

Supporting information

Brønsted acid catalysis opens a new route to polythiolesters via the direct condensation of thiolactic acid to thiolactide

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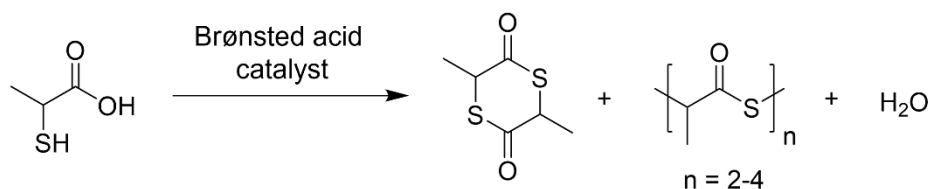
S1 Materials and Methods

S1.1 Materials

Thiolactic acid (Alfa Aesar, 97%), benzyl alcohol (Acros Organics, $\geq 98\%$, Extra dry, AcroSeal), sodium chloride (Roth, $\geq 99,5\%$), sodium bicarbonate (Honeywell Fluka, $\geq 99,7\%$), boric acid (Fischer Scientific, 99.5%), sulfuric acid (Acros Organics, 96%), nitric acid (Acros Organics, 65%), hydrochloric acid (Acros Organics, 37%), hydrofluoric acid (Sigma-Aldrich, 40%), trifluoromethanesulfonic acid (TCI Europe, $>98.0\%$), tetraethoxy silane (TEOS) (Fischer Scientific, $>99\%$), N,N,N,N-tetraethylammonium hydroxide (TEAOH) (Sachem, 35 wt% in water), tin chloride pentahydrate (Sigma-Aldrich, 98%), sodium hydroxide (Acros Organics, extra pure), sodium aluminate (Alfa Aesar, technical), L-lysine (Alfa Aesar, 98%), ammonium nitrate (Acros Organics, 98%), and lithium metaborate (Sigma-Aldrich, 99.9%) were used as received. Diphenyl phosphate (Sigma-Aldrich, 99%), 1-dodecanol (Merck, 98.0%) and p-toluenesulfonic acid monohydrate (Fluorochem limited, 98%) were dried overnight under vacuum before use. Triethylamine (Merck, $\geq 99\%$) is dried by refluxing and distilling it over pre-activated molecular sieves. Tin(II) 2-ethylhexanoate (Sigma-Aldrich, 92.5-100.0%) was purified and dried by vacuum distillation. Commercial ion-exchange resins Amberlyst 36 (Merck, 0.20 mL/g total pore volume), Dowex 50x2-100 (Acros Organics), Aquivion PW98 (Sigma-Aldrich, PFSA eq. wt. 980 g/mol SO_3H) were used as received. Commercial zeolites NH_4 -BEA 12.5 (Zeolyst, CP841E*, Si/Al = 12.5), H-BEA 19 (Zeolyst, CP814C*, Si/Al = 19), H-BEA 75 (Clariant, CZB 150, Si/Al = 75), H-BEA 150 (Zeolyst, CP811C-300, Si/Al = 150), H-BEA 255 (Tosoh, HSZ-900-931HOA, Si/Al = 255), ZSM-5 (Zeolyst, CBV 8014, Si/Al = 40), CBV 712 (Zeolyst, Si/Al = 6), CBV 720 (Zeolyst, Si/Al = 15), and CBV 760 (Zeolyst, Si/Al = 30) were used after calcination (under static air at 550°C for 1 h). Toluene (Acros Organics, 99.5%), o-xylene (Fischer Scientific, 99%), mesitylene (Sigma-Aldrich, $\geq 98.0\%$) (Acros Organics, $\geq 99.9\%$), chloroform (Acros Organics, $>99.8\%$), methanol (Acros Organics, 99.9%), tetrahydrofuran (Biosolve, unstabilized), ethyl acetate (Acros Organics, 99.5%), dichloromethane (Acros Organics, 99.9%, Extra dry, stabilized, AcroSeal), diethylether (Acros Organics, $> 99\%$), chloroform-d (Sigma-Aldrich, 100%, 99.96 atom% D, 0.03% (v/v) TMS) and dimethylsulfoxide-d6 (Sigma-Aldrich, 100%, 99.96 atom% D, 0.03% (v/v) TMS) were used as purchased. Toluene and tetrahydrofuran used to dissolve polymerization catalysts and initiators were purified and dried by a MB SPS-800 solvent purification system (MBRAUN).

S1.2 Methods

S1.2.1 Synthesis of thiolactide



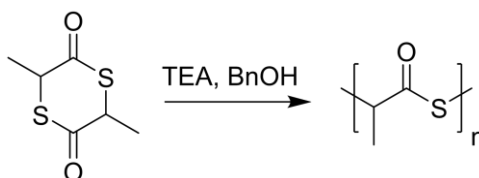
In a typical reaction for screening (Table 1, zeolite Fig. 3) 0.5 g (4.71 mmol) of thiolactic acid (TLA) (or 2-mercaptopropionic acid) is added to a 10 ml round bottom flask, together with 0.2825 mmol H^+ (p-toluenesulphonic acid (p-TSA), H_2SO_4 , methanesulfonic acid (MSA) or ion-exchange resin (IER)) or 0.25 g of Brønsted acid zeolite (0.25 g H-BEA (Si/Al = 12.5) is estimated to be equal to 0.2825 mmol H^+) and a magnetic stirring bar. Larger scale experiments were performed to enable sampling over time and reduce small scale variations (Figure 2). In a typical large scale experiment 5 g (47.1 mmol) of TLA is added to a 100 ml round bottom flask, together with 2.825 mmol H^+ (homogeneous acid or IER) or

2.5 g of zeolite. Homogeneous acids and IERs are used as received. Zeolites are calcined prior to use by heating them in a muffle oven till 550°C at a rate of 1°C/min and keeping it isothermal for 1-3 h. All reaction compounds are dissolved in 5 ml (or 50 ml (large scale)) of solvent (toluene, o-xylene or mesitylene) and heated in an oil bath at 135°C (toluene, boiling point (bp) = 111°C), 170°C (o-xylene, bp = 144°C) or 185°C (mesitylene, bp = 165°C). A custom-made Dean-Stark trap, filled with the same solvent, is used to remove the water formed during (thio)esterification under continuous reflux and stirring for 15 min up to 72 h. After reaction the mixture is allowed to cool down and 7.5 ml (or 75 ml (large scale)) of acetonitrile (ACN) is added to homogenize the whole. Heterogeneous catalysts are separated from the reaction mixture by filtering it over a glass frit filter under vacuum. Remaining zeolite/IER is rinsed with another 5 ml (or 50 ml (large scale)) of ACN. The (filtered) mixture is directly analyzed (without evaporation of the solvent) by ¹H-NMR (400 MHz, dmsO-d₆), HPLC and chiral GC (c-GC).

S1.2.3 Purification of thiolactide

Prior to ring-opening polymerization, thiolactide (TLD) is purified from the mixture obtained after cyclization of TLA. First, the remaining solvents (toluene, o-xylene or mesitylene and ACN) are removed via rotary evaporation. Second, the compounds are diluted in ethyl acetate and washed three times with a saturated aqueous NaHCO₃ solution to extract TLD from the linear oligomers, remaining TLA (and homogeneous acid catalyst). The organic layer is then washed additionally with a saturated NaCl solution, and the remaining water is removed by adding MgSO₄. MgSO₄ is removed by filtration and the mixture is dried to afford TLD with a purity of 90.9%. To further purify and dry the monomer, the compound is distilled in vacuo to obtain 99.5% pure TLD. The purity of TLD can be further increased by recrystallization in cold diethylether (unstabilized) to obtain a white powder with a purity of more than 99.9%.

S1.2.4 Ring-opening polymerization of thiolactide



In a typical ROP experiment a desired amount of TLD and a magnetic stirring bar are added to a flame-dried vial purged with argon. A solution of catalyst (triethylamine (TEA), diphenylphosphate (DPP), p-toluenesulfonic acid (p-TSA), triflic acid (TfOH) or Sn(II) ethylhexanoate (Sn(Oct)₂)) and benzylalcohol (BnOH) or 1-dodecanol (DDOH) as the initiator in anhydrous dichloromethane (DCM) (or tetrahydrofuran (THF) for p-TSA, or toluene for Sn(Oct)₂ and DDOH) are added to the monomer. Monomer:catalyst (m/c) ratios between 25 and 500 are used, while the amount of initiator added was half or 70% of the amount of catalyst (mol%) (i.e. m/i = 50-1000). For bulk ROP, the solvent is removed under a nitrogen flow and the vials are filled with argon. The vials are placed in an oven with a multi-position stirring plate at 40-80°C. For solution ROP, catalyst and initiator are added to a solution of the monomer in anhydrous DCM to reach a monomer concentration of 25 M in DCM. The reactions are stirred at room temperature (21-27°C) for 5 min to 48 h. After polymerization, the reactions are quenched by cooling and immediately diluted with CDCl₃ for ¹H-NMR (400 MHz) or with THF for GPC analysis.

S1.2.5 Reaction mixture and polymer analysis

^1H and ^{13}C -NMR spectra are recorded in $\text{dms}\text{-d}_6$ (Sigma-Aldrich) or CDCl_3 (Sigma-Aldrich) on a Bruker Advance 400 or 600 MHz spectrometer with a BBI 5 mm probe.

Quantitative ^1H -NMR (qNMR) is performed by addition of 1.5-2.5 mg of naphthalene as external standard to a 500 μL solution of $\text{dms}\text{-d}_6$ and the product mixture (0.1-0.2 g (no solvent removal)) to determine the absolute amounts of TLA and TLD in $\text{dms}\text{-d}_6$ as compared to the initial amount of TLA added to the reaction.

High pressure liquid chromatography (HPLC) is used to analyze the composition of the reaction mixture after TLA cyclization. A Shimadzu LC-20 apparatus is used, containing a CTO 20AC column oven and a SPD-20A UV-VIS detector (210 nm). A C-18 column is used with a length of 250 mm, internal diameter of 4.6 mm and a particle size of 5 μm . After reaction, 0.1 mL of reaction mixture is weighed and dissolved in ACN (30 mg/mL). The mobile phase is composed of two solvents: a) 95% milli-Q water and 5% ACN (V/V) enriched with 2 mL of 85% phosphoric acid (H_3PO_4) per L of solvent, b) 100% ACN enriched with 2 mL of 85% H_3PO_4 per L of solvent. The elution method (a/b, V/V) was the following: minute 0-1: 50/50; minute 1-44: linear ramp to 20/80; minute 44-49: isocratic at 20/80.

Chiral gas chromatography (c-GC) is used to determine the stereochemistry of TLD, separating L,L; D,D and L,D enantiomers. Separation is performed on a Hewlett Packard 6890 equipped with a chiral 25 m Agilent WCOT fused silica CP-Chirasil-DEX CB capillary column (0.32 mm internal diameter and 0.25 μm film thickness) and a FID detector held at 350°C. The temperature of the injection port was set at 220°C. The initial column temperature is kept at 50°C for 2 minutes and is subsequently ramped to 200°C at a heating rate of 15°C/min and held at this temperature for 3 minutes.

Gel permeation chromatography (GPC) is performed using a Shimadzu LC-10AD chromatograph liquid pump and CTO-10A column oven and a RID-20A refractive index detector. Separation is performed on an Agilent D-column 5 μm (mixed) with a 1 mL min^{-1} flow of THF at 35 °C. Polystyrene standards are used for calibration.

S1.2.6 Gas-phase adsorption measurements followed by FT-IR spectroscopy

Gas-phase adsorption measurements of pyridine, lactic acid (LA) and TLA over a H-BEA zeolite (Si/Al = 12.5) were followed with *in-situ* Fourier transform infrared (FT-IR) spectroscopy. Spectra were collected using a Nicolet 6700 instrument equipped with a DTGS (Deuterated Triglycine Sulfate) detector.¹ Time-profile adsorption spectra were collected with a cumulation of 128 scans at a resolution of 2 cm^{-1} . Before adsorption, the zeolite was self-pressed into a wafer (around 10 mg/cm^2) and degassed *in-situ* for 1 h at 400°C (200°C when studying the spent catalyst = after reaction) under vacuum (< 0.1 mbar).

