



# Acrylate Esters by Ethenolysis of Maleate Esters with Ru Metathesis Catalysts: an HTE and a Technoeconomic Study

# Pascal S. Engl,<sup>a §</sup> Alexey Tsygankov,<sup>a, b §</sup> Jordan De Jesus Silva,<sup>a</sup> Jean-Paul Lange,<sup>c, d</sup> Christophe Copéret,<sup>a</sup> Antonio Togni,<sup>a</sup> Alexey Fedorov,<sup>\*a, e</sup>

<sup>a</sup> Department of Chemistry and Applied Biosciences, ETH Zürich, Vladimir-Prelog-Weg 1-5, CH-8093 Zürich,

Switzerland

<sup>b</sup> A.N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences, Vavilova str. 28, 119991, Moscow, Russia

<sup>c</sup> Shell Research and Technology Center Amsterdam, Grasweg 31, 1031 HW Amsterdam, The Netherlands

<sup>d</sup> Sustainable Process Technology, University of Twente, Drienerlolaan 5, Enschede 7522 NB, The Netherlands

<sup>e</sup> Department of Mechanical and Process Engineering, ETH Zürich, Leonhardstrasse 21, CH-8092 Zürich, Switzerland

E-mail: fedoroal@ethz.ch

[<sup>§</sup>] These authors contributed equally

Dedicated to our colleague, friend and mentor Prof. Peter Chen on the occasion of his 60th birthday

**Abstract:** A high throughput experimentation (HTE) study identified active Ru metathesis catalysts and reaction conditions for the ethenolysis of maleate esters to the respective acrylate esters. Catalysts were tested at various loadings (75–10'000 ppm) and temperatures (30–60 °C) with maleate esters dissolved in toluene (up to ca. 44 wt%) or neat and at variable partial pressures of ethylene (0.2–10 bar). Ruthenium catalysts containing a PCy<sub>3</sub> ligand, such as 1<sup>st</sup> or 2<sup>nd</sup> generation Grubbs catalysts, as well as the state-of-the-art catalysts containing cyclic alkyl amino carbene (CAAC) ligands, are generally inferior to Hoveyda-Grubbs 2<sup>nd</sup> generation catalyst in ethenolysis of maleates. Productive turnover numbers could exceed 1900 if the ethenolysis reaction is performed at low ethylene pressures (0.2-3 bar) and reach 5200 when a polymeric phenol additive was used. Such catalytic performance falls well within the window practiced in industry. Moreover, a crude technoeconomic analysis finds similar production cost for the ethenolysis route and conventional technology, i.e. propene oxidation followed by esterification, justifying research to further improve the ethenolysis route.

Keywords: ethenolysis, high throughput experimentation, acrylates, Ru metathesis catalysts, technoeconomic analysis

#### Introduction

Ethenolysis, that involves the cross-metathesis reaction between ethylene and another olefin, has recently emerged as a powerful methodology for the production of  $\alpha$ -olefins and in particular the catalytic upgrading of biomass-derived feedstocks, e.g. the conversion of long-chain esters such as oleates to the corresponding terminal olefins.<sup>[1-8]</sup> The research focus has revolved around oleates and related esters owing to their abundance in vegetable oils and the high value of terminal olefins produced from those substrates and ethylene. Currently, ethenolysis of oleates serves as a benchmark reaction for the search of improved metathesis catalysts, often including screening of large catalyst libraries.<sup>[9-15]</sup> Achieving high productivity in ethenolysis can be hampered by deactivation of intermediate Ru methylidene species,<sup>[16, 17]</sup> [Ru=CH<sub>2</sub>], by a bimolecular coupling<sup>[18-21]</sup> or methylidene abstraction,<sup>[22]</sup> both processes being facilitated by the small size and the high reactivity of the methylidene ligand.<sup>[23]</sup> In addition, a  $\beta$ -hydrogen elimination pathway contributes significantly to

decomposition of unsubstituted ruthenacyclobutane intermediates.<sup>[24, 25]</sup> Ethenolysis of functionalized olefins such as esters is further exacerbated by the presence of functional groups and impurities in ester-containing feeds.<sup>[26]</sup> Catalyst decomposition is unfavorable also for reaction selectivity, as the decomposed catalyst could promote side reactions.<sup>[1, 27]</sup> In contrast to long-chain esters, ethenolysis of  $\alpha$ , $\beta$ -conjugated olefins, e.g. maleates, remains largely underexplored. Such substrates are challenging for olefin metathesis since nucleophiles (for instance, phosphine ligands of the catalyst initiator) can add to those Michael acceptors forming reactive basic species, that in turn decompose the catalyst or key metallacyclobutane intermediates of the Chauvin mechanism.<sup>[28-31]</sup> In addition, alkylidene intermediates with a carboxyl group, [Ru=CHCOOR], formed with maleate and acrylate substrates, are known to be highly reactive and unstable.<sup>[32]</sup> That said, ethenolysis of cheap and abundant maleate esters could represent an attractive strategy to produce industrially important acrylate monomers, provided efficient catalysts and reaction conditions are identified. A computational study

predicted that ethenolysis of dimethyl maleate is viable both kinetically and thermodynamically, with the overall reaction being slightly endothermic.<sup>[33]</sup> The use of a ruthenium catalyst previously allowed converting dimethyl maleate to methyl acrylate by the cross-metathesis with methyl 10-undecenoate.<sup>[34]</sup> Notably, ethenolysis of ethyl crotonate to ethyl acrylate and propene using the second

