Tungstosilicic Acid ($H_4SiW_{12}O_{40}$) Have Efficient Catalysts for Synthesis of 2,3-Dihydroxynaphthoquinone from Lawsone

Nassima Benferrah[1]*, Mohamed Hammadi[2]*, Hadjila Dokari[2] and Didier Villemin[3]

[1]URMPE Research Unit for Materials, Processes and Environment, University M'hamed Bougara Boumerdes, Faculty of Engineering Sciences, Boumerdes, 35000, Algeria

[2]Laboratory petrochemical synthesis University M'hamed Bougara Boumerdes, Faculty of hydrocarbons and chemistry, 35000, Boumerdes, Algeria

[3]Ensicaen, LCMT—UMR 6507 CNRS, University of Caen, Caen 14050, France

ABSTRACT

The Thiele–Winter reaction is of interest for synthesis of tetracetoxyaromatic precursors of hydroxynaphtoquinones. Solid acids such as Tungstosilicic acid ($H_4SiW_{12}O_{40}$) have an efficient catalyst in acetoxylation reaction of naphtoquinones without the use of organic solvent at room temperature. 1,2,3,4-Tetrahydroxynaphthalene was easily oxidized at room temperature in 2,3-Dihydroxynaphthoquinone by using (Pc[Co]/K10) and air (1 atm). We have also tested this type of reaction in 2-hydroxynaphthoquinone (Lawsone). Many naphthoquinones are natural products with interesting biological properties.

Keywords: Heteropolyacids, Without solvent, Room temperature, Lawsone, Catalytic system (Pc[Co]/K10)

INTRODUCTION

The founding principles of green chemistry are mainly based on:

- The removal, if possible, of pollutant solvents that do not respect the environment. Nowadays, the use of inorganic solid acid catalysts in dry reactions (without organic solvent) offers many possibilities in the field of organic synthesis. Indeed they provide a simplification of the experimental protocols, easy recycling, and thereby easy protection of the environment.

- The improvement in the energy efficiency that beneficially affects the economy and the environment that must be considered and should be minimized by the development of synthetic methods at room temperature conditions.

One of the main problems in the chemical industry is the search for tolerable procedures for chemical production. There is a growing demand for the development of selective, efficient, and environmentally appropriate synthetic methods. Organic solvents are not only expensive, but are often flammable, toxic, and hazardous. Generally the use of solvent is considered to be necessary in organic reactions. The hydroxynaphthoquinones [1] are well-known substances for their chemical and biologic properties [2]. The hydroxynaphthoquinones including Phthiocol [3], Lawsone [4,5], Juglone [6,7], and Atovaquone [8] have gained much interest due to their presence in natural products and their pharmacological properties as antitumoral, antiprotozoal, anti-inflammatory, antiviral, and antifungal [9,10].

We have used this methodology to prepare the acetoxylation reactions of 2-hydroxynaphtoquinone acid-catalyzed by heteropolyacid $H_4SiW_{12}O_{40}$, in the absence of solvent at room temperature.

Our attention has focused on the use of metallic phthalocyanines supported in the oxidative reactions of naphthotriols prepared from the Thiele–Winter reaction in order to synthesize hydroxynaphthoquinone natural products having antibiotic properties. The acetoxylation reaction of Lawsone with acetic anhydride $(CH_3CO)_2O$ catalyzed by sulfuric acid H_2SO_4 [11,12]

(Ho=-11.94), at room temperature is slow with low yields especially in the presence of substituents on the naphthoquinone as electron donors. Sulfuric acid (H_2SO_4) was replaced by chlorozincique acid [13] and tetrafluoroboric acid [1] with low yields. To overcome this problem where the acidity of the medium thus protonation of the 2-hydroxynaphtoquinone is the decisive step, we opted for the use of solid super acid as heterogeneous conditions in the heteropolyacid: $H_4SiW_{12}O_{40}$. In our work we are particularly interested in the synthesis of 2,3-dihydroxy-1,4-naphthoquinone (3). Transformation of lawsone into tetracetoxy (2) by the Thiele–Winter reaction. The saponification of (2) followed by catalytic oxidation *in situ* of naphthotriols is shown in Scheme 1.

MATERIALS AND METHODS

Melting points (m.p.) were determined with a Kofler hot apparatus and are uncorrected. Proton NMR spectra (PMR) were determined on Brucker AC 250 (250 MHz, CDCl3, Me4Si). The IR spectra were recorded as KBr pellets on Perkin Elmer 16 PC FT-IR spectrometer. UV–visible spectra (λmax log(ε)) were obtained with spectrophotometer Perkin-Elmer Lamda 15.