Acid sites quantification (pyridine adsorption): After degassing, the temperature on the system was cooled to 150°C and a reference spectrum of the activated material was recorded. Pyridine vapor was introduced onto the zeolite wafer with continuous addition of 5 mbar doses until saturation of the samples. Thermal desorption was carried out at 150°C under vacuum (< 0.1 mbar) in order to remove weakly adsorbed species.² After 20 minutes desorption, a spectrum was recorded and compared to a reference spectrum. The amount of BAS and LAS were determined by integrating the area of their characteristic bands: “v8a” at $\sim 1545 \text{ cm}^{-1}$ for pyridinium ions (PyH^+) and “v19b” at 1455 cm^{-1} for coordinated pyridine (PyL) on Al Lewis sites, and using their respective molar absorption coefficient: $\epsilon(\text{PyH}^+) = 1.67 \text{ cm}/\mu\text{mol}$ and $\epsilon(\text{PyL-Al}) = 2.22 \text{ cm}/\mu\text{mol}$.³

LA and TLA adsorption and desorption: After degassing, the temperature on the system was cooled down to 50°C, after which LA or TLA vapors were added onto the zeolite wafer. Adsorption was followed until an equilibrium was reached (no more significant difference between consecutive spectra). After equilibrium, a thermal desorption step was performed under vacuum (< 0.1 mbar) for a temperature range between 50°C and 200°C. The strength of interaction of both LA and TLA with the zeolite surface was estimated by the fraction of residual species at the desorption temperature. Occasionally, pyridine vapor was introduced on the zeolite wafer after the desorption step at 150°C, in order to study the poisoning (competitive adsorption) effect of LA or TLA, translated by a decrease in the amount of BAS and LAS calculated earlier.

S1.2.7 Thermogravimetric analysis (TGA)

TGA of the zeolites is conducted on a TGA Q500 (TA Instruments). Zeolites measured after reaction are dried in a muffle oven at 60°C overnight prior to TGA measurements. The analysis is performed under nitrogen by heating till 700°C at a heating rate of 10°C/min while continuously measuring the weight of the zeolite samples.

S1.2.8 Powder X-ray diffraction (PXRD)

PXRD data were collected on a high-throughput STOE STADI P Combi diffractometer in transmission mode with focusing Ge(111) monochromatic X-ray inlet beams ($\lambda = 1.5406 \text{ \AA}$, Cu K α source).

S1.2.9 Low-temperature N₂-physisorption

Nitrogen adsorption isotherms in the relative pressure range of 0-1 bar were measured on a Tristar II 3020 instrument. All the samples were dried at 200°C for 6 h prior to analysis. The textural properties of all samples were then obtained from the adsorption isotherms. The Brunauer-Emmett-Teller (BET) specific surface area (S_{BET}) was calculated according to the Rouquerol method⁴ The micropore volume (V_{mic}) was deducted from the t-Plot method.

S1.2.10 Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES)

ICP-AES analyses were conducted on a PerkinElmer Optima 3300 DV apparatus. A different pretreatment method is used for the determination of Si/Al and Si/Sn ratios.

Si/Al

Prior to ICP-AES measurements, 10 mg of sample is dissolved using 0.4 ml HF and 0.2 ml aqua regia. After 3 hours, the mixture is neutralized using 5.0 ml boric acid and diluted with 14.4 ml milli-Q water. After 2 more hours, the samples are diluted 10 times using 0.42 M HNO₃ in water.

Si/Sn

Prior to ICP-AES measurements, 50 g of the sample is mixed with 250 g of lithium borate for 24 h. Subsequently, the mixture is placed in a graphite crucible and put inside a muffle oven for 10 minutes at 1000°C. Subsequently the hot sample is transferred to a 10 wt% HCl solution in water and stirred for 10 minutes. After 2 more hours, the whole is diluted 5 times by using another 10 wt% solution of HCl.

S1.2.11 Custom zeolite synthesis

Synthesis of Sn-BEA zeolite (Si/Sn = 162)

The procedure is based on the method by Cambor *et al.*⁵

In a typical synthesis, 20.000 g of TEOS (tetraethyl orthosilicate) and 21.812 g of TEOH (tetraethylammonium hydroxide) were mixed together and kept under vigorous stirring. When the

two-phase system reached homogeneity, 0.200 g of tin chloride salt (SnCl_4) was added. The mixture was stirred continuously at room temperature until complete TEOS hydrolysis and evaporation of ethanol and water. Subsequently, 2.593 g of HF was added dropwise as a mineralizing agent in an equimolar amount to the OSDA. The viscous solution became a dry gel, which was milled with a spatula to obtain fine particles. At the end of the procedure the following batch composition was reached:

Si:168Sn⁻¹:0.54TEAOH:0.54HF:7.50H₂O

Finally, the gel was transferred into a Teflon-lined stainless steel autoclave, which was kept in an oven at 140 °C for 25 days. After crystallization, the zeolitic product was separated from a two-phase mixture by centrifugation (6200 rpm, 5 minutes). The product was washed by centrifuging with 50 ml milli-Q water per gram until a pH below 10 was reached. The product was dried overnight at 60°C. Prior to use, the dried product was calcined in a muffle oven under static air (heating until 550°C over 9 h and keeping it isothermal for 6 h).

Synthesis of Al-rich BEA zeolite (Si/Al = 7)

The procedure is based on the method by Zhang *et al.*⁶

In a typical synthesis, 15.200 g of TEOS (tetraethyl orthosilicate), 16.884 g of TEAOH (tetraethylammonium hydroxide), 0.136 g of NaOH, 3.200 g of L-lysine, and 4.785 g of water were mixed together and kept under vigorous stirring. When the two-phase system reached homogeneity, 0.797 g of NaAlO₂ was added. The mixture was stirred continuously at room temperature until complete TEOS hydrolysis and evaporation of ethanol. At the end of the procedure the following batch composition was obtained:

Si:7.50Al⁻¹:0.55TEAOH:0.18Na⁺:0.30Lys:12.00H₂O.

After evaporation, the solution was transferred into a Teflon-lined stainless steel autoclave, and was preheated in an oven at 80°C for two days. Next, the sample was placed into another oven for crystallization at 140°C for two more days. After crystallization, the zeolitic product was washed with milli-Q water until a neutral pH was reached, and dried overnight at 60 °C. The dried product was calcined as described above for SnBEA.

The Na-form of the Al-rich BEA zeolite was turned into its H-form by an ion-exchange procedure. 30 g of a 1 M NH₄NO₃ solution was used to exchange 1 g of zeolite sample. Two ion-exchange steps (12 h and 6 h) were conducted at 75°C. After each stage, the zeolites were separated from the mother solution by centrifugation (6200 rpm, 5 minutes) and washed once with milli-Q water. After both stages, the ion-exchanged zeolites were dried overnight in a static oven at 60°C and calcined under static air with the following program in a muffle oven (heating until 450°C over 6 h and keeping it isothermal for another 6 h).

S2 Results and Discussion

S2.1 Catalytic synthesis of TLD from TLA

S2.1.1 Analysis of reaction mixture

¹H-NMR

Reaction mixtures were immediately analyzed after removal of heterogeneous catalysts, if present, by filtration, without evaporation of the reaction solvents (toluene, o-xylene or mesitylene and acetonitrile). ¹H-NMR spectra are recorded in dms_o-d₆ on a Bruker Advance 400 or 600 MHz spectrometer. A spectrum of a typical reaction mixture can be consulted in Figure S 1. The product mixture compositions are determined by relatively comparing the signals of thiolactic acid (TLA), thiolactide (TLD) and linear oligomers in mol% thiolactyl units.

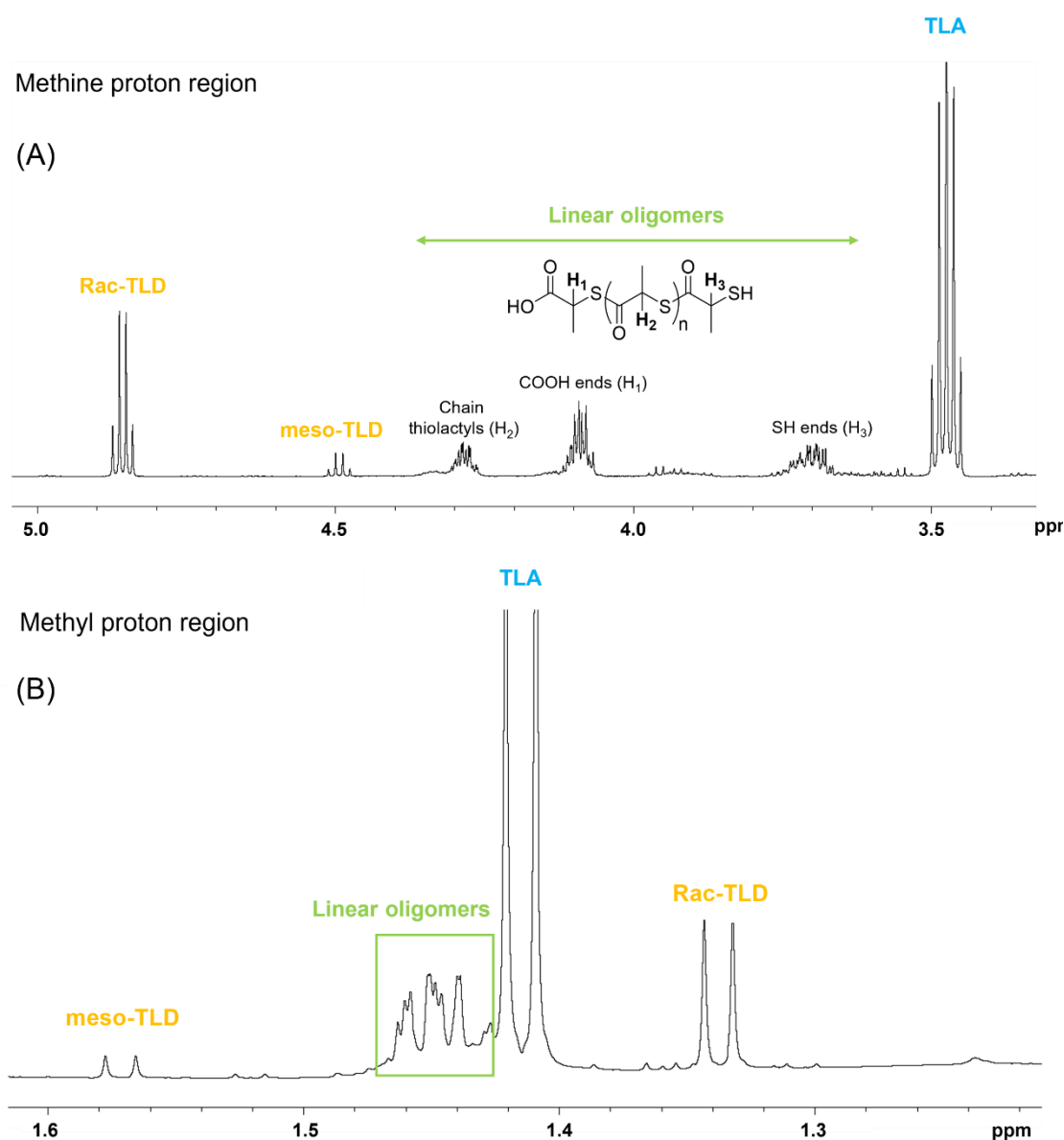


Figure S 1: ¹H-NMR (400MHz, dms_o-d₆) spectrum of a typical reaction mixture after racemic thiolactic acid (*rac*-TLA) condensation to thiolactide (TLD) in o-xylene. (A) Methine proton region and (B) Methyl proton region of the reaction mixture composed of TLA, TLD and linear oligomers of TLA. Product distributions are determined in mol% of thiolactyl units.