with methyl 10-undecenoate.<sup>[34]</sup> Notably, ethenolysis of ethyl crotonate to ethyl acrylate and propene using the second generation Hoveyda-Grubbs (HG-2) catalyst gave turnover numbers (TON) around 350 under ca. 18 bar of ethylene, and decreasing ethylene pressure was reported to lower the TON.<sup>[35]</sup> This study also demonstrated that ethyl acrylate undergoes self-metathesis to diethyl fumarate, suggesting that ethenolysis of ethyl crotonate is equilibrium limited. In addition, the catalyst stability was identified as a key factor to achieve high TON values.<sup>[35]</sup> However, conversion of cinnamic acid or ethyl cinnamate in the ethenolysis with HG-2 catalyst to respective acrylates and styrene was shown to depend critically on ethylene pressure, and highest conversion of substrates were achieved using ca. 1 bar ethylene while decreasing sharply at higher ethylene pressure.<sup>[36]</sup> These contrasting results point at an entangled dependence of yield of acrylates produced via ethenolysis on the catalyst stability, including at high ethylene pressures and high product concentrations, and position of the thermodynamic ethenolysis equilibrium.

Only two experimental reports on the ethenolysis of maleates have appeared to this date, both in the patent literature and exploiting the second generation Hoveyda-Grubbs (HG-2) catalyst. These patents present diverging results regarding catalytic performance: a more recent patent described only several productive metathesis turnovers from a maleate to the acrylate ester using HG-2 catalyst,<sup>[37]</sup> while in the earlier patent, the activity of HG-2 catalyst was orders of magnitude higher, reaching up to ca. 3600 turnovers in the presence of p-cresol or benzoquinone,<sup>[38]</sup> and under 1 bar of ethylene.<sup>[39]</sup> Note, however, that those high turnover numbers were achieved at yields of ethyl acrylate not exceeding ca. 30 %.<sup>[39]</sup>

Here, we report the investigation utilizing high throughput catalytic testing of several Ru-based metathesis catalysts that confirm high activity of the HG-2 catalyst. However, this activity is only attainable at low partial pressure of ethylene (0.2–3 bar). Turnover numbers exceeding 1900 could be achieved when converting dimethyl maleate to methyl acrylate in toluene or neat and using the HG-2 catalyst. Turnover numbers can be pushed to ca. 5200 with a polymeric phenol resin additive that is found to stabilize the HG-2 catalyst al low loadings. Conversion of dimethyl maleate appears to be limited by catalyst decomposition at high yields of methyl acrylate (ca. 65-70%). Technoeconomic analysis reveals that the ethenolysis pathway to acrylates by ethenolysis of maleates merits further consideration for possible industrial utilization.

### **Results and Discussion**

**Primary catalyst screening.** We examined the activity of a library of Ru metathesis catalysts in the ethenolysis of maleate esters,<sup>[40]</sup> and report the key results below. Widely-used 2nd generation Grubbs catalysts with SIMes and SIPr ligands (1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene and 1,3-bis(2,6-diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene, respectively, **Ru-1** and **Ru-2**),<sup>[41, 42]</sup> the so-called third generation Grubbs catalyst (**Ru-3**),<sup>[43]</sup> 2nd generation Piers (**Ru-4**),<sup>[44]</sup> and 2nd generation Hoveyda-Grubbs catalysts (**Ru-5**, Scheme 1, top),<sup>[45, 46]</sup> were tested in the ethenolysis of methyl, iso-propyl and *n*-butyl maleate esters (**1-OMe**, **1-OiPr**, **1-OnBu**, respectively, Scheme 1, bottom). The catalysts were injected to a solution of esters in toluene after equilibration to the desired temperature and ethylene pressure (10 bar, quasi-isobaric conditions), remembering that high ethylene pressure was reported to increase the TON values in

ethenolysis of ethyl crotonate.<sup>[35]</sup> Table 1 presents results of the initial screening of the parameter space including 3 substrates and 5 catalysts tested at 10 bar ethylene pressure and variable temperature, catalyst loading and reaction time. Results reveal that the least sterically bulky ester, dimethyl maleate (1-OMe), typically yields the respective acrylate (2-OMe) with a higher selectivity (>90%) compared to 1-OiPr (<12%) and 1-OnBu (<23%). Conversion of maleate esters in these experiments was low, i.e. ca. 3-7 % (Table 1, entries 1-5). Noteworthy, acrylates can be separated from maleates by distillation owing to a large difference in boiling points (204 and 80 °C for 1-OMe and 2-OMe, respectively). While the first generation Grubbs and Hoveyda-Grubbs catalysts were inactive in ethenolysis of esters 1 in these conditions (data not shown), catalysts Ru-1 and Ru-2 gave turnover numbers (TONs) based on the yield of the desired acrylate ester reaching ca. 300, which is 2-3 times higher than for Ru-3 and Ru-4 catalysts (Table 1, entries 1-6). Gas uptake curves recorded during the ethenolysis reactions at 35-60 °C revealed that catalysts Ru-1-5 deactivate rapidly, within first ca. 10-15 min after their injection. Catalyst Ru-5 performs better at 50-60 °C compared to catalysts Ru-1-4 and increasing its loading to 0.5 and 1 mol% (5000 and 10000 ppm) allows for a higher conversion of 1-OMe, reaching 39 and 59 %, however accompanied by a decrease in selectivity to 68 and 60% respectively (Table 1, entries 7-9). To summarize, our preliminary screening identified 2<sup>nd</sup> generation Hoveyda-Grubbs catalyst Ru-5 and 1-OMe as preferred catalyst and maleate ester for further optimization studies owing to the higher stability and selectivity to the ethenolysis product 2-OMe, with product yields reaching 35%.



Scheme 1. Selected Ru metathesis catalysts (top) and synthesis of acrylate esters by ethenolysis of maleate esters (bottom).

