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Effective Aerobic Allylic Oxidation of β-ionone and Series of Olefins Catalyzed by Phosphomolybdic Acid

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Oxidation of olefins in particular is a key reaction in the synthesis of complex organic molecules and fine chemicals.[1] The use of molecular oxygen as an oxidant for such processes is especially attractive from both economic and environmental perspectives.[2] 4-oxo-β-ionone, which is a kind of valuable flavors and chemical intermediates that can be extensively used in food, makeup fragrances and medication,[3-4] can be prepared from oxidation of β-ionone. As is known to all, allylic oxidation and epoxidation of double carbon bond are two competing processes both *in vivo* and *in vitro*.[5] So most of the methods have been developed for conversion of β-ionone to the corresponding 4-oxo-β-ionone or 5,6-epoxy-β-ionone and the major emphasis is the selectivity of the reaction. The terminal oxidant such as $NaClO_3$/NaI[6] or copper halide or active copper powder catalyzed *tert*-butyl alcohol peroxide system[7] was used in the reported methods. We[8] have reported catalytic aerobic oxidation using 20 mol % *N*-hydroxyphthalimide (NHPI) as the key catalyst combined with some co-catalysts, including transition metals $Co(acac)_2$ with almost 100% conversion and 82.1% selectivity for allylic oxidation product, but in work-up processing it has trouble to get rid of the excessive *N*-hydroxyphthalimide. So it is desirable in developing a new efficient and feasible catalytic procedure for selective catalytic oxygenation of hydrocarbons such as β-ionone or other olefins compounds with inexpensive and nonpolluting O_2 along with convenient work-up processing.[9-10]

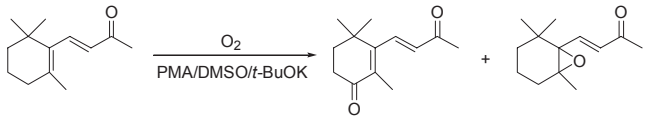
Heteropoly acid (HPA) can meet the demands as it consists of a central atom (P, As, Ge or Si *etc*) and assemblies of metal-oxygen polyhedrons, including components of molybdenum, tungsten or fragments of oxide crystal grating.[11] HPA catalysts have received much attention in both academia and industry due to their unique properties owing to their specific acidity, redox, high reactive selectivity, tunable catalytic ability and environmentally benign and a variety of synthetically useful transformations have been achieved in the oxidation of alcohols,[12] esterification,[13] ring-opening of epoxides[14] and dehydration[15] using HPAs as catalysts.

As a kind of heteropoly acid, phosphomolybdic acid (PMA) has been successfully used in many fine chemical reactions. Murphy *et al*.[16] have achieved a successful aerobic oxidation of isophorone to ketoisophorone with 99.1% conversion and 70.3% selectivity. Yadav and co-workers[17] first reported the preparation of 4-hydroxypiperidines *via* aza-prins-cyclization in 96% yields and with 93.7% selectivity using 10 mol % PMA under mild reaction conditions.

Here we report a series of allylic aerobic oxidation reactions using β-ionone **1** as model reaction, PMA/DMSO/*t*-BuOK as catalytic system to obtain 4-oxo-β-ionone **2** to optimize the reaction conditions and then expand to series of olefins for their oxo-products (Table 1).

The results show that strong polar aprotic solvent is better for getting 4-oxo-β-ionone **2** in the reaction. When DMF as solvent, it gives a better conversion but poor selectivity of **2**, while unfavorable results are obtained in solvent-free condition or using weak polar solvent dioxane as solvent. In the other hand, using DMSO as solvent leads to a considerable increase in both conversion (100%) and selectivity (100%). Because protons produced in the allylic oxidation could be abstracted,[18] which is in favor of the reaction. The influence of temperature is another important factor for the conversion and selectivity (Entry 4 ~ 9). After an initial increase for the reaction conversion and selectivity, an optimum temperature is obtained at about 115 °C, followed by an obvious drop (especially in selectivity) after 125 °C, which means that the reaction reach a thermo-

Table 1. The aerobic oxidation of β-ionone with PMA/DMSO/*t*-BuOK at different conditions

