Biomass Conversion **Hot Paper**

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Production of Diethyl Terephthalate from Biomass-Derived Muconic Acid

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Abstract: *We report a cascade synthetic route to directly obtain diethyl terephthalate, a replacement for terephthalic acid, from biomass-derived muconic acid, ethanol, and ethylene. The process involves two steps: First, a substituted cyclohexene system is built through esterification and Diels–Alder reaction; then, a dehydrogenation reaction provides diethyl terephthalate. The key esterification reaction leads to improved solubility and modulates the electronic properties of muconic acid, thus promoting the Diels–Alder reaction with ethylene. With silicotungstic acid as the catalyst, nearly 100 % conversion of muconic acid was achieved, and the cycloadducts were formed with more than 99.0 % selectivity. The palladium-catalyzed dehydrogenation reaction preferentially occurs under neutral or mildly basic conditions. The total yield of diethyl terephthalate reached 80.6 % based on the amount of muconic acid used in the two-step synthetic process.*

Synthetic polyesters play an essential and ubiquitous role in the area of polymer materials. Purified terephthalic acid (PTA) is used mainly as a monomer for the synthesis of polyesters, especially for polyethylene terephthalate (PET). The global consumption of PTA was over 50 million tons in 2014, which utilizes huge amounts of fossil oil.[1] As an abundant and renewable resource, biomass has the potential to serve as a feedstock for the production of liquid fuels and chemicals.[2] Therefore, methods for the efficient conversion of biomass into PTA and its derivatives are of great importance for the development of the biopolymer industry.[3]

Terephthalic acid comprises a benzene ring with dicarboxylic acid groups at the 1- and 4-position. Some important strategies have been proposed to construct aromatic structures by catalytic biorefinery routes. One of these is based on the fact that lignocellulosic biomass can undergo a fast catalytic pyrolysis process in the presence of zeolites as the catalyst to produce aromatic compounds.[4] However, it is a challenge to directly convert cellulose-based platform chemicals into aromatic compounds because of the absence of benzene rings in the molecular structure. C5 and C6 sugars can be converted into a BTX (benzene, toluene, and xylenes) stream by bioforming technology, which is based on aqueous-phase reforming and conventional chemical processing and was developed by Virent.[5] Furan-based compounds, which are important platform chemicals and can be produced from glucose and other biomass feedstock, have a conjugated diene structure.[6] Recently, several groups applied Diels–Alder reactions between a conjugated diene and an alkene to form substituted cyclohexenes and further dehydration or dehydrogenation to obtain aromatic compounds. For example, furfural,[7] 2,5-dimethylfuran,[8] and oxidized variants of 5-hydroxymethylfurfural[9] have been used to construct aryl rings. Biomass-derived ethylene,[10] isoprene,[11] methyl coumalate,[12] and sorbic acid[13] can also be used as starting materials in Diels–Alder reactions. However, further oxidation is required to form the two carboxylic acid groups.

Muconic acid has garnered significant interest owing to its potential as starting material for the synthesis of adipic acid, a bulk chemical for the production of Nylon-6,6.[14] It contains a conjugated diene and two carboxylic acid moieties, which render it an attractive candidate for the synthesis of terephthalic acid. Frost et al. have described the formation of terephthalic acid through a Diels–Alder reaction between muconic acid and ethylene and further dehydrogenation in a patent.[15] This method constitutes a very promising route to produce renewable terephthalic acid. However, the solubility of muconic acid is very poor in many solvents, and its molecular structure contains two electron-withdrawing carboxylic acid groups, rendering its reaction with a dienophile difficult.[9,13]

Herein, we propose a synthetic route to diethyl terephthalate (DET), using *trans*,*trans*-muconic acid (TTMA), ethanol, and ethylene as the reactants, through a cascade process combining esterification, Diels–Alder cycloaddition, and dehydrogenation (Scheme 1). The key esterification reaction improves the solubility of the reaction products in ethanol and modulates the electronic properties of TTMA, thus promoting the Diels–Alder reaction with ethylene. Various metal catalysts were examined for the dehydrogenation reaction, and palladium catalysts showed the most efficient performance under neutral or mildly basic conditions. This work serves as a proof of concept for utilizing biomass molecules by rational design of the functional groups present in the platform chemicals.