Table 1. Ethenolysis of maleate esters with catalysts Ru-1-5 in toluene (ca. 44 wt%). Conversions and selectivities were determined by GC andconfirmed by <sup>1</sup>H NMR. Ru-4 was added to reaction mixtures before pressurizing with ethylene. The ethylene pressure was set to 10 bar. Conversion,yield, selectivity, and productive turnover number (TON) were calculated as follows: Conv. =  $1 - n_{(1-OR)final} / n_{(1-OR)final} / 2 \times n_{(1-$ 

Entry	Substrate	Catalyst	Loading, [Ru, ppm]	Time, [min]	T, [°C]	Conv. [%]	Sel. [%]	Yield [%]	TON
1	1-OMe	Ru-1	210	300	35	7	>99	7	330
2	1-OMe	Ru-1	500	30	50	5	>99	5	100
3	1-OMe	Ru-2	210	300	35	4	>99	4	190
4	1-OMe	Ru-2	500	30	50	3	>99	3	60
5	1-OMe	Ru-3	1'000	30	60	5	99	5	50
6	1-OMe	Ru-4	2000	30	60	21	96	20	100

7	1-OMe	Ru-5	500	30	50	8	>99	8	160
8	1-OMe	Ru-5	5'000	30	60	39	68	27	60
9	1-OMe	Ru-5	10'000	30	60	59	60	35	30
10	1-OiPr	Ru-1	500	30	35	41	<1	<1	<1
11	1-OiPr	Ru-4	2000	30	60	41	12	5	30
12	1-OiPr	Ru-5	500	30	35	41	7	3	60
13	1-O <i>n</i> Bu	Ru-1	500	30	35	42	4	2	40
14	1-O <i>n</i> Bu	Ru-1	500	30	50	42	8	3	60
15	1-O <i>n</i> Bu	Ru-4	2'000	30	60	54	23	12	60
16	1-O <i>n</i> Bu	Ru-5	500	30	35	44	8	3	60
17	1-O <i>n</i> Bu	Ru-5	500	30	50	46	10	5	100

**Solvent and ethylene pressure effects**. Further optimization of reaction conditions using **Ru-5** and **1-OMe** revealed that decreasing the ethylene pressure from 10 bar to 1-3 bar drastically improves conversion of **1-OMe** and selectivity to **2-OMe** at high conversions, resulting in productive TON of ca. 1400 and 920 in toluene and THF, respectively with yields of **2-OMe** equal to 36 and 23%, respectively (Table 2, entries 1-2). These data suggest that catalyst instability at 10 bar of ethylene was responsible for the observed lower TON values (Table 1). Decreasing the reaction temperature from 60 to 35 °C does not improve conversion or selectivity (Table S2). Conversion and selectivity are generally higher in toluene or chlorobenzene than in benzene, THF, or iPrOH and the resulting yield of **2-OMe** reaches 67% (Table 2, entries 1-7).<sup>[47]</sup> Notably, the reaction proceeded in neat **1-OMe**, although it was accompanied by the formation of dimethyl fumarate (Table 2, entry 8-10).

Conversion of 1-OMe did not improve when Ru-5 was added in three injections such that additional two injections of Ru-5 were made after ethylene consumption ceased (Table 2, entry 11). This result may be explained by the presence of thermodynamic equilibrium in the ethenolysis of dimethyl maleate. To verify this hypothesis, we have conducted a reverse reaction, viz. the self-metathesis of methyl acrylate. We observe that at room temperature in C6D6 solution (ca. 28 wt % of 2-OMe), 540 ppm of Ru-5 provides no detectable 1-OMe but delivers 10 % yield of its thermodynamically favored isomer, dimethyl fumarate, after 90 min reaction time under Ar atmosphere (1 bar). Moreover, the yield of dimethyl fumarate increases to 18 % when the reaction mixture is diluted 10-fold. Therefore, the expected equilibrium between maleate and acrylate should not be limiting as formed acrylate will be consumed to dimethyl fumarate. Because dimethyl fumarate is not observed in significant amounts (>1%) in most of our experiments (with an exception of reactions conducted in neat 1-OMe), we suggest that the thermodynamic equilibrium does not limit our catalytic optimization results. Consistent with this inference, no ethylene uptake was observed when additional 1-OMe was injected into the reaction mixture that had reached ca. 66 % conversion of 1-OMe, suggesting that the deactivation of Ru-5 at these high levels of 1-OMe conversion plays a role. To summarize, control experiments indicate that 1) the catalytic ethenolysis reaction between 1-OMe and 2-OMe does not appear to be limited by the thermodynamic equilibrium under the tested conditions, 2) high concentrations of 2-OMe are likely responsible for deactivation Ru-5 at low ethylene pressures (1-3 bar), and that 3) Ru-5 deactivates in the presence of 1-OMe at high ethylene pressure (10 bar) even at low concentrations of 2-OMe.

The presented data indicates two regimes of catalyst' instability: at 10 bar ethylene pressure, **Ru-5** provides low TON to acrylates disregard of the maleate conversion, while at 1-3 bar ethylene pressure, high TON values can be achieved, yet the yield of **2-OMe** does not exceed ca. 67%, pointing at the product-induced decomposition of **Ru-5** at those high yields of **2-OMe**.

 Table 2. Solvent screen for the ethenolysis of dimethyl maleate (1-OMe) with Ru-5 at 60 °C. Conversion and selectivity values were determined by

 GC-FID. Except for entries 1-3, experiments were performed on the 96-parallel autoclave (ILS GmbH).<sup>[48]</sup>

Entry	Solvent	Loading, [Ru, ppm]	Time, [min]	P, [bar]	Conv. [%]	Sel. [%]	Yield [%]	TON
1	toluene	250	120	3	67	53	36	1440
2	THF	250	120	3	24	98	23	920
3	iPrOH	250	120	3	9	75	7	280
4	toluene	500	70	1	66	99	66	1320
5	$C_6 D_6$	500	70	1	44	99	44	880
6	C <sub>6</sub> H₅CI	500	70	1	67	99	67	1340
7	C <sub>6</sub> H₅CI	250	70	1	24	99	24	960
8	neat	125	120	3	21	96 <sup>[a]</sup>	20	1600
9	neat	250	120	3	45	81 <sup>[a]</sup>	36	1440
10	neat	500	70	1	41	99 <sup>[a]</sup>	41	820
11	toluene	3×500	90	3	56	99	56	370

[a] Formation of methyl fumarate was observed.

