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Catalytic Oxidative Decarboxylation of Malic Acid into Dimethyl Malonate in Methanol with Dioxygen

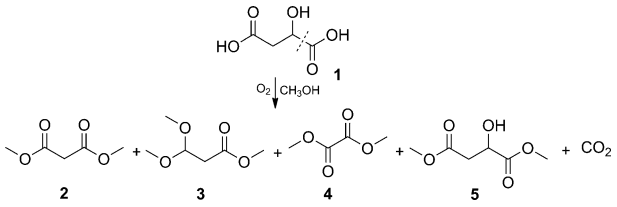
Junxia Liu,[a, b] Zhongtian Du,[a] Yanliang Yang,[a, b] Tianliang Lu,[a, b] Fang Lu,[a] and Jie Xu*[a]

The production of valuable chemicals from biomass has attracted much attention recently.[1] Carbohydrate biomass can be readily converted into a variety of organic acids, such as succinic, malic, aspartic, glutamic, and itaconic acid. These acids contain a large number of oxygen atoms with a specific structure.[2] Making full use of these existing oxygen atoms to produce oxygenated chemicals is an effective strategy.

Decarboxylation is an important transformation at both the laboratory and industrial level. The reaction often occurs in biological systems. For example, the oxidative decarboxylation of pyruvate links the glycolysis and citric acid cycles.[3] In industry, cyclopentanone is nowadays mostly produced via decarboxylation of adipic acid.[4] Transforming biomass and its derivatives into valuable chemicals through decarboxylation would be a valuable approach for chemists.

Malonic ester is an important reagent for the preparation of carboxylic acid by what is known as the malonic ester synthesis. However, it is difficult to obtain this ester from petrochemical feedstocks because they are deficient in oxygen atoms. For example, the hydrogen cyanide process for the production of malonic ester is based on the highly toxic raw materials chloroacetic acid and sodium cyanide.[5] The development of an environmentally benign process is thus an attractive prospect. Malic acid has been identified as one of twelve promising sugar-derived building blocks in biomass conversion.[2] Similar to malonic acid, malic acid contains both a carboxyl group and a methylene group. The conversion of malic acid into malonic acid is an interesting prospect. Herein, we present preliminary results on the transformation of malic acid into dimethyl malonate through selective oxidative decarboxylation (Scheme 1).

We recently reported the vanadium-catalyzed oxidative C–C bond cleavage of 5-hydroxymethylfurfural (HMF) into maleic anhydride.[6] We anticipated that conversion of malic acid into malonic acid could be achieved via selective oxidation by removing the carboxyl group. However, malonic acid itself is rather unstable as it readily undergoes thermal decarboxylation;[7] in contrast, dimethyl malonate is much more stable than malonic acid. It would be attractive to obtain malonic ester directly from malic acid via one-pot oxidative decarboxylation and esterification. Thus, a catalyst with both redox and acid property is preferred. On the basis of previous reports,[8] we selected phosphovanadomolybdates as the bifunctional catalysts.



Scheme 1. Oxidative decarboxylation of malic acid into dimethyl malonate.

The reactions were performed in absolute methanol, using oxygen as terminal oxidant. As expected, dimethyl malonate was obtained from malic acid when $H_5[PMo_{10}V_2O_{40}]$ was employed as catalyst (Table 1, entry 1). About 99% of malic acid was converted within 10 h at 100 °C; dimethyl malonate and methyl 3,3-dimethoxypropionate (**2** and **3**) were obtained as the main products with 68% and 16% selectivity respectively (entry 1). About 8% of dimethyl oxalate **4** and 2% of dimethyl malate **5** were also observed. In contrast, few products of C–C bond cleavage were detected in the absence of the catalyst, and the main product was **5** via esterification with methanol. Besides ester in the liquid phase, carbon dioxide was released in the gas phase, derived from carboxyl groups. Using $H_4[PMo_{11}VO_{40}]$ or $H_6[PMo_9V_3O_{40}]$ instead of $H_5[PMo_{10}V_2O_{40}]$, the

Table 1. Catalytic oxidation of malic acid in absolute methanol.[a]

Entry	Catalyst	Conv. [mol%]	Products in liquid phase [mol%]				
			2	**3**	**4**	**5**	others
1	$H_5[PMo_{10}V_2O_{40}]$	99	68	16	8	2	6
2	$H_4[PMo_{11}VO_{40}]$	99	61	16	6	2	15
3	$H_6[PMo_9V_3O_{40}]$	99	45	27	14	1	13
4[b]	$H_5[PMo_{10}V_2O_{40}]$	94	62	16	6	2	14
5	$H_3[PW_{12}O_{40}]$	95	1	n.d.	n.d.	98	1
6	$H_3[PMo_{12}O_{40}]$	95	1	1	n.d.	98	n.d.
7[c]	$H_3[PMo_{12}O_{40}]$	99	62	18	9	1	10
8[d]	$H_5[PMo_{10}V_2O_{40}]$	97	1	n.d.	n.d.	98	1

[a] Reaction conditions: 2.5 mmol DL-malic acid, 1 mol% catalyst based on vanadium content, and 0.5 mol% catalyst for entries 5 and 6, 3 mL methanol, 100 °C, 1.0 MPa O_2, 10 h. Conversion of malic acid was determined by HPLC, and selectivity was based on GC. [b] L-malic acid was used as substrate. [c] 0.5 mol% $H_3[PMo_{12}O_{40}]$ + 1 mol% $VOPO_4$. [d] N_2 atmosphere.

