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A novel and environmentally benign selective route for Vitamin K_3 synthesis

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Abstract

The oxidation of 2-methylnaphthalene was carried out in acetic acid with aqueous hydrogen peroxide. 2-Methyl-1,4-naphthoquinone was obtained in a selectivity of nearly ≥90% at 100 °C for 3 h. The reaction has been studied by varying different parameters like concentration of hydrogen peroxide, strength of acetic acid, molar ratio of 2-methylnaphthalene to hydrogen peroxide, reaction temperature and time. Compared to the conventional preparation of Vitamin K_3, this method could be economical and ecofriendly as the use of mineral acid and chromium salts are avoided.

Keywords: Oxidation; 2-Methylnaphthalene; Acetic acid; Hydrogen peroxide; Vitamin K_3

1. Introduction

It is well known that quinones possess pronounced bio-activity and find important medicinal applications [1]. Ever since the Vitamin K_3 (menadione) was found to be more active than Vitamin K_1 and Vitamin K_2 as antihemorrhagic agent [2], many methods have been described to bring about the controlled oxidation of 2-methylnaphthalene (**I**) using various oxidizing agents in the presence of catalyst [3–9]. In a well-known process, 2-methylnaphthalene is oxidized with a solution of sulfuric acid and chromic acid to give Vitamin K_3 (2-methyl-1,4-napthoquinone, (**II**)) in 30–60% of yield [10,11]. However, in this stoichiometric oxidation about 18 kg of chromium containing waste is produced for the synthesis of 1 kg of the product and there is a necessary treatment of chromium containing waste water. Adam and co-workers [12–14] described the use of acetic acid, hydrogen peroxide and methyl trioxorhenium (conversion of 2-methylnaphthalene was 81%, affording 47% of 2-methyl-1,4-naphthoquinone and 7% of 6-methyl-1,4-naphthoquinone, (**III**)) or Pd^{II}-polystyrene sulphonic acid resin [15] as catalysts. The rhenium catalyzed oxidation of 2-methylnaphthalene, using 85% H_2O_2 solution gave a conversion 93% at 40 °C after 4 h. However, this reaction is rather hazardous, as concentrated hydrogen peroxide is potentially explosive [16]. In another method, metalloporphyrin catalyzed oxidation of 2-methylnaphthalene by potassium monopersulphate was reported [17], with the selectivity upto 53% for 2-methyl-1,4-naphthoquinone. The economics associated with the use of all these catalysts and the present day's stringent environmental concerns on the disposal of

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catalysts make it difficult to proceed with them any more.

We have now studied the oxidation of 2-methylnaphthalene in detail using H_2O_2 in the presence of acetic acid and without a solid acid catalyst. In the present work, we report here for the first time, a very highly selective formation of 2-methyl-1,4- naphthoquinone in comparison with H_2SO_4/CrO_3 catalyzed reactions.

2. Experimental

We mainly used 30% of H_2O_2 solution that was prepared by diluting the 50% H_2O_2 (Qualigens fine chemicals) in distilled water at room temperature. 2-Methyl naphthalene (Lancaster, 97%), 2-methyl-1,4-naphthoquinone (Aldrich) and glacial acetic acid (Loba Chemie) were of analytical purity and used without further purification.

To a solution of 2-methylnaphthalene, 1 g in 20 ml of acetic acid, 9 ml of 30% H_2O_2 was added slowly at 100 °C and stirred for 3 h, while carefully monitoring the reaction. The product mixture was extracted with CH_2Cl_2. The combined organic phase was washed with water and the collected organic extract was dried at 20–40 °C in vacuum. The preliminary product analysis was made by a Chemito 8510 gas chromatography (GC) using 20% SE-30 column coupled with FID. The product was identified using standards. The products were confirmed by GC–MS and ^{1}H NMR. The experiments were repeated by varying the temperature, reaction time and concentration of H_2O_2 and acetic acid.

3. Results and discussion

The influence of hydrogen peroxide concentration and the role of acetic acid strength on the oxidation of 2-methylnaphthalene were studied in detail. In the presence of acetic acid, 2-methylnaphthalene (**I**) is oxidized by hydrogen peroxide preferentially to the 2-methyl-1,4-naphthoquinone (**II**) (Scheme 1).

3.1. Effect of hydrogen peroxide strength

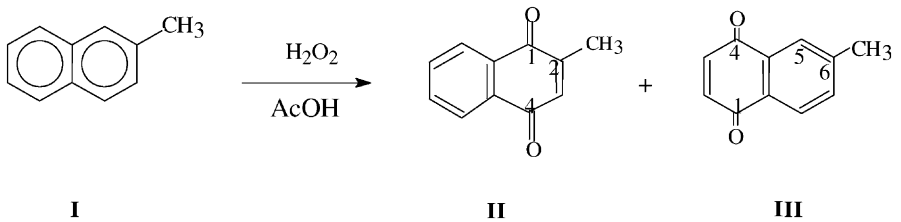
Initially, we investigated the influence of H_2O_2 (10–50wt.%) on the reaction at 100 °C and molar ratio of 2-methylnaphthalene:H_2O_2 as 1:10. We found that 30% H_2O_2 gave >95% conversion of 2-methylnaphthalene with nearly ≥90% selective formation of 2-methyl-1,4-naphthoquinone (**II**). When we used 50% H_2O_2, we observed that there was a formation of 6-methyl-1,4-naphthoquinone (**III**) along with 2-methyl-1,4-naphthoquinone (Fig. 1).