**Catalyst decomposition studies.** Further insight into the reactivity and stability of **Ru-5** in ethenolysis of maleates was obtained from in situ <sup>1</sup>H-NMR experiments. While **Ru-5** is stable for at least 1 hour at 23 °C in the presence of 10 equiv. of **1-OMe**, keeping this solution at 60 °C for 1 hour induces decomposition of ca. 30 % of **Ru-5**, as indicated by the decrease of the benzylidene <sup>1</sup>H-NMR resonance signal, as well as the formation of metathesis products, 1-isopropoxy-2-vinylbenzene and methyl (E)-3-(2-isopropoxyphenyl)acrylate (Figure S3). The rate of **Ru-5** decomposition increases when ethylene is introduced to the Young tube. For instance, in the presence of 10 equiv. **1-OMe** and 0.7 bar of ethylene, ca. 50 % of **Ru-5** decomposes in 2 hours at 23 °C (Figure S4). After 72 h, complete decomposition of **Ru-5** is observed accompanied by formation of methyl fumarate, likely owing to the isomerization of **1-OMe** by the decomposition products of **Ru-5**. However, these catalyst life times are still substantially longer than the duration of the ethylene uptake after injection of 500 ppm of **Ru-5** to **1-OMe** at 3 bar ethylene pressure and 60 °C, which proceeds only for ca. 15-20 min under these conditions (Figure S1). This suggests that at low ethylene pressure (1-3 bar), methyl acrylate strongly undermines catalyst stability.

**Optimization of the catalytic performance**. We tested **Ru-5** in the ethenolysis of **1-OMe** in toluene (44 wt% solution) at a decreased partial pressure of ethylene, comparing results at 0.2, 1 and 3 bar and at 500 ppm catalyst loading at 60 °C. There is a modest increase of TON from 920 to ca. 1100 with decreasing ethylene pressure from 3 and to 1 bar, but no

further notable increase under 0.2 bar of ethylene (Table 3, entries 1-3). These relatively stable TON values at variable low ethylene pressures are consistent with no catalyst deactivation by ethylene at 1-3 bar (in the time scale of the catalytic reaction). In addition, it shows that catalyst productivity (assessed by TON) is not limited by ethylene concentration. Thus, 1 bar ethylene pressure was chosen for testing 3 lower temperatures (50, 40, 30 °C) that gave similar turnover numbers ranging from 1260 at 50 °C and 1020 at 30 °C (Table 3, entries 4-6). Notably, using twice less catalyst (250 ppm) and 0.2 bar ethylene partial pressure allowed for nearly doubling turnover number to 1960, which was achieved at identical conversion (56%) but slightly lower selectivity (99% vs. 87%, Table 3, entries 1 and 7). Interestingly, substitution of chlorine by bromine ligands in **Ru-6** slightly increases TON when compared to **Ru-5** (Scheme 2 and Table 3, entries 2, 8).<sup>[49]</sup> However, at 1 bar ethylene decreasing the loading of **Ru-6** to 250 ppm decreases TON from 1380 to 1000, in contrast to what was described above for **Ru-5** at 0.2 bar ethylene partial pressure. Ruthenium metathesis catalysts featuring cyclic alkyl amino carbene (CAAC) ligands, such as **Ru-7-8** (Scheme 2), have previously been shown to exhibit exceptionally high turnover numbers in ethenolysis of linear olefins.<sup>[10]</sup> To our surprise, catalysts **Ru-7-8** demonstrated little or no activity in ethenolysis of **1-OMe** (Table 3, entries 10-11).

We have further screened various additives (alcohols,<sup>[50]</sup> o-phenylenediamine, 1,2-benzenedithiol or 1,5-hexadiene,<sup>[7]</sup> see Table S3) with the objective of finding conditions to lower the loading of **Ru-5**, or increase yield of **2-OMe**. Notably, a polymeric phenol resin that was previously identified as an effective additive for cross-metathesis of acrylate esters using phosphine-based metathesis catalysts such as **Ru-2**,<sup>[30]</sup> also increases TONs of phosphine-free **Ru-5**. For instance, with 5000 ppm of the commercial polymeric phenol additive, TON at 3 bar of ethylene and 250, 125 and 75 ppm or **Ru-5** are 2320, 3520 and 5200, respectively (Table 3, entries 12-14). These increasing TON values with decreasing loadings are consistent with no deactivation of **Ru-5** at low concentration of **1-OMe**. An alternative explanation is that catalyst deactivation occurs via dimerization of Ru species, which is slowed downs at low concentrations of **Ru-5**. From a practical standpoint, this data suggests that polymeric phenol additive can quench the decomposition of **Ru-5** by Brønsted bases such as enolates, which can be formed by a nucleophilic addition to **2-OMe**. Yet this polymeric phenol additive does not increase the yield of **2-OMe** at conversions of **1-OMe** around 65-70%.



Scheme 2. Additional tested Ru metathesis catalysts.