The esterification and the Diels–Alder reaction of TTMA with ethanol and ethylene, respectively, took place at 200 °C in the presence of a silicotungstic acid catalyst. The crude

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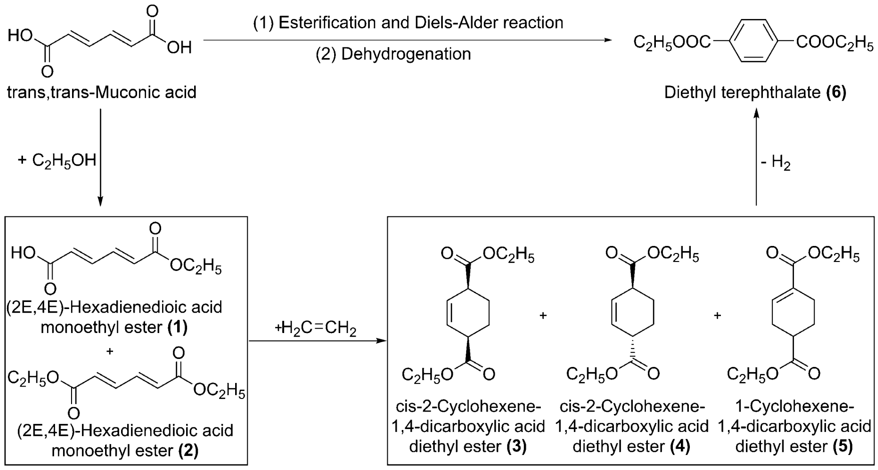

Scheme 1. Cascade process for the production of diethyl terephthalate (DET) from *trans,trans*-muconic acid (TTMA).

reaction mixture was directly used as the feedstock of the dehydrogenation reaction (Scheme 1). Typically, the two primary ethyl esters of TTMA and three cycloadducts were detected by GC-MS, including the (2*E*,4*E*)-hexadienedioic acid monoethyl ester (**1**), (2*E*,4*E*)-hexadienedioic acid diethyl ester (**2**), *cis*-2-cyclohexene-1,4-dicarboxylic acid diethyl ester (**3**), *trans*-2-cyclohexene-1,4-dicarboxylic acid diethyl ester (**4**), and 1-cyclohexene-1,4-dicarboxylic acid diethyl ester (**5**; see the Supporting Information, Figure S2 a,b). The desired product, DET (**6**), and other side products of the dehydrogenation reaction could be also identified (Figure S8 a,b).

The ethylene pressure exerts a great influence on the product selectivity of the esterification and Diels–Alder reaction (Figure 1). At an ethylene pressure of 0.1 MPa, mainly the products of the esterification reaction were present. Monoester **1** and diester **2** were formed with selectivities of 4.2 % and 92.1 %, respectively. With increasing ethylene pressure, the amount of **1** and **2** dropped significantly, whereas the amount of the cycloadducts (**3**, **4**, and **5**) increased. Compounds **1** and **2** were not detected at an ethylene pressure of 3.0 MPa, and the cycloadducts were formed with an overall selectivity of > 99.0 %. Among the three cycloadducts, *cis* product **3** was the major product because of the stereospecificity of the Diels–Alder reaction.[16] Therefore, a suitably high ethylene pressure promotes the Diels–Alder reaction.

To further investigate the reaction of TTMA with ethanol and ethylene, we let the reactions run for different periods of time at an ethylene pressure of 2.0 MPa (Figure 2). TTMA reacted rapidly in the initial stage of the reaction, and its conversion reached up to 87.9 % in the first twelve minutes. At this point, **1** and **2** had been formed with selectivities of 37.8 % and 37.0 %, respectively. Upon prolonging the reaction time to 30 minutes, the amount of **1** decreased while the amount of **2** slightly increased, implying that the formation rate of **2** was greater than its consumption rate within the first 30 minutes. Upon further extending the reaction time, the amounts of **1** and **2** decreased while those of the cycloadducts increased gradually.

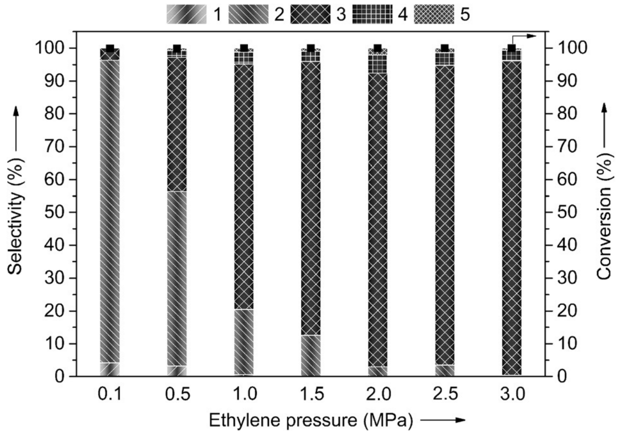

Figure 1. The effect of ethylene pressure on the selectivity of the esterification and Diels–Alder reaction of TTMA with ethanol and ethylene. Reaction conditions: TTMA (0.5 mmol), ethanol (20 mL), silicotungstic acid (0.005 mmol), 200 °C, 240 min.

