

Rhenium-catalyzed oxidation of arenes—an improved synthesis of vitamin K₃¹

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Abstract

2-Methylnaphthalene **1** is oxidized to 2-methyl-1,4-naphthoquinone **2** by virtue of a new catalyst system in high yields and selectivity. A mixture of aqueous hydrogen peroxide and acetic anhydride is used as oxidant in the presence of methyltrioxorhenium(VII) dissolved in acetic acid as solvent. The concentration of acetic acid in the reaction mixture plays a crucial role for the activation of acetic anhydride mediated by methyltrioxorhenium(VII). © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Methyltrioxorhenium; Arene oxidation; Hydrogen peroxide; Acetic anhydride; Vitamin K₃

1. Introduction

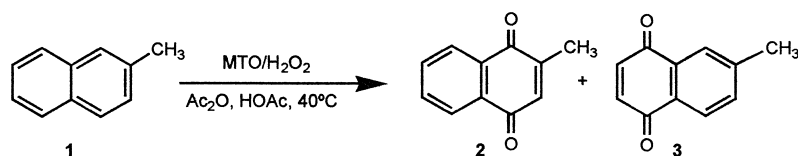
Vitamin K₃ (2-methyl-1,4-naphthoquinone, ‘menadione’) **2** displays the antihemorrhagic activity of vitamin K (phylloquinone). The compound is produced on industrial scale, e.g., by stoichiometric oxidation of 2-methylnaphthalene with chromium trioxide in sulfuric acid [1]. The drawbacks of this method are obvious: production of inorganic salts as by-product (18 kg of salt per kg of product) and a necessary treatment of chromium-containing waste-water. Other stoichiometric procedures have been proposed in the literature [2,3] but remain question-

able both from an economic and environmental point of view. Therefore, the use of hydrogen peroxide as a ‘clean’ oxidant in catalytic processes represents a beneficial alternative (Scheme 1).

Rhenium complexes like methyltrioxorhenium(VII) (CH₃ReO₃, MTO) **4** show catalytic activity in olefin epoxidation, Baeyer–Villiger-oxidation and oxidation of arenes such as methylnaphthalene, phenanthrene, methoxybenzene and alkylsubstituted phenol derivatives yielding the respective *p*-quinones [4–8]. Major advantages of rhenium-mediated oxidations are their versatility and low-waste technology (salt-free and halogen free oxidation processes). The catalyst can be readily obtained from dirheniumheptoxide and tetramethyltin as starting material or by a novel procedure allowing perrhenate recycling [4,5].

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¹ Communication 173 of the series Multiple Bonds between Main-Group Elements and Transition Metals. Preceding paper, Ref. [14].



Scheme 1. Catalytic oxidation of 2-methylnaphthalene **1** by H₂O₂ in acetic anhydride/acetic acid with methyltrioxorhenium(VII) as catalyst.

When hydrogen peroxide is added to MTO, the rhenium compound is stepwise converted to the monoperoxo- and bisperoxorhenium complex CH₃Re(O₂)₂O · H₂O. The latter has been isolated and characterized by X-ray crystallography and exhibits high activity and selectivity in the conversion of arenes to quinones and is considered to be the catalytically active species [4,5].

Previous catalytic experiments with MTO and H₂O₂ in different solvents have shown an increase of reactivity by application of carboxylic acids in contrast to non-acidic conditions (THF) [8]. In both cases the catalyst lifetime has been limited by slow hydrolysis of the active species to catalytically inactive perrhenate salts as a direct consequence of the inevitable formation of water as oxidation product [4,5,9,10].

In this paper we report how acetic anhydride can serve as a water-trapping agent and as a precursor for percarboxylic acid leading to an increase in catalytic activity and further improvement of the catalyst's lifetime.

2. Results and discussion

The role of MTO as catalyst and the role of acetic anhydride as an auxiliary agent was studied in detail.