Entry	Catalyst	Loading, [Ru, ppm]	Time, [min]	P, [bar]	T, [°C]	Conv. [%]	Sel. [%]	Yield [%]	TON
1	Ru-5	500	60	0.2	60	56	99	56	1120
2	Ru-5	500	90	1	60	65	85	55	1100
3	Ru-5	500	90	3	60	65	71	46	920
4	Ru-5	500	90	1	50	63	99	63	1260
5	Ru-5	500	90	1	40	57	93	53	1060
6	Ru-5	500	90	1	30	56	93	51	1020

Table 3. Ethenolysis of dimethyl maleate (ca. 44 wt% in toluene). Conversions and selectivities were determined by GC-FID and turnovers calculated based on GC yields of methyl acrylate.

7	Ru-5	250	60	0.2	60	56	87	49	1960
8	Ru-6	500	90	1	60	73	94	69	1380
9	Ru-6	250	90	1	60	40	63	25	1000
10	Ru-7	500	90	1	60	23	33	8	160
11	Ru-8	500	90	1	60	6	-	-	-
12 <sup>[a]</sup>	Ru-5	250	60	3	60	64	92	58	2320
13 <sup>[a]</sup>	Ru-5	125	60	3	60	50	87	44	3520
14 <sup>[a]</sup>	Ru-5	75	60	3	60	44	89	39	5200

<sup>[a]</sup> In the presence of 5000 ppm of a polymeric phenol resin.

**Industrial potential**. The technical progress reported above and summarized for a representative experimental result in Table 4 warrants a first evaluation of the industrial potential of the maleate-to-acrylate ethenolysis reaction. First, the catalytic performance achieved here was compared to general industrial targets proposed in the literature.<sup>[51]</sup> According to Table 4, the ethenolysis of dimethyl maleate meets the general selectivity (up to 90%), productivity (up to 1.1 kg L<sup>-1</sup> h<sup>-1</sup>) and product concentration (up to 40 wt%) criteria for industrial operation. The obtained catalyst life-time productivity of 600-800 g product (g catalyst)<sup>-1</sup> is also close to industrial requirements, making this reaction a viable target for further development, in particular in terms of compatibilities of all criteria under the same conditions.

Table 4. Comparison of industrial targets and obtained catalytic performance.

Target / Experiment	Selectivity, %	Product concentration, wt%	Product formation rate, g $L^{-1} h^{-1}$	Product / Catalyst ratio, g (product) g (Ru) <sup>-1</sup>
Industrial target	> 90	> 10	> 100	1000
Table 3, entry 3	71	~22	~880 <sup>[a]</sup>	~1570

[a] Taking into account that ethylene uptake terminates in ca. 15 min (Figure S1).

An initial assessment of the economic viability of the ethenolysis route to the state-of-the-art technology, i.e. the oxidation of propylene via acrolein, was performed. To this end, we estimated the raw material cost by assuming a stoichiometric consumption of the various reactants and using a consistent set of market prices from commercial data bases (available at Shell Research and Technology Center). The remaining cost contribution, i.e. investment, fixed costs, catalysts and energy costs, etc., were lumped into a 'conversion cost' and assumed to amount to  $200 t^{-1}$  of total feed consumed, as proposed elsewhere.<sup>[51]</sup> The conversion of maleic anhydride to **2-OMe** was assumed to proceed in two steps, i.e. esterification and ethenolysis steps. The propene route consisted of 2.5 steps, i.e. the two-step oxidation, first to acrolein then to acrylic acid, which was counted as 1.5 step owing to the absence of the product workup between the steps, followed by an esterification step. Next, we considered basic economic sensitivities by varying the feed prices by +/- 10% and by varying the conversion cost by +/- 25% for all steps. Notice that a penalty of +10% on the feed price corresponds to a penalty of -10% of overall product selectivity.

The ethenolysis route falls in the same band of manufacturing cost as the propylene oxidation route (the diagonal band of  $1250-1500 t^{-1}$ ), i.e. within the uncertainty band discussed above and represented by the size of the bubbles in Figure

**1**. The ethenolysis route shows a higher raw material cost, mainly owing to the price of maleic anhydride. However, this additional cost is largely offset by lower conversion cost, resulting from a lower number of process steps (2 instead of 2.5), combined with a lower overall feed intake (1.1 t feed/t product instead of 1.42 t/t). The cost of the catalysts in the ethenolysis route is assumed to be moderate, at this stage falling within the inaccuracy of the method.

We also calculated the production cost when starting from butane and propane, i.e. by including the oxidation of butane to maleic anhydride or the oxidative dehydrogenation of propane to propene into the overall manufacturing process. This does not dramatically change the conclusions since both routes still falls within the band of \$1250-1500 t<sup>-1</sup> production cost, although with a larger uncertainty that is due to the higher capex that is needed (Figure 1).

Finally, we tested the robustness of this analysis by evaluating an earlier concept to produce methyl acrylate from maleic anhydride, namely the selective decarboxylation of maleic acid.<sup>[52]</sup> This methodology has not been commercialised and is therefore expected to be more expensive than the routes discussed above. We assessed the decarboxylation route by assuming that it also proceeds with a quantitative yield and requires two process steps, i.e. esterification of maleic anhydride to its mono-methyl ester and decarboxylation to methyl acrylate. We find that this route is uncompetitive by about \$1000 t<sup>-1</sup> because of the unaffordable raw material cost and slightly disadvantaged conversion cost (Figure 1). Despite its intrinsic inaccuracy, our approach is apparently capable of identifying uncompetitive processes.

This analysis has so far focused on the manufacture of methyl acrylate. But one may wish to produce acrylic acid or another acrylate ester (e.g. butyl acrylate). When manufacturing acrylic acid, we need to remove the cost of MeOH for both routes, remove the esterification step for the propene route and add a hydrolysis step for the maleic anhydride route. This would lower the cost of the propene route to ca.  $950 t^{-1}$  and raise that of the maleic anhydride route to ca.  $1650 t^{-1}$ , which is a notable penalty for the maleic anhydride route. When producing another ester, the relative cost of both routes would be affected if we need to use an alcohol that is incompatible with the ethenolysis step. In such case, the maleic anhydride route would come with a modest economic disadvantage of ca.  $200 t^{-1}$  by requiring an additional transesterification step, while the propene route would simply switch its esterification step to using an alcohol other than MeOH. Such  $200 t^{-1}$  penalty is significant, but it still falls largely within the uncertainty band. A more detailed evaluation would be needed to reliably label the ethenolysis route as uncompetitive. Alternatively, this penalty would justify further study to improve the ethenolysis step and make it compatible with the desired alcohol.