Microwave irradiation was carried out with a commercial microwave oven (Toschiba ER 7620) at 2,450 MHz, Mass spectra were carried out on a Nermag Riber R10; TLC analyses were performed by using Kieselgel Schleicher and Shull F 1500 Ls 254 and Merck 60F 254. The grinding of products was carried out on analytical grinder A 10 of Janke and Kenkel-IKA Labortechnik.

Spectroscopic characterization of lawsone (2-Hydroxy-1,4-naphthoquinone)

Orange solid, yield: 79%, m.p: 194°C; UV-visible λmax log(ε) (dioxane/H_2O) nm: 276.3 (4.48), 334.3 (3.28); IR (KBr) cm^{-1}: 3166 (υ OH), 1676 (υ C=O), 1592, 1170, 874, 668, 536; ^{1}H NMR (CDCl3): δ 6.37 (s, 1H, OH); 7.26 (s, 1H, H arom.); 7.25-8.14 (m, 4H, H arom); $C_{10}H_6O_3$, calcd: H, 3.47%; C, 68.97%; found: H, 3.53%; C, 68.92%.

Phthalocyanine (Co) supported on K10 (1)

Preparation of montmorillonite K10 exchanged by Co^{2+}

In a 250 ml flask, the Montmorillonite K10 (20 g) was added to a solution of metallic salt CoCl2 (0.2 mol) dissolved in 100 ml of distilled water. The reaction al mixture was stirred for 24 h at room temperature. The suspension was washed twice with distilled water then centrifuged. The Montmorillonite exchanged by Co^{2+} was washed with methanol and recentrifuged. The solid was dried for 24 h in vacuum then finely ground. The final product was a clear beige color.

Phthalocyanine intercalated in the montmorillonite K10

A solution of phthalonitrile (20 mmol; 2.56 g) dissolved in 20 ml of dichloromethane was added to the solid Montmorillonite K10 (5 g) exchanged with some metallic cations (Co^{2+}). After contact for 2 h, the remaining liquid was evaporated under reduced pressure. The activation of the solid under microwave irradiation (MO): p=power, t=time of irradiation) was carried out in a resonance cavity. After cooling, the solid was successively washed with water, acetone (20 ml), and then with dichloromethane (20 ml). The solid was dried under

reduced pressure and the extracted with acetonitrile as a solvent using a Soxhlet for 8 h. Catalysts were characterized by FT-IR; electronic spectra of metalated phthalocyanine intercalated into Montmorillonite were very close to those observed with pure metalated phthalocyanine, but the bands were shifted.

Pc[Co] supported on K10 (1)

Microwaves irradiation Resonance Cavity. (p=630 W, t=10 min); Purple solid, m.p > 300°C $C_{32}H_{16}CoN_8$; yields: 85%, UV-visible λmax log(ε) / (1-chloronaphthalene) nm: 669.5 (4.42); 642.1 (3.88); 604.2 (3.78); 580.1 (3.22); IR (KBr) cm^{-1}: 1636, 1522, 1400, 1044, 870, 796, 756, 532, 525, 466.

Acetoxylation reaction under heterogeneous conditions (solid acids)

In a typical experiment, 10 mmol of Lawsone were dissolved in acetic anhydre (0.2 mol; 21.64 g). One gram of catalyst ($H_4SiW_{12}O_{40}$) was added and the mixture was stirred at room temperature. After 48 h, the products were separated by chromatography on a silica column eluted successfully with ethyl acetate/cyclohexane (10/90). The different fractions gave, respectively, a yellow solid (unreacted quinone) and a beige solid (1,2,3,4- tetracetoxynaphthalene) (2). It must be noted that traces of products of diacetylation could be detected by thin-layer chromatography (TLC).
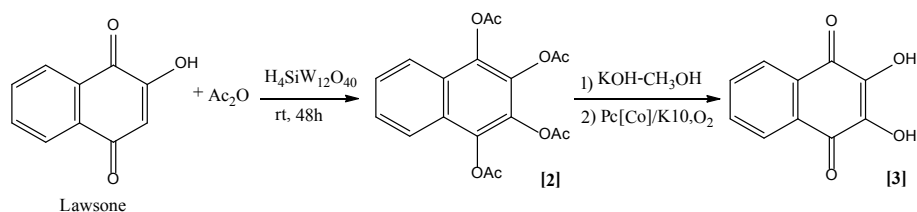
Scheme 1: Synthesis of 3 from Lawsone

1,2,3,4-tetracetoxynaphthalene (2)

Beige solid, yield 66%, m.p: 140-143°C, $C_{18}H_{16}O_8$; IR (KBr) cm^{-1} : 3012 (υ CH arom.), 1760 (υ OCOCH$_3$), 1718; ^{1}H NMR (CDCl$_3$): δ 2.39 (s, 6H, OCOCH$_3$); 2.44 (s, 6H, OCOCH$_3$); 7.46-8.14 (m, 4H, H arom.); MS m/z (%); 360 (M$^+$; 24.46), 318 (3.41), 276 (16.38), 192 (100), 146 (11.95), 105 (23.55).