From an industrial point of view acetic anhydride has two additional advantages. As an inexpensive, organic solvent it improves the solubility of naphthalene derivatives in the reaction. It can be easily removed from the reaction mixture together with the solvent since any reaction of acetic anhydride (hydrolysis, in situ formation and subsequent reactions of peroxy-

acetic acid) gives acetic acid (solvent) as a final product facilitating the work-up procedure. No multi-component mixtures are produced and the use of drying agents like magnesium sulfate or sodium sulfate can be avoided, i.e., the oxidation process can still be carried out under salt- and halogen-free conditions.

2.1. Influence of acetic anhydride on catalytic activity of methyltrioxorhenium(VII)

For kinetic studies, a standard experiment was employed: 2-methylnaphthalene was chosen as a probe and oxidized with H₂O₂ (85 wt.%) at 40°C for 4 h under nitrogen to exclude any influence of oxygen. The molar ratio of arene/oxidant (1:7) was held constant throughout all experiments. The course of the reaction was monitored quantitatively by GC.

Fig. 1 shows the formation of 2-methyl-1,4-naphthoquinone in three different experiments performed under standard conditions as mentioned above.

In the uncatalyzed reaction (experiment (a)) the oxidation of 2-methylnaphthalene in a mixture of acetic anhydride/acetic acid (1:2) occurs rather slowly giving 2-methyl-1,4-naphthoquinone in 10% yield. Experiment (b) was performed in the presence of 1.0 mol% MTO in acetic acid as sole solvent (molecular ratio of arene:H₂O₂:MTO = 1:7:0.01) yielding 20% menadione. Finally, experiment (c) was carried out in the presence of 1.0 mol% MTO in acetic anhydride/acetic acid (1:2). Under these conditions a maximum yield of 46% menadione is obtained.

Comparison of experiment (a) and (c) in Fig. 1 clearly shows the catalytic role of MTO. In

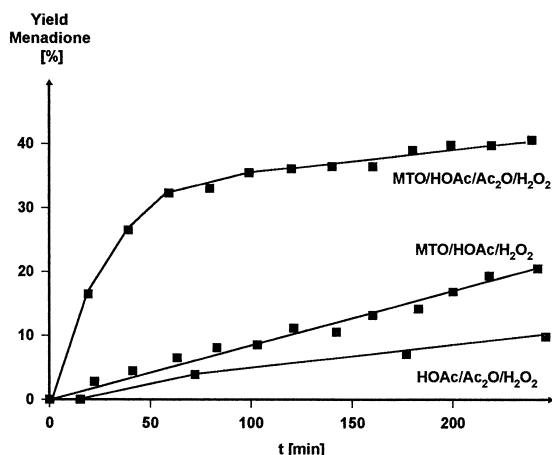


Fig. 1. Formation of 2-methyl-1,4-naphthoquinone under standard conditions: (a) uncatalyzed reaction acetic anhydride/acetic acid (1:2), (b) MTO-catalyzed reaction (1.0 mol%) in acetic acid, (c) MTO-catalyzed reaction (1.0 mol%) in acetic anhydride/acetic acid (1:2). Abbreviations: MTO = methyltrioxorhenium(VII), Ac_2O = acetic anhydride, HOAc = acetic acid, H_2O_2 = hydrogen peroxide.

addition to this fact, comparison of the experiments (b) and (c) indicates an increase of menadione yield from 20 to 40% caused by the change from acetic acid as solvent to the acetic anhydride/acetic acid system. Thus, a simple accumulation effect by methylbisperoxorhenium(VII) mediated oxidation and oxidation caused by in situ formation of peracid without contribution of MTO can be clearly ruled out (see Fig. 1).

The anhydride/acid ratio also has a pronounced effect on the activity of the system. For a detailed study, the standard experiment was performed with 1.0 mol% MTO and systematic variation of the acetic anhydride/acetic acid ratio (molecular ratio of arene/ H_2O_2 /MTO 1:7:0.01). The results are shown in Fig. 2.

