Chinese Chemical Letters Vol. 10, No. 6, pp. 443–444, 1999

Synthesis of *d,l*-α-Tocopherol Catalyzed by Heteropoly Acids

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Abstract: *d,l*-α-Tocopherol (vitamin E) is found to be synthesized by condensing trimethylhydroquinone with isophytol catalyzed by heteropoly acids (HPA) $H_3PW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ at room temperature. These HPA are efficient catalysts for the synthesis of *d,l*-α-Tocopherol and can easily be separated from the reaction mixture and reused.

Keywords: *d,l*-α-Tocopherol, heteropoly acids, synthesis.

d,l-α-Tocopherol (vitamin E) is generally synthesized by condensing trimethyl-hydroquinone (TMHQ) with phytol or isophytol catalyzed by various Brönsted and Lewis acids such as $ZnCl_2$-HCl[1] and $AlCl_3$[2]. An essential disadvantage of these catalysts is their high consumption. The ratio of $ZnCl_2$ to TMHQ is about 1:1. Futhermore, the catalysts are difficult to be recovered and reused. Recently, I.V. Rozhevnikov and co-workers[3] reported that the reaction could be catalyzed by heteropoly acids (HPA) $H_3PW_{12}O_{40}$ and $H_4SiW_{12}O_{40}$. The consumption of these HPA was low, but the reaction was carried out at elevated temperature 90-150°C.

In the present study, we have found that the condensation of TMHQ with isophytol catalyzed by heteropoly acids $H_3PW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ can be carried out at room temperature, thereby reducing the energy consumption and high temperature equipment cost.

Isophytol (95%, 14g) was added dropwise for 3 h to a stirred mixture of TMHQ (98%, 7g) and $H_3PW_{12}O_{40}$ or $H_3PMo_{12}O_{40}$ (0.5) in dichloromethane (20ml), isopropyl ether (5ml) and AcOH (10ml) at room temperature under nitrogen. When the addition was filtered, the mixture was stirred for another 30 min at the same temperature, then the catalyst was filtered off, which could be reused. The filtrate was concentrated under reduced pressure and to give an oil. This oil was dissolved in toluene (150ml) and washed with 50% aqueous methanol, 2% aqueous NaOH and saturated brine successively. After dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure to give crude *d,l*-α-Tocopherol as a brown oil.

In order to compare with HPA, the activity of $ZnCl_2$ was also investigated under the similar conditions.

Table 1 shows the results of reactions under various reaction conditions.

Table 1. Synthesis of *d,l-α*-Tocopherol under various conditions

Run	Catalyst (g)	AcOH (ml)	Yield (%)[a]	Purity (%)[b]
1	—	10	4	16
2	$H_3PW_{12}O_{40}$ (0.5)	2	76	65
3	$H_3PW_{12}O_{40}$ (0.5)	4	85	77
4	$H_3PW_{12}O_{40}$ (0.5)	6	93	80
5	$H_3PW_{12}O_{40}$ (0.5)	8	97	83
6	$H_3PW_{12}O_{40}$ (0.5)	10	93	97
7	$H_3PW_{12}O_{40}$ (0.5)[c]	10	92	97
8	$H_3PW_{12}O_{40}$ (0.5)	12	88	94
9	$H_3PW_{12}O_{40}$ (0.5)	10	96	95
10	$H_3PMo_{12}O_{40}$ (0.5)	6	63	64
11	$H_3PMo_{12}O_{40}$ (0.5)	8	77	76
12	$H_3PMo_{12}O_{40}$ (0.5)	10	87	82
13	$H_3PMo_{12}O_{40}$ (0.5)	12	81	79
14	$ZnCl_2$(6.8)	1	97	94

a)Yield based on crude *d,l-α*-Tocopherol. b)Purity based on crude *d,l-α*-Tocopherol, determined by ceriometry. c)Use recovered catalyst.

As shown in **Table 1**, the catalytic activity of HPA is obviouly higher than that of $ZnCl_2$. The yield and purity of *d,l-α*-Tocopherol catalyzed by HPA are markedly dependent on the amout of AcOH. This may be due to the fact that AcOH can increase HPA's acid strength, thereby increasing the activity of catalyst, but excessive AcOH may lead to side reactions such as dehydration of isophytol to produce a mixture of isomeric phytodienes. The catalytic activity of $H_3PW_{12}O_{40}$ is higher than that of $H_3PMo_{12}O_{40}$ It may be due to the different acid strength.

In summary, HPA are promising catalysts for the synthesis of *d,l-α*-Tocopherol. This is mainly due to their high activities, mild reaction conditions and the catalyst is easy to separate and reuse.

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Received 4 November 1998