3.2. Effect of molar ratio of 2-methylnaphthalene to H_2O_2

Keeping the reaction temperature at 100 °C and using 30% H_2O_2 and 17 M of acetic acid, we examined the effect of molar ratio of 2-methylnaphthalene and H_2O_2 from 1:2 to 1:10. At molar ratio of 1:10, both the conversion and selectivity reached ≥90% after 3 h (Fig. 2).

3.3. Effect of acetic acid strength

The strength of acetic acid also has a pronounced effect on the system when all other conditions being identical. For detailed study, the concentration of acetic acid was varied from 5 to 17 M. The conversion of 2-methylnaphthalene increased from 35 to ≥90% as the strength of acetic acid increased from 5 to 17 M (Fig. 3), even though, the selectivity of 2-methyl-1,4-naphthoquinone remains unchanged nearly ≥90%.



I **II** **III**

Scheme 1. The oxidation of 2-methylnaphthalene (**I**) by H_2O_2 in acetic acid.

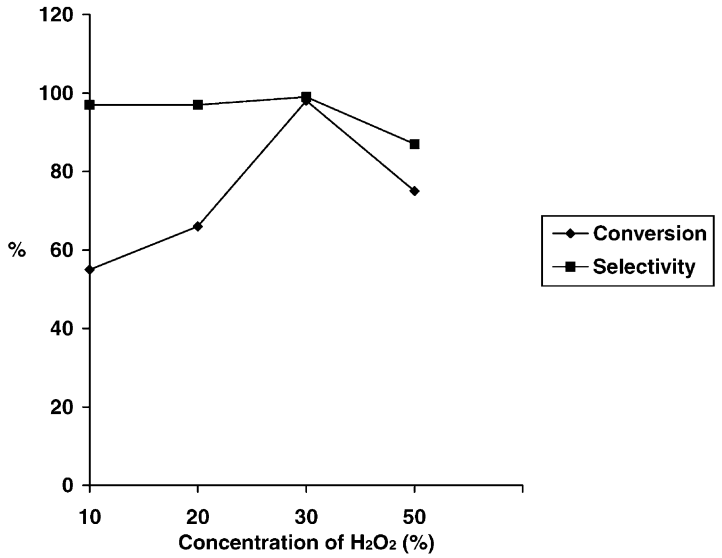


Fig. 1. Influence of H_2O_2 concentration on oxidation of 2-methylnaphthalene: reaction temperature = 100 °C, reaction time = 3 h, molar ratio of 2-methylnaphthalene:H_2O_2:acetic acid (17 M) = 1:10:50.

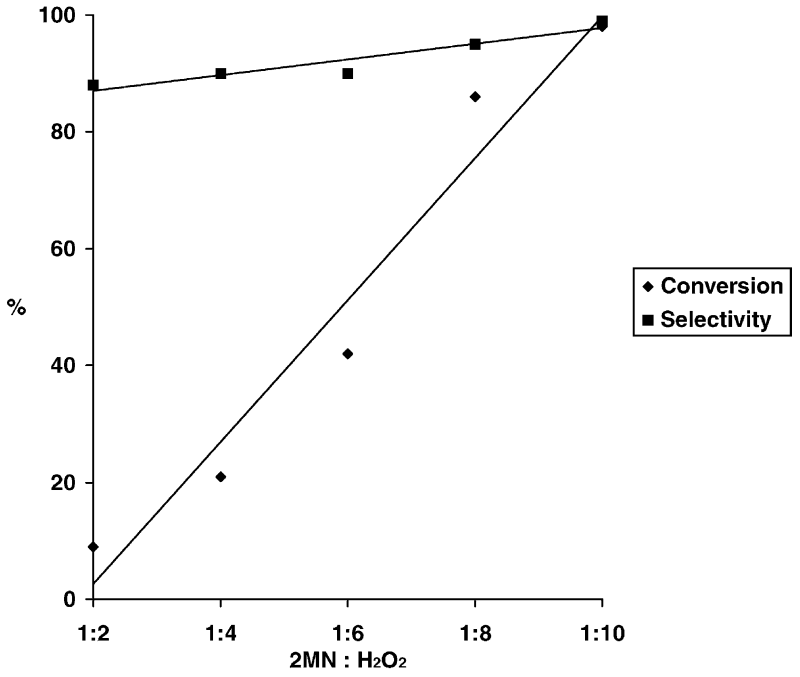


Fig. 2. Influence of molar ratio of 2-methylnaphthalene to H_2O_2: reaction temperature = 100 °C, reaction time = 3 h, acetic acid (17 M) = 20 ml.