Starting from acetic acid as solvent, catalytic activity rises together with increasing acetic anhydride quantities to reach peak activity at a molar ratio of Ac_2O /HOAc (1:2). As the concentration of acetic anhydride increases further, the activity of the system decreases, finally leading to 5% conversion of 2-methylnaphthalene in pure anhydride. The following con-

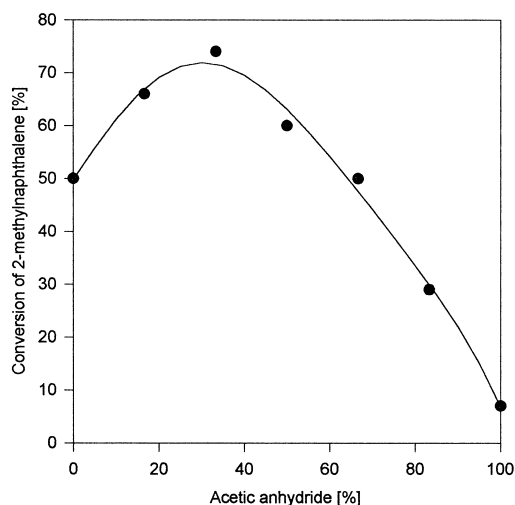


Fig. 2. Peak activity depending on acetic anhydride concentration. Oxidation of 2-methylnaphthalene on acetic anhydride/acetic acid ratio under standard conditions (arene/ H_2O_2 /MTO (1:7:0.01); 40°C, 4 h, N_2 -atmosphere).

clusions can be drawn from these observations: As to its potential use as water-trapping agent, hydrolysis of acetic anhydride seems to play a less important role in the catalytic cycle. This can be seen from the reaction in pure acetic anhydride: fast acetic anhydride hydrolysis would increase the acetic acid concentration resulting in an enhanced conversion of 2-methylnaphthalene which, however, has not been observed within reaction time (cf. Fig. 3). This means the presence of acetic acid is necessary for the reaction system to be activated since MTO does not work as efficient catalyst in pure

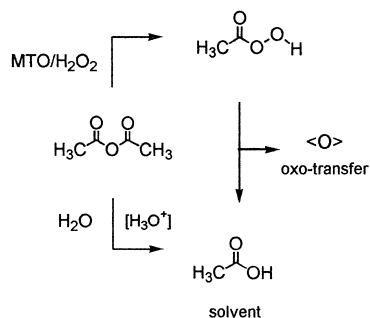


Fig. 3. Acetic anhydride proposed as auxiliary agent (precursor for peroxyacetic acid and water-trapping agent) improving catalyst performance and lifetime.

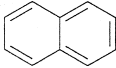
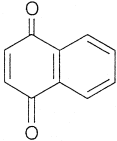
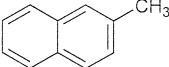
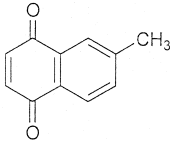
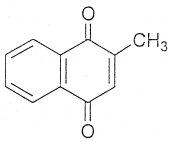
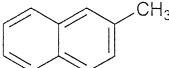
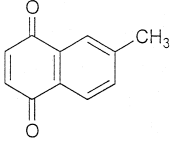
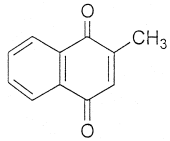
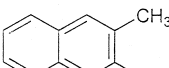
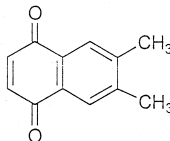
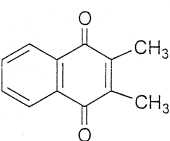
acetic anhydride. In this context the observation of peak reactivity for an anhydride/acid ratio of 1:2 is remarkable since the molar amount of acetic anhydride is equal to the molar amount of hydrogen peroxide in the reaction solution under starting conditions.

