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Bio-derived muconates via cross-metathesis and their conversion to terephthalates

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Abstract: Polyethylene terephthalate that is 100% bio-derived is in high demand in the market guided by the ever more exigent sustainability regulations with the challenge remaining the production of renewable terephthalic acid. Renewable terephthalic acid or its precursors can be obtained via Diels-Alder cycloaddition and further dehydrogenation of biomass-derived muconic acid. The *cis,cis*-isomer of the dicarboxylic acid is typically synthesized using fermentation with genetically modified microorganisms, a process that requires complex separations to obtain a high yield of the pure product. Furthermore, the *cis* isomer has to be transformed into the *trans,trans*-form and has to be esterified before being suitable for the terephthalate synthesis. To overcome these challenges we have investigated the synthesis of dialkyl muconates via cross-metathesis. The Ru-catalyzed cross-coupling of sorbates with acrylates, which can be bio-derived, proceeds selectively to yield up to 41% di-ester muconates using very low catalyst amounts (0.5 – 3.0 mol.%) and no solvent. In the optimized procedure, the muconate precipitates as a solid and is easily recovered from the reaction medium. GC-MS and NMR analysis showed that this method delivers exclusively the trans,trans isomer of dimethyl muconate. The Diels-Alder reaction of dimethyl muconate with ethylene was studied in various solvents to obtain the 1,4-bis(carbomethoxy) cyclohexene. The cycloaddition proceeded in very high conversion (77 – 100%) and yield (70 − 98%) in all solvents investigated, methanol and tetrahydrofuran being the best. Next, the aromatization of 1,4-bis(carbomethoxy) cyclohexene to dimethyl terephthalate over Pd/C catalyst resulted in up to 70% yield in tetrahydrofuran and an air atmosphere. Due to the high yield of the reaction of dimethyl muconate to 1,4-bis(carbomethoxy) cyclohexene, no separation step is needed before the aromatization. This is the first time that cross-metathesis has been used to produce bio-derived trans,trans-muconates as precursors to renewable terephthalates, important building blocks in the polymer industry.

Introduction

The production of industrial chemical intermediates from renewable resources is an alternative to petrochemicals, often offering energy savings and contributing to sustainable development.[1] Among these intermediates, renewable polymer building blocks are especially attractive,[2] as many of them are oxygenates (as is biomass) and they are used in very large quantities.[3] Purified terephthalic acid (PTA), a building block of poly(ethylene terephthalate) (PET), is a very high-demand, commodity chemical. The industrial manufacture of PTA is primarily based on the catalytic aerobic oxidation of petroleum-based p-xylene in acetic acid, over cobalt-, manganese-, and bromide-based catalysts, known as the AMOCO process.[4] There is strong interest to develop sustainable processes for the production of 100% renewable PET.[5] The current bio-PET in the market is in fact only 30% renewable—accounting for the mono ethylene glycol, which is already produced from biomass.[6] The other building block, PTA, is fossil-fuel derived.[7] Bio-PTA production will allow for the production of 100% bio-based PET.

A number of routes have been investigated for the synthesis of bio-based p-xylene: via pyrolysis of waste biomass (with yields of up to 11%),[8] using bio-ethylene (49% yield),[9] from isobutanol (18.7% yield)[10] and from 5-hydroxymethylfurfural (HMF) (90% yield).[11] Most of these reaction paths have insufficient selectivity to p-xylene and an additional oxidation step is needed to produce the PTA.[12] While the highest yield to p-xylene from the aforementioned routes is from HMF,[13] the problematic separation and high production cost of HMF[14] limit its use as a PTA precursor.[15]

Several biomass-based PTA synthesis routes that avoid p-xylene as an intermediate have also been proposed. Limonene, extracted from orange peels for example, can afford PTA after only two steps: i) dehydrogenation to p-