The average chain length of the oligomeric fraction was determined by end-group analysis. $^1\text{H-NMR}$ analysis shows three groups of peaks in the methine proton region belonging to oligomers: (1) the chain thiolactyl units, (2) the $-\text{COOH}$ end groups and (3) the $-\text{SH}$ end groups (Figure S 1). The linear dimer only shows two groups of peaks (both SH and COOH end-groups (2 and 3)). Longer chains show small shifts in ppm in the three peak regions compared to the linear dimer peaks. In addition, small shifts are also observed when oligomers are composed of TLA units with different stereochemistry. As a consequence, three groups of multiplets are observed, representing a mixture of linear oligomers and dimers. Comparing the amount of chains (based on the amount of end-groups) against the total amount of oligomers allows determination of the average chain length of the oligomeric fraction in TLA units (n), if the groups are clearly distinguishable.

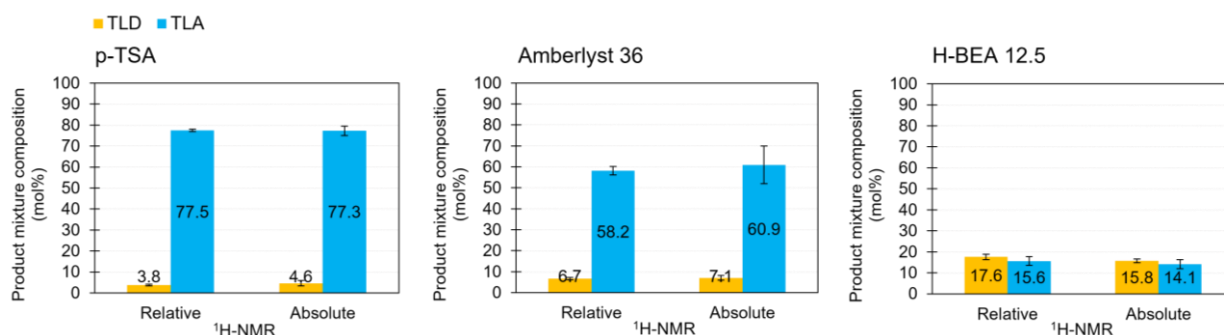


Figure S 2: Mol% of TLA and TLD in the reaction mixture as determined by relative $^1\text{H-NMR}$ or quantitative (absolute) $^1\text{H-NMR}$ for the synthesis of TLD from *rac*-TLA with p-TSA, Amberlyst 36 or H-BEA 12.5 as the catalyst. Reaction conditions: 0.5 g *rac*-TLA, 170°C, 3 h, 5 ml *o*-xylene, 0.2825 mmol H^+ (catalyst). Error bars are obtained by performing three NMR measurements on three separate samples from the same product mixtures.

Comparing the product mixture composition obtained by relative NMR with the results obtained by quantitative NMR with naphthalene as external standard proved the effectiveness of the relative method for quantitative analysis of the reaction mixture (Figure S 2).

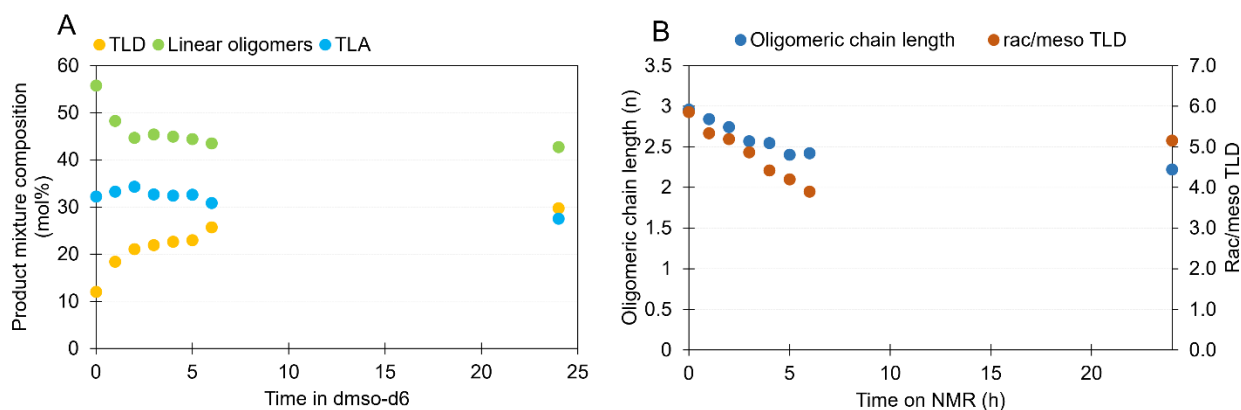


Figure S 3: (A) Changes in product mixture composition (mol%) and (B) changes in oligomeric chain length and *rac*/*meso* TLD ratio after a specific amount of time in dms0-d6 for $^1\text{H-NMR}$ analysis. Reaction conditions: 0.5 g *rac*-TLA, 170°C, 1 h, 5 ml *o*-xylene, 0.25 g H-BEA 12.5. Zeolite is removed from the reaction mixture prior to analysis.

Immediate analysis of the reaction mixture is key, since changes in reaction mixture composition were observed after prolonged time in dms0-d6 (e.g. in a waiting line to be measured in NMR) as shown in Figure S 3. Almost a tripling of the TLD yield happened after 24 h in dms0-d6. Most probably dms0 acts as a catalyst for back-biting of linear oligomers, since both the amount and length of the oligomers seemed to decrease over time. *HPLC*

The reaction mixtures were analyzed on HPLC. A typical spectrum can be found in Figure S 4.

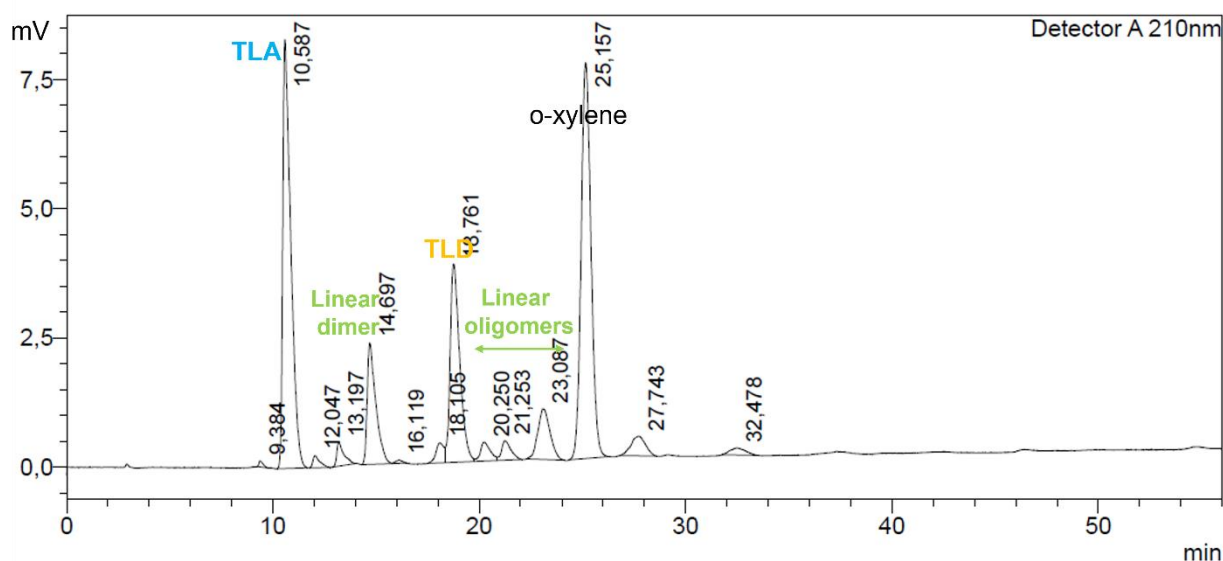


Figure S 4: HPLC spectrum of a typical reaction mixture after *rac*-TLA condensation to TLD, composed of TLA, TLD and linear oligomers of TLA.

It has to be mentioned that when comparing results on HPLC and on $^1\text{H-NMR}$ it was noticed that some degradation of TLD took place during HPLC analysis or after prolonged time in the waiting queue. The presence of water and strong acid (H_3PO_4 , necessary to protonate the acids for analysis) in the mobile phase at 40°C possibly induced some hydrolysis reactions. As a consequence, HPLC was only used as a qualitative analysis tool and quantitative results were based on $^1\text{H-NMR}$ analysis.

Chiral GC

Chiral GC (c-GC) was used to determine the relative quantities of the different chiral structures of TLD: (L,L) and (D,D)-TLD (or *rac*-TLD) and (D,L)-TLD (or *meso*-TLD). A typical c-GC spectrum is presented in Figure S 5.

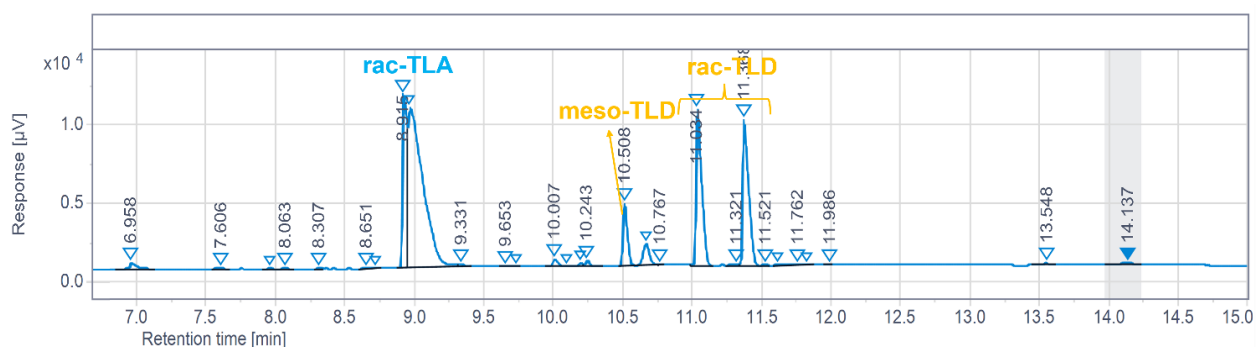


Figure S 5: Chiral GC (c-GC) spectrum of a typical reaction mixture after *rac*-TLA condensation to TLD, composed of TLA, TLD ((L,L) and (D,D)-TLD (or *rac*-TLD) and (D,L)-TLD (or *meso*-TLD)) and linear oligomers of TLA.

It has to be mentioned that, when comparing NMR and c-GC data, degradation of *meso*-TLD was observed during GC analysis (GC showed a higher *rac*/*meso* ratio than NMR). Therefore, $^1\text{H-NMR}$ was used as the main analysis method to compare relative quantities of *meso* and *rac*-TLD. However, c-GC proved that the amount of (L,L)- and (D,D)-TLD was always equal.

