

# Aerobic oxidation of aryl-himachalene using a combination of N-hydroxy phthalimide and cobalt(II) acetoacetate

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## Abstract

An efficient aerobic oxidation of Ar-himachalene as bio-natural sesquiterpene employing the N-hydroxyphthalimide (NHPI), under mild conditions in presence of cobalt (II) afforded the corresponding alcohol, aldehyd and carboxylic acid in excellent yield and good selectivities.

**Keywords :** Aerobic oxidation, Ar-himachalene, sesquiterpene, NHPI.

## 1. Introduction

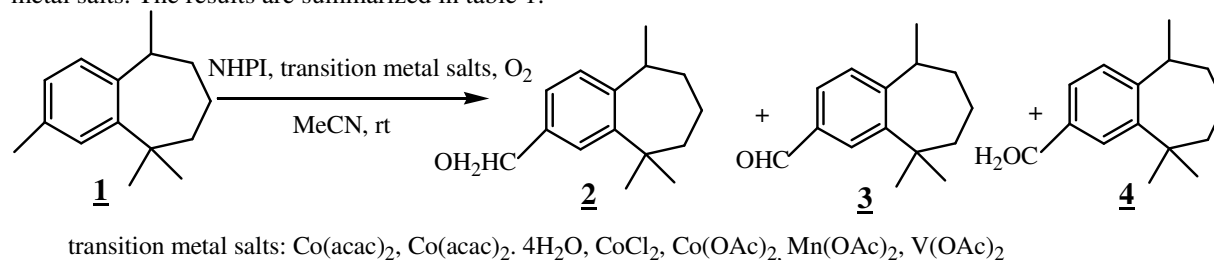
The Atlas cedar forests have an important role in the socio-economy of Morocco, for the exploitation of this floral we have directed our research towards the Atlas cedar. The essential cedar oil is mainly composed of the sesquiterpene hydrocarbons  $\alpha$ -,  $\beta$ - and  $\gamma$ -himachalene, which together can make up almost 70% of the composition (Chalchat et al. 1994), and male-produced pheromone component of the flea beetle *Aphthona flava* (Lis-Balchin et al. 1998) constitute only 0.5% in total of the oil. Essential oils are an extremely useful source of starting material for several industrial processes used for the synthesis of fragrances and pharmaceutical compounds.

The oxidation of methyl aromatic hydrocarbons is of great scientific, technological, and commercial importance (Mori 2005) especially for the production of oxygen-containing compounds like alcohols, aldehydes, and carboxylic acids. Several methods reported, such as the oxidation by potassium permanganate in aqueous trifluoroacetic acid (Partenheimer 1995), surfactant assisted permanganate oxidation (Suresh et al. 2000).

As a part of our ongoing program in developing various new functionalized sesquiterpene high added value compounds, using cheap and eco-friendly materials as catalysts (Ziyat et al. 2004a, 2004b; Hossini et al. 2011a, 2011b; Abouhamza et al. 2001). Herein, we report an efficient oxidation of aromatic alkyl by aerobic oxidation of Ar-himachalene using the NHPI catalyst, in the presence of catalytic amount cobalt salt, to give selectively corresponding alcohol, aldehyd, and carboxylic acid with excellent yield.

## 2. Result and discussion

Our initial studies were focused on the optimization of the reaction conditions for oxidation reaction of aryl-himachalene (**1**), under dioxygen atmosphere (1atm) in the presence of a catalytic amount of NHPI and transition metal salts. The results are summarized in table 1.



