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Synthesis of Biobased Terephthalic Acid from Cycloaddition of Isoprene with Acrylic Acid

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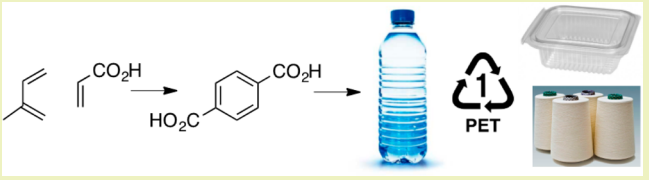
Supporting Information

ABSTRACT: A reaction sequence has been elaborated that could enable the 36×10^9 kg/y of terephthalic acid currently synthesized from *p*-xylene and used in the manufacture of poly(ethylene terephthalate) (PET) to instead be synthesized via cycloaddition of biobased acrylic acid and biobased isoprene. A central challenge in this cycloaddition is isoprene polymerization catalyzed by acrylic acid that is accelerated by the same Lewis acid catalysts needed to improve para selectivity in the cycloaddition. Esterifying acrylic acid to avoid diene polymerization while enabling Lewis acid catalyzed cycloaddition is not atom economical. A solution has been found with $TiCl_4$ (2 mol %) catalyzed cycloaddition of acrylic acid and isoprene. At room temperature and in the absence of solvent, cycloaddition (94% yield) gives a 23:1, para:meta selectivity. Pd(0)-catalyzed aromatization (77% yield) of the para cycloaddition product affords *p*-toluic acid that is converted (94% yield) into terephthalic acid with a Co^{2+}/Mn^{2+}-catalyzed O_2 oxidation.

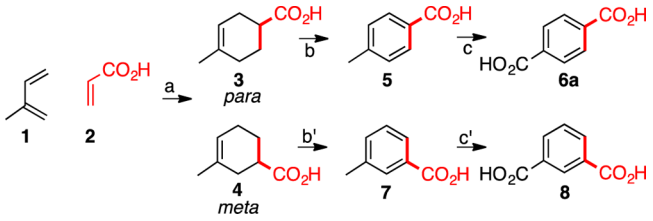


KEYWORDS: *Terephthalic acid, Isophthalic acid, Acrylic acid, Isoprene, Biobased*

INTRODUCTION

Microbial synthesis of isoprene **1** from glucose,[1] synthesis of acrylic acid **2** from glucose,[2,3] and synthesis of biobased terephthalic acid **6a** are areas of disparate research uniquely connected by the Alder reaction sequence (Scheme 1). Alder first used cycloaddition with acrylic acid **2** to trap isoprene **1** formed during ring-opening of methylenecyclobutane.[4] Later, reaction (Scheme 1) of isoprene **1** and acrylic acid **2** (1:1, mol/mol) at 95 °C in a high pressure reaction vessel afforded a 79% cycloaddition yield with 3:1, *para*-**3**:*meta*-**4** selectivity.[5] This neat reaction avoids the toxicity, volatility, and recycling issues frequently associated with solvent use. However, catalysis options were needed to increase para selectivity, reduce temperature, and eliminate elevated pressures in the cycloaddition.

Scheme 1[a]



[a](a) $TiCl_4$ (2 mol %), neat, rt, 94%, 23:1, **3**:**4**. (b)/(b′) 5 wt % Pd on C, 240 °C, 0.11 bar, 77%(b)/69%(b′). (c)/(c′) $Co(OAc)_2$ (0.5 mol %), $Mn(OAc)_2$ (0.5 mol %), *N*-hydroxysuccinimide, O_2, HOAc, 100 °C, 94%(c)/88%(c′).

Beyond the central importance of the cycloaddition of **1** with **2**, catalytic alternatives had to be elaborated to Alder's[4] and Tong's[6] aromatizations of *para*-**3** to *p*-toluic acid **5** in concentrated H_2SO_4 and stoichiometric $KMnO_4$ oxidation of **5** to terephthalic acid **6a** (Scheme 1). The catalytic alternatives that were developed were also examined for aromatization of *meta*-**4** to *m*-toluic acid **7** and oxidation of **7** to isophthalic acid **8** (Scheme 1). PET contains 3−5% of isophthalic acid **8** to inhibit crystallization, which enhances transparency and lowers the melting point of PET.[7] Access to biobased isophthalic acid is therefore a prerequisite to synthesis of PET with 100% biobased carbon content.