S2.1.2 Homogeneous catalysis

p-Toluenesulphonic acid

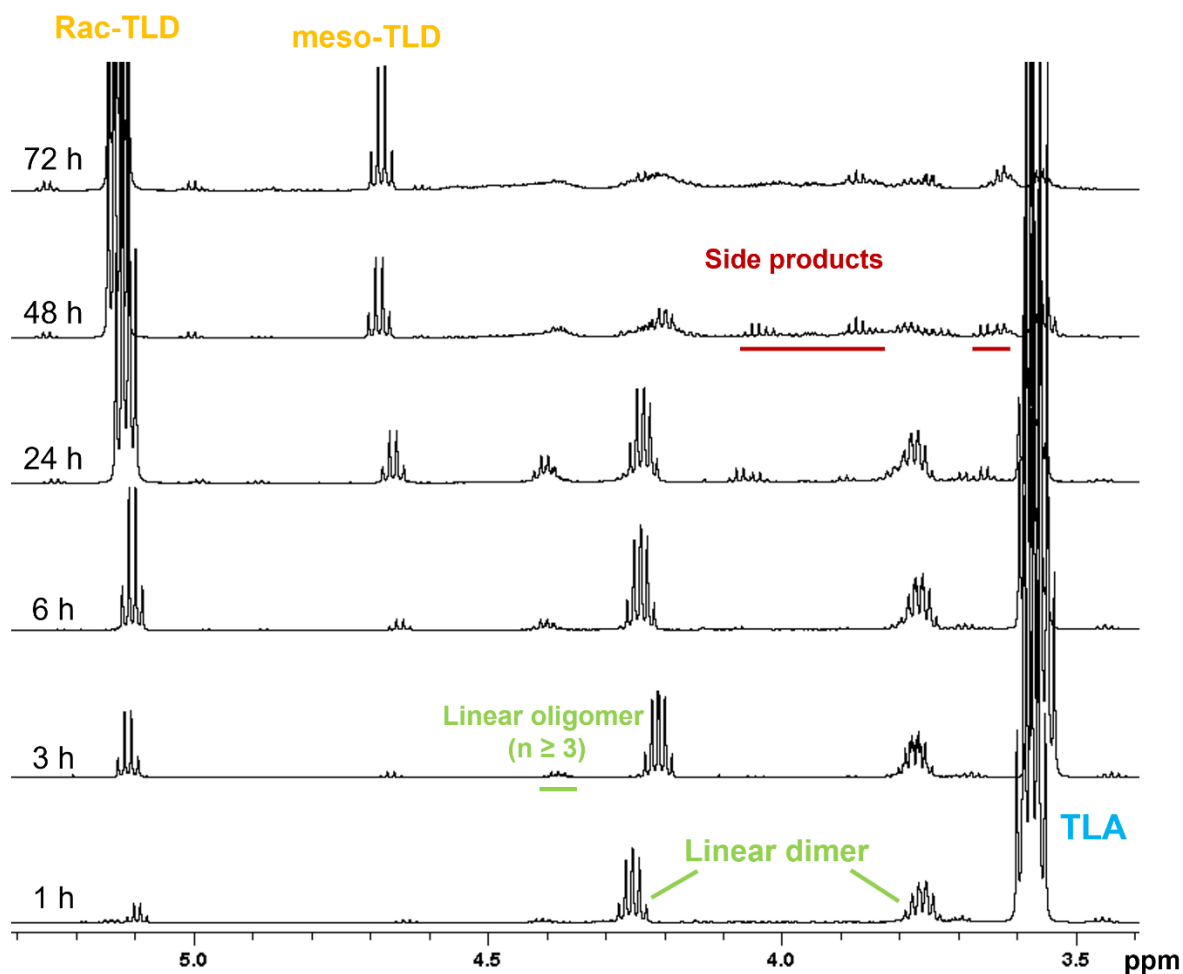


Figure S 6: ¹H-NMR (400 MHz, dms_o-d₆) spectra of the methine proton region of the product mixture after reacting *rac*-TLA in the presence of *p*-TSA for 1–72 h. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.565 mmol H⁺ (*p*-TSA)/g of TLA.

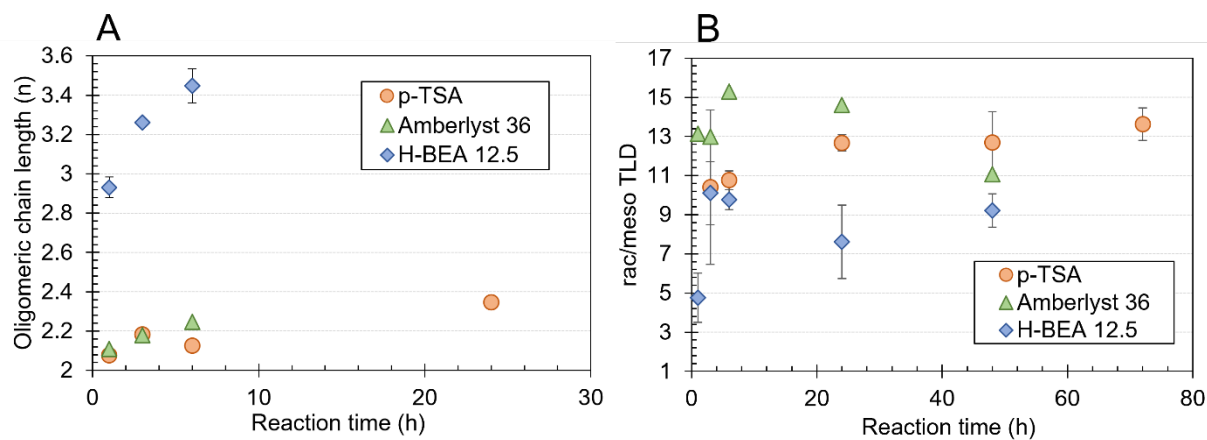


Figure S 7: (A) Linear oligomeric chain length in TLA units (n) and (B) *rac*/*meso* TLD ratio as a function of reaction time for TLA cyclization reactions with *p*-TSA, Amberlyst 36 or H-BEA 12.5 as the catalyst. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.565 mmol H⁺ (catalyst)/g of TLA.

Reaction temperature and solvent

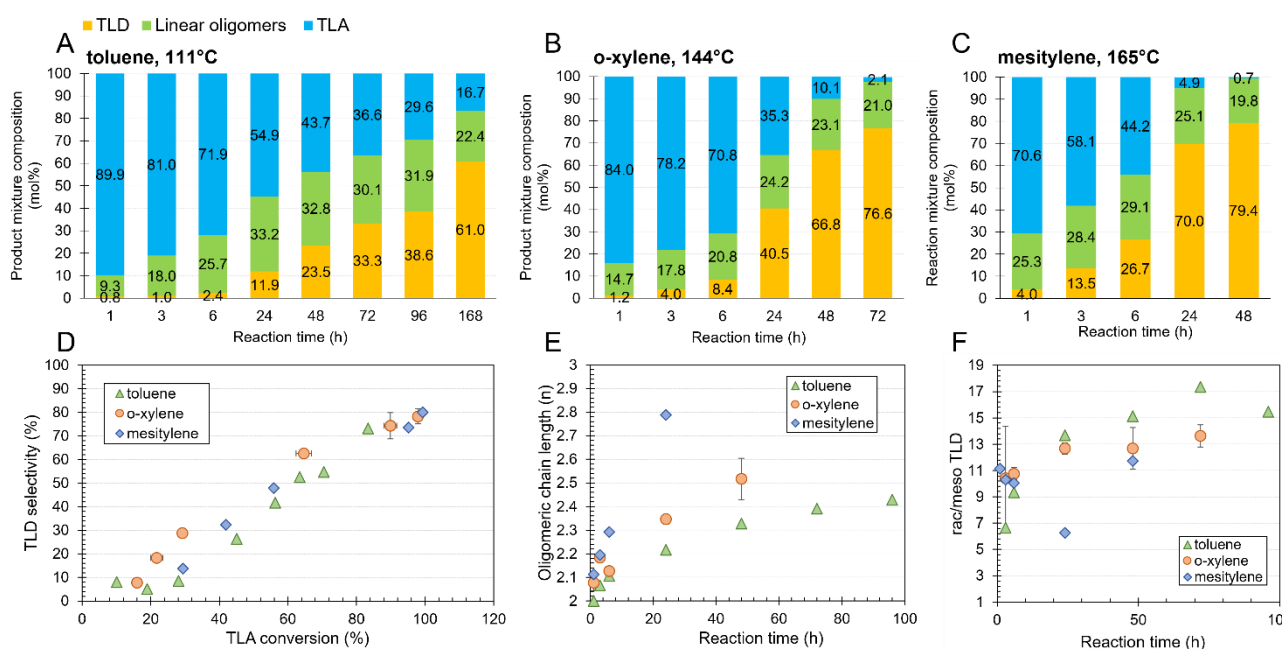


Figure S 8: (A)-(C) Product mixture distribution as a function of reaction time (h), (D) TLD selectivity (%) as a function of TLA conversion (%), (E) oligomeric chain length as a function of reaction time (h) and (F) rac/meso TLD ratio as a function of reaction time (h) for TLA cyclization reactions at 111°C (toluene), 144°C (o-xylene) or 165°C (mesitylene). Reaction conditions: 5 g *rac*-TLA, 50 ml solvent, reflux, 0.565 mmol H⁺ (p-TSA)/g of TLA.

Concentration of substrate

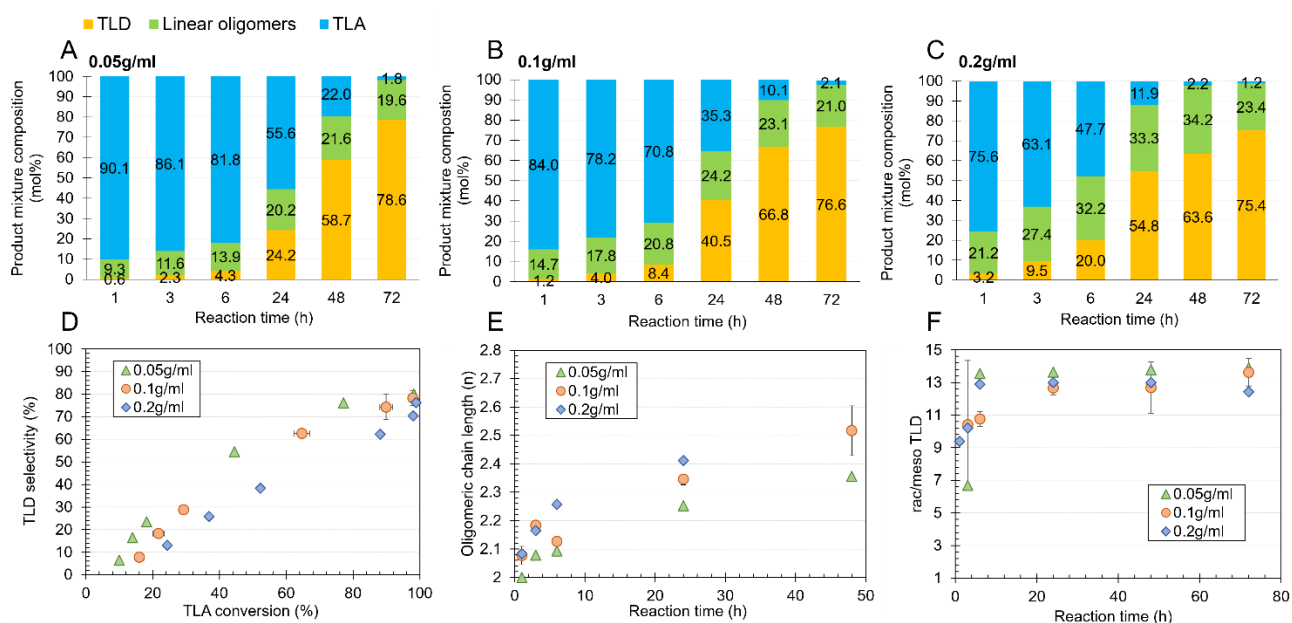


Figure S 9: (A)-(C) Product mixture distribution as a function of reaction time (h), (D) TLD selectivity (%) as a function of TLA conversion (%), (E) oligomeric chain length as a function of reaction time (h) and (F) rac/meso TLD ratio as a function of reaction time (h) for TLA cyclization reactions at TLA concentrations of 0.05 g/ml, 0.1 g/ml or 0.2 g/ml. Reaction conditions: 2.5-10 g *rac*-TLA, 50 ml o-xylene, 144°C, 0.565 mmol H⁺ (p-TSA)/g of TLA.

