An efficient heteropolyacid catalyzed acylation of pyruvate esters to α-acyloxyacrylate esters as potential candidate monomers for bio-based polymers

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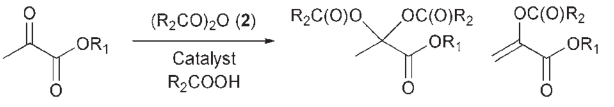
α-Acyloxyacrylate esters were efficiently synthesized from pyruvate esters and carboxylic anhydrides under mild conditions. These esters are potential candidate monomers for bio-based polymers with high durability and transparency. Tungsten-based Keggin type heteropolyacids, especially $H_3PW_{12}O_{40}$, worked more effectively as catalysts for this reaction than other typical acids.

Recently, technologies for biorefinery have been focused on as new procedures for producing various energies and chemicals.[1] In polymer industries, it is also desirable to produce various so-called "bio-based polymers" and "bio-based plastics" from biomass feedstock. α-Acyloxyacrylate esters have similar structures to methacrylate esters and polymers of α-acyloxyacrylate esters show higher thermal durability than poly methyl methacrylate (PMMA).[2] PMMA is widely used as sheets, displays, water cisterns, optical fibres and coating resins, because of its high transparency and high durability. Our starting materials, pyruvate esters, are obtained from lactate esters,[3] that are derivatives of lactic acid. Lactic acid is regarded as one of the most important products obtained by the fermentation of glucose. In addition, various important chemicals could be directly derived from lactic acid.[4] Therefore, developing an effective procedure to convert pyruvate esters to α-acyloxyacrylate esters is significant from the perspective of biorefinery.

The α-acyloxyacrylate esters (**4**) have been synthesized by acylation of pyruvate esters (**1**) with *p*-toluenesulfonic acid (*p*-TsOH)[5] or pyridine.[6] Unfortunately, these procedures have some problems, such as severe reaction conditions, low product yields, and difficulties in purifying the products. Meanwhile, β-acetoxyacylate esters have been synthesized by oxidative coupling between acrylate esters and acetic acid using $Pd(OAc)_2$ and Mo-based Keggin type heteropolyacids (HPAs), molybdovanadophoshates, as catalysts.[7] In this paper, we describe an efficient acylation of **1** to **4** catalyzed by tungsten (W)-based Keggin type heteropolyacids (HPAs).

We investigated the reaction between **1** and carboxylic anhydride (**2**) in carboxylic acid as a solvent at 343 K for 1 h (Table 1). As shown in Table 1, 2,2-diacyloxypropionate ester (**3**) was generated as a side product besides formation of the desired product (**4**). Both **3** and **4** have been characterized by using ^1H-, ^{13}C-NMR and HRMS after appropriate purifications.[8] It is worth noting that W-based Keggin type HPAs, $H_3PW_{12}O_{40}$ (entry 1) and $H_4SiW_{12}O_{40}$ (entry 2), showed high yields for **4a** with very low yields of **3a**. Acylation selectivity (sum of **3** and **4** yields per conversion) was almost 100%. $H_3PW_{12}O_{40}$ was determined as the most efficient catalyst for formation of **4a** (entry 1). In contrast, the yields of **4a** with Mo-based Keggin type HPAs, $H_3PMo_{12}O_{40}$, $H_4PMo_{11}V_1O_{40}$, and $H_4SiMo_{12}O_{40}$ (entries 3–5), were much lower than those with $H_3PW_{12}O_{40}$ and $H_4SiW_{12}O_{40}$. Moreover, typical mineral

Table 1 Acylation of pyruvate ester (**1**) with carboxylic anhydride (**2**) in the presence of various acid catalysts[a]



1 **3** **4**

1a: $R_1 = C_2H_5$ **2a**: $R_2 = CH_3$ **3a, 4a**: $R_1 = C_2H_5$, $R_2 = CH_3$
1b: $R_1 = CH_3$ **2b**: $R_2 = C_2H_5$ **3b, 4b**: $R_1 = CH_3$, $R_2 = CH_3$
3c, 4c: $R_1 = C_2H_5$, $R_2 = C_2H_5$