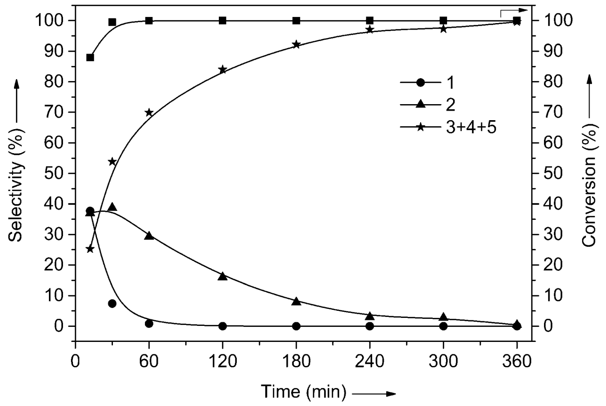

Figure 2. Time course of the esterification and Diels–Alder reaction of TTMA with ethanol and ethylene. Reaction conditions: TTMA (0.5 mmol), ethylene (2.0 MPa), ethanol (20 mL), silicotungstic acid (0.005 mmol), 200 °C.

The combined esterification and Diels–Alder reaction of TTMA with ethanol and ethylene was studied by real-time in situ FT-IR spectroscopy (Figure 3). Owing to the limitations of our spectrometer, relatively low temperature and ethylene pressure (125 °C and 0.4 MPa) were selected. After background correction (see Figure S15), TTMA (reactant), (2*E*,4*E*)-hexadienedioic acid diethyl ester (esterification product), and *cis*-2-cyclohexene-1,4-dicarboxylic acid diethyl ester (primary cycloadduct) gave rise to characteristic absorptions at 1690 cm^{-1}, 1715 cm^{-1}, and 1740 cm^{-1} (stretching vibrations of C=O), which could be used to measure

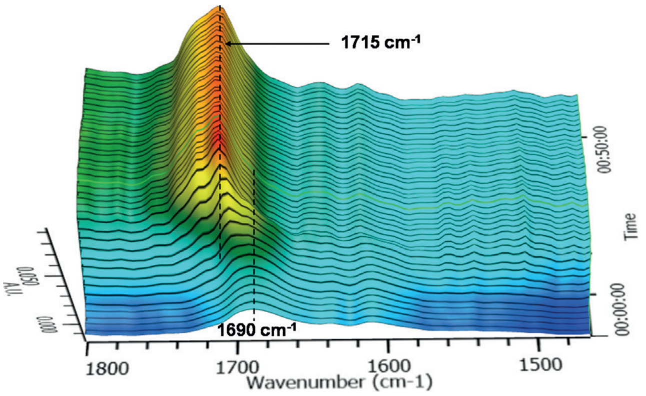

Figure 3. Real-time in situ FT-IR spectroscopic analysis of the esterification and Diels–Alder reaction of TTMA with ethanol and ethylene. The peaks at 1690 cm^{-1} and 1715 cm^{-1} correspond to the C=O stretching vibrations of TTMA and **2**, respectively. Reaction conditions: TTMA (1.8 mmol), ethylene (0.4 MPa), ethanol (10 mL), silicotungstic acid (0.018 mmol), 125 °C.

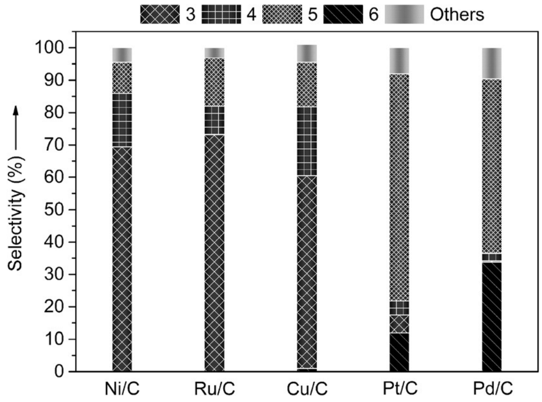

Figure 4. Dehydrogenation of the liquid products from the esterification and Diels–Alder reaction of TTMA with ethanol and ethylene using various catalysts. Reaction conditions: 0.1 MPa initial N_2 pressure, 200 °C, 360 min; 30 mol % Ni or Cu, 2.5 mol % Ru, Pt, or Pd with respect to TTMA. "Others" refers to a combination of diethyl adipate, 1,4-cyclohexanedicarboxylic diethyl ester, and (*E*)-2-hexenedioic acid diethyl ester.

