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Selective Aerobic Oxidation of Isophorone Catalyzed by Molybdovanadophosphate Supported on Carbon (NPMoV/C)

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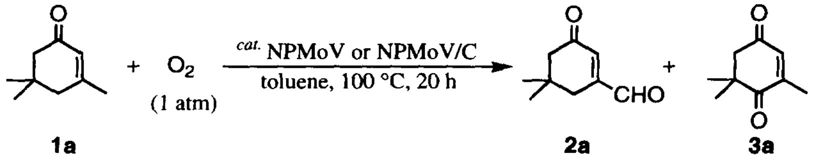
Abstract: Isophorone was smoothly oxidized with molecular oxygen by molybdovanadophosphate supported on the active carbon (NPMoV/C) to give 3-formyl-5,5-dimethyl-2-cyclohexen-1-one in relatively high selectivity. The regioselectivity of the oxidation by NPMoV/C was found to be just opposite to that of the conventional oxidations. The pore size of the supports appears to be an important factor governing the regioselectivity.

The selective oxidation of organic compounds utilizing molecular oxygen as the oxidant will become more important in synthetic organic chemistry from both economical and environmental points of view. Selective conversion of α-isophorone (**1a**) to 3-formyl-5,5-dimethyl-2-cyclohexen-1-one (**2a**) or 3,5,5-trimethyl-2-cyclohexene-1,4-dione (**3a**) is an attractive reaction, since **2a** and **3a** are useful precursors for preparing pharmaceutical materials and flavorings.¹⁾ **1a** was reported to be oxidized to **3a** along with a small amount of **2a** with ^{t}BuOOH by palladium (II) and copper (I) catalysts.$^{2)}$ Similarly, the oxidation of **1a** with air by a combined catalytic system comprised of phosphomolybdic acid, potassium dichromate and cupric sulfate produces **3a** as the major product.$^{3)}$ An obvious alternative approach to obtain **3a** is the Mn or Co complex-catalyzed aerobic oxidation of β-isophorone (3,5,5-trimethyl-3-cyclohexen-1-one),$^{4)}$ which is available by the isomerization of **1a**. To our knowledge, however, there has been little study so far of the selective oxidation of **1a** to **2a**$^{5)}$ except the unoxidative preparation of **2a**.$^{6)}$

In a previous paper, we reported that a mixed addenda heteropolyoxometalate, molybdovanadophosphate (NPMoV), whose average composition is indicated as $(NH_4)_5H_4PMo_4V_{7.8}O_{40} \cdot nH_2O$,$^{7)}$ and NPMoV supported on the active carbon, NPMoV/C,$^{8)}$ catalyzed efficiently the aerobic oxidation of benzylic



1a **2a** **3a** (1)

compounds and phenols to the corresponding oxygen-containing compounds.[9)] We now find that **1a** is selectively oxidized with molecular oxygen by NPMoV/C to **2a** rather than **3a** which results from conventional oxidations (eq. 1).[2-3)]

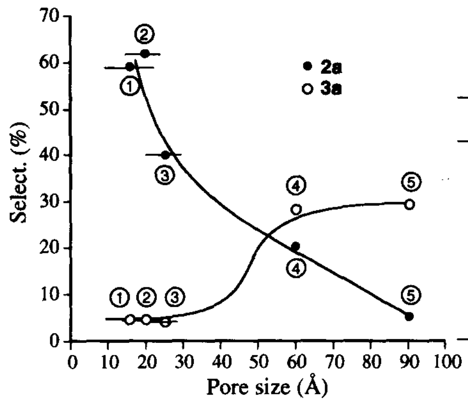
A typical reaction was carried out as follows : To a solution of isophorone **1a** (2 mmol) in toluene (10 mL) was added NPMoV (35 mg) or NPMoV/C (350 mg) loading 10 wt% of NPMoV on active carbon, and the mixture was stirred under atmosphere oxygen (1 atm) at 100 °C for 20 h. Products were isolated by column chromatography on silica gel with hexane/ethyl acetate (10/1).

Table 1 shows the representative results for the oxidation of **1a** with dioxygen in the presence of a catalytic amount of NPMoV or NPMoV/C under various conditions. The oxidation of **1a** by NPMoV in toluene at 100 °C for 20 h afforded 3,5,5-trimethyl-2-cyclohexene-1,4-dione, **3a**, as the major product along with a complex mixture of over-oxidation products, in low conversion (15%) (run 1). It is interesting to note that the oxidation of **1a** by NPMoV supported on the active carbon, NPMoV/C, under these conditions led to **2a** (62%) in 88% conversion (run 2). The regioselectivity was found to be different from that obtained by the NPMoV catalyst which produces **3a** as the principal product. In a previous paper, we reported that the catalytic activity of NPMoV in the aerobic oxidation of benzylic alcohols and phenols was considerably enhanced by supporting it on the active carbon, although these substrates were difficult to be oxidized by non-supported NPMoV.[8)] When the reaction was carried out in an acidic medium, the selectivity of **1a** to **2a** increased. For example, the oxidation of **1a** by

Table 1. Oxidation of Isophorone (**1a**) Using NPMoV or NPMoV/C Under Various Conditions[a]

Run	Catalyst	Temp. / °C	Conv. / %	Select. / %	
				2a	**3a**
1	NPMoV	100	15	trace	47
2	NPMoV/C	100	88	62	5
3[b]	NPMoV/C	80	93	75	5
4[b]	NPMoV	80	2	trace	trace
5[c]	NPMoV/C	80	95	66	4
6[d]	NPMoV/C	80	90	71	5
7	NPMoV/C[e]	100	82	59	5
8	NPMoV/C[f]	100	53	40	4
9	NPMoV/SiO_2	100	48	21	29
10	NPMoV/Al_2O_3	100	20	5	30

[a] Isophorone (**1a**) (2 mmol) was allowed to react with O_2 (1atm) in the presence of NPMoV (35 mg) or NPMoV/S (S=C, SiO_2, Al_2O_3) (350 mg) in toluene (10 mL) at 100 °C for 20 h. [b] CH_3SO_3H (0.1 mL) was added. [c] H_2SO_4 (0.1 mL) was added instead of CH_3SO_3H. [d] H_3PO_4 (0.1 mL) was added instead of CH_3SO_3H. [e] Active carbon (Kurare BP-25) was used. [f] Active carbon (Star coal W-AC) was used.