Thus, it is reasonable to assume two reaction pathways: direct oxidation by in situ formed rhenium bisperoxo complex and simultaneously MTO-catalyzed in situ generation of peroxyacetic acid as oxidant from acetic anhydride.

The results under ‘anhydride conditions’ (MTO/H₂O₂/Ac₂O/HOAc) strongly suggest MTO-catalyzed in situ formation of peroxyacetic acid as additional oxidant which has not played a major role in acetic acid as solvent so far [8]. This hypothesis is supported by a series of control experiments [11,12]: iodometric titration for determination of the total oxidative active oxygen content, followed by a permanganometric titration for determination of the H₂O₂-content. The difference of these two titra-

Table 1

Comparison of naphthoquinone formation under optimized conditions (arene/H₂O₂/MTO (1:7:0.01) in Ac₂O/HOAc (1:2); 40°C, 4 h, N₂-atmosphere)

Substrate	Conv. [%]	M.B. ^[a] [%]	Product and Yields ^[b] [%]	
	55	56		11
	65 ^[c]	79 ^[c]		5 (8) ^[c]
				39 (60) ^[c]
	89	63		6 (7)
				46 (52)
	72	94		10 (14)
				56 (77)

^aM.B. = mass balance of isolated, characterized product and recovered starting material.

^bThe yields in parentheses are corrected for converted starting material.

^cInstead of 1.0 mol% an amount of 0.5 mol% MTO was used.

tions represents the amount of in situ formed peroxyacetic acid: under ‘anhydride conditions’ (MTO/H₂O₂/Ac₂O/HOAc) 37% of hydrogen peroxide was converted into peroxyacetic acid which corresponds to 2.6 equivalents of peracid with respect to the substrate. This result accounts for the function of acetic anhydride as a more favorable peracid precursor than direct formation from acetic acid. On the other hand, the excess of peroxyacetic acid needed for the increase in reactivity also shows a lower efficiency of the peracid pathway compared to the rhenium bisperoxo complex mediated pathway.

2.2. Comparison of naphthalene derivatives as substrates in the MTO-catalyzed oxidation under ‘anhydride conditions’

Working with an optimized anhydride/acid ratio, our attention now focuses on oxidation activity and regioselectivity of the MTO/H₂O₂/Ac₂O/HOAc system towards electron-rich arenes as substrates. Naphthalene, 2-methylnaphthalene and 2,3-dimethylnaphthalene were chosen as substrates for a comparative study (Table 1).

Two tendencies can be seen from Table 1: (1) The conversion of arene and the yield of quinone rises with the number of methyl groups as electron-donating substituents at the aromatic ring. Naphthalene, representing the most electron-deficient derivative, shows the lowest reactivity (11% 1,4-naphthoquinone at 55% total conversion). Due to its higher reactivity 2-methylnaphthalene yields 46% 2-methyl-1,4-naphthoquinone at 89% conversion. The best quinone yield (56%) is obtained for 2,3-dimethylnaphthalene. (2) The high regioselectivities found compare well with known results from the literature [9]. In the case of 2-methylnaphthoquinone a 89:11 ratio for 2- and 7-methylnaphthoquinone and 85:15 for 2,3-methylnaphthoquinone regioisomers are obtained. The high excess of quinone with the higher number of substituents at the quinoid ring is a characteristic feature of the rhenium-catalyzed process.

These results remarkably differ from regioselectivities obtained with porphyrin systems: in a recent study, B. Meunier used metalloporphyrins (5 mol%) as catalyst in the oxidation of 2-methylnaphthalene with caroate as oxidant [13]. Although higher total quinone yields (86%) were reported, a vitamin K₃ selectivity of 53% indicate a shift towards the less favored regioisomer.

3. Conclusion

The application of acetic anhydride in combination with acetic acid as solvent system improves the known MTO-catalyzed oxidation procedure for aromatic compounds. Best results are obtained with an anhydride/acid ratio of 1:2.