		Substrate			Yield (%)[b]			
Entry	Catalyst	1	2	Conversion (%)[b]	3		4	
1	$H_3PW_{12}O_{40}$	**1a**	**2a**	68	**3a**	7	**4a**	61
2	$H_4SiW_{12}O_{40}$	**1a**	**2a**	65	**3a**	13	**4a**	52
3	$H_3PMo_{12}O_{40}$	**1a**	**2a**	32	**3a**	2	**4a**	6
4	$H_4PMo_{11}V_1O_{40}$	**1a**	**2a**	24	**3a**	0	**4a**	5
5	$H_4SiMo_{12}O_{40}$	**1a**	**2a**	27	**3a**	1	**4a**	4
6	H_2SO_4	**1a**	**2a**	21	**3a**	12	**4a**	8
7	HCl	**1a**	**2a**	0	**3a**	0	**4a**	0
8	HNO_3	**1a**	**2a**	4	**3a**	0	**4a**	3
9	H_3PO_4	**1a**	**2a**	0	**3a**	0	**4a**	0
10	p-TsOH·H_2O	**1a**	**2a**	13	**3a**	3	**4a**	5
11	$AlCl_3$	**1a**	**2a**	22	**3a**	0	**4a**	2
12	$H_3PW_{12}O_{40}$	**1b**	**2a**	68	**3b**	9	**4b**	48
13	$H_3PW_{12}O_{40}$	**1a**	**2b**	70	**3c**	8	**4c**	56

[a] Reaction conditions: **1** (2 mmol), **2** (20 mmol), catalyst (entries 1–10, 12, 13; 7.5 mol% as H^+ *vs.* **1**, entry 11; 2.5 mol% *vs.* **1**), carboxylic acid (1.20 g), 343 K, 1 h. [b] Conversion of **1** and yields of **3** and **4** were determined by GC using *n*-butyl acetate as an internal standard.

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acids, H_2SO_4, HCl, HNO_3, and H_3PO_4 (entries 6–9), showed very low yields. *p*-TsOH·H_2O (entry 10), which has often been used as a catalyst,[5] was also not effective under our conditions. $AlCl_3$ (entry 11), which often catalyzed Friedel–Crafts acylation as a Lewis acid, did not work as well.

HPAs have been actively utilized as important catalysts.[9] Because their strong acidities and excellent redox properties are attractive to organic reactions, many useful chemicals, such as methacrylic acid, *tert*-butanol, acetic acid, and ethyl acetate, have been produced industrially.[10–12]

The acid strength of these HPAs in polar solvents follows the order: $H_3PW_{12}O_{40} > H_4SiW_{12}O_{40} > H_3PMo_{12}O_{40} > H_4PMo_{11}V_1O_{40} > H_4SiMo_{12}O_{40}$.[13] Since the stability of Mo-containing HPAs in solution is rather low, they may decompose or become deeply reduced during a reaction. Owing to these instabilities of Mo-based HPAs, side reactions would be promoted and acylation selectivity would result in a low value. Additionally, acid strength of HPAs is much stronger than that of other typical acids, such as H_2SO_4, HCl, HNO_3, H_3PO_4, and *p*-TsOH·H_2O. These are the main reasons why $H_3PW_{12}O_{40}$ shows the highest performance toward **4a** formation. When **1b** was used as a substrate (entry 12), selectivity of **4b** and mass balance clearly decreased. It is guessed that decomposition of **1b** will easily occur compared to **1a**.[14] Compound **4c** (entry 13) was formed with almost the same yield as that of **4a**.

To clarify the pathway of this reaction, we have observed the correlation between reaction time and yield for **3a** and **4a** at 343 K with $H_3PW_{12}O_{40}$ (Fig. 1). At the beginning of the reaction, **3a** was produced, and gradually the yield of **3a** decreased, whereas the yield of **4a** increased, suggesting that **3a** is the intermediate species and **4a** may be consecutively formed through **3a**. Furthermore, we have also confirmed that through the reaction of **3a** as a substrate in the presence of $H_3PW_{12}O_{40}$ and acetic acid at 343 K, **4a** was observed as a product. Indeed, **3a** was not converted unless $H_3PW_{12}O_{40}$ was added at 343 K. As the reaction temperature increases, accumulation of **3a** decreases, and **4a** forms more rapidly than at low reaction temperature. In the case of reaction at ambient temperature between **1a** and **2a** with $H_3PW_{12}O_{40}$, **3a** was the main product after 3 h (52% yield).

From an industrial point of view, heterogeneous catalysts are more useful than homogeneous catalysts because of their advantages in the separation process of products and catalysts.

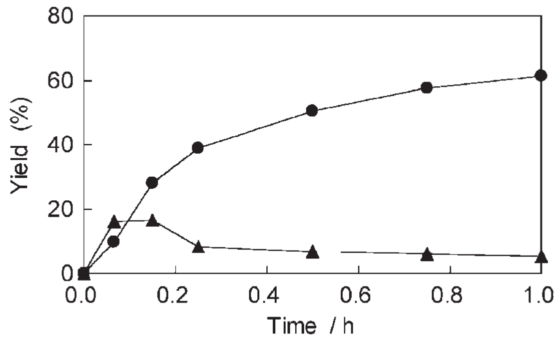
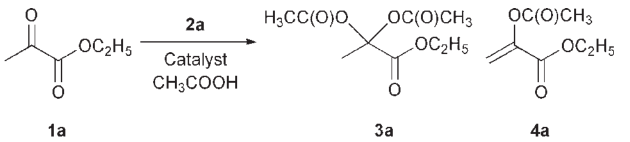


Fig. 1 The correlation between reaction time and yield for **3a** (▲) and **4a** (●). Reaction conditions: **1a** (2 mmol), **2a** (20 mmol), $H_3PW_{12}O_{40}$ (2.5 mol% *vs.* **1a**), acetic acid (1.20 g), 343 K.