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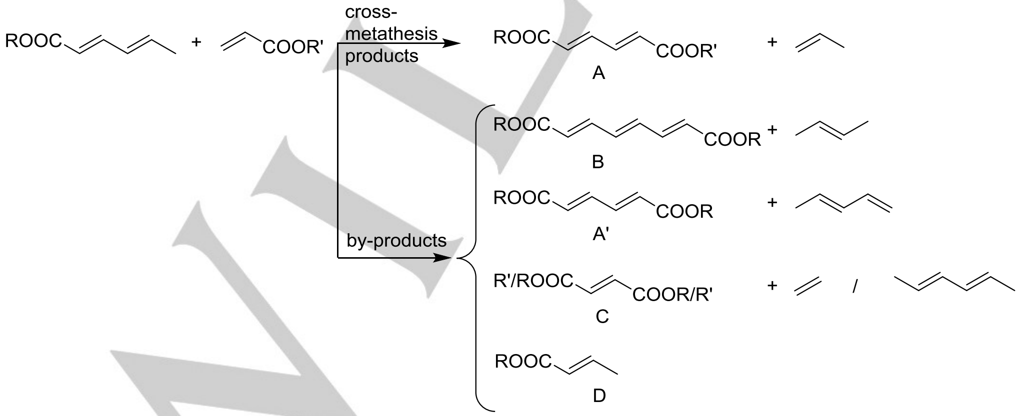
cymene and ii) oxidation to PTA.[16] However, the limited production capacity of limonene, and its competitive uses as food and perfume additives restrict its use as PTA feedstock. Diels-Alder cycloaddition of isoprene with acrylic acid leads to 4-methyl-1-cyclohexene-1-carboxylic acid and the subsequent oxidation of this cycloadduct forms terephthalic acid in 78% yield.[17] The main drawbacks here are the competitive demands for the high value-added starting materials and the strongly corrosive homogeneous catalysts used for the oxidation. Diels-Alder reaction with ethylene has also been applied to biomass-derived chemicals, such as in the reaction of 2,5-furandicarboxylic acid (FDCA), or its esters, with ethylene and subsequent dehydration, which gives PTA.[18] While this route would have only 4-5 steps from fructose to PTA, the reported yields are very low (0.14 % according to one example disclosed in the patent[18b]). Other Diels-Alder reactions with ethylene for the production of bio-PTA involve renewable sorbic acid[15b] and muconic acid.[19] While the renewable sorbic acid route comprises fewer steps to para-substituted toluates, namely the cycloaddition with ethylene and the consecutive aromatization, the yields in each step are low, i.e., 13% and 30% respectively.[15b] The cycloaddition of the muconic acid or its esters with ethylene gives cyclohex-2-ene-1,4-dicarboxylic acid, which, upon catalytic dehydrogenation, can be transformed to PTA in high yields (80-98%).[20] Although this method is very promising, muconic acid can only be produced via fermentation of biomass glucose by genetically modified strains and in low yields (<30%).[21] Furthermore, the use of genetically engineered microorganisms, their sensitivity to muconic acid and the costly multi-step process of the product recovery from the synthesis broth,[20c, 21b, 22] detract from the process efficiency.The fermentation route affords only the cis,cis-isomer of the muconic acid, To date, other methods can only produce the *cis,cis* isomers of the muconic acid, which, in order to be transformed in to terephthalates, has to undergo two additional steps: i) the isomerization to the all *trans isomer* and ii) esterification of the acid to increase solubility.[23] It is then clear that an alternative route to muconic acid or its esters would be highly desirable, to facilitate its use as a PTA precursor.

Olefin metathesis is one of the most powerful modern methods for the formation of new carbon-carbon bonds.[24] Its mechanism, proposed in the 70s by Herisson and Chauvin,[25] involves the [2+2] cycloaddition of an alkene double bond to a transition metal alkylidene to form a metallacyclobutane intermediate. Cleavage of this intermediate can then yield a new alkene and alkylidene. Interaction with the d-orbitals on the metal catalyst lowers the activation energy enough so the reaction can proceed rapidly at modest temperatures.[26] Catalysts that can be used for cross-metathesis reactions between olefins with functional groups are typically ruthenium carbenes, owing to their functional group tolerance.[27] Cross-metathesis of unsaturated fatty acid derivatives with electron deficient substrates, such as acrylic acid or its equivalents, has been studied in the last decades as a route to bio-sourced monomers used for the production of polyesters.[28] Cross-metathesis has, however, never been considered for the synthesis of important PET precursors, such as muconic acid. Previous work has shown that it is possible to synthesize muconates, although in relatively low yields (~30%) for high catalyst amounts (5.0 mol.%), via the cross-metathesis route from unsaturated carboxylic acids.[29] Inspired by this chemistry, we have investigated an alternative approach to muconates via the cross-metathesis reaction of sorbates with acrylates (Scheme 1).



Scheme 1. Synthesis of muconates via cross-metathesis of sorbates and acrylates and its byproducts.

One of the main challenges with the cross-metathesis reaction is the selectivity towards the cross-coupled product. As illustrated in Scheme 1, the main side products expected from the metathesis reaction of sorbate and acrylate esters are the self-metathesis products, the resulting gaseous compounds and compound D which is a product of secondary metathesis reactions between A and propene, or B and butene.