Scheme 1. Aerobic oxidation of aryl-himachalene

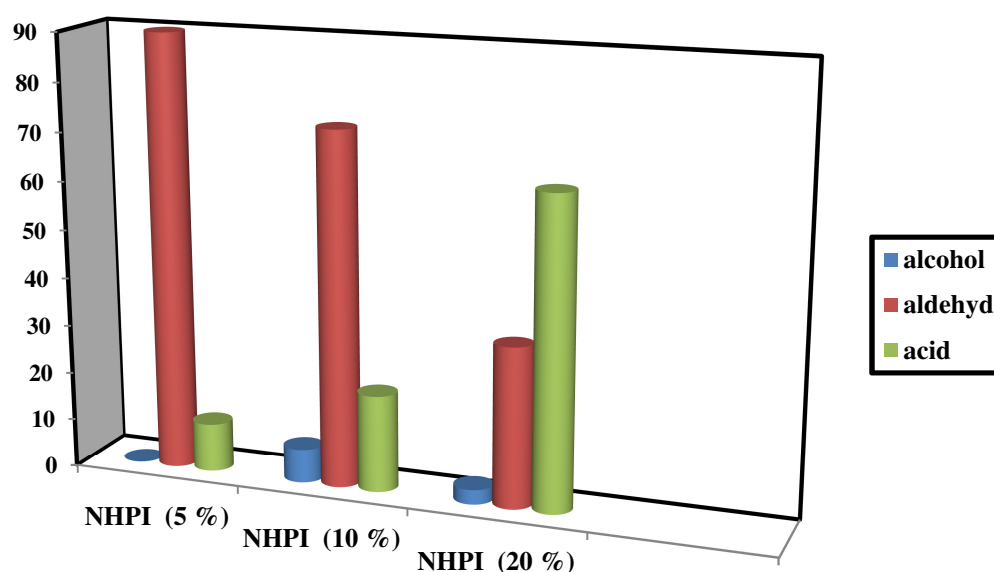
Table1. Oxidation of ar-himachalene (1) catalysed by NHPI at r.t in the presence of transition metal salts.

Entry <sup>a</sup>	Catalyst/metal salts <sup>b</sup>	Time (h)	Conversion %	Selectivity <sup>a</sup> %		
				2	3	4
1	NHPI	16	none	-	-	-
2	NHPI/Co(OAc) <sub>2</sub>	16	67	7	73	20
3	NHPI/ Mn(OAc) <sub>2</sub>	22	59	17	71	12
4	NHPI/V(OAc) <sub>2</sub>	22	51	14	74	16
5	NHPI/Co(acac) <sub>2</sub>	20	63	10	75	15
6	NHPI/Co(OAc) <sub>2</sub> .4H <sub>2</sub> O	24	49	14	80	6
7	NHPI/CoCl <sub>2</sub>	24	52	22	78	-

<sup>a</sup> All entries were carried out in acetonitrile. <sup>b</sup> NHPI/metal salt (10 %, 1%). <sup>c</sup> Selectivity obtained by CPV.

As it can be seen from table 1, all used metal salts have allowed to the selective oxidation of benzyl methyl. Cobalt salts are the most effective, especially Co (OAc)<sub>2</sub> which gives a much higher conversion (67%), in just 16h. we note also that only the benzylic methyl was oxidized while the saturated ring of our substrate remains intact. The Co(acac)<sub>2</sub> also gives a fairly good conversion which is 63% after 20h of reaction. For other salts, the conversions obtained are modest; this may be explained in part by their low solubility in acetonitrile.

In order to optimize the amount of NHPI, three ratio of NHPI/Ar-himachalene waere used in combination with Co(acac)<sub>2</sub> to catalyse the oxidation of ar-himachalene in acetonitrile. The follow diagram illustrates the obtained results.



**Figure1.** Effect of the ratio (NHPI/Ar-himachalene) on the oxidation of aryl-himachalene

With 5% of NHPI, we get only the aldehyd (3) and carboxylic acid (4), while with larger quantities we get more alcohol (2). We also note that when we minimize the studied ratio, the formation of the aldehyd (3) is preferred (90%), in the contrary the formation of carboxylic acid (4) is the preferred (64%).

To inspect suitable solvents to convert 1 to 2, 3 and 4, the effect of several solvents was studied under NHPI (10%) and O<sub>2</sub> (1atm) at room temperature for 16 to 20h (Table 2).