Table 2 Acylation of ethyl pyruvate (**1a**) with acetic anhydride (**2a**) in the presence of various solid acid catalysts[a]

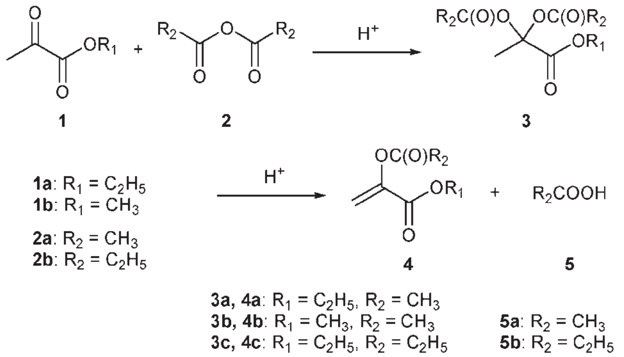


Entry	Catalyst	Conversion (%)[b]	Yield (%)[b] 3a	4a
1	20%$H_3PW_{12}O_{40}/SiO_2$	61	7	46
2	H-Y (Si/Al = 5.5)	0	0	0
3	H-BEA (Si/Al = 150)	25	5	20
4	MCM-41	0	0	0
5	SiO_2	17	0	1
6	Amberlyst-15H	44	4	34

[a] Reaction conditions: **1a** (2 mmol), **2a** (20 mmol), catalyst (entry 1; 0.85 g, entries 2–5; 0.10 g, entry 6; 0.34 g), acetic acid (1.20 g), 343 K, 1 h. [b] Conversion of **1a** and yields of **3a** and **4a** were determined by GC using *n*-butyl acetate as an internal standard.

Solid catalysts, such as supported-HPAs, zeolites, mesoporus silica, silica, and ion-exchange resin, were examined in the reaction between ethyl pyruvate (**1a**) and acetic anhydride (**2a**) (Table 2). Among them, 20% $H_3PW_{12}O_{40}/SiO_2$ (SiO_2: CARiACT Q-10, 75–500 μm, FUJI SILYSIA CHEMICAL LTD.) showed the highest yield of **4a**. Amberlyst-15H (MP Biomedicals, Inc.), which is a cation-exchange resin bearing sulfonic groups as strong acid sites, showed moderate performance. The origin of the low performance of H-Y (Si/Al = 5.5), H-BEA (Si/Al = 150), MCM-41, and SiO_2 may be explained by their lower acidities compared to $H_3PW_{12}O_{40}$. Albeit, during the reaction with 20% $H_3PW_{12}O_{40}/SiO_2$, leaching of $H_3PW_{12}O_{40}$ from SiO_2 was partly observed. Hereafter, some improvements for the supporting method of $H_3PW_{12}O_{40}$ are necessary.

As shown in Scheme 1, **1** is initially transformed into **3**. This type of acid catalyzed acylation is known as a protection reaction of aldehydes. There are many studies of the syntheses of 1,1-diacetate compounds from various aldehydes, such as benzaldehydes.[15] To the best of our knowledge, **3a–c** are new compounds. And then, **4** would consecutively be generated from **3** through one R_2COOH (**5**) elimination by an acid catalyst. The synthesis of **4a** with $H_3PW_{12}O_{40}$ was examined at various reaction temperatures: 323, 343 and 363 K. Using the initial formation rate of **4a**, the apparent activation energy (E_a) was



Scheme 1 Supported reaction pathway.

Table 3 Comparison of polymer properties

Polymer[a]	PEAA	PMMA	PLA
Transmittance (%T)[b]	93	93	Translucent[d]
T_g/K[c]	406	378	333

[a] Molecular weights (Mw) of PEAA and PMMA were both approximately 100 000. *LACEA*® (*H*-100) was used as PLA. [b] The value of %T was measured in reference to the method of JIS K 7105 published by the Japanese Industrial Standards Committee. [c] The value of T_g was determined by differential scanning calorimetry (DSC). [d] It was so low that we couldn't measure the value of %T.

calculated by the Arrhenius method. As a result, E_a was determined as 31.6 kJ mol^{-1}. This value would be comparable with the Friedel–Crafts acylation reaction with HPAs.[16] Further kinetic studies are under investigation in our laboratory.