This route has the potential to produce a valuable product from inexpensive materials.[30] Moreover, the starting materials, i.e., sorbates and acrylates, can be derived from renewable carbon sources[31]. Plant-derived sorbic acid was first obtained from the extraction of the essential oil of nonedible mountain-ash berries (*Sorbus aucuparia*).[32] Since this method gives limited quantities of the sorbic acid, other bio-routes to sorbic acid have been proposed. Bio-sourced sorbic acid can be synthesized from bioethanol after its oxidation to acetaldehyde, trimerization to 2,4-hexadienal (sorbaldehyde), and, finally, oxidation to sorbic acid.[30b] Hydrogenation of the renewable 4-hydroxy-6-methyl-2-pyrone (HMP) to 4-hydroxy-6-methyltetrahydro-2-pyrone (4-HMTHP) and its further dehydration by contacting it with a solid acid catalyst also generates parasorbic acid (PSA).[33] On the other hand, bio-acrylic acid can be prepared from the glucose-derived 3-hydroxypropionic acid,[17, 34] or from the dehydration of biomass-derived methyl lactate.[35] Muconic acid or its esters are excellent precursors for other polymer building blocks, including adipic acid.[22c, 36]

The goal of this research was to take advantage of the versatile metathesis chemistry, combined with the availability of renewable and inexpensive starting materials to produce a sustainable and low cost precursor to PTA, i.e., muconate esters. Using Ru-catalysts the cross-metathesis between methyl sorbate and methyl acrylate affords the *trans,trans* isomer of dimethyl muconate in yields up to 40% for low catalyst amounts (only 3.0 mol.%). The subsequent Diels-Alder cyclization of the muconate with ethylene proceeds very selectively to yield up to 98% dimethyl cyclohex-2-ene-1,4-dicarboxylate, which can then be readily transformed to dimethyl terephthalate without prior purification via oxidative dehydrogenation in tetrahydrofuran over a Pd/C catalyst. The method reported here keeps the carboxyl groups of the starting materials in the final PTA after three reactions, and accordingly has a very high atom economy to the target product.

Results and Discussion

Catalysts screening. Several commercially available Ru-catalysts were investigated for the reaction between ethyl-substituted sorbate and acrylate esters (Figure 1). One of the major drawbacks of ruthenium carbene catalysts in many reactions is the lifetime and efficiency of these catalysts.[37] For the cross-metathesis reaction between ethyl-substituted sorbate and acrylate esters, first (catalyst **I**) and second-generation (catalyst **II**) Hoveyda-Grubbs catalysts were investigated. Catalyst **I**, containing a phosphine ligand, gave the lowest conversion and selectivity towards the desired product, diethyl muconate, when compared to all the catalysts tested. The second generation Hoveyda-Grubbs catalyst **II**, containing an N-heterocyclic carbene (NHC) ligand, demonstrated a higher metathetic activity. The increased reactivity of NHC-based catalysts relative to phosphine-based catalysts in cross-metathesis is attributed to their higher tolerance toward functionalized olefins.[38] In addition, it has been shown that this catalyst (**II**) can be recycled via silica gel chromatography.[39] Two other variations of the second generation of Hoveyda-Grubbs catalyst **II** were also tested, namely catalysts **III** and **IV**, due to the fact that they can be recovered from the reaction mixture either by water extraction (catalyst **III**),[40] or by filtration through a short pad of silica gel (catalyst **IV**).[41] These potentially recyclable catalysts were selected in consideration of the high cost of these materials and to avoid waste.

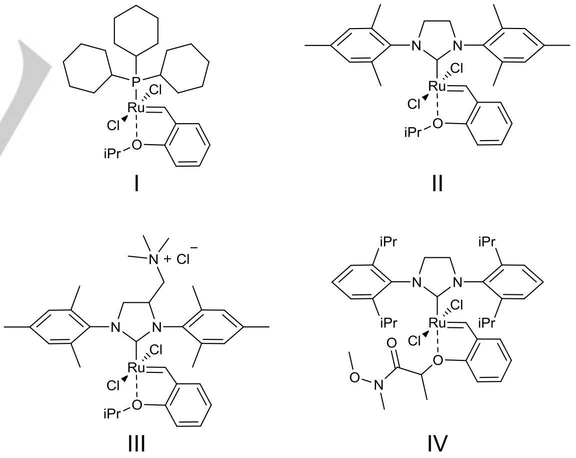


Figure 1. Ru-catalysts tested for the cross-metathesis reaction

Among the ruthenium catalysts investigated, the activity and was highest for catalyst **IV** (Table 1). This could be due to its higher reaction rates at low concentration, and its improved stability.[41] As seen in Table 1, the increasing activity for the catalysts (from **I** to **IV)** correlates well with the attained yield of the cross-metathesis product, A. When using a catalyst

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with low metathetic-activity the Type II olefin involved in the reaction (the acrylate) has a lower probability of participating in the cross-metathesis reaction and will act almost as a Type III olefin (no homodimerization activity). That is why cross-metathesis probability, and, thus, selectivity to A, is higher for catalyst with good activity when Type I and II olefins are involved in the reaction. Similar findings for styrene and stilbene cross-metathesis have been reported[24a].

