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Synthesis of (all-*rac*)-α-tocopherol using Nafion resin/silica nanocomposite materials as catalysts

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The reaction of trimethylhydrochinone and isophytol over novel Nafion resin/silica nanocomposite materials with 40 wt% of Nafion in silica produces (all-*rac*)-α-tocopherol in high yield. The *in situ* prepared nanocomposite materials are more stable than the dispersed Nafion catalysts on *pre-formed* SiO_2-supports with respect to solvent leaching.

KEY WORDS: Nafion resin/silica nanocomposite; solid acid catalyst; Friedel-Crafts alkylation; vitamin E.

1. Introduction

Nafion resin, a perfluorosulfonic acid resin, which is a copolymer of tetrafluoroethene and a perfluorosulfonylether derivative, is known to be a strong Brønsted acid [1]. However, the activity of this material in non-swelling solvents or in the gas phase is very low due to the very low surface area. This fact has limited the use of the pure Nafion as a catalyst. In order to increase the acid site accessibility, Nafion composite materials were produced by depositing nanometer-sized Nafion particles on different *pre-formed* supports or by an *in situ* entrapment in silica [2,3]. The highly dispersed and entrapped Nafion resin/silica nanocomposite *via* the *in situ* sol gel technique is unattainable using the *pre-formed* silica support. Not only the catalytic activity but also the stability is higher for the *in situ* nanocomposite versus using a *pre-formed* support. The *in situ* developed Nafion resin–silica nanocomposite materials have opened up a large number of applications due to the increase in the catalytic activity and selectivity [4–9].

The pure Nafion resin NR50 as well as Nafion/SiO_2 with 15 wt% Nafion supported on SiO_2 were already examined as catalysts in the industrially relevant reaction of trimethylhydroquinone (TMHQ) **1** with isophytol (IP) **2** to yield (all-*rac*)-α-tocopherol 3 (synthetic vitamin E, Scheme 1) [10,11].

These heterogeneous catalysts seem promising as replacement for good but hazardous Lewis and Brønsted acids such as zinc chloride or mineral acids [12]. Major disadvantages of the homogeneous catalysts are corrosion problems and potential contamination of waste water.

As reported in literature, the Nafion systems, NR50 as well as supported Nafion/SiO_2 showed a remarkably high conversion of isophytol ($>95\%$) and good yields of tocopherol ($\sim92\%$) when the reaction was carried out in a two-phase solvent system of non-polar heptane and of polar propylene carbonate [10,11]. Even in toluene, the results obtained with NR50 in the range of 72–75% yield are comparable with those of the Nafion/SiO_2 supported material. Obviously, the same dependency of the solvent polarity in the case of both catalysts could be found. Nevertheless, the major drawback of both materials is their low stability. A decomposition of the pure Nafion material takes place in propylene carbonate at the reaction temperature (100 °C). In the case of the supported material Nafion/SiO_2, leaching of the Nafion particles from the *pre-formed* silica support in polar as well as in non-polar solvent was observed [11].

Alternatively, as we found now, the more stable Nafion systems for the synthesis of tocopherol are the *in situ* produced Nafion resin/silca nanocomposite materials as strong acid catalysts. In figure 1, the results of the condensation of trimethylhydroquinone and isophytol in propylene carbonate/heptane in the presence of 0.9 wt% Nafion resin/silica nanocomposites (SAC) with different loading of Nafion in silica are depicted.

According to the different activity of the composites with varying amounts of Nafion, the yield of tocopherol raises from 61% for SAC05 (5 wt% of Nafion in silica) to 73% for SAC13 and 88% for SAC40.

The higher catalytic performance of SAC40 is attributed to the higher quantity of strong acid centers related to the increased amount of Nafion on silica. However, in the case of SAC80, the number of the acid sites is too high and responsible for decreased selectivity

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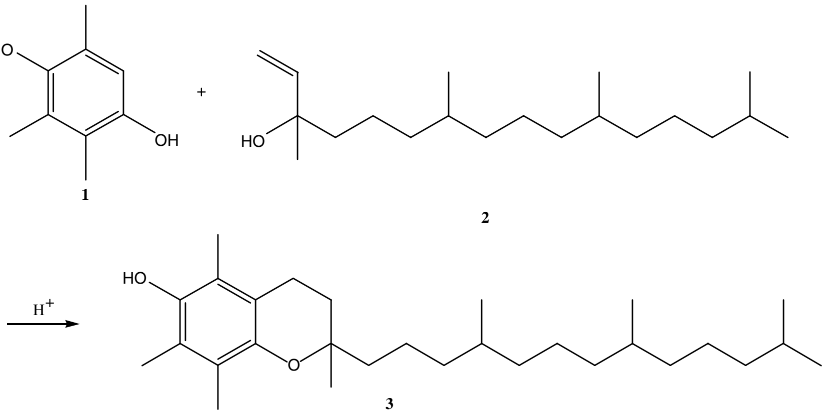

Scheme 1. Synthesis of (all-*rac*)-α-tocopherol.