Catalyst/substrate ratio

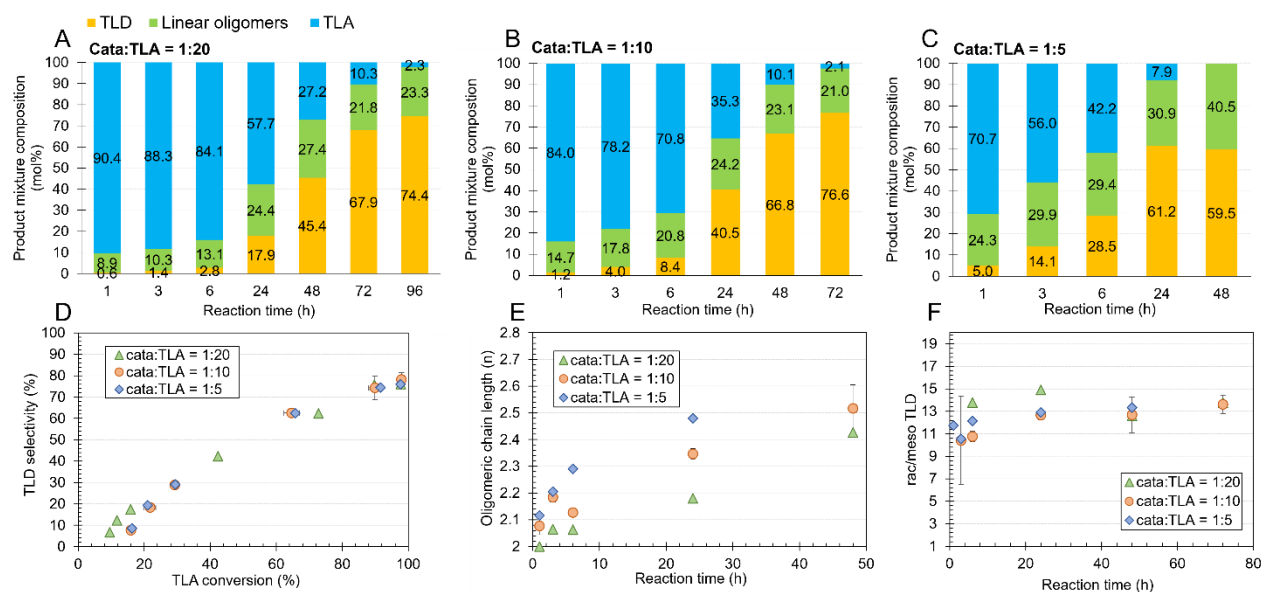


Figure S 10: (A)-(C) Product mixture distribution as a function of reaction time (h), (D) TLD selectivity (%) as a function of TLA conversion (%), (E) oligomeric chain length as a function of reaction time (h) and (F) rac/meso TLD ratio as a function of reaction time (h) for TLA cyclization reactions with a p-TSA:TLA ratio (wt) of 1:20, 1:10 or 1:5. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.2825-1.13 mmol H⁺ (p-TSA)/g of TLA.

Type of homogeneous catalyst

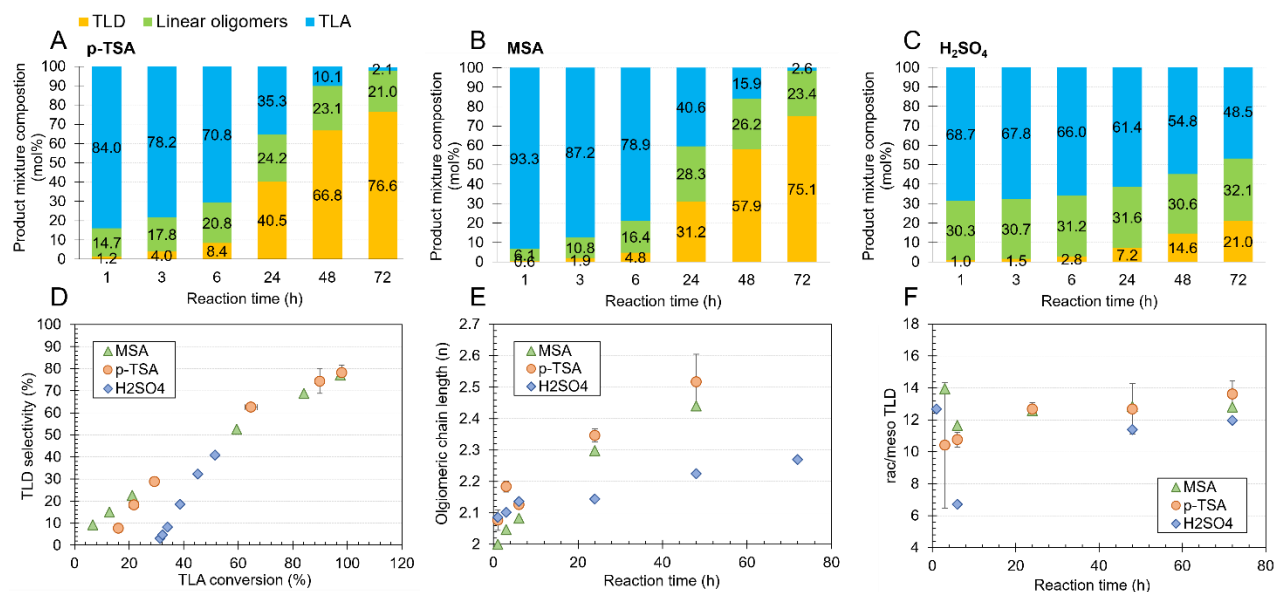


Figure S 11: (A)-(C) Product mixture distribution as a function of reaction time (h), (D) TLD selectivity (%) as a function of TLA conversion (%), (E) oligomeric chain length as a function of reaction time (h) and (F) rac/meso TLD ratio as a function of reaction time (h) for TLA cyclization reactions with p-toluenesulphonic acid (p-TSA), methanesulphonic acid (MSA) or sulfuric acid (H₂SO₄, assuming 2 moles of H⁺ per mole of H₂SO₄) as the homogeneous catalyst. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.565 mmol H⁺ (catalyst)/g of TLA.

Re-usability of *p*-TSA

To evaluate the possible loss in reactivity of *p*-TSA after a 24 h reaction in mesitylene (165°C), a fresh amount of *rac*-TLA was added to the mixture after reaction followed by heating it again for another 24 h. The ¹H-NMR spectra after the first and second reaction are shown in Figure S 12. The spectra show that after both the first and second reaction almost no TLA is left and the main reaction product is TLD, proving that no loss in reactivity of *p*-TSA is observed after two consecutive 24 h reactions at 165°C. The total TLD yield after two reactions (i.e. 80.1%) is determined by qNMR and compared to the total amount of TLA added.

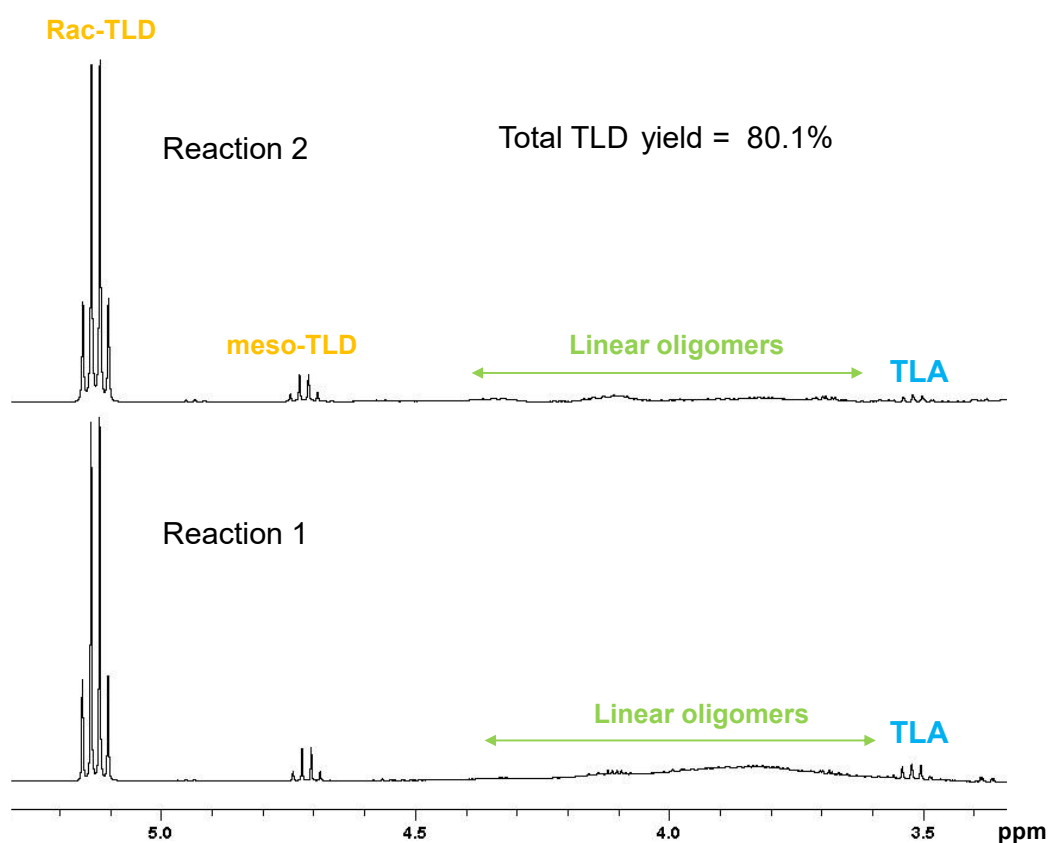


Figure S 12: ¹H-NMR (400 MHz, dms_o-d₆) spectra of the methine proton region of the product mixture after TLA cyclization (reaction 1) and after adding a fresh amount of *rac*-TLA and performing a second reaction (reaction 2). Reaction conditions: 0.5 (+ 0.5) g *rac*-TLA, 5 ml mesitylene, 165°C, 0.565 mmol H⁺ (*p*-TSA)/g of TLA.

S2.1.3 Heterogeneous catalysis

Ion-exchange resins

Table S 1: Properties of commercial sulfonic acid-based ion-exchange resins.

Type	Acid exchange capacity (meq/g;meq/ml)	Surface area (m ² /g)	Average pore diameter (Å)	Total pore volume (ml/g)	Matrix	Active group	Max. operation temperature (°C)
Amberlyst 15	4.7;1.7	53	300	0.40	PS-DVB* (macroreticular)	sulfonic acid	120
Amberlyst 36	5.40;1.95	33	240	0.20	PS-DVB* (macroreticular)	sulfonic acid	150
Dowex 50x2 (100)	- ;0.6	-	-	-	PS-DVB* (gel)	sulfonic acid	150
Aquivion PW98	0.98-1.06;-	-	-	-	Copolymer of tetrafluoroethylene and sulfonyl fluoride vinyl ether	sulfonic acid	150-160

*Polystyrene (PS) crosslinked with divinylbenzene (DBV)

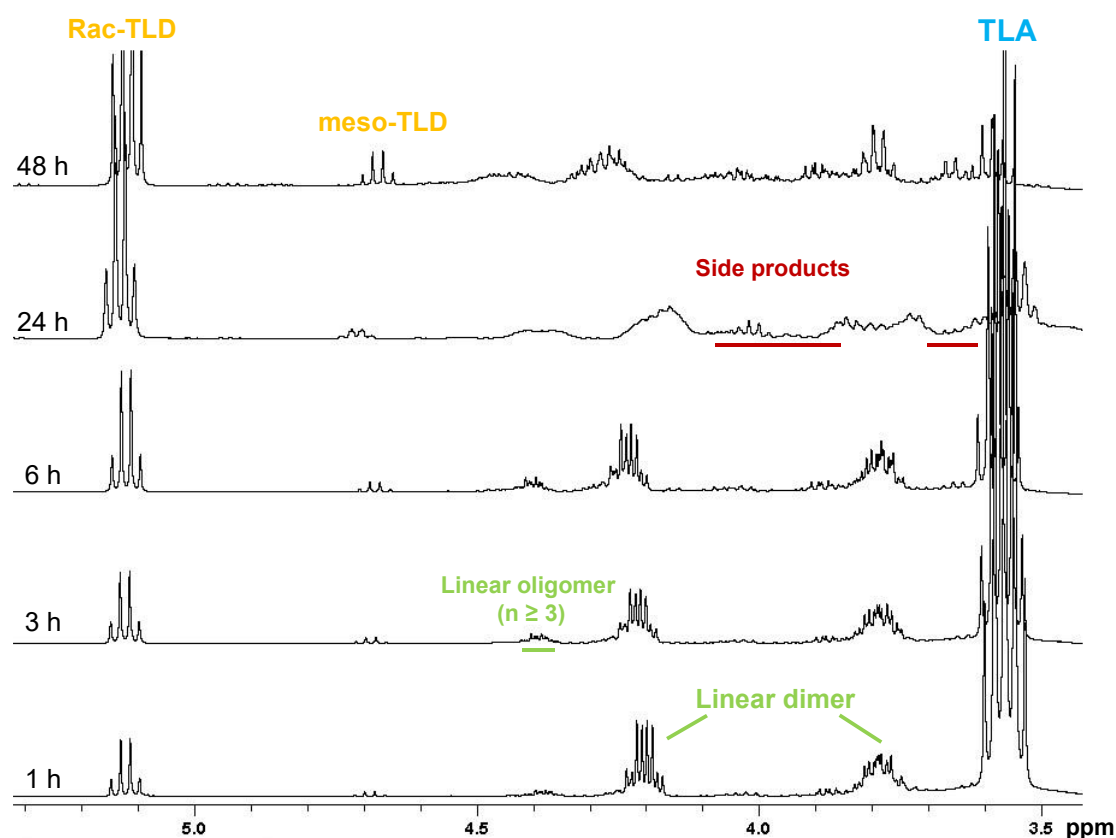


Figure S 13: ¹H-NMR (400 MHz, dms_o-d₆) spectra of the methine proton region of the product mixture after reacting *rac*-TLA in the presence of Amberlyst 36 for 1-48h. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.565 mmol H⁺ (Amberlyst 36)/g of TLA