RESULTS AND DISCUSSION

Catalysis leading to acyloxyborane and acylboronate intermediacy can enhance para selectivity in the cycloaddition of **1** and **2**.[6,8−10] Use of BH_3[6,8] (15 mol %) and 2-bromophenylboronic acid[9,10] (20 mol %) affords 80−90% yields of *para*-**3** cycloaddition product in CH_2Cl_2. However, the solvent choice, high mole percent catalyst loading, and the multiple steps/expense for synthesis of BH_3 and 2-bromophenylboronic acid detract from their potential utility in commodity chemical synthesis. Lewis acid catalysis is an attractive alternative due to the greater availability of many of these catalysts. For example, Lewis acid $TiCl_4$ is also an intermediate in the Kroll process[11] for refining Ti^0 and a starting material for manufacture of TiO_2.[11]

Lewis acid-catalyzed reaction of *β*-acylacrylic acids in the presence of diisopropylethylamine (DIPEA) has been reported to improve para selectivity with use in separate reactions of

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$SnCl_4$ (200 mol %), $TiCl_4$ (150 mol %), and $Sc(OTf)_3$ (10 mol %) as catalysts in various solvents.[12] An example in the patent literature reports reaction of acrylic acid with 1,3-butadiene in benzene catalyzed by $TiCl_4$ (20 mol %) that afforded a 44% of cycloaddition product.[13−15] Relative to 1,3-butadiene, isoprene **1** is more reactive toward Lewis acid-catalyzed polymerization.[16]

Lewis acid catalysts were screened using a 1:1 (mol/mol) ratio of **1**/**2** under neat reaction conditions at rt to identify improved yield and para selectivity. Acrylic acid **2** was first added to the Lewis acid under Ar followed by addition of isoprene **1** at 0 °C. The reaction was then allowed to warm to rt where reaction proceeded for 24 h. In lieu of added Lewis acid, reaction at rt and 1 bar pressure of neat **1** and **2** (1:1, mol/mol) afforded a 27% yield with 3:1, *para*-**3**:*meta*-**4** selectivity (entry 1, Table 1).

Table 1. Cation Impact on Cycloaddition[a] of Isoprene 1 and Acrylic Acid 2

entry	catalyst	temp	yield[b]	para/meta[c]
1	none	rt	27%	3:1
2	CuCl	rt	8%	3:1
3	$CuCl_2$	rt	8%	3:1
4	$NiCl_2$	rt	11%	3:1
5	YCl_3	rt	11%	4:1
6	$FeCl_2$	rt	11%	4:1
7	$AlCl_3$	rt	15%	6:1
8	$FeCl_3$	rt	17%	7:1
9	$ZnCl_2$	rt	20%	5:1
10	$MgCl_2$	rt	21%	4:1
11	$TiCl_3$	rt	34%	8:1
12	$SnCl_4$	rt	37%	11:1
13	$ScCl_3$	rt	48%	8:1
14	$SnCl_2$	rt	59%	15:1
15	$HfCl_4$	rt	73%	12:1
16	$ZrCl_4$	rt	76%	12:1
17	$TiCl_4$	rt	94%[d]	23:1
18[e]	$TiCl_4$	0 °C	94%	37:1
19[f]	$TiCl_4$	−20 °C	94%	50:1

[a]Neat reaction for 24 h of 5 mmol/5 mmol, **1**/**2** using 2 mol % catalyst. [b]Determined by NMR. [c]Determined by GC. [d] ±1%. [e]48 h reaction. [f]100 h reaction.