Table 1
Oxidation of 2-methylnaphthalene with H_2O_2 in the presence of acetic acid[a]

S. no.	Temperature (°C)	Time (h)	Conversion (**I**) (%)	Yield (**II**) (%)	Selectivity (**II**) (%)
1	40	3	7	6.5	93
2	60	3	40	37	93
3	80	3	52	47	90
4	100	3	95	86	91
5	100	0.5	48	43	90
6	100	1.0	86	77	90
7	100	1.5	87	78	90
8	100	2.0	95	86	90

[a] 2-Methylnaphthalene:H_2O_2:acetic acid (20 ml) = 1:10:50 molar ratio.

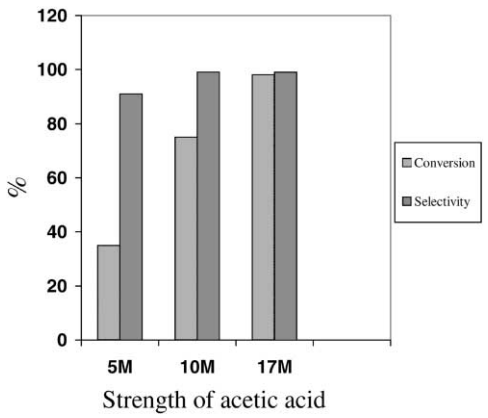


Fig. 3. Effect of acetic acid strength on oxidation of 2-methylnaphthalene: reaction temperature = 100 °C, reaction time = 3 h, molar ratio of 2-methylnaphthalene: H_2O_2 = 1:10.

3.4. Effect of temperature

Effect of temperature was studied over the reaction keeping the reaction time constant for 3 h. The influence of temperature on the oxidation of 2-methylnaphthalene is depicted in the Table 1. It may be noted that 2-methylnaphthalene (**I**) conversion dropped to 7% when the temperature was lowered from 100 to 40 °C, even though, the quinone selectivity remained unchanged at nearly ≥90%. The conversion of 2-methylnaphthalene increased with time and reached ≥90% after 3 h of reaction (Table 1). The reaction was monitored with the variation of time period. The conversion of 2-methylnaphthalene was increased with the increase in the time. The reaction was carried for 0.5, 1.0, 1.5, 2.0 and 3.0 h. As given in the fourth row, selective formation of 2-methyl-1,4-naphthoquinone is maximum when the reaction was carried out for 3 h.

4. Conclusion

Oxidation of 2-methylnaphthalene with hydrogen peroxide in the acetic acid yields 2-methyl-1,4-naphthoquinone at 100 °C without the involvement of any other catalyst. From the detailed study, it implies that this process is a very efficient one for the synthesis of Vitamin K_3 with ≥90% selectivity in the absence of a mineral acid catalyst or a solid catalyst. The use of acetic acid and hydrogen peroxide complies with the clean technology concept and clearly represents advancement for an oxidation process under economically and environmentally acceptable conditions, which hitherto used mineral acid, chromium and manganese salts for oxidation of this reaction.

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References

[1] J. Rodriguez, E. Quinoa, R. Riguera, B.M. Peters, L.M. Abrell, P. Crews, Tetrahedron 48 (1992) 6667.

[2] L.F. Fieser, M. Tushler, W.L. Sampson, J. Biol. Chem. 137 (1941) 659.
[3] M. Periasamy, M.V. Bhatt, Tetrahedron Lett. 4 (1978) 4561.
[4] R.P. Kreh, R.M. Spotnitz, J.T. Lundquist, J. Org. Chem. 54 (1989) 1526.
[5] J. Karzewski, Tetrahedron 40 (1984) 4997.
[6] S. Torri, H. Janaka, S. Nakane, Bull. Chem. Soc. Jpn. 55 (1982) 1673.
[7] H. Hiranuma, S.I. Miller, J. Org. Chem. 47 (1982) 5083.
[8] A.B. Sorokin, A. Tuel, New J. Chem. 23 (1999) 473.
[9] J. Kowalski, J. Ploszynska, A. Sobkowiak, J. Appl. Electrochem. 28 (1998) 1261.
[10] L.F. Fieser, J. Biol. Chem. 133 (1940) 391.
[11] R.A. Sheldon, Top. Curr. Chem. 164 (1993) 21.
[12] W. Adam, W.A. Herrmann, J. Lin, C.R. Saha-Moller, R.W. Fischer, J.D.G. Correia, Angew. Chem. 106 (1994) 25456.
[13] W. Adam, W.A. Herrmann, J. Lin, C.R. Saha-Moller, R.W. Fischer, J.D.G. Correia, Angew. Chem. Int. Ed. 33 (1994) 2475.
[14] W.A. Herrmann, J.J. Haider, R.W. Fischer, J. Mol. Catal. A Chem. 138 (1999) 115.
[15] S. Yamaguchi, M. Inoue, S. Enomoto, Chem. Lett. (1985) 827.
[16] W. Adam, W.A. Herrmann, J. Lin, C.R. Saha-Moller, J. Org. Chem. 59 (1994) 8281.
[17] R. Song, A. Sorokin, J. Bernadou, B. Meunier, J. Org. Chem. 62 (1997) 673.