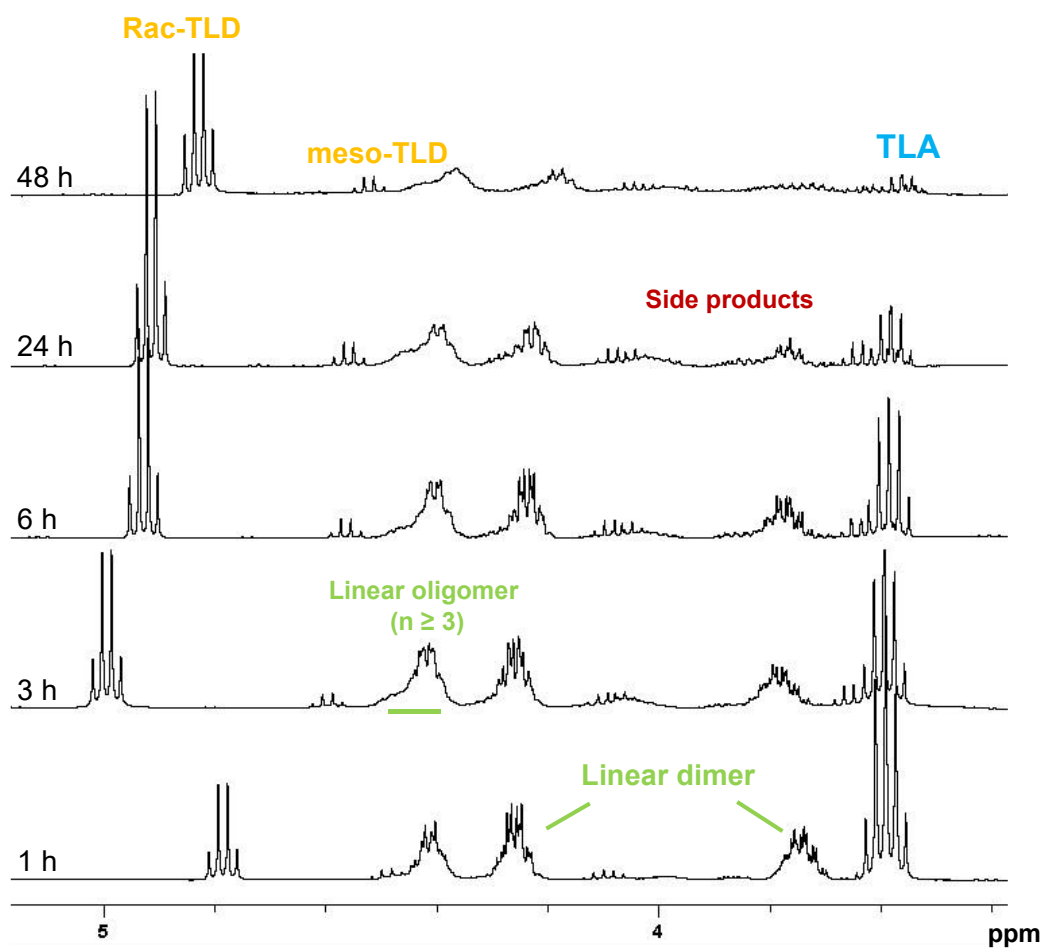


Figure S 14: ¹H-NMR (400 MHz, dms_o-d₆) spectra of the methine proton region of the product mixture after reacting *rac*-TLA in the presence of H-BEA 12.5 for 1-48h. Reaction conditions: 5 g *rac*-TLA, 50 ml *o*-xylene, 144°C, 0.565 mmol H⁺ (H-BEA 12.5, i.e. 0.5 g)/g of TLA

S2.2 Mechanistic insights into the zeolite catalysis

S2.2.1 Characterization of zeolites

Commercial zeolites

Characteristics of commercial zeolites were determined. Amounts of Brønsted acid (BAS) and Lewis acid sites (LAS) of all used commercial zeolites were determined by Fourier-Transform Infrared (FT-IR) (Table S 2). For the commercial BEA zeolites the average pore diameter, the pore volume (total and micropore) and the surface area (specific and external) were determined by N₂ physisorption measurements (Table S 3).

Table S 2: Overview of all commercial zeolites used with their supplier, Si/Al ratio (provided by manufacturer), cation and amount of Brønsted acid (BAS) and Lewis acid sites (LAS) as determined by FT-IR at 150°C.

Catalysts / Supplier code	Supplier	Si/Al	Cation	BAS (150°C)	LAS (150°C)
FAU				μmol/g	μmol/g
CBV712	Zeolyst	6	H (from NH ₄ ⁺)	421	103
CBV720	Zeolyst	15	H ⁺	371	221
CBV760	Zeolyst	30	H ⁺	138	61
BEA					
CP814E*	Zeolyst	12.5	H (from NH ₄ ⁺)	234	219
CP814C*	Zeolyst	19	H (from NH ₄ ⁺)	245	109
CZB150	Clariant	75	H ⁺	73	13
CP811C-300	Zeolyst	150	H ⁺	52	5
HSZ-980HOA	Tosoh	255	H ⁺	23	3
MFI (ZSM-5)					
CBV8014	Zeolyst	40	H (from NH ₄ ⁺)	177	40

Table S 3: Average pore diameter (nm), pore volume (cm³/g) (total and micropore) and surface area (m²/g) (specific and external) for the most acidic commercial BEA zeolites as determined by N₂ physisorption.

Zeolite	Average pore diameter (nm)	Specific surface area (BET surface area) (m ² /g)	External surface area (m ² /g)	Total pore volume (cm ³ /g)	Micropore volume (cm ³ /g)
H-BEA 12.5	3.79	629	192	0.47	0.13
H-BEA 19	2.32	579	137	0.36	0.19
H-BEA 75	3.88	571	165	0.49	0.16

Custom-made zeolites

Table S 4: Si/Al or Si/Sn ratio as determined by ICP-AES, Brønsted (BAS) and Lewis acid sites (LAS) density as determined by FT-IR, and BET surface area and micropore volume as determined by N₂ physisorption for custom made H-BEA and SnBEA.

Zeolite	Si/Al ratio	Si/Sn ratio	BAS (μmol/g)	LAS (μmol/g)	Specific surface area (BET surface area) (m ² /g)	Micropore volume (cm ³ /g)
H-BEA 7	7.2	-	242	137	640	0.15
SnBEA	-	161.9	3	14	581	0.18

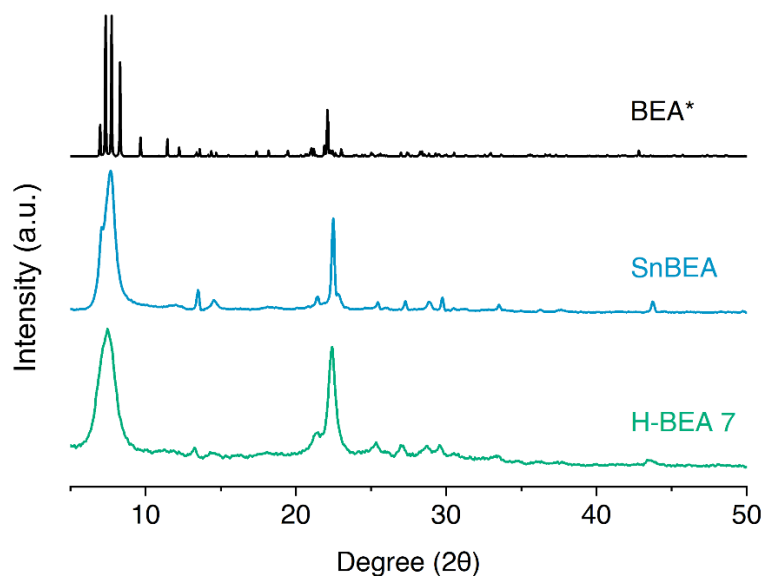


Figure S 15: Powder XRD spectra of custom-made SnBEA and H-BEA 7 and compared to a typical BEA pattern of combined polymorphs A and B (1:1 ratio).

S2.2.2 Zeolite screening

Table S 5: Zeolite screening for the cyclization reaction of TLA. TLA conversion (%), TLD selectivity (%) and average oligomeric chain length expressed in units TLA (n). Reaction conditions: 0.5 g *rac*-TLA, 5 ml *o*-xylene, 144°C, 1 h, TLA:catalyst (wt) = 2:1 for zeolites. For H₂SO₄ and p-TSA the catalyst amounts used are equivalent to the same amount of H⁺ in H-BEA 12.5 (i.e. 0.565 mmol H⁺/g TLA).

Entry	Catalyst	Reaction mixture composition (¹ H-NMR)		End-group analysis (¹ H-NMR)
		TLA conversion (%)	TLD selectivity (%)	Oligomeric chain length (units TLA (n))
1	-	4.7	0	2.0
2	H ₂ SO ₄	42	38	2.1
3	p-TSA	10	7.0	2.1
4	SnBEA	3.9	7.7	2.0
5	H-BEA 7	60	22	2.8
6	H-BEA 12.5	68	20	3.0
7	H-BEA 19	70	15	2.7
8	H-BEA 75	50	23	2.7
9	H-BEA 150	26	29	2.3
10	H-BEA 255	26	27	2.4
11	H-MFI 40	30	3.4	2.2
12	H-FAU 6	37	19	2.5
13	H-FAU 15	40	11	2.7
14	H-FAU 30	37	13	2.6

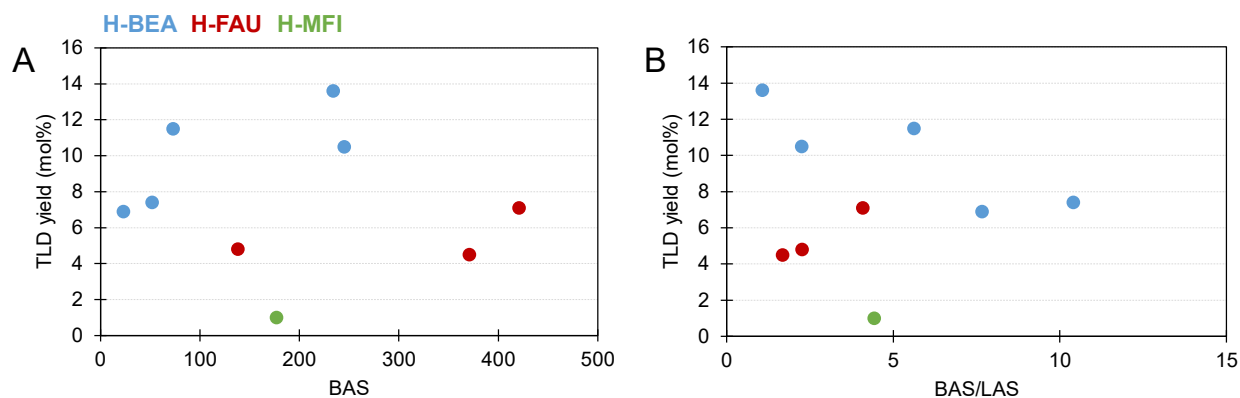


Figure S 16: (A) TLD yield (mol%) as a function of the amount of Brønsted acid sites (BAS) in the used zeolites (H-BEA, H-FAU or H-MFI), (B) TLD yield (mol%) as a function of the amount of BAS divided by the amount of Lewis acid sites (LAS) (BAS/LAS) of the used zeolites (H-BEA, H-FAU or H-MFI). Reaction conditions: 0.5 g *rac*-TLA, 5 ml *o*-xylene, 144°C, 1 h, 0.25 g of zeolite.