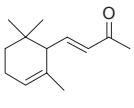
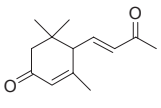
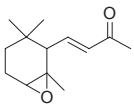
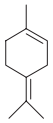
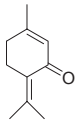
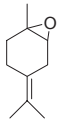
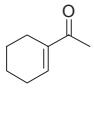
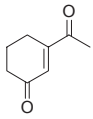
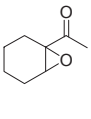
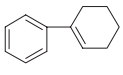
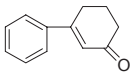
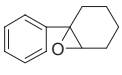
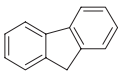
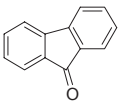


1 2 3

Entry	Solvent	Temp. (°C)	Conversion (%)	Selectivity of **2** (%)
1	Solvent-free	115	45.5	76.1
2	DMF	115	93.6	11
3	Dioxane	115	38.8	13.3
4	DMSO	85	70.4	78.8
5	DMSO	95	78.3	78.9
6	DMSO	105	98.6	91.3
7	DMSO	115	100	100
8	DMSO	125	100	85.3
9	DMSO	135	97	81.8

Reaction conditions: β-ionone (5 g, 0.026 mol); time (20 h); *t*-BuOK (1 mmol) in 20 mL solvent

Table 2. Serial allylic oxidations on various alkenes

Entry	Substrate	Product		Conversion (%)	time (h)	Selectivity (%)	
		b	c			b	c
1	 **4a**	 **4b**	 **4c**	100	20	94.1	6.8
2	**5a**	**5b**	**5c**	97.2	20	90.6	8.9
3	 **6a**	 **6b**	 **6c**	89.5	20	81.4	15.3
4	 **7a**	 **7b**	 **7c**	90.7	20	93.1	6.4
5	 **8a**	 **8b**	 **8c**	79.6	20	82.4	12.8
6	 **9a**	 **9b**		85.3	20	80.7	

dynamic equilibrium at low temperature. The decrease of conversion and selectivity at higher temperature can be rationalized as follows: the raise of temperature results in the decrease of equilibrium conversion for its strong exothermic effect in the aspect of thermodynamics and polymerization may occur at high temperature, which deeply affects the selectivity of **2**. The concentration of PMA, *t*-BuOK for the reaction is also investigated, and the optimum molar ratios of PMA and **1**, **1** and *t*-BuOK are respectively 0.43% and 26 from the results.

In order to examine the reproducibility and feasibility of the method, a series of alkenes are carried out the allylic aerobic oxidation with the same method (Table 2).

The results show that some alkenes are allylic oxidzed with oxygen by PMA/DMSO/*t*-BuOK system and selectivity of oxo-products (b) is generally moderate to good. Somewhat differences are observed in proportion of the mixture resulting as the electronic effect and neighboring group effect of the substituents in olefins. The larger steric hindrance, the lower conversions and selectivities of oxo-products (b) were obtained. Especially, oxidation of terpinolene **6a**, phenylecylohexene **8a** and fluorene **9a** relatively gave a low allylic oxidation results with 81.4% to 89.7% selectivity and 79.6% to 89.5% conversion.

In conclusion, an one-pot route to 4-oxo-β-ionone *via* allylic oxidation of β-ionone using PMA/DMSO/*t*-BuOK system under moderate conditions is reported. β-ionone can be oxidized to 4-oxo-β-ionone as the only product, and a series of olefins also give corresponding oxo-products with 85% to 100% conversion and 80% to 94% selectivity. Mild reaction conditions, simple experimental procedures, high conversion, clean oxidant, easy post-processing and good selectivity are the noteworthy advantages of this protocol.

General procedure for allylic aerobic oxdation of olefins with O_2/PMA/DMSO/*t*-BuOK system. A mixture of β-ionone, PMA, *t*-BuOK and DMSO was successively added to a three-necked flask under an atmosphere of O_2 (1 atm). The mixture was stirred at a definite temperature for the reported. The progress of the reaction was monitored by thin-layer chromatography (TLC). After the reaction finishing, the reaction organic layer was separated and washed with water. The organic layer was evaporated on a rotary evaporator and the oily residue was obtained. Then the sample was taken to GC-MS to analyze conversion and selectivity. And the residue was purified by column chromatography to obtain the sample for NMR to determine the structure of the products.

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