Table 1. Cross-metathesis of ethyl sorbate with ethyl acrylate using different ruthenium catalysts[a]

Entry	Catalyst	Conversion / %[b]	Yield$_A$ / %[b]	Selectivity$_A$/ %[b]
1	I	2.6	0.9	34.6
2	II	5.1	2.2	43.1
3	III	13.2	6.3	47.7
4	IV	16.5	10.8	65.5

[a]Reaction conditions: catalyst 0.5 mol %, reflux, 5 equiv. excess ethyl acrylate, 323 K, 1 h, N_2 atmosphere.
[b]Determined by GC.

Acrylic acid derivatives, which are α,β-unsaturated substrates, are known to undergo homodimerization at a low rate, if at all, and, thus, fall into the Type II category (slow homodimerization)[24a]. This prediction was verified by the resulting conversion of no more than 4.2% of ethyl acrylate when it reacts alone in the presence of catalyst **IV** (0.10 mol.%) in methanol (3.00 mol/L) at 323 K over 2 hours. The resulting product from the GC analysis of the reaction mixture is dimethyl fumarate (C). Ethyl sorbate, on the other hand, reacted much faster to reach a conversion of up to 40% at the same reaction conditions. The main products in this case were the self-coupled product, B (diethyl (2E,4E,6E)-octa-2,4,6-trienedioate, 41% selectivity), which precipitates as a deep red solid, and some D (ethyl crotonate, 38% selectivity). The fast self-metathesis reaction of ethyl sorbate indicates that it belongs to the type I olefins. Thus, having olefins of two different types means that their reaction can result in selective cross-metathesis.[24a] In addition, note that ethyl crotonate (D) is a very stable compound, which is a type III or even type IV olefin (no homodimerization or inert to cross-metathesis). When tested as a reactant in a control experiment, its reaction with ethyl sorbate gave almost the same products as the self-metathesis of ethyl sorbate at the same reaction conditions. This means that the formation of ethyl crotonate does not favor the cross-metathesis mechanism. Similar results were obtained when methyl-substituted sorbate and acrylate esters were used in control experiments.

One of the main goals in developing a green and sustainable process is to reduce the use of solvents,[42] since solvents can be of great environmental concern and make up an important part of the process cost. Since catalyst **IV** was one of the most effective catalysts in our study (Table 1), it was used to understand the solvent dependence on the cross-metathesis between ethyl sorbate and ethyl acrylate. Two commonly used solvents in cross-metathesis reactions are dichloromethane (DCM) and toluene.[43] DCM performs slightly better than toluene (Table 2) although the differences are small. In fact, more polar solvents[44] and those with smaller molecular sizes[45] tend to give better results in the cross-metathesis. However, the neat reaction using ethyl acrylate as the solvent and as the reactant in 5-fold excess provided higher conversion and selectivity towards the di-ester muconate (Table 2).

Table 2. Solvent effect on the cross-metathesis of ethyl sorbate with ethyl acrylate[a]

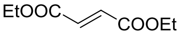
Entry	Solvent	Conversion/ %[b]	Yield$_A$/ %[b]	Selectivity$_A$/ %[b]
1	No solvent	16.5	10.8	65.5
2	DCM	9.2	5.3	57.6
3	Toluene	6.3	3.2	50.8

[a]Reaction conditions: catalyst **IV** (0.5 mol %), reflux, 5 equiv. excess ethyl acrylate, 323 K, 1 h, N_2 atmosphere.
[b]Determined by GC.

It is established that the intermediate enoic carbenes, [Ru]=CHCOOR, formed from the reaction of the catalyst with the acrylate,[44], are stabilized by excess acrylate owing to its lack of metathesis reactivity during the course of the reaction.[46] Not only does the absence of solvent provide a more sustainable process, as it decreases waste, but the separation of the product from the reaction medium is also easier when fewer chemical species are present

Reactant substituent effects. Steric effects of the reactant molecules are an important factor in metathesis reactions[24a, 27b, 47] and they were investigated by changing the size of the substituent of the acrylate ester reacting with the ethyl sorbate (Table 3). The behavior of differently substituted acrylates as substrates for the cross-metathesis with ethyl sorbate shows the same correlations that have been reported in previous reports.[48] A larger carboxylic group substituent decreases the reaction rate of metathesis by making it more difficult for the molecules to reach the Ru active site.[49] As seen in Table 3, the smaller the substituent of the acrylate, the higher is the conversion to the cross-metathesis product. Moreover, when the fumarate is used as a reactant (Table 3, entry 5) the reactivity for cross-metathesis is further diminished, due to the steric hindrance and the high stability of the di-ester.