S2.2.3 Diffusion limitation

Pore diffusion limitation

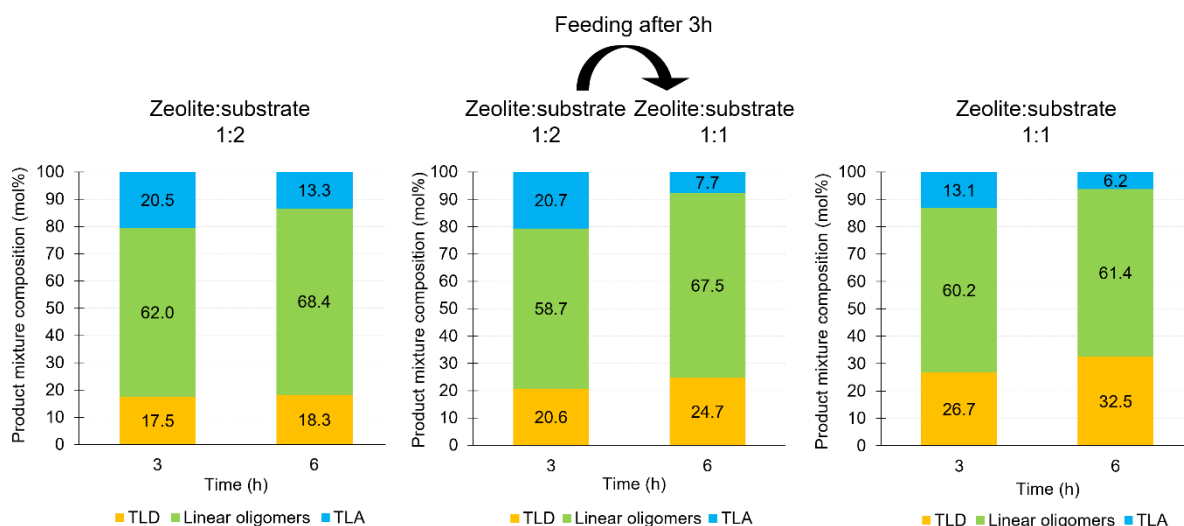


Figure S 17: Product mixture composition (mol%) after a 3 h or 6 h reaction. Reaction conditions: 0.5 g *rac*-TLA, 5 ml toluene, 111°C, H-BEA 12.5, (left) zeolite:substrate = 1:2 over 3 and 6 h of reaction, (middle) zeolite:substrate = 1:2 for 3 h of reaction and after 3 h the same fresh zeolite is added ('feeding') to react for another 3 h, (right) zeolite:substrate = 1:1 over 3 and 6 h of reaction.

Film diffusion limitation

The presence of film diffusion limitation was checked by performing reactions at different stirring rates at 111°C in toluene for up to 1 h. The results are shown in Figure S 18.

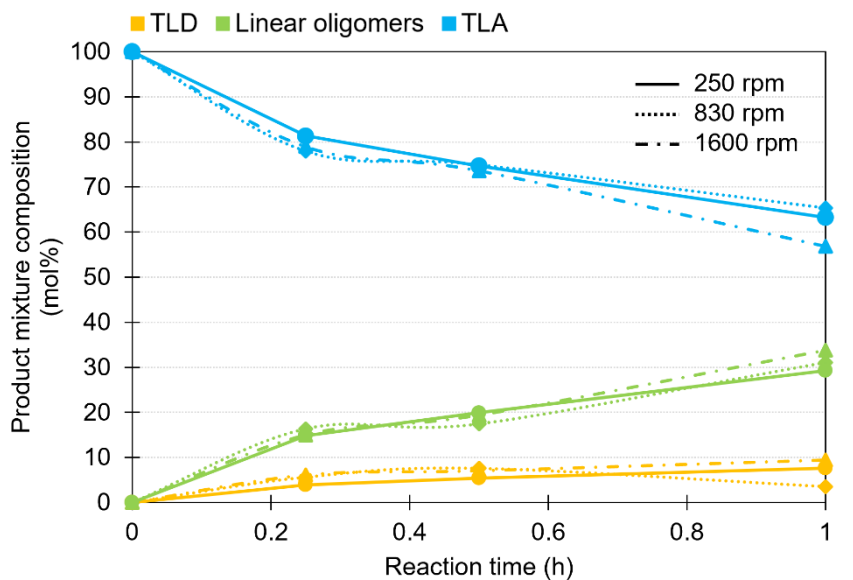


Figure S 18: Film diffusion limitation check by performing reactions at different stirring rates (250 rpm, 830 rpm, 1600 rpm). Reaction conditions: 0.5 g *rac*-TLA, 5 ml toluene, 111°C, 15 min-1 h 0.25 g H-BEA 12.5,

S2.2.4 Thermogravimetric analysis of zeolite

Thermogravimetric analysis (TGA) was performed on pure H-BEA 12.5, H-BEA 12.5 after contact with o-xylene at reflux conditions and H-BEA 12.5 after a TLA cyclization reaction of 1 h in o-xylene. The results are shown in Figure S 19.

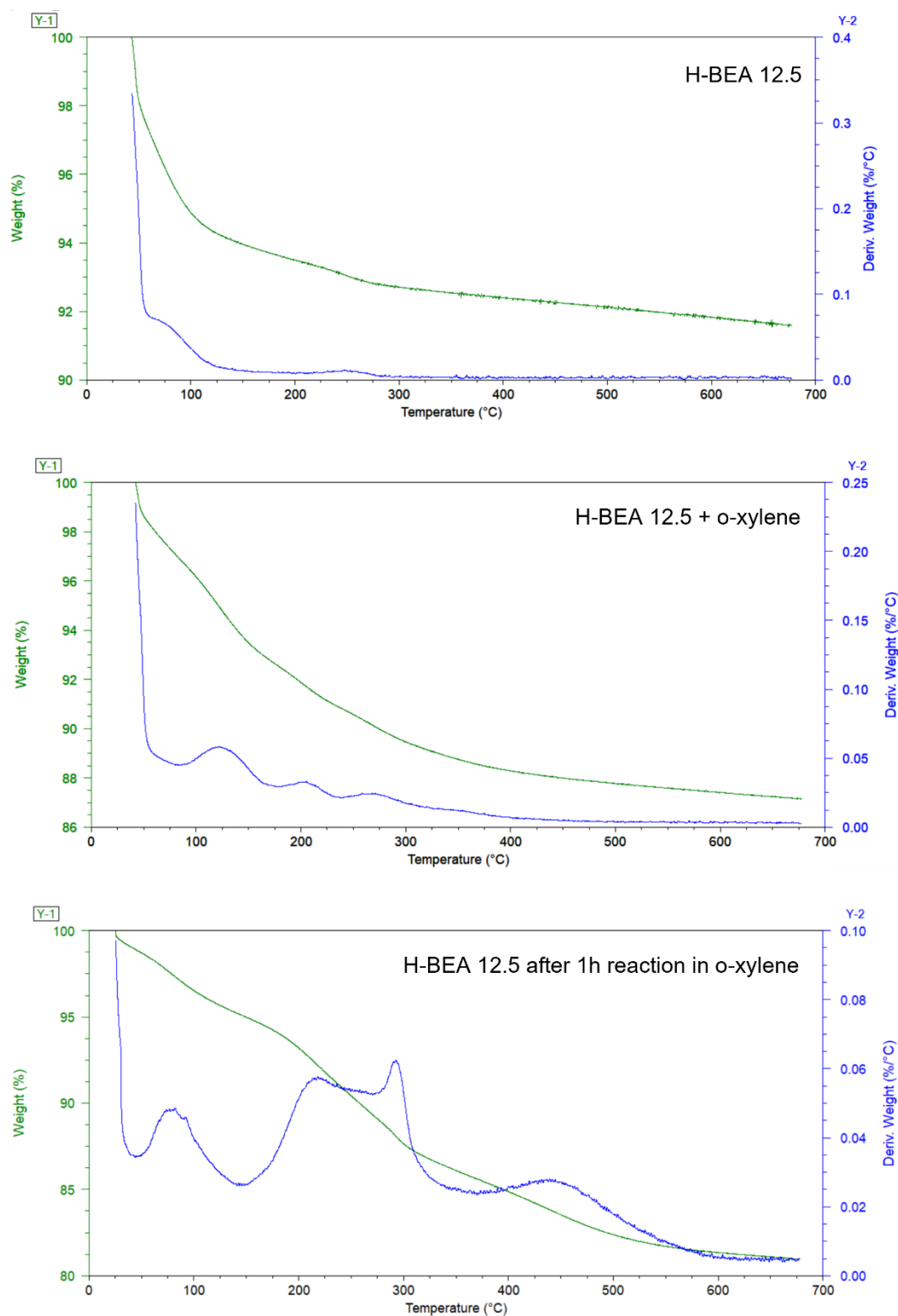


Figure S 19: Variation in weight (%), y1-axis and first derivative of weight (%/°C, y2-axis) as a function of temperature determined by TGA for pure H-BEA 12.5 (upper), H-BEA 12.5 brought in contact with o-xylene for 10 min at reflux conditions (middle) and H-BEA 12.5 after TLA cyclization in o-xylene for 1 h.

S2.2.5 N₂ physisorption

Table S 6: Comparison of BET surface area (m²/g) and microporous volume (cm³/g) of zeolites before (neat) and after reactions with TLA or TLD (non-calcined) as determined by N₂ physisorption measurements (dried at 200°C for 6 h prior to analysis). Reaction conditions: 0.5 g *rac*-TLA or TLD, 5 ml *o*-xylene, 144°C, 1 or 24 h, 0.25 g H-BEA 12.5 or SnBEA (Si/Sn = 162).

Zeolite	BET surface area (m ² /g)	Microporous volume (cm ³ /g)
H-BEA 12.5 (neat)	629	0.13
H-BEA 12.5, 1 h, TLA	361	0.05
H-BEA 12.5, 24 h, TLA	296	0.03
H-BEA 12.5, 24 h, TLD	437	0.07
SnBEA (neat)	581	0.18
SnBEA, 1 h, TLA	551	0.17

S2.2.6 XRD

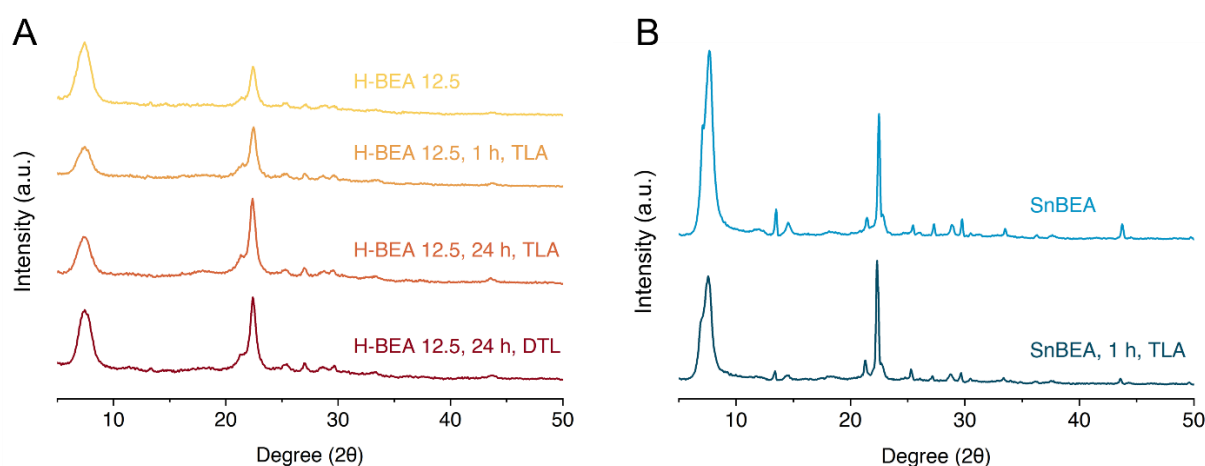


Figure S 20: Powder XRD spectra of (A) H-BEA 12.5 after a 1 h or 24 h reaction with TLA or a 24 h reaction with TLD, (B) SnBEA after a 1 h reaction with TLA as compared to a neat, calcined (A) H-BEA 12.5 or (B) SnBEA zeolite.