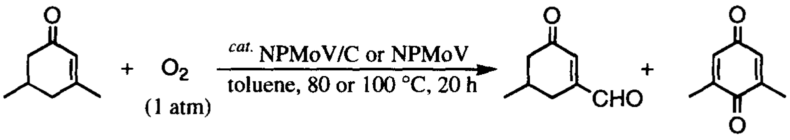
	Support	Pore size (Å)
①	carbon (Kurare BP-25)	8-24
②	carbon (Wako Pure Chemical)	15-25
③	carbon (Star coal W-AC)	20-30
④	silica gel (Merck silica gel 60)	60
⑤	alumina (Merck Alumina 90)	90

Fig. 1. The Relationship between Regioselectivity and Pore Size of Supports

NPMoV/C in the medium acidified with CH_3SO_3H at 80 °C gave **2a** in 75% selectivity in 93% conversion; however, under the same conditions NPMoV itself was inert (runs 3 and 4). Almost the same results were obtained when H_2SO_4 or H_3PO_4 was used in place of CH_3SO_3H (runs 5 and 6). The acids may facilitate the enolization of **1a**.

In order to clarify the influence of the supports on the regioselectivity, NPMoV was loaded on other two active carbons (Kurare BP-25, pore size 8-24 Å and Star coal W-AC, pore size 20-30 Å),[10] silica gel (Merck silica gel 60, pore size *ca.* 60 Å)[10] and alumina (Merck Alumina 90, activated neutral, pore size *ca.* 90 Å)[10] in the same way as the NPMoV/C catalyst. The oxidation of **1a** by NPMoV supported on the active carbons having large pore size resulted in slight decreases in the conversion as well as the selectivity to **2a**. The oxidation of **1a** by NPMoV/SiO_2 afforded **2a** and **3a** in a ratio of 4 : 6 in 48% conversion (run 9). NPMoV/Al_2O_3 was less active than NPMoV/C or NPMoV/SiO_2 and gave **2a** (5%) and **3a** (30%) in low selectivity (run 10).

It is difficult to explain clearly the effect of the supports on the regioselectivity, but the ratio of **2a** to **3a** seems to depend on the pore size of the supports, *i.e.*, the selectivity of **1a** to **2a** decreases sharply with increasing of the pore size of the supports (Fig. 1). This is because the adsorption of **1a** on the catalysts having small pore size would be unfavorable for the oxidation of the sterically crowded allylic methylene group. As a consequence, the sterically less hindered methyl group of **1a** is



1b **2b** **3b**

(2)

Catalyst	Conv. / %	Select. / %	
		2b	**3b**
NPMoV/C	74	65	12
NPMoV	10	trace	50

preferentially oxidized by such catalysts to form **2a** rather than **3a**.

To survey the generality of the present oxidation, 3,5-dimethyl-2-cyclohexen-1-one (**1b**) was allowed to react with O_2 in the presence of a catalytic amount of NPMoV/C or NPMoV at 80 °C or 100 °C, respectively, for 20 h (eq. 2). In a similar fashion to **1a**, **1b** was oxidized by NPMoV/C to 3-formyl-5-methyl-2-cyclohexen-1-one (**2b**) in relatively high selectivity, in which the allylic methyl group was selectively formylated, while 2,6-dimethyl-1,4-benzoquinone (**3b**) was obtained by NPMoV as the major product, although the conversion was low (10%).

In conclusion, the selective aerobic oxidation of isophorone **1a** to **2a**, which was difficult to obtain by the conventional methods, was achieved using NPMoV/C as the catalyst. The ratio of **2a** to **3a** was found to depend on the pore size of the supports employed.

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8 NPMoV/C was prepared as follows: To a solution of NPMoV (1 g) in an excess water was added 9 g of active carbon (Wako Pure Chemical, surface area: 1450 m^2/g, pore size: 15 - 25 Å, pore volume: 0.58 mL/g), and the suspended solution was stirred vigorously at room temperature for 0.5 h. After filtration, the precipitate was dried overnight in vacuo (20 mmHg) at *ca.* 90 °C to obtain NPMoV/C in which 10 wt% of NPMoV was supported on the active charcoal. The surface area and pore volume of NPMoV/C were estimated as 1250 m^2/g and 0.52 mL/g, respectively. IR (KBr): 1059, 943, 854, 777 cm^{-1} (around 1100 - 700 cm^{-1}).

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10 Active carbon: Kurare BP-25 (Kurare Chemical, surface area: 2420 m^2/g, pore size: 8 - 24 Å, pore volume: 1.20 mL/g), Active carbon: Star coal W-AC (Hokutan-kasei, surface area: 1100 m^2/g, pore size: 20 - 30 Å, pore volume: 0.7 mL/g), Silica gel: Merck silica gel 60 (surface area: 490 m^2/g, pore size: *ca.* 60 Å), Alumina: Merck Alumina 90 (surface area: 200 m^2/g, pore size: *ca.* 90 Å)

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