Table 3. Cross metathesis of ethyl sorbate and acrylates with different substituents [a]

Entry	Reactant 2	Conversion/ %[b]	Yield$_A$/ %[b]	Selectivity$_A$/ %[b]
1	 COOMe	21.2	14.3	67.5
2	 COOEt	16.5	10.8	65.5
3	 COOBut	11.2	6.6	58.9
4	 COO*tetr*-But	9.5	4.6	48.4
5	 EtOOC COOEt	5.0	2.1	42.0

[a]Reaction conditions: catalyst **IV** (0.5 mol %), reflux, 5 equiv. excess ethyl acrylate, 323 K, 1 h, N_2 atmosphere.

[b]Determined by GC.

Optimizing conditions for the synthesis of dimethyl muconate. Consideration of the results described above guided the optimization of the dialkyl muconate synthesis. In particular, methyl sorbates and acrylates were used as reactants in the rest of the experiments as they showed the highest reaction rate. The cross-metathesis product, dimethyl muconate, is an off-white solid which due to symmetry and better packing, precipitates quickly upon formation. Producing a solid, hardly soluble compound in this case is advantageous because it drives the reaction forward. Further, the separation of the product from the reaction mixture can be easily accomplished by filtration.

Table 4. Methyl sorbate conversion and dimethyl muconate yield in the cross-metathesis of methyl sorbate with methyl acrylate at different reaction conditions[a].

Entry	Atm.	T / K	$n_{cat.}$/ mol.%	Reaction time/ h	Conversion / %[b]	Yield / %[b]	Selectivity/ %	TON[c]
1	Air	293	0.5	1	16	1.4	8.8	2.7
2	N_2	293	0.5	1	28	5.1	18.2	10
3	N_2	293	0.5	24	26	6.4	24.6	0.5
4	N_2	323	0.5	0.5	19	10.5	55.3	20
5	N_2	323	0.5	1	35	18.7	53.4	37
6	N_2	323	0.5	6	34	18.1	53.2	35
7	N_2	323	0.5	24	36	19.1	53.1	37
8	N_2	323	3.0	1	61	40.7	66.7	80

[a]Reaction conditions: catalyst **IV**, reflux, 10 equiv. excess methyl acrylate. [b]Determined by GC and solid product analysis.

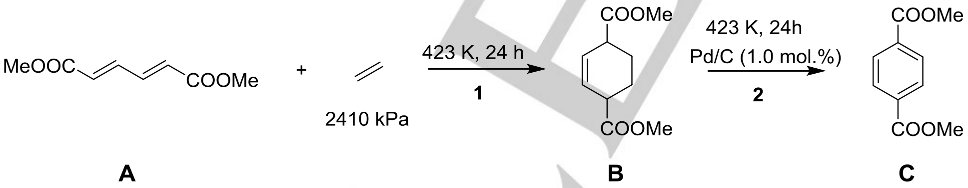
[c]TON= moles of dimethyl muconate/ moles of catalyst

The cross-metathesis reaction conducted at room temperature using methyl sorbate and methyl acrylate results in low conversion (Table 4, entries 1 – 3), compared to reactions carried out at 323 K at otherwise identical conditions. Although the ruthenium catalyst IV, like other second generation Hoveyda-Grubbs catalysts, is more resistant towards deactivation by oxygen from the atmosphere,[50] it still deactivates under an air atmosphere for the typical reaction times, giving a low TON (see entry 1, Table 4). To determine the stability of the catalyst under the reaction conditions, the time course of the cross-metathesis of methyl sorbate with methyl acrylate was investigated using a series of independent experiments (entries 4 – 7). Our results show that most of the conversion happens within the first hour of the reaction, and there is little or no changes even after 24 hours of reaction (entry 7). Termination of product formation before equilibrium has been reached is indicative of catalyst decomposition[45]. Entry 8 in Table 3 shows that although for practical reasons we kept the catalyst loading at very low levels (only 0.5 mol.%), the conversion and yield of the final product can be easily increased by increasing the amount of catalyst. The TON for this case is however low, due to catalyst deactivation over the course of reaction. Adding the Ru-catalyst gradually over the course of the reaction can reduce the problem of deactivation,[29] but this was not part of this investigation. Another reported way to improve cross-metathesis efficiency by using low catalyst doses is to add other compounds, e.g. *p*-cresol, iodites, that act as catalyst stabilizers.[47, 51] Such compounds are usually toxic and their use would defy our efforts for a clean process with minimum harmful waste. The turn over frequencies of the catalytic reactions are also shown for comparison in Table 4. The conditions that generate the highest TON in this case are the conditions depicted in entry 5.