[a] *J. Liu,[+] Dr. Z. Du,[+] Y. Yang, T. Lu, Dr. F. Lu, Prof. Dr. J. Xu*
Dalian National Laboratory for Clean Energy
State Key Laboratory of Catalysis
Dalian Institute of Chemical Physics
Chinese Academy of Sciences
Dalian 116023 (PR China)
Fax: (+86) 411-84379245
E-mail: xujie@dicp.ac.cn

[b] *J. Liu,[+] Y. Yang, T. Lu*
Graduate University of the Chinese Academy of Sciences
Beijing 100039 (PR China)

[+] *These authors contributed equally to this work.*

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conversion of malic acid was still high, and the selectivities towards dimethyl malonate were 61 and 45%, respectively (entries 2 and 3). These results indicate that phosphovanadomolybdate catalysts are effective for the direct conversion of malic acid into dimethyl malonate in methanol. Moreover, the relative configurations of malic acid did not significantly influence this transformation. Both the conversion and product distribution were similar when L-malic acid and DL-malic acid were oxidized (entries 1 and 4). By contrast, when we carried out experiments using $H_3[PW_{12}O_{40}]$ or $H_3[PMo_{12}O_{40}]$ as catalyst, the product distribution varied significantly: the main product was **5** and only small amounts of **2** were detected (entries 5 and 6). A controlled experiment under N_2 atmosphere also gave **5** as main product (entry 8). These results suggest that decarboxylation does not proceed without vanadium or dioxygen. Moreover, when a catalytic amount of $VOPO_4$ was used in combination with $H_3[PMo_{12}O_{40}]$,[9a] the selectivity to oxidation products **2** and **3** increased remarkably (entries 6 and 7). Figure 1 shows

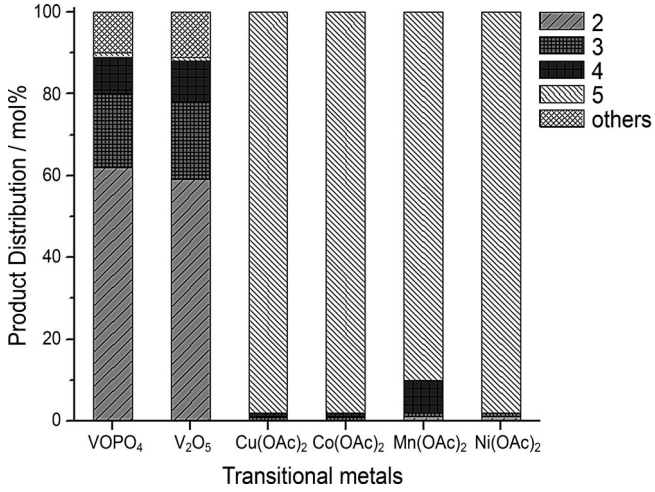


Figure 1. Catalytic oxidation of malic acid with $H_3[PMo_{12}O_{40}]$ in combination with transitional metals. The conversion of malic acid was >95% in all experiments. Reaction conditions: 2.5 mmol DL-malic acid, 0.5 mol% $H_3[PMo_{12}O_{40}]$, 1.0 mol% transition metal, 3 mL absolute methanol, 100 °C, 1.0 MPa O_2, 10 h.

the conversion of malic acid catalyzed with $H_3[PMo_{12}O_{40}]$ and other transitional metals. Besides $VOPO_4$, other vanadium compound such as V_2O_5 also proved effective for the formation of C3 products (**2** and **3**). In contrast, dimethyl malate via esterification was observed as the main product when $Cu(OAc)_2$, $Co(OAc)_2$, $Mn(OAc)_2$, and $Ni(OAc)_2$ were used. In line with the initial assumption, these observations suggest that vanadium is a key component for catalytic oxidative decarboxylation with molecular oxygen, while the heteropolyacid is effective for the esterification with methanol.

