaction mixture. Nevertheless, resorcinol could not be detected in the reaction solution. Therefore, it might be that the unchanged resorcinol is adsorbed on the SAC 80 and might be responsible for coke formation on the catalyst.

The easy adsorption of resorcinol can be demonstrated by stirring the catalyst separately with each reactant, resorcinol as well as acrylic acid, under the reaction conditions in toluene. In the case of resorcinol, the catalysts becomes rapidly dark. ^{13}C MAS NMR measurements with treated SAC 80 explained the supposed strong adsorption of resorcinol (Fig. 5). The ^{13}C NMR measurements were carried out after washing the catalyst several times with acetone.

With the adsorption on SAC 80, the symmetry of resorcinol is lost. In the spectrum of the adsorbed resorcinol, more signals for the nonequivalent positions can be observed. The signals at 106.6 and 154.3 ppm (spectra A) are characteristic for symmetric carbons of the original resorcinol. On the other hand, four signals at 110.4, 118.2, 151.9, and 164.7 ppm in the spectra of treated catalyst (spectra B) are observable. The peak at 29.3 ppm can be assigned to toluene.

Treatment with acrylic acid did not result in catalyst deactivation. By ^{13}C MAS NMR, it was not possible to detect any acrylic acid on the catalyst after washing with acetone. After treatment in acrylic acid solution, the colorless SAC 80 showed its maximal performance when it was used again in the synthesis of 7-hydroxy-3,4-dihydrocoumarin **5**. In this way, it could be concluded that resorcinol but not acrylic acid adsorption constitutes the main cause for catalyst deactivation.

Due to the high deactivation of the Nafion resin/silica composites by coke, a consecutive regeneration step is necessary. The best method to achieve the original performance of the catalyst proved here to be the regeneration with aqueous H_2O_2. Also in this case, a complete catalyst regeneration is possible.

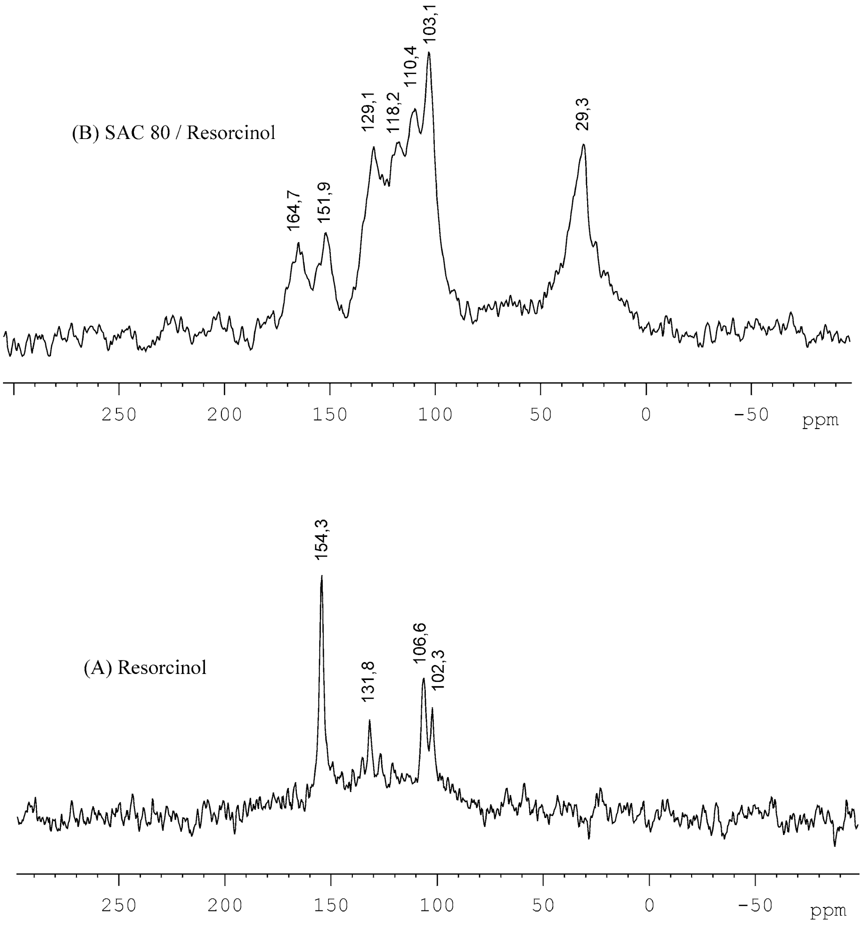


Fig. 5. ^{13}C MAS NMR measurements of contaminated SAC 80 and resorcinol.