The purified dimethyl muconate obtained from the cross-metathesis of methyl sorbate and methyl acrylate was identified using GC-MS. Commercial *trans,trans*-dimethyl muconate (Aldrich, CAS No.: 1733-37-5) was also analysed to confirm the MS spectra and the isomer type (*E,E*-); methanol was used as a solvent. X-ray diffreaction patterns of the as-synthesized and commercial dimethyl muconate differed only in the presence of additional small diffraction peaks coming from the tamuate impurity in the synthesized dimethyl muconate product. ^{1}H and ^{13}C NMR spectral analysis of the product also confirmed the chemical structure of the as-synthesized *trans,trans*-dimethyl muconate and the triene impurity.[23a, 52] ^{1}H NMR spectra (400 MHz, CD_3OD) of t*rans,trans*-dimethyl muconate: δ 7.35 (dd, 2H), 6.30 (d, 2H), 3.75 (s, 6H). ^{13}C NMR spectra (400 MHz, CD_3OD) of *trans,trans*-dimethyl muconate: δ 51.6, 128.4, 141.6, 167.1. ^{1}H NMR spectra (400 MHz, CD_3OD) of dimethyl tamuate: δ 7.38 (dd, 2H), 6.79 (dd, 2H), 6.13 (d, 2H), 3.76 (s, 6H).

Elemental ICP-OES analysis showed that after filtration and purification of the dimethyl muconate product by recrystallization in ethanol, its ruthenium content is below the 50 ppm detection limit of ICP-OES. Most of the ruthenium impurities remain in the liquid product mixture (reaction product filtrate) of the cross-metathesis reaction using 0.5 mol.% of catalyst **IV**, which after silica flash chromatography, affords a product mixture in which the residual Ru content is less than 100 – 160 ppm (by ICP-OES analysis).

Dimethyl terephthalate synthesis from dimethyl muconate. Frost et al.[20c] also described the formation of terephthalic acid by a Diels–Alder reaction between *cis,cis*-muconic acid and ethylene and further dehydrogenation.[22b] Starting from a *trans,trans*-isomer of the muconate is much better and it is crucial for cyclization with ethylene to prepare a terepthalic acid percursor[23b] (Scheme 2).



Scheme 2. One-pot, two-step process of dimethyl terephthalate synthesis from the Diels-Alder reaction of dimethyl muconate with ethylene and the subsequent aromatization of the Diels-Alder adduct in the presence of a Pd/C catalyst.

The Diels–Alder reaction proceeds at high ethylene pressure (here 2410 kPa), temperatures of around 423 K and without catalyst.[20b] *m*-Xylene was initially used as a solvent,[20c] but the solubility of the muconate was not sufficiently high in *m*-xylene. Due to the low solubility of the dimethyl muconate in non-polar solvents, polar solvents were tested, including ethyl acetate (EtOAc), methanol (MeOH), tetrahydrofuran (THF) and also acetic acid (Table 5). The Diels-Adler reaction proceeds in high conversion and yields in all solvents tested, especially in methanol (Table 5, entry 3 and 4), in which the conversion and selectivity are the highest. The final product mixture from the Diels-Alder reaction contains mainly the substituted cyclohexene product (**B**, scheme 2), the unreacted dimethyl muconate and the tamuate impurity of the muconate. The high yields of the product **B** and the neat product mixture makes product separation and purification unnecessary; it is possible to use the crude reaction mixture from the first step (**1** in scheme 2) as the starting material for the dehydrogenation reaction with only the addition of Pd/C catalyst (**2** in scheme 2). The impurity present in the muconate product, i.e., dimethyl tamuate, undergoes cycloaddition with ethylene in low conversions (<15%), but it does not affect the stoichiometry of the cyclohexene formation, due to the ethylene excess in the reactor. This was verified in a control experiments with pure, commercial dimethyl terephthalate, which was converted to the same extend as the synthesized one at the same reaction conditions.