As mentioned above, **4**-type esters are potential candidate monomers for bio-based polymers. We have also confirmed the properties of the homo-polymer of **4a**, poly ethyl α-acetoxyacrylate (PEAA). The optical transmittance and glass transition temperature (T_g) of PEAA were compared with PMMA and poly lactic acid (PLA) (Table 3). PEAA shows higher heat resistance than PLA and PMMA and is as transparent as PMMA. Additionally, the thermal stability of PEAA and PMMA was investigated by thermogravimetric analysis (TGA) under a nitrogen atmosphere. 5% weight loss temperatures of these polymers were in the range of 553 to 563 K, which means that their thermal degradation properties are comparable. Compound **4** can also be co-polymerized with various different monomers.[17] Further investigations of these polymer materials are now underway.

In conclusion, we have developed HPA-catalyzed acylation for α-acyloxyacrylate ester synthesis from pyruvate ester and carboxylic anhydride under mild conditions. The most important requirement for the catalyst is strong acidity. This requirement is especially well met by HPA, in particular $H_3PW_{12}O_{40}$. Furthermore, we have identified the intermediate species, a *gem*-diacetate compound, for this reaction. Because the pyruvate esters can be converted from lactic acid, one of the most important glucose fermentation products, the facile and efficient transformation of pyruvate ester to a useful polymer component will open new possibilities for lactic acid platform utility.

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8 General procedure: the reaction was carried out in a 10 ml test tube with a cap. After completion, the reaction mixture was cooled in iced water. When HPA was used as a catalyst, an excess of Cs_2CO_3 was added to precipitate the catalyst. After *n*-butyl acetate, as an internal standard, was added to this suspension, with mixing, the precipitate ($Cs_3PW_{12}O_{40}$) was removed with a centrifuge. The top layer was analyzed by GC and product yields were calculated. Further purification and characterization of the product in general was as follows. After the catalyst was removed, the reaction mixture was evaporated by rotary evaporator at first. Saturated aqueous $NaHCO_3$ solution was added to this condensed mixture. Then, diethyl ether was added to extract products from the aqueous layer. The ether layer was collected with a separatory funnel. This operation was repeated as necessary. After drying extracts with anhydrous Na_2SO_4, this solution was evaporated until an oily product was obtained. This oily product was analyzed by ^1H-, ^{13}C-NMR, and HRMS. If the purity of product is low, it is better to execute column chromatography of SiO_2, with chloroform–hexane = 5 : 1 (v/v) as a developing solvent. The HRMS measurement was carried out by the Centre for Instrumental Analysis, Hokkaido University. We are grateful to Ms Seiko Oka in this centre for MS analyses. Ethyl 2,2-diacetoxypropionate (**3a**): ^1H-NMR (400 MHz, $CDCl_3$) δ 1.27 (3H, t, J = 7.2 Hz, $C\mathit{H}_3CH_2O$); 1.94 (3H, s, $C\mathit{H}_3$–$C(OAc)_2COOC_2H_5$); 2.09 (6H, s, 2 × $CH_3C(O)O$); 4.23 (2H, q, J = 7.2 Hz, $CH_3C\mathit{H}_2O$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3CH_2O); 21.3 (2 × $\mathit{C}H_3C(O)O$); 22.1 ($\mathit{C}H_3$–$C(OAc)_2C(O)OC_2H_5$); 62.5 ($CH_3\mathit{C}H_2O$); 98.4 (CH_3–$\mathit{C}(OAc)_2$-$C(O)OC_2H_5$); 166.8 ($\mathit{C}(O)OC_2H_5$); 168.3 (2 × $CH_3C(O)O$). HRMS (ESI-TOF, NaI) calculated for $^{12}C_9{}^1H_{14}{}^{23}Na_1{}^{16}O_6$ ($[M+{}^{23}Na]^+$) 241.06881, found 241.06974.Ethyl α-acetoxyacrylate (**4a**): ^1H-NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, t, J = 7.2 Hz, $C\mathit{H}_3CH_2O$); 2.22 (3H, s, $C\mathit{H}_3C(O)O$); 4.25 (2H, q, J = 7.2 Hz, $CH_3C\mathit{H}_2O$); 5.47 (1H, d, J = 1.8 Hz, $CH_2{=}C$); 6.02 (1H, d, J = 1.8 Hz, $CH_2{=}C$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 ($\mathit{C}H_3CH_2O$); 20.2 ($\mathit{C}H_3C(O)O$); 61.7 ($CH_3\mathit{C}H_2O$); 113.5 ($\mathit{C}H_2{=}C$); 144.8 ($CH_2{=}\mathit{C}$); 161.3 ($CH_3\mathit{C}(O)O$); 168.8 ($\mathit{C}(O)OC_2H_5$). HRMS (ESI-TOF, NaI) calculated for $^{12}C_7{}^1H_{10}{}^{23}Na_1{}^{16}O_4$ ($[M+{}^{23}Na]^+$) 181.04768, found 181.04690.

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