changes in the reaction process. The intensity of the peak at 1690 cm^{-1} was very low at the beginning owing to the poor solubility of TTMA in ethanol at room temperature (0.18 g per 100 mL ethanol, Table S1). The reaction of TTMA with ethanol leads to diester **2**, which has a better solubility (9.86 g per 100 mL ethanol), promoting the esterification reaction. Therefore, the intensity of the peak at 1715 cm^{-1} increased rapidly. However, no peak was observed at 1740 cm^{-1} peak over the whole reaction, revealing that the cycloadduct had not been formed. Therefore, the Diels–Alder reaction requires more rigorous conditions to proceed.

The reaction time course data and integration of the real-time in situ FT-IR results indicate that the esterification and Diels–Alder reaction take place sequentially: First, TTMA reacts with ethanol to form the monoester and diester in a stepwise process, which then undergo the Diels–Alder reaction to form the cycloadducts. We surmise that two factors are crucial in determining the reaction sequence, namely that cycloaddition is preceded by esterification: 1) Ethanol serves as both the solvent and the esterification reagent. The product of esterification, **2**, is significantly more soluble in ethanol than the starting material. 2) Diesters possess two electron-donating ethoxy groups, which facilitate the reaction with a dienophile in a Diels–Alder process compared to TTMA.

To construct stable aromatic compounds, cyclohexenes need to eliminate 2 equiv of H_2. We tested different metals supported on activated carbon (Ni/C, Cu/C, Ru/C, Pt/C, and Pd/C) as dehydrogenation catalysts. The crude liquid product mixture of the first step was used as the feed for the dehydrogenation reaction. Typically, the reaction was conducted at 200 °C in nitrogen atmosphere. As illustrated in Figure 4, Ni/C and Ru/C were inactive, and Cu/C showed only 1.0 % selectivity towards the formation of DET. For Pt/C and Pd/C, the selectivity increased to 11.9 % and 33.7 %, respectively. The distribution of the cycloadducts changed after the reaction. In particular, the amount of **5** increased to 70.2 % and 53.8 % in the reactions catalyzed by Pt/C and Pd/C whereas the amount of **5** was only 2.2 % in the feed solution. These findings imply that isomerization and dehydrogenation reactions proceed simultaneously in the presence of these metal catalysts.[17] Owing to the absence of an additional hydrogen acceptor, other hydrogenated products were detected, including diethyl adipate, 1,4-cyclohexanedicarboxylic diethyl ester, and (*E*)-2-hexenedioic acid diethyl ester (see Figures S10–S12).

Further studies were performed on the palladium-catalyzed dehydrogenation reaction (Table 1). The yield of DET increased from 34.0 % to 75.5 % upon increasing the amount of Pd from 2.5 to 10 mol % with respect to TTMA (entries 1–3). However, doubling the Pd amount from 5 mol % to 10 mol % only resulted in a slight increase in DET yield while

Table 1: Palladium-catalyzed dehydrogenation of the liquid products from the esterification and Diels–Alder reaction of TTMA with ethanol and ethylene.[a]

Entry	Pd [mol %][b]	OH^-/H^+[c]	Specific rate[d] [$mol_{DET} mol_{Pd}^{-1} h^{-1}$]	Yield [%][e]
1	2.5	–	2.3	34.0
2	5	–	2.4	70.5
3	10	–	1.3	75.5
4[f]	5	–	0.6	19.1
5	5	1	2.7	80.6
6	5	2	2.7	80.1
7	5	4	2.3	69.0
8	5	8	2.2	66.6
9	5	11	1.7	50.3