Overall, the present methodology does not reveal major differences between those routes to produce methyl acrylate or any acrylate ester that is compatible with the ethenolysis step. The ethenolysis route shows neither obvious cost advantage nor economic flaws. It is thereby worthy of further economic analysis, considering experimental yields, precise energy demands and evaluation of major equipment requirements.



**Figure 1**. Preliminary economic screening of the production of methyl acrylate from various feedstock (NB: The diagonal lines represent line of identical total manufacturing cost; the size of the bubbles represents the uncertainties of +/-10% on raw material and +/-25% on conversion cost).

#### Conclusions

A screening of a library of Ru metathesis catalysts for the ethenolysis of dimethyl maleate to methyl acrylate yielded productive turnover numbers approaching 2000 using the second generation Hoveyda-Grubbs-type catalyst, with selectivity in several cases exceeding 80% and conversion reaching 70%, likely limited by the product-induced catalyst decomposition. Addition of a polymeric phenol resin was found to stabilize Hoveyda-Grubbs-2 catalyst at low loadings (75 ppm), allowing for higher turnover numbers of ca. 5200. Based on these experimental results, a first technoeconomic analysis was performed that showed no major differences between the ethenolysis route to methyl acrylate compared to other conceivable routes. The ethenolysis route is therefore poised for further development and optimization, with prospects of industrial implementation.

#### **Supplementary Material**

Supporting information for this article is given *via* a link at the end of the document.

#### Acknowledgements

The authors are grateful to the Scientific Equipment Program of ETH Zürich and the SNSF (R'Equip grant 206021\_150709/1) for financial support of the high throughput catalyst screening facility (HTE@ETH). J.D.J.S. was supported by the Luxembourg National Research Fund (AFR Individual Ph.D. Grant 12516655).

## **Author Contribution Statement**

J.P.L., A.F. and C.C. designed research; P.E., A.Ts., J.D.J.S. performed catalytic and NMR tests; J.P.L. performed the technoeconomic analysis; all authors analyzed the data; A.F. and J.P.L. wrote the paper with contributions from all authors.

# References

- [1] J. Bidange, C. Fischmeister, C. Bruneau, 'Ethenolysis: A Green Catalytic Tool to Cleave Carbon-Carbon Double Bonds', *Chem. Eur. J.* **2016**, *22*, 12226-12244.
- [2] C. S. Higman, J. A. M. Lummiss, D. E. Fogg, 'Olefin Metathesis at the Dawn of Implementation in Pharmaceutical and Specialty-Chemicals Manufacturing', *Angew. Chem. Int. Ed.* **2016**, *55*, 3552-3565.
- [3] J. Spekreijse, J. P. Sanders, J. H. Bitter, E. L. Scott, 'The Future of Ethenolysis in Biobased Chemistry', *ChemSusChem* **2017**, *10*, 470-482.
- [4] J. Allard, I. Curbet, G. Chollet, F. Tripoteau, S. Sambou, F. Caijo, Y. Raoul, C. Crevisy, O. Basle, M. Mauduit, 'Bleaching Earths as Powerful Additives for Ru-Catalyzed Self-Metathesis of Non-Refined Methyl Oleate at Pilot Scale', *Chem. Eur. J.* 2017, 23, 12729-12734.
- [5] K. A. Burdett, L. D. Harris, P. Margl, B. R. Maughon, T. Mokhtar-Zadeh, P. C. Saucier, E. P. Wasserman, 'Renewable monomer feedstocks via olefin metathesis: Fundamental mechanistic studies of methyl oleate ethenolysis with the firstgeneration Grubbs catalyst', Organometallics 2004, 23, 2027-2047.
- [6] T. Seidensticker, A. J. Vorholt, A. Behr, 'The mission of addition and fission catalytic functionalization of oleochemicals', *Eur. J. Lipid Sci. Technol.* **2016**, *118*, 3-25.
- [7] J. Julis, S. A. Bartlett, S. Baader, N. Beresford, E. J. Routledge, C. S. J. Cazin, D. J. Cole-Hamilton, 'Selective ethenolysis and oestrogenicity of compounds from cashew nut shell liquid', *Green Chem.* **2014**, *16*, 2846-2856.
- [8] S. Chikkali, S. Mecking, 'Refining of Plant Oils to Chemicals by Olefin Metathesis', *Angew. Chem. Int. Ed.* **2012**, *51*, 5802-5808.
- [9] R. M. Thomas, B. K. Keitz, T. M. Champagne, R. H. Grubbs, 'Highly selective ruthenium metathesis catalysts for ethenolysis', *J. Am. Chem. Soc.* **2011**, *133*, 7490-7496.
- [10] V. M. Marx, A. H. Sullivan, M. Melaimi, S. C. Virgil, B. K. Keitz, D. S. Weinberger, G. Bertrand, R. H. Grubbs, 'Cyclic alkyl amino carbene (CAAC) ruthenium complexes as remarkably active catalysts for ethenolysis', *Angew. Chem. Int. Ed.* 2015, *54*, 1919-1923.