Because of their ability to modulate Lewis acidity, triflates, chlorides, and bromides were examined as counteranions.[17] Cu^{2+}, Fe^{3+}, and Sn^{2+} triflates in acrylic acid **2** catalyzed a violent reaction upon addition of isoprene **1**. This reactivity was controlled upon addition of 10 mol % DIPEA, triethylamine, or lutidine, but only small improvements in yields and selectivities were observed. Violent reaction upon addition of isoprene **1** to catalyst complexed with acrylic acid **2** was also avoided with use of chloride as the counteranion (entry 2−19, Table 1). Significant improvement in yield and selectivity were observed for Sc^{3+}, Sn^{2+}, Hf^{4+}, and Zr^{4+} (entry 13−16, Table 1). However, Ti^{4+} (entry 17, Table 1) was singular in the yield and para selectivity achieved. Lower temperature improved the selectivity of $TiCl_4$-catalyzed cycloaddition of **1** with **2** (entry 18−19, Table 1). Chloride was the only Ti^{4+} counteranion that afforded high yield and selectivity for the cycloaddition (Table 2).

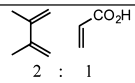
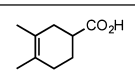
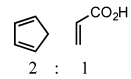
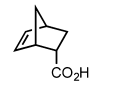
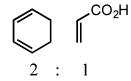
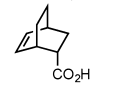
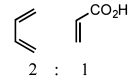
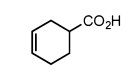
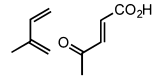
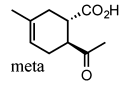
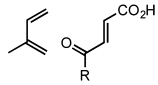
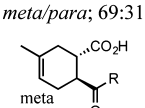
To determine whether $TiCl_4$ catalysis was unique to cycloaddition of isoprene **1** and acrylic acid **2**, a preliminary survey (Table 3) was made of other $TiCl_4$-catalyzed, solvent-free cycloadditions involving dienophile carboxylic acids. Neat reaction of acrylic acid **2** with 2,3-dimethyl-1,3-butadiene, 1,3-cyclohexadiene, cyclopentadiene and 1,3-butadiene all gave >80% cycloaddition yields using $TiCl_4$ catalysis. Similar yields were realized in the $TiCl_4$-catalyzed reactions of isoprene **1** with β-acylacrylic acids. A quantity of liquid diene is required to at least partially solubilize the dienophile carboxylic acids. This is the reason for the higher mole ratio of diene to dienophile for the cycloadditions summarized in Table 3 relative to the 1:1, mol/mol ratio used in the reaction of isoprene with acrylic acid.

Table 2. Anion Impact on Cycloaddition[a] of Isoprene 1 and Acrylic Acid 2

entry	catalyst	temp	yield[b]	para/meta[c]
1	$TiBr_4$	rt	58%	18:1
2	TiF_4	rt	1%	14:1
3	$Ti(O_3SCF_3)_2Cl_2$[d]	rt	23%	5:1
4	$Ti(OiPr)_4$	rt	8%	4:1
5[e]	$Ti(Cp)_2Cl_2$	rt	13%	3:1

[a]Neat reaction for 24 h of 5 mmol/5 mmol, **1**/**2** using 2 mol % catalyst. [b]Determined by NMR. [c]Determined by GC. [d]0.1 mol % catalyst. [e]Cp = cyclopentadienyl.

Table 3. $TiCl_4$-Catalyzed Cycloadditions[a] of Dienophile Carboxylic Acid

Entry	Substrates mol:mol	Time Temp [$TiCl_4$]	Product	Yield[b] (Yield)[c]
1	 2 : 1	22 h rt 2 mol%		82% (13%)
2	 2 : 1	0.7 h 0°C 2 mol%	 *endo/exo*; 84:16	82% (31%)
3	 2 : 1	23 h rt 10 mol%	 *endo/exo*; 99:1	84% (3%)
4	 2 : 1	18 h rt 10 mol%		86% (4%)
5	 10 : 1	22 h rt 2 mol%	 *meta/para*; 69:31	82% (14%)
6	 10 : 1 R=4-Me-C_6H_4	1 h rt 10 mol%	 *meta/para*; 70:30	88% (0%)

[a]Neat reaction. [b]Isolated yield for $TiCl_4$-catalyzed cycloaddition. [c]NMR yield of control cycloaddition lacking $TiCl_4$.