We further investigated the reaction progress profile by using $H_5[PMo_{10}V_2O_{40}]$ as catalyst. The esterification of malic acid proceeded swiftly in excess methanol. In controlled experiments under N_2, 52% of dimethyl malate was obtained within 30 min, and more than 90% of malic acid was converted into diester after 90 min in the presence of $H_5[PMo_{10}V_2O_{40}]$ (Figure S5, in situ IR investigation). The distribution of main products at different reaction times also showed that dimethyl malate was the main product initially and that the proportion of dimethyl malonate then increased gradually with diminishing amounts of dimethyl malate (Figure 2). When dimethyl malate was oxidized in place of malic acid under the same re-

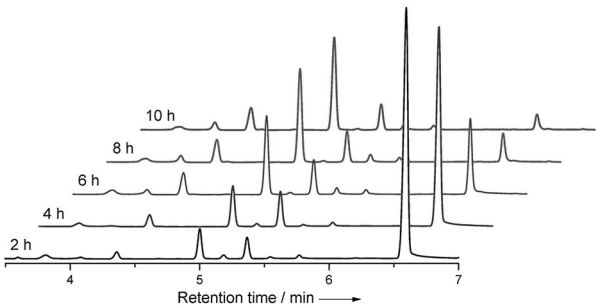


Figure 2. GC traces at different reaction times. The retention times correspond to the following compounds: 4.36 min (**4**), 5.00 min (**2**), 5.36 min (**3**), and 6.60 min (**5**).

action conditions, a similar product distribution was detected. This observation is in agreement with the low selectivity towards dimethyl malate after 10 h (entries 1–4). Therefore, most malic acid is first converted into dimethyl malate before decarboxylation in methanol.

Excess methanol as solvent was preferred for stabilizing products by means of esterification. Dimethyl malonate is much more stable than malonic acid under oxidative reaction conditions. Malonic acid and dimethyl malonate were tested for oxidation under the same reaction conditions in different solvents (Table S1). Most dimethyl malonate remained intact, either in methanol or acetonitrile, under oxidative reaction conditions (Table S1, entries 1 and 2). In contrast, malonic acid readily decomposed into acetic acid and carbon dioxide in acetonitrile, water, and sulfolane, and the recovery was much lower than that in methanol (Table S1, entries 3–6), because malonic acid was readily converted into dimethyl malonate in excess methanol in the presence of $H_5[PMo_{10}V_2O_{40}]$ catalyst. The formation of malonic ester hinders the formation of the six-membered ring transition state, which may reduce the decomposition of malonic acid (Scheme S1).

The conversion of malic acid into malonate involves oxidative C–C bond cleavage of α-hydroxycarboxylic acid. The properties of C=O groups in carboxylic acids (esters) are different from those in aldehydes or ketones due to electron delocalization. It is more difficult to oxidize α-hydroxycarboxylic acid than α-hydroxy ketone. Previously, Bregeault et al. described the efficient catalytic oxidative cleavage of α-hydroxy ketones with $H_5[PMo_{10}V_2O_{40}]$ under 0.1 MPa dioxygen;[9] however, under similar reaction conditions, most malic acid was converted into dimethyl malate through esterification. We found that the oxygen pressure has a strong influence on the catalytic oxidative of α-hydroxycarboxylic acid. In this work, the oxidation was performed with 1.0 MPa dioxygen, and oxidative decar-

boxylation of malic acid proceeded smoothly. Isotope-labeling experiments were also carried out (Figure S6–S8). When $^{18}O_2$ (97% ^{18}O-labeled) was employed as oxidant the dimethyl malonate was significantly enriched in ^{18}O: approximately 41% of dimethyl malonate had incorporated ^{18}O atoms (Figure 3).[10]

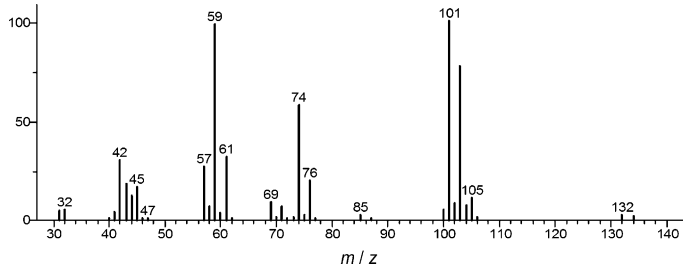


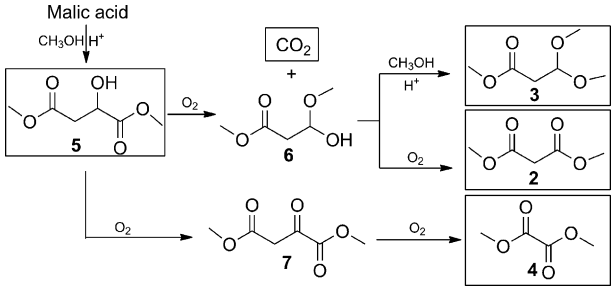
Figure 3. MS of dimethyl malonate when employing $^{18}O_2$.