A comparison with other results from the literature shows a very low need of catalyst (0.5–1.0 mol% or 25–50% of our previously published procedure [9], respectively) and yields vitamin K₃ with a regioselectivity of up to 89%. The reaction concept presented is not limited to the acetic anhydride/acetic acid system and can be generally transferred to other anhydride/acid systems which are under current investigations and will be reported at a later time. The use of acetic anhydride, acetic acid and hydrogen peroxide complies with the demand for low-waste technologies and clearly represents an advance for an oxidation process under environmentally acceptable conditions.

4. Experimental

4.1. Materials and methods

4.1.1. Materials

Methyltrioxorhenium(VII) was prepared according to the previously reported methods [4,5]. H₂O₂ (85%) was purchased from Peroxid, Pullach bei München, Germany. Naphthalene (Merck), 2-methylnaphthalene (Aldrich), 2,3-di-

methylnaphthalene (Roth), 2-methyl-1,4-naphthoquinone (Aldrich), diethyleneglycol dibutylether (Merck), concentrated acetic acid (Aldrich) and acetic anhydride (Fluka) were of analytical purity and used without further purification. 2,3-Dimethylnaphthoquinone was synthesized according to the general method given in the section below.

4.1.2. Instrumentation

The reaction course was monitored by quantitative gas chromatography on a Hewlett-Packard (HP 5970 B) instrument equipped with a mass-selective detector (HP 5970 B) and integration unit (HP 3394). Calibration curves for naphthalene, 2-methylnaphthalene and 2-methyl-1,4-naphthoquinone were recorded using diethyleneglycol dibutylether as internal standard. The regioselectivity was determined by GC/MS. The regioisomers could be clearly identified due to different patterns of decay in the mass spectra and comparison with reference substances.

All reactions were carried out by careful control of temperature in a thermostated reaction vessel at 40°C. Although no difference was observed between inert and non-inert conditions all reactions were performed under inert conditions to exclude any influence of oxygen.

4.2. MTO-catalyzed oxidation of naphthalene derivatives

4.2.1. General procedure (A) for the oxidation of naphthalene in acetic anhydride / acetic acid

To a solution of 2-methylnaphthalene 1.00 g (7 mmol), 500 mg of diethyleneglycol dibutylether (internal standard) and 17 mg CH_3ReO_3 (70 μmol) in 5 ml acetic anhydride and 10 ml acetic acid, 49 mmol aqueous hydrogen peroxide (85 wt.%) were added and stirred for 4 h at 40°C under careful control of the reaction temperature. The course of the reaction was monitored by GC. Samples were taken at 20 min intervals.

For product isolation 10 ml water were added followed by extraction with 3×20 ml CH_2Cl_2 . The collected organic extracts were dried over sodium sulfate and the solvent was removed in vacuo. The raw product obtained was recrystallized in purity higher than 98% ($^1\text{H-NMR}$) from ethanol (yield: 550 mg, 45%). Naphthalene and 2,3-dimethylnaphthalene were oxidized following the same procedure.

4.2.2. General procedure (B) for the oxidation of 2-methylnaphthalene under varying acetic anhydride / acetic acid ratio

Method A was followed except for systematic variation of the acetic anhydride/acetic acid ratio (0:6, 1:5; 1:2; 1:1, 2:1; 5:1; 6:0).

4.2.3. General procedure (C) for the oxidation of 2-methylnaphthalene with peroxyacetic acid in acetic acid (control experiment)

To a solution of 1.00 g (7 mmol) 2-methylnaphthalene, 500 mg of diethyleneglycol dibutylether (internal standard) and CH_3ReO_3 (14 μmol) in 5 ml acetic acid, 10 ml peroxyacetic acid (32 wt.%) was added and vigorously stirred for 4 h at 40°C under careful control of the reaction temperature. The product was isolated as in general procedure A.

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