- [11] P. S. Engl, A. Fedorov, C. Copéret, A. Togni, 'N-Trifluoromethyl NHC Ligands Provide Selective Ruthenium Metathesis Catalysts', Organometallics 2016, 35, 887-893.
- P. Wyrębek, P. Małecki, A. Sytniczuk, W. Kośnik, A. Gawin, J. Kostrzewa, A. Kajetanowicz, K. Grela, 'Looking for the [12] Noncyclic(amino)(alkyl)carbene Ruthenium Catalyst for Ethenolysis of Ethyl Oleate: Selectivity Is on Target', ACS Omega 2018, 3, 18481-18488.
- [13] S. Monfette, J. M. Blacquiere, D. E. Fogg, 'The Future, Faster: Roles for High-Throughput Experimentation in Accelerating Discovery in Organometallic Chemistry and Catalysis†', Organometallics 2011, 30, 36-42.
- Y. Schrodi, T. Ung, A. Vargas, G. Mkrtumyan, C. W. Lee, T. M. Champagne, R. L. Pederson, S. H. Hong, 'Ruthenium [14] Olefin Metathesis Catalysts for the Ethenolysis of Renewable Feedstocks', Clean: Soil, Air, Water 2008, 36, 669-673.
- S. C. Marinescu, R. R. Schrock, P. Muller, A. H. Hoveyda, 'Ethenolysis Reactions Catalyzed by Imido Alkylidene [15] Monoaryloxide Monopyrrolide (MAP) Complexes of Molybdenum', J. Am. Chem. Soc. 2009, 131, 10840-10841
- S. H. Hong, A. G. Wenzel, T. T. Salguero, M. W. Day, R. H. Grubbs, 'Decomposition of Ruthenium Olefin Metathesis [16] Catalysts', J. Am. Chem. Soc. 2007, 129, 7961-7968.
- S. H. Hong, A. Chlenov, M. W. Day, R. H. Grubbs, 'Double C-H Activation of an N-Heterocyclic Carbene Ligand in a [17] Ruthenium Olefin Metathesis Catalyst', Angew. Chem. Int. Ed. 2007, 46, 5148-5151.
- [18] P. E. Romero, W. E. Piers, 'Mechanistic studies on 14-electron ruthenacyclobutanes: degenerate exchange with free ethylene', J. Am. Chem. Soc. 2007, 129, 1698-1704.
- F. C. Courchay, J. C. Sworen, I. Ghiviriga, K. A. Abboud, K. B. Wagener, 'Understanding structural isomerization during [19] ruthenium-catalyzed olefin metathesis: A deuterium labeling study', *Organometallics* **2006**, *25*, 6074-6086. J. Engel, W. Smit, M. Foscato, G. Occhipinti, K. W. Tornroos, V. R. Jensen, 'Loss and Reformation of Ruthenium
- [20] Alkylidene: Connecting Olefin Metathesis, Catalyst Deactivation, Regeneration, and Isomerization', J. Am. Chem. Soc. 2017, 139, 16609-16619.
- G. A. Bailey, M. Foscato, C. S. Higman, C. S. Day, V. R. Jensen, D. E. Fogg, 'Bimolecular Coupling as a Vector for [21] Decomposition of Fast-Initiating Olefin Metathesis Catalysts', J. Am. Chem. Soc. 2018, 140, 6931-6944.
- W. L. McClennan, S. A. Rufh, J. A. Lummiss, D. E. Fogg, 'A General Decomposition Pathway for Phosphine-Stabilized Metathesis Catalysts: Lewis Donors Accelerate Methylidene Abstraction', *J. Am. Chem. Soc.* **2016**, *138*, 14668-14677. [22]
- P. Vignon, T. Vancompernolle, J. L. Couturier, J. L. Dubois, A. Mortreux, R. M. Gauvin, 'Cross-metathesis of biosourced [23] fatty acid derivatives: a step further toward improved reactivity', ChemSusChem 2015, 8, 1143-1146.
- [24] D. L. Nascimento, A. Gawin, R. Gawin, P. A. Gunka, J. Zachara, K. Skowerski, D. E. Fogg, 'Integrating Activity with Accessibility in Olefin Metathesis: An Unprecedentedly Reactive Ruthenium-Indenylidene Catalyst', J. Am. Chem. Soc. **2019**, *141*, 10626-10631.
- [25] B. K. Keitz, R. H. Grubbs, 'Probing the origin of degenerate metathesis selectivity via characterization and dynamics of ruthenacyclobutanes containing variable NHCs', J. Am. Chem. Soc. 2011, 133, 16277-16284.
- Y. Schrodi, in Handbook of Metathesis (Ed.: R. H. Grubbs, Wenzel, A. G.), Wiley-VCH: Weinheim, 2015, pp. 323-342. [26] [27] C. S. Higman, A. E. Lanterna, M. L. Marin, J. C. Scaiano, D. E. Fogg, 'Catalyst Decomposition during Olefin Metathesis Yields Isomerization-Active Ruthenium Nanoparticles', ChemCatChem 2016, 8, 2446-2449.
- [28] G. A. Bailey, D. E. Fogg, 'Acrylate metathesis via the second-generation Grubbs catalyst: unexpected pathways enabled by a PCy3-generated enolate', J. Am. Chem. Soc. 2015, 137, 7318-7321.
- [29] G. A. Bailey, J. A. M. Lummiss, M. Foscato, G. Occhipinti, R. McDonald, V. R. Jensen, D. E. Fogg, 'Decomposition of Olefin Metathesis Catalysts by Bronsted Base: Metallacyclobutane Deprotonation as a Primary Deactivating Event', J. Am. Chem. Soc. 2017, 139, 16446-16449.
- [30] A. G. Santos, G. A. Bailey, E. N. dos Santos, D. E. Fogg, 'Overcoming Catalyst Decomposition in Acrylate Metathesis: Polyphenol Resins as Enabling Agents for PCy3-Stabilized Metathesis Catalysts', ACS Catal. 2017, 7, 3181-3189.
- B. J. Ireland, B. T. Dobigny, D. E. Fogg, 'Decomposition of a Phosphine-Free Metathesis Catalyst by Amines and Other [31] Bronsted Bases: Metallacyclobutane Deprotonation as a Major Deactivation Pathway', ACS Catal. 2015, 5, 4690-4698.
- [32] M. Ulman, T. R. Belderrain, R. H. Grubbs, 'A series of ruthenium(II) ester-carbene complexes as olefin metathesis initiators: metathesis of acrylates', *Tetrahedron Lett.* **2000**, *41*, 4689-4693. S. Fomine, M. A. Tlenkopatchev, 'Cross-metathesis of dimethyl maleate and ethylene catalyzed by second generation
- [33]
- ruthenium carbene complexes: B3LYP and MPW1K comparison study', J. Organomet. Chem. 2006, 691, 5189-5196. [34] A. Behr, S. Toepell, S. Harmuth, 'Cross-metathesis of methyl 10-undecenoate with dimethyl maleate: an efficient protocol with nearly quantitative yields', RSC Adv. 2014, 4, 16320.
- D. Schweitzer, K. D. Snell, 'Acrylates via Metathesis of Crotonates', Org. Process Res. Dev. 2015, 19, 715-720. [35]
- [36] J. Spekreijse, J. Le Nôtre, J. van Haveren, E. L. Scott, J. P. M. Sanders, 'Simultaneous production of biobased styrene and acrylates using ethenolysis', Green Chem. 2012, 14.
- M. J. Burk, P. Pharkya, S. J. Van Dien, A. P. Burgard, C. H. Schilling, in US8026386, Vol. US 8026386, Genomatica, [37] Inc., US, 2011
- [38] S. H. Hong, D. P. Sanders, C. W. Lee, R. H. Grubbs, 'Prevention of Undesirable Isomerization during Olefin Metathesis', J. Am. Chem. Soc. 2005, 127, 17160-17161.
- [39] A. V. Nizovtsev, T. M. Dolgina, N. B. Bespalova, V. E. Fedorov, in RU2326733, OOO "ob'edinennyj tsentr issledovanij i razrabotok", RU, 2007.
- P. S. Engl, C. B. Santiago, C. P. Gordon, W. C. Liao, A. Fedorov, C. Coperet, M. S. Sigman, A. Togni, 'Exploiting and [40] Understanding the Selectivity of Ru-N-Heterocyclic Carbene Metathesis Catalysts for the Ethenolysis of Cyclic Olefins to alpha, omega-Dienes', J. Am. Chem. Soc. 2017, 139, 13117-13125.
- [41] M. Scholl, S. Ding, C. W. Lee, R. H. Grubbs, 'Synthesis and Activity of a New Generation of Ruthenium-Based Olefin Metathesis Catalysts Coordinated with 1,3-Dimesityl-4,5-dihydroimidazol-2-ylidene Ligands', Org. Lett. 1999, 1, 953-956
- [42] M. B. Dinger, J. C. Mol, 'High Turnover Numbers with Ruthenium-based Metathesis Catalysts', Adv. Synth. Catal. 2002, 344.671-677.
- J. A. Love, J. P. Morgan, T. M. Trnka, R. H. Grubbs, 'A Practical and Highly Active Ruthenium-Based Catalyst that [43] Effects the Cross Metathesis of Acrylonitrile', Angew. Chem. Int. Ed. 2002, 41, 4035-4037.
- P. E. Romero, W. E. Piers, R. McDonald, 'Rapidly Initiating Ruthenium Olefin-Metathesis Catalysts', Angew. Chem. [44] Int. Ed. 2004, 43, 6161-6165.
- S. Gessler, S. Randl, S. Blechert, Synthesis and Metathesis Reactions of a Phosphine-free Dihydroimidazole Carbene [45] Ruthenium Complex', Tetrahedron Lett. 2000, 41, 9973-9976.