An increase of the abundance of ^{18}O in carbon dioxide was also observed. These results further affirm that one oxygen atom transfers from the dioxygen to the products during the C–C bond cleavage. On the other hand, little change was observed in the relative abundance $^{18}O/^{16}O$ for methyl 3,3-dimethoxypropionate, which would be attributed to fast isotopic exchange in excess methanol. This is also in agreement with the result that the abundance of ^{18}O in dimethyl malonate was only 41%, rather than 100%.

To the best of our knowledge, catalytic oxidation of malic acid into dimethyl malonate is a novel transformation. This approach is free of cyanide and halides, which is important for sustainability and environmental criteria. Besides malic aid, other α-hydroxycarboxylic acids such as lactic acid and mandelic acid could also be oxidized through decarboxylation under the same reaction conditions (Scheme S2 and S3). When lactic acid was tested, methyl acetate was obtained as the main product. As for mandelic acid, the main products derived from decarboxylation were methyl benzoate (31%), benzaldehyde (18%), and benzaldehyde dimethyl acetal (24%). Hence, this approach would be potentially useful for selective oxidative decarboxylation of α-hydroxycarboxylic acid.

The formation pathway of products was studied in more detail. Firstly, the corresponding hemiacetal could form with the release of carbon dioxide after C–C bond cleavage of α-hydroxycarboxylic acid. The α-hydroxycarboxylic acid is believed to coordinate with vanadium(V) readily, and it has been proved that the oxidative C–C bond fission of malic acid with stoichiometric quinquevalent vanadium yields the corresponding aldehyde.[11] During the catalytic oxidation of malic acid with molecular oxygen, methyl 3,3-dimethoxypropionate was observed, which proved the occurrence of hemiacetal after oxidative decarboxylation. Secondly, dimethyl oxalate might be derived from oxalacetic acid or its ester. When oxalacetic acid was oxidized in a controlled experiment, dimethyl oxalate was detected. Due to its instability,[12] oxalacetic acid would not be observed after catalytic oxidation. Moreover, the oxidation of malic acid into oxalacetic acid is plausible because the oxidation of alcohols catalyzed by vanadium compounds with dioxygen has been described elsewhere.[13] Because α-ketophenylacetic acid is much more stable than oxalacetic acid, it was indeed detected when mandelic acid was subjected to oxidation, which confirmed that the oxidation of secondary hydroxyl group did occur besides the oxidative decarboxylation.

On the basis of the experiments above, we propose a reaction pathway for the oxidation of malic acid to methanol (Scheme 2). Malic acid is converted into dimethyl malate swiftly. C–C bond fission takes place over the phosphovanadomolybdate catalyst, and hemiacetal **6** is proposed as the intermediate to form **2** and **3**. Dimethyl malonate is derived from **6** via further oxidation. The formation of malonic acid is circumvented by catalytic oxidation and esterification, consecutively, in methanol. Dimethyl oxalate **4** is generated from **7**, which is formed from dimethyl malate via oxidation of its secondary hydroxyl group.



Scheme 2. Proposed reaction pathway for the catalytic oxidation of malic acid in methanol with molecular oxygen over $H_5[PMo_{10}V_2O_{40}]$.

In summary, we report a novel approach to obtain dimethyl malonate from malic acid via a facile one-pot process, which is cyanide- and halide-free. Phosphovanadomolybdate is used as bifunctional catalyst to achieve the oxidative decarboxylation and esterification consecutively. Hemiacetal is firstly formed after oxidative C–C bond cleavage. This work provides an example of producing valuable oxygenated chemicals by fully utilizing the existing oxygen atoms and specific structure of biomass products.

Experimental Section

Phosphovanadomolybdates ($H_5[PMo_{10}V_2O_{40}]$, $H_4[PMo_{11}VO_{40}]$, and $H_6[PMo_9V_3O_{40}]$) were prepared by using a known standard method.[14] $H_3[PW_{12}O_{40}]$ and $H_3[PMo_{12}O_{40}]$ are commercially available and were used as-received. Methanol was of HPLC grade.

Typically, 2.5 mmol malic acid and 0.5 mol% $H_5PV_2Mo_{10}O_{40}$ were loaded into an autoclave, followed by 3 mL methanol. The autoclave was sealed and charged with 1.0 MPa oxygen. The reaction mixture was kept at 100 °C under stirring for 10 h. The autoclave was then cooled to room temperature and carefully depressurized to atmospheric pressure. All of the reaction mixture was transferred. The amounts of dicarboxylic acids, such as malic acid and malonic acid, were determined by HPLC. Dimethyl malonate, methyl 3,3-dimethoxypropionate, dimethyl oxalate, and dimethyl malate were measured by GC using an internal standard. More experimental details can be found in the Supporting Information.

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Keywords: biomass · malic acid · malonic ester · oxidation · sustainable chemistry

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