Table 5. Diels-Alder and consecutive aromatization conditions and results (conversion of the dimethyl muconate, A; yield of the cycloaduct, B; conversion of the cycloaduct, B; yield of the dimethyl terephthalate, C) for the production of dimethyl terephthalate from dimethyl muconate

			Diels-Alder		Aromatization	
Entry	Solvent	Atmosphere of 2	Conversion$_A$ / %	Yield$_B$ / %	Conversion$_B$ / %	Yield$_C$ / %
1	*m*-Xylene	N_2	77	76	-	-
2	EtOAc	N_2	88	76	-	-
3	MeOH	N_2	100	98	93	33
4	MeOH	Air	98	96	62	55
5	THF	N_2	96	75	73	49
6	THF	Air	98	77	97	68
7	THF	O_2	95	74	54	32
9	Acetic Acid	Air	85	70	61	44

Diels-Alder reaction: 0.03 M dimethyl muconate in a solvent, 2400 kPa ethylene, 423 K, 24 h.
Aromatization reaction: 15 ml of the product mixture from the Diels-Alder reaction, 0.5 g of 10wt.% Pd/C catalyst, 3450 kPa N_2/Air/O_2.

An optimal solvent for the production of terepthalates from muconates was identified to carry out both reaction steps (**1** and **2** in Scheme 2) in a one-pot, same-solvent fashion. An appropriate solvent for both steps would make the process suitable for a continuous flow reactor plant. While the cycloaddition of the muconate with ethylene proceeds in high yields of B, its conversion to dimethyl terephthalate is highly dependent on the solvent and the atmosphere in the reactor during the dehydrogenation reaction. The main side product of the aromatization step is the fully hydrogenated cyclohexane dicarboxylate.[53] Methanol turned out to be an unsuitable solvent for the dehydrogenation step as it undergoes partial decomposition over the palladium catalyst independently of the atmosphere of the reaction (entries 3 and 4 in Table 5)[54]. Acetic acid is a good solvent for the dimethyl muconate, but its high reactivity with the catalyst and the metal walls of the reactor makes it a poor candidate for our sequential transformations. THF, on the other hand, gives a good yield in the first cycloaddition step and in the oxidative dehydrogenation step it gives yields up to 68% when air (as source of oxidant) is present in the reactor headspace. When the reactor is filled with pure oxygen (1380 kPa) as oxidant, THF is consumed in side reactions and the efficiency of the dehydrogenation reaction decreases significantly (only 32% yield of **C**). In the absence of an oxidant and in inert atmosphere (N_2, entry 5 Table 5), the aromatization of **B** to **C** proceeds up to 49% yield. These results show that relatively low partial pressures of oxygen promote the oxidative dehydrogenation reactions over Pd catalysts at moderated temperatures.[55] High oxygen pressure in the reactor, consumes the solvent in side reactions and drives the disproportionation of the products towards the cyclohexane dicarboxylate.[56]

Conclusions

This report showed that dialkyl muconates can be successfully synthesized via cross-metathesis. Low amounts (up to 3.0 mol.%) of the second generation, NHC-based Hoveyda-Grubbs catalyst can be used efficiently (up to 41% yield) for this synthesis, due to their high metathetic activity and stability. The starting reagents, sorbate and acrylate esters, are inexpensive and can be derived from biomass waste. Moreover, no solvent is used in the muconates synthesis, adding more sustainability value to this process. NMR and GC-MS analysis established the formation of the trans,trans-isomer of dimethyl muconate. The trans form of muconates is important, as it makes them readily transformable precursors to important polymer building blocks, such as terephthalic or adipic acid, making this synthesis route superior to other bio-synthesis methods, which can only produce the cis isomer of muconic acid. The as-synthesized trans,trans-dimethyl muconate is further transformed into dimethyl terephthalate by undergoing a Diels-Alder cyclization with ethylene to give 1,4-Bis(carbomethoxy) cyclohexene (up to 98% yield), which is then dehydrogenated in the same pot and solvent into dimethyl terephthalate over a Pd/C catalyst (68% yield). This method for obtaining bio-derived dimethyl muconate via cross-metathesis as a precursor to renewable dimethyl terephthalate, can also be applied to produce other bio-derived polymer building blocks, like terephthalic acid, its other esters, trimellitic acid, adipic acid, etc. Although the yield of the methyl muconate remains low for commercial interest, our results point towards the focus of future research for improving the synthesis of bio-sourced terephthalates.

Experimental Section

All of the reagents were purchased from SigmaAldrich and were used as received, without further purification. The metathesis catalysts (Figure 1) were purchased from Aldrich (Hoveyda−Grubbs I, CAS No. 203714-71-0; Hoveyda−Grubbs II, 301224-40-8) and Strem Chemicals (GreenCat, 1448663-06-6; StickyCat Cl, CAS No. 1452227-72-3).