- [46] S. B. Garber, J. S. Kingsbury, B. L. Gray, A. H. Hoveyda, 'Efficient and Recyclable Monomeric and Dendritic Ru-based Metathesis Catalysts', J. Am. Chem. Soc. 2000, 122, 8168-8179.
- [47] M. Bieniek, A. Michrowska, D. L. Usanov, K. Grela, 'In an Attempt to Provide a User's Guide to the Galaxy of Benzylidene, Alkoxybenzylidene, and Indenylidene Ruthenium Olefin Metathesis Catalysts', *Chem. Eur. J.* 2008, 14, 806-818.
- [48] A. Fedorov, H. J. Liu, H. K. Lo, C. Coperet, 'Silica-Supported Cu Nanoparticle Catalysts for Alkyne Semihydrogenation: Effect of Ligands on Rates and Selectivity', J. Am. Chem. Soc. 2016, 138, 16502-16507.
- [49] R. M. Thomas, A. Fedorov, B. K. Keitz, R. H. Grubbs, 'Thermally Stable, Latent Olefin Metathesis Catalysts', Organometallics **2011**, *30*, 6713-6717.
- [50] G. S. Forman, A. E. McConnell, R. P. Tooze, W. J. van Rensburg, W. H. Meyer, M. M. Kirk, C. L. Dwyer, D. W. Serfontein, 'A convenient system for improving the efficiency of first-generation ruthenium olefin metathesis catalysts', *Organometallics* 2005, 24, 4528-4542.
- [51] J.-P. Lange, 'Catalysis for biorefineries performance criteria for industrial operation', *Catal. Sci. Technol.* **2016**, *6*, 4759-4767.
- [52] L. A. Pine, B. La Rouge, US, 1969.

тос



HTE Screening: Ru catalysts and conditions TON up to 5200 Methyl acrylate yield up to 69%