Saponification and oxidation in situ

In a typical experiment, a current of air is passed through a U tube fitted with a filter flask. The tube contains the (Pc(Co)/K10 (0.1 g) in suspension in a solution of product (2) (0.6 g) dissolved in CH$_3$OH (20 ml) and KOH (2 g) for 6 h at room temperature. After filtration and evaporation of the methanol, the product (3) is crystallized.

2,3-Dihydroxy-1,4-naphthoquinone (3)

Beige clear solid, yield: 91%, m.p: 201°C, $C_{10}H_6O_4$, UV-visible λmax log(ε) (dioxane/H$_2$O) nm: 289.3 (4.77), 339.3 (3.27); IR (KBr) cm^{-1}: 3172 (υ OH), 1678 (γ C=O), 1589, 1174, 878, 536; ^{1}H NMR (CDC$_{l3}$): δ 6.41 (s, 1H, OH); 6.42 (s, 1H, OH); 7.31-8.11 (d, 4H, H arom).

Table 1: Acetoxylation of Lawsone at 20°C

Catalyst	Aspect	Hammet: Ho	Experimental	M.p.(°C)	IR vester (cm^{-1})	Yield (%)
ClSO$_3$H	Liquid	-13.80	20°C, 20 h	149	1772	54
H$_3$PW$_{12}$O$_{40}$	Solid	-13.6	20°C, 48h	149	1768	61
H$_3$PMo$_{12}$O$_{40}$	Solid	-	20°C, 48 h	-	-	-
H$_4$SiW$_{12}$O$_{40}$	Solid	-	20°C, 48 h	152	1760	66

Table 2: Tungstosilicic acid (H$_4$SiW$_{12}$O$_{40}$) as catalyst for oxidation by molecular oxygen