Table 2. Effect of solvent on the oxidation of ar-himachalene

Entry <sup>a</sup>	Solvent	Time (h)	Conversion%	Selectivity <sup>b</sup> %		
				2	3	4
2	MeCN	16	67	7	73	20
8	AcOH	20	54	15	79	16
9	AcOEt	20	49	19	67	14

<sup>a</sup> All entries were allowed in the presence of NHPI (10%) and O<sub>2</sub> (1atm) at room temperature in other study, the oxidation reaction of aryl-himachalene was checked in several solvents to recognize the efficiency of the solvent. The best conversion is obtained in acetonitrile with 67%, after 16h of reaction. In addition, all solvents promote oxidation of ar-himachalene to the corresponding aldehyd (3). The largest conversion to alcohol (2) was obtained in the use of ethyl acetate, while acetic acid allows to the best conversion to corresponding aldehyde (3) which is 79%. We have also studied the effect of temperature on the course of the oxidation of ar-himachalene. Table 3 summarizes representative results for this oxidation.

Table 3. Effect of the temperature on the course of ar-himachalene oxidation

Entry	Temp (°C)	Conversion %	Alcohol	Aldehyd	Acide
2	r.t	67	7	73	20
10	50 °C	81	11	35	54
11	100 °C	97	0	13	87

It results from this study that the increase of temperature has a beneficial effect on the conversion of the reaction, since it rose from 67% at room temperature to 97% at 100 °C. Moreover, at 50°C the conversion stops at 81%, favoring the formation of acid with a loss of conversion to aldehyd

In order to detail these results, the evolution of the oxidation of aryl-himachalene at 100°C was followed by gas chromatography. The results obtained are shown in the following diagram (fig 2).

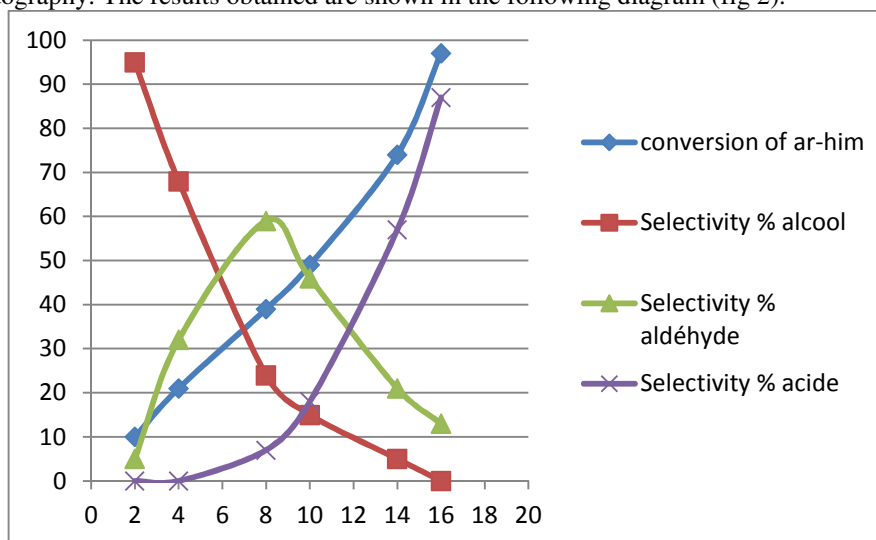


Figure2. Time dependence curves for the oxidation of ar-himachalene in the presence of 10%NHPI and 1% Co(OAc)<sub>2</sub> at 100°C.

It was found that at the beginning of the reaction, the ar-himachalene was mainly oxidized in the corresponding alcohol but with very low conversions that do not exceed 25%.

From 10 hours of reaction, the selectivity of the acid continues to increase up to 87% at the end of the reaction, while the alcohol disappears completely, and the aldehyd selectivity not exceeds 13%. These results can be explained by the oxidation of alcohol (**2**) to the aldehyd (**3**), which oxide also to the carboxylic acid (**4**) (figure 3)

### 3. Conclusion

By employing N-hydroxyphthalimide (NHPI) as the catalyst, a novel aerobic oxidation of ar-himachalene, which surpasses the conventional autoxidations in conversion and selectivity, has been achieved under mild conditions. This oxidation method provides entry to a diverse array of significant oxygen containing compounds.