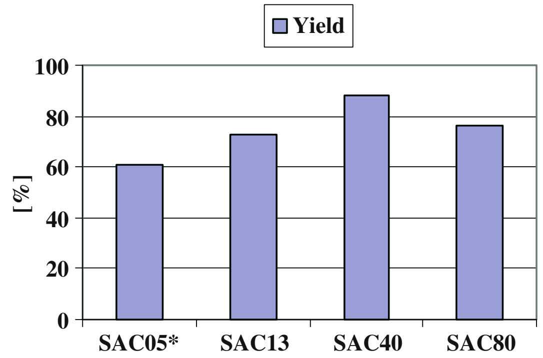

Figure 1. Synthesis of (all-*rac*)-α-tocopherol with different Nafion/silica resin nanocomposite materials (SAC). Conditions: 49.5 mmol TMHQ, 33 mmol IP, propylene carbonate/heptane (50 ml/50 ml), 1 g (0.9 wt%) catalyst, 1 h (*14 h), 100 °C.

to tocopherol. The main by-products in this reaction are phytadienes and furan derivatives. By using a very active catalyst like SAC80, formation of considerable amounts of higher molecular by-products is favored. Another disadvantage of SAC80 composite is the decreased stability in the strong polar medium propylene carbonate at the reaction temperature (100 °C). So, the material loses its mechanical hardness and causes difficulties with filtering-off. The Nafion composite with 40 wt% of Nafion (SAC40) was the best catalyst not only because of its high catalytic performance but also because of its high thermal stability in polar solvents. The higher stability of SAC40 compared with that of SAC80 can be explained by the higher amount of silica in the composite.

Further optimization of the reaction conditions led to 91% yield of tocopherol when only 0.6 wt% SAC40 was used as catalyst (figure 2).

In order to examine the leaching resistance or the decomposition behavior of the used heterogeneous catalysts, the recovered propylene carbonate phase was reused without the catalyst. On the one hand, in the case of SAC40, only a negligibly low conversion of isophytol in the range of ca. 1% could be observed. On the other hand, the recovered propylene carbonate phase after reaction over Nafion/SiO_2 or over the pure Nafion NR50 showed a conversion of isophytol of ca. 30%.

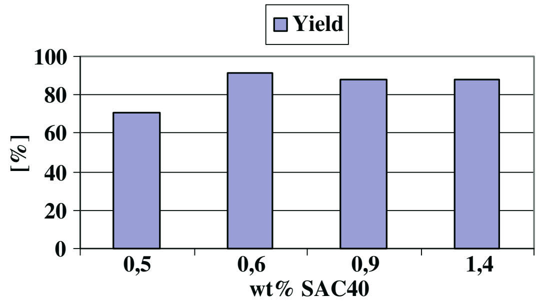

Figure 2. Synthesis of (all-*rac*)-α-tocopherol with different amount of catalyst SAC40. Conditions: 49.5 mmol TMHQ, 33 mmol IP, propylene carbonate/heptane (50 ml/50 ml), 1 h, 100 °C.

Consequently, the SAC40 material produced by the sol–gel technique has, in contrast to the supported Nafion material Nafion/SiO_2 or to the pure resin NR50, improved stability with the same or even higher catalytical performance in polar propylene carbonate. A high stability of those catalysts in propylene carbonate (used in a two-phase system with heptane) is desired particularly since the results in other solvents are clearly inferior [10,11].

In further experiments, the recycle of SAC40 was investigated. For this purpose, SAC40 was filtered-off, rinsed with acetone and dried under ambient conditions for 2 h after each experiment. As presented in figure 3, there is a decrease in the yield of tocopherol from 88% to 78% after the first catalyst recycle.

After a second catalyst cycle, unfortunately, the conversion decreases another 20%. For the reactivation of used SAC40, a washing procedure with oxidizing agents, diluted nitric acid or hydrogen peroxide solution at 80 °C can be applied [3].

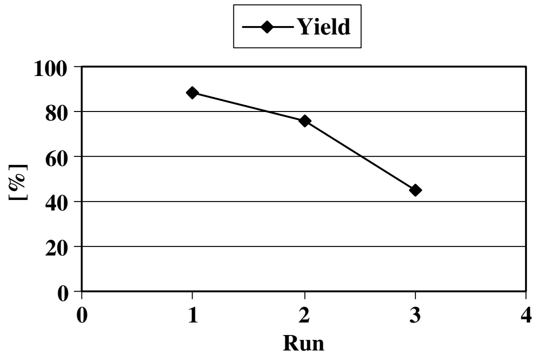

Figure 3. Synthesis of (all-*rac*)-α-tocopherol with reused, non-regenerated SAC40. Conditions: 49.5 mmol TMHQ, 33 mmol IP, propylene carbonate/heptane (50 ml/50 ml), 1 g (0.9 wt%) catalyst, 1 h, 100 °C.

2. Experimental section

2.1. General

Trimethylhydroquinone **1** and all used solvents were purchased from Fluka. Isophytol **2** was obtained from Lonza AG. All these compounds were used without further purification. All liquid reagents and solvents were degassed by three freeze thaw cycles before use.

The pure Nafion resin NR50 and the composite materials were kindly provided by DuPont de Nemours & Company, Wilmington. Before use, all resins were dried at 150 °C under vacuum for 4 h.

2.2. Reaction procedure

The catalytic reactions were carried out in a batch reactor under an argon atmosphere using Schlenk techniques. 11.6 ml (33.0 mmol) isophytol **2** were added (0.2 ml/min) to a mixture of 7.6 g (49.5 mmol) trimethylhydroquinone **1** and 0.5–1.5 wt% catalyst in propylene carbonate/heptane (50 ml/50 ml) at 100 °C. The reaction mixture was stirred for further 60 min at 100 °C with azeotropic removal of water. After filtering-off the catalyst from the two-phase solvent mixture, the heptane phase containing tocopherol **3** was separated and the solvent removed under vacuum. The crude product was analyzed by GC with an internal standard. Excess **1** contained in the propylene carbonate phase may be reused.

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