1) Thiele-Winter: tetracetoxyaromatic	2) [Saponification–oxidation] *in situ*
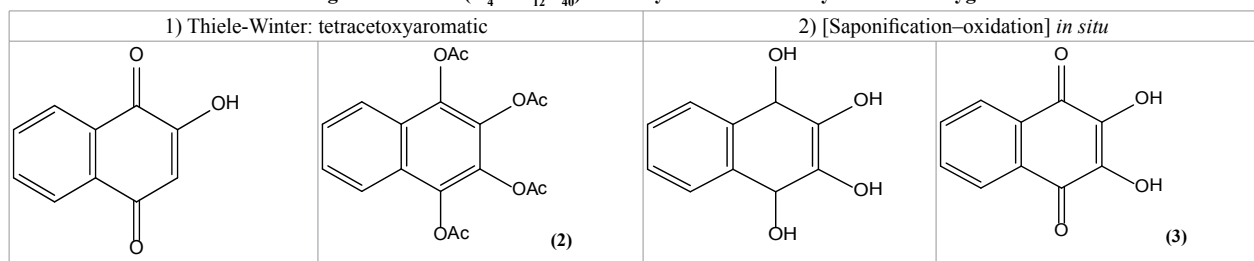
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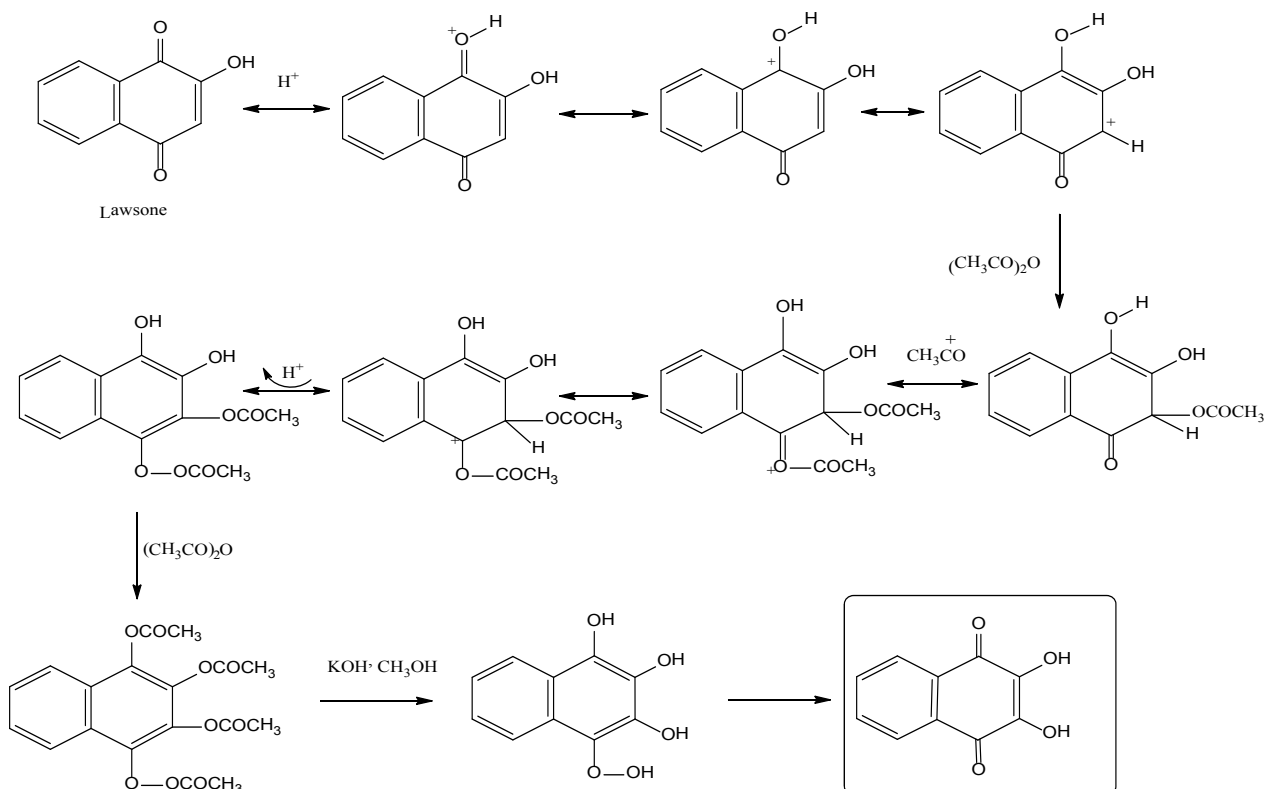
RESULTS AND DISCUSSION

Thiele–winter reaction

The 2-hydroxynaphthoquinone (Lawsone) treated with acetic anhydride in the presence of solid acid converts into the 1,2,3,4-tetracetoxynaphthalene (2) (yield 66%).

We have studied this reaction with strong acids. Chlorosulfonique acid (Ho=13.80) [14-16] led to the desired product. The reaction with solid super acids shows a high Brônsted acidity.

Heteropolyacids (HPAs also called polyoxometalates) are catalysts of very great interest [17,18]. The display has a very high Brônsted acidity close to super acids.

We decided to test three heteropolyacids $H_3PW_{12}O_{40}$ (PW), $H_4SiW_{12}O_{40}$ (SiW), and $H_3PMo_{12}O_{40}$ (PMO). The SiW provided the product with a yield of 66% whereas a yield of 61% was achieved with the PW. It has been noticed that the SiW appeared a better catalyst than the PW. This could be because of the higher ratio of the number of protons in SiW [19].

We have noticed that no product (3) was obtained with the $H_3PMo_{12}O_{40}$ (PMO). The reaction medium color changed from green to deep blue, proving the reduction of PMO. The result with PMO is not surprising owing to its high redox potential resulting from the presence of the molybdenum atom. Results of acetoxylation of Lawsone by acetic anhydride obtained from different acids catalysts are reported in Table 1.

The 1,2,3,4-tetracetoxynaphthalene (2) was easily transformed into (3) by saponification basic and oxidation with potassium hydroxide (KOH) in methanol (CH_3OH) in the presence of air at room temperature. The yield of 2,3-dihydroxy-1,4-naphthoquinone from (3) is good (91%). The results obtained from the two-step sequence (tetracetoxyaromatic and saponification–oxidation *in situ*) are reported in Table 2.

CONCLUSION

In conclusion it appears that heteropolyacids ($H_4SiW_{12}O_{40}$) can easily catalyze the Thiele-Winter reaction. This work represents the first example of catalysis of this reaction by solid acids. The sequence of the two steps (acetoxylation, saponification-oxidation) constitutes a new synthesis of 2,3-dihydroxynaphthoquinones from Lawsone.

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