### Experimental Section

#### Instruments

All the reagents and solvents used in the experiments were purchased from commercial sources as received without further purification (Aldrich, Fluka, Acros), and Ar-himachalene were prepared in our laboratory [10]. NMR studies were performed on a Bruker Avance 300 spectrometer in  $\text{CDCl}_3$ , chemicals shifts are given in ppm relative to external TMS and coupling constant (J) in Hz. Liquid chromatography was performed on silica gel (Merk 60, 220-440 mesh; eluent: hexane/ethylacetate).

#### Catalytic studies

An acetic acid solution 5 ml of ar-himachalene, NHPI and  $\text{Co}(\text{OAc})_2$  was placed in a 50 ml pear-shaped flask with a balloon filled with  $\text{O}_2$ . The mixture was stirred at suitable temperature for aforesaid time in table 1. After the completion of reaction, the solvent was removed under reduced pressure, and the products were purified by column chromatography on silica gel to give the corresponding oxygenated products. The conversions and selectivities of products were obtained by CPV analysis.

(5,9,9-Trimethyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-2-yl)-methanol **2**, a yellow oil,  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ): 1,39 (1H, m, CHH), 1,45 (3H, s, CH<sub>3</sub>), 1,53 (3H, d, J 6.9, CHCH<sub>3</sub>), 1,58 (3H, s, CH<sub>3</sub>), 1,76 (1H, m, CHH), 1,91 (4H, m, CH<sub>2</sub>), 3,42 (1H, m, CHCH<sub>3</sub>), 5,47 (2H, s, ArCH<sub>2</sub>), 7,31 (1H, d, J 8,1, ArH), 7,33 (1H, dd, J 1,2; 8,1, ArH), 7,49 (1H, d, J 1,2, ArH);

$\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 20.9, 23.9, 28.8, 33.9, 34.8, 36.2, 39.7, 40.9, 75.5, 126.0, 127.2, 127.9, 129.4, 145.9, 148.7.

5,9,9-Trimethyl-6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carbaldehyde **3**, a yellow oil,  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ): 1,15 (1H, m, CHH), 1,25 (3H, s, CH<sub>3</sub>), 1,27 (3H, d, J 6.9, CHCH<sub>3</sub>), 1,31 (3H, s, CH<sub>3</sub>), 1,6 (1H, m, CHH), 1,91 (4H, m, CH<sub>2</sub>), 3,25 (1H, m, CHCH<sub>3</sub>), 7,29 (1H, d, J 8,1, ArH), 7,56 (1H, dd, J 1,5; 8,1, ArH), 7,81 (1H, d, J 1,5, ArH), 9,85 (2H, s, ArCH<sub>2</sub>)

$\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 20.3, 23.4, 29.8, 33.3, 34.9, 35.9, 39.4, 40.9, 126.1, 127.5; 127.7, 134.9, 146.7, 151.2, 192.5.

5,9,9-Trimethyl-6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carboxylic acid **4**, a yellow oil,  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ ): 1,15 (1H, m, CHH), 1,25 (3H, s, CH<sub>3</sub>), 1,27 (3H, d, J 6.9, CHCH<sub>3</sub>), 1,31 (3H, s, CH<sub>3</sub>), 1,6 (1H, m, CHH), 1,91 (4H, m, CH<sub>2</sub>), 3,25 (1H, m, CHCH<sub>3</sub>), 7,29 (1H, d, J 8,1, ArH), 7,56 (1H, dd, J 1,5; 8,1, ArH), 7,81 (1H, d, J 1,5, ArH), 9,85 (2H, s, ArCH<sub>2</sub>)  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ ): 20.3, 23.4, 29.8, 33.3, 34.9, 35.9, 38.9, 40.7, 126.3, 127.6; 127.7, 134.9, 148.7, 150.2, 191.5.

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