[a] Reaction conditions: 0.1 MPa initial N_2 pressure, Pd/C, 200 °C, 360 min. [b] The amount of metallic palladium with respect to TTMA. [c] The protons result from the silicotungstic acid added in the first step; entries 1–4: no base; entries 5–9: OH^- added as KOH. [d] The specific rate is defined as the number of moles of DET produced by one mole of the catalyst per hour. [e] The yield of DET was determined by HPLC analysis; for entry 4, the yield of terephthalic acid is given. [f] The feeds are the reaction mixtures containing cyclohexene-1,4-dicarboxylic acid that were prepared by the reaction of TTMA (0.5 mmol) and ethylene (2.0 MPa) in deionized water (20 mL) for 360 min at 200 °C.

the specific rate was reduced by almost one half. Therefore, we selected a Pd amount of 5 mol% for the following experiments. Using water as the solvent, the overall yield of terephthalic acid was only 19.1% (entry 4), compared to 70.5% DET when ethanol was used as both reactant and solvent under otherwise identical reaction conditions (entry 2). This is due to the fact that the solubility of TTMA in deionized water is rather low at room temperature (0.02 g per 100 mL water, see Table S1). As TTMA reacts with ethanol, diester **2** is formed, which has a very high solubility in ethanol and can thus easily undergo the Diels–Alder reaction with ethylene. Therefore, the esterification reaction is necessary to obtain DET in high yield.

We also conducted several experiments to study the influence of the acidity/basicity of the reaction mixture by adding base to the solution (Table 1, entries 5–9). When the same amount of hydroxide ions as that of protons resulting from the silicotungstic acid used in the first step is added, the yield of DET increased to 80.6% (entry 5). Doubling the OH^-/H^+ molar ratio resulted in a slight decrease in the yield to 80.1% (entry 6). However, upon further increasing the basicity of the reaction system, the yield decreased rapidly (entries 7–9). Obviously, the palladium-catalyzed dehydrogenation reaction preferentially proceeds under neutral or mildly basic conditions.

The block flow diagram for the production of DET starting from biomass-derived TTMA, ethylene, and ethanol is depicted in Figure 5.

The whole process can be conducted in a single reactor followed by one separation system. Compared to the reported routes for the production of biomass-derived PTA (see Figures S21 and S22), our process has the following features:

1) The process enables the direct formation of DET, a replacement for terephthalic acid. The commonly employed oxidation step is avoided, and the diethyl terephthalate product could be separated and purified by a common distillation method.
2) TTMA has a very low solubility at room temperature in many solvents. Subjecting TTMA to a key esterification reaction with ethanol leads to a significant increase in solubility. Furthermore, the diester of TTMA possesses two electron-donating ethoxy groups, facilitating the reaction with a dienophile.
3) The raw materials used in this process can all be derived from biomass. More specifically, TTMA can be produced from D-glucose and lignin by microbial synthesis.[14a,c] Furthermore, Toste et al. and Zhang et al. have proposed catalytic chemical routes to synthesize TTMA and its esters from biomass-derived mucic acid in excellent yield (99.0%).[18] The production of bioethanol has been commercialized, and ethylene can be manufactured by the dehydration of bio-ethanol on large scale. Additionally, unreacted ethanol and ethylene can be recycled in our process.

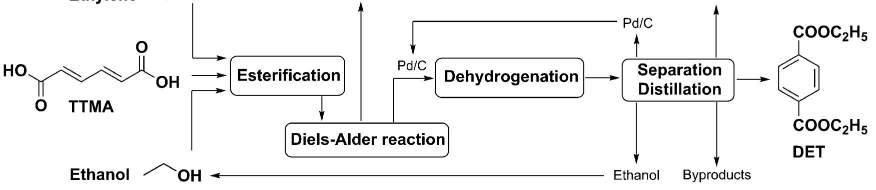

Figure 5. Block flow diagram for the production of DET from biomass-derived TTMA.

In conclusion, a synthetic route to directly obtain diethyl terephthalate (DET) from biomass-derived *trans,trans*-muconic acid (TTMA) through a cascade process combining esterification, Diels–Alder cycloaddition, and dehydrogenation in a single reactor has been developed. A palladium-based catalyst gave the best overall yield of DET, namely up to 80.6% based on the amount of TTMA. The key esterification reaction significantly increases the solubility of the diester product in ethanol and promotes the Diels–Alder reaction by modulating the electronic properties of TTMA. The dehydrogenation reaction preferentially occurs under neutral or mildly basic conditions. This work provides an example of producing high-value aromatic chemicals by fully utilizing the existing specific structures of biomass-derived feedstock. By rational design of the functional groups, the utilization of biomass can thus become more economic and environmentally friendly.

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Keywords: biomass · catalysis · cycloaddition · muconic acid · terephthalic acid

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