As previously reported,[4,6] para cycloaddition product **3** was aromatized in concentrated H_2SO_4 at 100 °C. Significant charring was observed in route to a 79% yield of *p*-toluic acid **5**. Aromatization in H_2SO_4 at 100 °C of a 1:1 mixture of *para*-**3**:*meta*-**4** led to a low 9% yield of *m*-toluic acid **7**. By contrast, distillation of para cycloaddition product **3** at 0.11 bar and 240 °C through Pd on C dispersed in macroporous silica gel (Scheme 1) afforded *p*-toluic acid in 77% yield along with *trans*- and *cis*-4-methylcyclohexanecarboxylic acids in 12% and 9% yields, respectively. Likewise distillation through Pd on C of the

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para-**3**:*meta*-**4** mixture resulting from uncatalyzed cycloaddition led to a 69% yield of *m*-toluic acid **7** (Scheme 1) along with formation of *trans*- and *cis*-3-methylcyclohexanecarboxylic acids in 10% and 13% yields, respectively.

p-Xylene is commercially oxidized to terephthalic acid **6a** under high pressure reaction conditions using $Co(OAc)_2$/$Mn(OAc)_2$ catalyst, acetic acid as solvent, air as oxidant, and an alkyl bromide as a radical chain carrier.[18] To avoid elevated pressures during oxidation of of *p*-toluic acid, *N*-hydroxysuccinimide was used as the radical chain carrier (Scheme 1).[19,20] This enabled the oxidation of *p*-toluic acid **5** catalyzed by $Co(OAc)_2$/$Mn(OAc)_2$ in acetic acid solvent to proceed under 1 atm O_2 at 100 °C and afforded terephthalic acid **6a** (94%) and 4-formylbenzoic acid (1%) with 2% unreacted *p*-toluic acid. Oxidation of *m*-toluic acid **7** led to isophthalic acid **8** in 88% yield. *p*-Toluic acid **5** and *m*-toluic acid **7** were significantly more reactive than *p*-xylene. Under identical reaction conditions, *p*-xylene oxidation led to terephthalic acid **6a** (69%), 4-formylbenozoic acid (3%), and *p*-toluic acid **5** (5%).

The Alder reaction sequence affording biobased terephthalic acid **6a** avoids elevated temperatures such as the 450−550 °C required for aromatization of the C_8 intermediates derived from biobased isobutanol.[21−24] There are no complex product mixtures to separate like those encountered with catalytic reforming of sorbitol.[25] Two of the three steps in the Alder reaction sequence as modified in this report require no reaction solvents. The Alder reaction sequence (Scheme 1) and use of limonene[26] as starting material provide the two highest overall yields of terephthalic acid **6a** synthesized from biobased starting material. Unlike the route from limonene, the Alder reaction sequence enables synthesis of both terephthalic acid **6a** and isophthalic acid **8**. Esterification and subsequent ester hydrolysis as used in routes from biobased succinic acid[27−29] and malic acid[30−32] are avoided.

Only one combination of metal (Ti^{4+}, Table 1) and anion (Cl^-, Table 2) has thus far been discovered to catalyze a highly para selective cycloaddition of isoprene **1** and acrylic acid **2** along with other cycloadditions involving dienophile carboxylic acids (Table 3). Integration of $TiCl_4$-catalyzed cycloaddition with Pd(0)-catalyzed, vapor-phase aromatization and subsequent oxidation of an aryl methyl group catalyzed by Co^{2+}/Mn^{2+} establishes the Alder reaction sequence (Scheme 1) from isoprene **1** and acrylic acid **2** to terephthalic acid **6a** as an intriguing option for the synthesis of this essential polymer building block.[33] These same three catalyzed steps can be applied to synthesis of isophthalic acid **8** (Scheme 1) from isoprene **1** and acrylic acid **2**. Pure, biobased terephthalic acid **6a** derived from $TiCl_4$-catalyzed cycloaddition could conceivably be combined with a biobased mixture of terephthalic **6a** and isophthalic **8** acids derived from an uncatalyzed cycloaddition. The result would be a tunable ratio of terephthalic acid **6a** to isophthalic acid **8**. Subsequent polymerization with biobased ethylene glycol could establish a route to the first PET with 100% biobased C atom content.

■ ASSOCIATED CONTENT

Supporting Information

General methods and product analyses for all cycloadditions, aromatizations, and oxidations. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ ABBREVIATIONS

PET, poly(ethylene terephthalate)
DIPEA, diisopropylethylamine
rt, room temperature

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