ICP-OES analysis for evaluating the Ru content (method: GLI Procedure ME-70) were done by the Galbraith Laboratories, Inc. (Knoxville,TN). XRD patterns were collected using a Bruker D8 diffractometer with CuKα radiation source. The pattern was collected for 0.5 s at each increment of 0.02^0 between 5 and 50^0. NMR spectra were recorded on a Bruker DRX-400 spectrometer and were referenced to the residual protons of the solvent (CD_2Cl_2, 5.32 ppm; CD_3OD, 4.87 ppm). The spectra were analyzed with the MestReNova software. All liquid products were analyzed with a GC-MS (Agilent 7890B GC system and 5977A MSD) equipped with an FID. A DB-5 column (30.0 m x 250 µm x 0.25 µm) was used with the following temperature program for all analysis: hold at 313K for 4 min, 10 K min^{-1} ramp to 523 K, and a final hold for 4 min. Retention times and calibrations of reactants and products were determined from calibration solutions of the commercial compounds.

The cross-metathesis reaction was conducted in a 25 ml round bottom flask connected to a condenser and a Schlenk line to assure the absence of moisture and an inert atmosphere (nitrogen). The acrylate and sorbate esters were mixed in a molar ratio of 5 – 10, with excess of acrylate. The ruthenium catalyst was added in a predefined amount (0.1 – 3.0 molar ratio of the catalyst with respect to the sorbate) to the reaction mixture. The reaction mixtures were analyzed using GC-MS. Conversion and yield of the reaction were calculated on the sorbate basis as follows:

$$Conversion\ (X) = \frac{Moles\ of\ reactant\ converted}{Moles\ of\ reactant\ fed} \qquad 1$$

$$Yield\ (Y) = \frac{Moles\ of\ desired\ product}{Moles\ of\ reactant\ fed} \qquad 2$$

The selectivity of the products is defined as the ratio of the desired product, A, to the rest of the detectable products by GC-MS. Gaseous byproducts are not considered in this analysis.

When a solid muconate product was formed, it was separated from the reaction mixture via filtration and thoroughly washed with ethanol. The liquid product mixture of the reaction was purified from ruthenium residues by flash chromatography using Merck silica gel 60 (230 – 400 mesh)[41]. The solid dimethyl muconate contained dimethyl tamuate (dimethyl 2,4,6-octatrienedioate, CAS No. 13160-88-8)[52] as impurity. The ratio of the muconate to tamuate determined from ^{1}H-NMR was 7:1.

The Diels-Alder and dehydrogenation-aromatization reactions were conducted in a 5512-series Parr reactor. For the Diels-Alder reaction, the Parr reactor internal Teflon liner was loaded with the dimethyl muconate (0.1 g) in a solvent (0.03 M). After assembly of the Parr reactor, its contents were degassed three times with N_2 (2760 to 3450 kPa). The internal pressure was then allowed to decrease to a relative pressure 0 kPa, at which point ethylene (Air Liquide, 99.6%) was introduced up to the desired pressure (2400 kPa). Following the detachment of the gas feed lines, the contents of the Parr reactor were heated to 423 K. After the desired amount of time, the reaction was quenched by cooling in an ice bath to room temperature, and it was degassed by opening the exhaust valve. The contents of the reactor were then analyzed by GC-MS. For the dehydrogenation reactions, the product mixture from the Diels-Alder cyclization reaction described above, served as a starting solution for the aromatization reaction to produce dimethyl terephthalate. 0.5 g of 10wt.% Pd/C catalyst were added to 15 ml of the reaction mixture in the Parr reactor. Independently of the gas atmosphere present in the reactor, its content was always pressurized with N_2 to 3450 kPa, to maintain overpressure for all experiments. After the reaction was complete, the catalyst was removed by filtration and the reaction mixture was analysed by GC-MS. The conversions and yields for the Diels-Alder and dehydrogenation reactions were calculated using equations **1** and **2** above.

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Keywords: terephthalate • muconate • metathesis • Diels-Alder • bio-derived chemical

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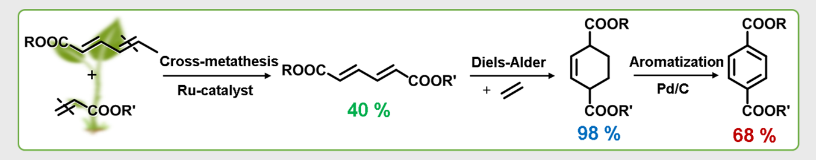

Cross-road to green terephthalate rings metathesized: Cross-metathesis was used for the first time to produce renewable terephthalate PET precursors. Moderate amounts of Ru-catalyst and no solvents gave pure trans isomer of the muconates, which can then be readily converted to terephthalates by combining consecutive Diels-Alder and aromatization reactions in the same solvent with very high efficiency.

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