4. Conclusion

Nafion resin/silica nanocomposite materials have been shown to give excellent activity in the synthesis of 7-hydroxycoumarins. The synthesis of 7-hydroxy-4-methylcoumarin (81–96% yield) from resorcinol and ethyl acetoacetate in toluene is performed very satisfactorily and with short reaction time by using composites with 40% (SAC 40) and 80% (SAC 80) content of Nafion on silica. The composites are directly recyclable; only a low catalyst deactivation occurs.

Similar reaction conditions were applied in the synthesis of 7-hydroxy-3,4-dihydrocoumarin (86–88% yield) from resorcinol and acrylic acid. Composites with 40% (SAC 40) and 80% (SAC 80) loading of Nafion on silica are again the most promising catalysts. However, in this last case, high deactivation of the catalysts occurs due to the strong resorcinol adsorption and the catalyst has to be regenerated by treatment with H_2O_2 solutions.

Acknowledgment

The authors are grateful to DuPont de Nemours & Company for the provided Nafion resin/silica nanocomposites.

References

[1] R.D.H. Murray, J. Medez, S.A. Brown, The Natural Coumarins: Occurrence, Chemistry and Biochemistry, Wiley, New York, 1982.
[2] E.A. Gunnewegh, A.J. Hoefnagel, R.S. Downing, H. van Bekkum, Recl. Trav. Chim. Pays-Bas 115 (1996) 226.
[3] W.-C. Sun, K.R. Gee, R.P. Haugland, Bioorg. Med. Chem. Lett. 8 (1998) 3107.
[4] J. Oyamada, C. Jia, Y. Fujiwara, T. Kitamura, Chem. Lett. (2002) 380.
[5] E.C. Horning, in: Organic Synthesis, Vol. III, Wiley, New York, 1955, p. 281.
[6] D.A. Chaudhari, Chem. Ind. (1983) 568.
[7] E.A. Gunnewegh, A.J. Hoefnagel, H. van Bekkum, J. Mol. Catal. A: Chem. 100 (1995) 87.
[8] B.M. Reddy, V.R. Reddy, D. Giridar, Synth. Commun. 31 (2001) 3603.
[9] T.S. Li, Z.H. Zhang, F. Yang, C.G. Fu, J. Chem. Res. (S) (1998) 38.
[10] A. De la Hoz, A. Moreno, E. Vázques, Synlett (1999) 608.
[11] G.A. Olah, S.I. Pradeep, G.K.S. Prakash, Synthesis (1986) 513.
[12] G.A. Olah, in: J. Fraissard, L. Petrakis (Eds.), Acidity and Basicity of Solids, Kluwer, Dordrecht, The Netherlands, 1994, p. 305.
[13] A.M. Harmer, W.E. Farneth, Q. Sun, J. Am. Chem. Soc. 118 (1996) 7708.
[14] A.M. Harmer, Q. Sun, A.J. Vega, W.E. Farneth, A. Heidekum, W.F. Hoelderich, Green Chem. (2000) 7.
[15] A. Heidekum, M.A. Harmer, W.F. Hoelderich, Catal. Lett. 47 (1997) 243.
[16] A. Heidekum, M.A. Harmer, W.F. Hoelderich, Am. Chem. Soc. Polym. Prepr. (1996) 763.
[17] A. Heidekum, M.A. Harmer, W.F. Hoelderich, J. Catal. 176 (1998) 260.
[18] A. Heidekum, M.A. Harmer, W.F. Hoelderich, J. Catal. 181 (1999) 217.
[19] A. Heidekum, M.A. Harmer, W.F. Hoelderich, J. Catal. 188 (1999) 230.
[20] M.A. Harmer, Q. Sun, Appl. Catal. A 221 (2001) 45.
[21] P.B. Venuto, Micropor. Mater. 2 (1994) 297.