S2.2.7 FT-IR

Pyridine adsorption analysis followed by FT-IR spectroscopy was performed on a neat H-BEA 12.5 zeolite and compared to H-BEA 12.5 exposed to several reaction conditions: 1 h reaction with TLA or 24 h reaction with TLA or TLD. Similar measurements were additionally performed on a neat SnBEA (Si/Sn = 162) and compared to the SnBEA sample after 1 h reaction with TLA (see Table S 7).

Table S 7: Comparison of Brønsted acid sites (BAS) and Lewis acid sites (LAS) density (μmol/g) of zeolites before (neat) and after reactions with TLA or TLD (non-calcined) as determined by FT-IR spectroscopy after pyridine adsorption. Reaction conditions: 0.5 g *rac*-TLA or TLD, 5 ml *o*-xylene, 144°C, 1 or 24 h, 0.25 g H-BEA 12.5 or SnBEA (Si/Sn = 162).

Zeolite	BAS (μmol/g)	LAS (μmol/g)
H-BEA 12.5 (neat)	234	219
H-BEA 12.5, 1 h, TLA	35	44
H-BEA 12.5, 24 h, TLA	24	33
H-BEA 12.5, 24 h, TLD	75	34
SnBEA (neat)	3	14
SnBEA, 1 h, TLA	2	10

S2.2.8 Zeolite recycling and stability

Recycling reactions

The recyclability and stability of H-BEA 12.5 was tested by capturing and calcining the zeolite after each TLA cyclization reaction for three consecutive reactions. The product mixture distribution as determined by $^1\text{H-NMR}$ is shown in Figure S 21.

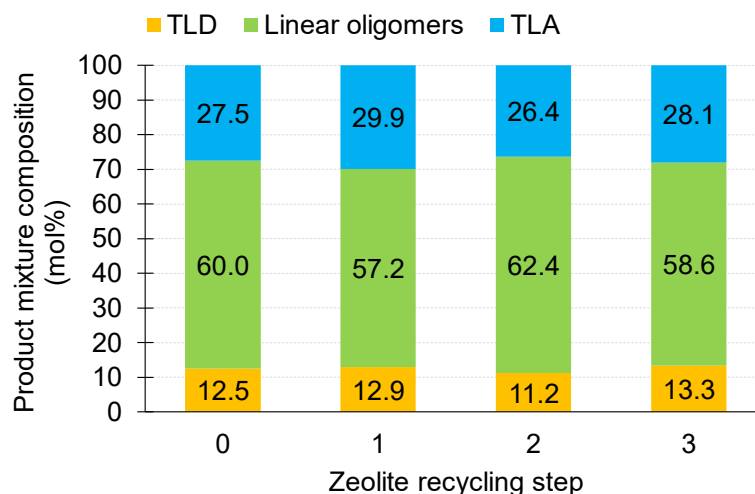


Figure S 21: Product distribution (mol%) after TLA cyclization in the presence of a H-BEA 12.5 zeolite that was 0, 1, 2 or 3 times recycled after calcination at 550°C (heating 1°C/min) for 3 h. Reaction conditions: 0.6 g *rac*-TLA, 6 ml *o*-xylene, 144°C, 1 h, 0.3 g H-BEA 12.5 in the first run. In consecutive runs, corrections in TLA feedstock and solvent were done based on recovered calcined weight.

XRD

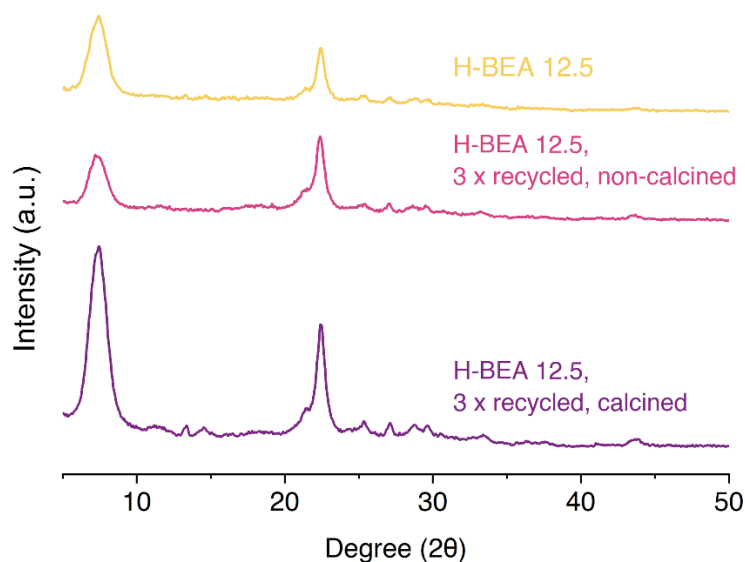


Figure S 22: Powder XRD spectra of H-BEA 12.5 after 3 recycling steps before and after calcination and compared to a neat, calcined H-BEA 12.5 zeolite.

N_2 physisorption

N_2 physisorption analysis was performed on a neat, calcined H-BEA 12.5 zeolite and compared to H-BEA 12.5 that was recycled and re-used three times for TLA cyclization reactions. The recycled zeolite was tested by N_2 physisorption both before and after calcination. The results are shown in Table S 8.

Table S 8: Comparison of BET surface area (m^2/g) and microporous volume (cm^3/g) of H-BEA 12.5 as determined by N_2 physisorption before and after TLA cyclization with a three times recycled zeolite before and after calcination at 550°C (heating $1^\circ\text{C}/\text{min}$) for 3 h. Reaction conditions: 0.5 g *rac*-TLA, 5 ml *o*-xylene, 144°C , 1 h, TLA:catalyst (wt) = 2:1.

Zeolite	BET (m^2/g)	Microporous volume (cm^3/g)
H-BEA 12.5	629	0.13
Recycling step 3 (not calcined)	391	0.06
Recycling step 3 calcined)	607	0.13

FT-IR
















Pyridine adsorption analysis followed by FT-IR spectroscopy was performed on a neat, calcined H-BEA 12.5 zeolite and compared to H-BEA 12.5 exposed to 3 reaction cycles with and without calcination.







Table S 9: Comparison of Brønsted acid sites (BAS) and Lewis acid sites (LAS) density ($\mu\text{mol}/\text{g}$) of H-BEA 12.5 before (neat) and after three reaction cycles with and without calcination as determined by FT-IR spectroscopy after pyridine adsorption. Reaction conditions: 0.5 g *rac*-TLA, 5 ml *o*-xylene, 144°C , 1 h, 0.25 g H-BEA 12.5.

Zeolite	BAS ($\mu\text{mol}/\text{g}$)	LAS ($\mu\text{mol}/\text{g}$)
H-BEA 12.5 (neat)	234	219
H-BEA 12.5, recycling step 3 (not calcined)	20	26
H-BEA 12.5, recycling step 3 calcined)	215	196

S2.3 Principles of green chemistry

Table S 10: Principles of green chemistry assessed against the method with p-TSA as homogeneous catalyst presented in this work and compared to the methods by Suzuki *et al.* and Wang *et al.*

Principle of green chemistry	Suzuki <i>et al.</i> ⁷	Wang <i>et al.</i> ⁸	This work
Waste prevention^a	 E-factor ₁ = 214.7 E-factor ₂ = 13.8	 E-factor ₁ = 20.9 E-factor ₂ = 3.1	 E-factor ₁ = 13.7 E-factor ₂ = 0.67
Atom economy (AE)	 AE = 7.8 Excess amounts of extra reagents are used (BOP PF ₆ , DMAP)	 AE = 24.3 Stoichiometric amounts of extra reagents are used (DCC)	 AE = 66.4 Except for TLA, no extra reagents are used.
Less hazardous chemical synthesis	 Use of toxic compounds (BOP PF ₆ , DMAP) Formation of toxic compounds (HMPA)	 Use of toxic compounds (DCC, DMAP)	 No toxic compounds added
Safer solvents & auxiliaries	 Use of hazardous solvent (DCM)	 Use of hazardous solvent (DCM)	 Use of hazardous solvents (toluene, o-xylene or mesitylene)
Design for energy efficiency	 24 h reaction at room temperature	 Cooling at 0°C for 10 min 3 h reaction at room temperature	 Heating at 185°C for 24 h

<p>Use of renewable feedstock</p>	<p style="text-align: center;"></p> <p>BOP PF₆ and DMAP are non-renewable compounds</p>	<p style="text-align: center;"></p> <p>DCC and DMAP are non-renewable compounds</p>	<p style="text-align: center;"></p> <p>TLA (only reagent) can be synthesized from alanine, a renewable amino acid</p>
<p>Catalysis (vs. stoichiometric)</p>	<p style="text-align: center;"></p> <p>Excess of reagents is used in absence of a catalyst</p>	<p style="text-align: center;"></p> <p>DMAP is used as a homogeneous catalyst</p>	<p style="text-align: center;"></p> <p>p-TSA is used as homogeneous catalyst</p>

Seven of the twelve principles of green chemistry are selected, the remaining 5 principles (designing safer chemicals, reducing derivatives, design for degradation, real-time analysis for pollution prevention and inherently safer chemistry for accident prevention) are not relevant for comparing these routes.

^a*E-factor₁ includes all waste, E-factor₂ does not take solvents into account*

S2.3.1 Atom economy (AE)

$$AE = \frac{\text{molecular mass of desired product}}{\text{molecular masses of reactants}} * 100\%$$

Suzuki et al.

MW	Reactants			Desired product
	TLA	BOP PF₆	DMAP	TLD
MW (g/mol)	106.14	442.29	122.17	176.25
Stoichiometric MW (g/mol)	212.28	884.58	244.34	176.25
Total MW (g/mol)	1341.2			176.25 (100% yield) 103.99 (59% yield)
AE (%)	13.1 (100% yield) 7.8 (59% yield)			

Wang et al.

	TLA	DCC	TLD
MW (g/mol)	106.14	206.33	176.25
Stoichiometric MW (g/mol)	212.28	412.66	176.25
Total MW (g/mol)	660.98		176.25 (100% yield) 160.39 (91% yield)
AE (%)	26.7 (100% yield) 24.3 (91% yield)		

This work

	TLA	TLD
MW (g/mol)	106.14	176.25
Stoichiometric MW (g/mol)	212.28	176.25
Total MW (g/mol)	212.28	176.25 (100% yield) 141.00 (80% yield, p-TSA) 66.98 (38% yield, IER) 49.35 (28% yield, H-BEA)
AE (%)	83.0 (100% yield) 66.4 (80% yield, p-TSA) 31.6 (38% yield, IER) 23.2 (28% yield, H-BEA)	

S2.3.2 Ecology factor (E-factor)

$$E\text{-factor} = \frac{\text{mass of total waste}}{\text{mass of product}}$$

Suzuki et al.^a

MW	Waste compounds					Desired product
	BOP PF₆	DMAP^e	HMPA	1-HBT^f	DCM	TLD
Mass (g)	5.00	4.15	4.05	3.05	332.5	1.18
Total mass (g)	348.76					1.18
Total mass (no solvents) (g)	16.26					1.18
E-factor	296.80					
E-factor (no solvent)	13.84					

Wang et al.^a

	DCU	DMAP	Acetic acid	DCM	TLD
Mass (g)	329.46	1.8	15.75	1995	112.12
Total mass (g)	2342.01				112.12
Total mass (no solvents) (g)	347.01				
E-factor	20.89				
E-factor (no solvent)	3.09				

This work (zeolite)^b

	TLA	Oligomers	H ₂ O	Zeolite	o-Xylene	TLD
Mass (g)	0.25	2.92	0.66	2.5	43.95	1.16
Total mass (g)	50.28					1.16
Total mass (no solvent) (g)	6.33					
E-factor	43.3					
E-factor (no solvent)	5.5					
E-factor (no zeolite, no H₂O)	40.5					
E-factor (no solvent, no zeolite, no H₂O)	2.7					

This work (IER)^c

	TLA	Oligomers	H ₂ O	IER	o-Xylene	TLD
Mass (g)	0.51	2.33	0.89	0.523	43.95	1.57
Total mass (g)	48.20					1.57
Total mass (no solvents) (g)	4.25					
E-factor	30.6					
E-factor (no solvent)	2.7					
E-factor (no IER, no H₂O)	29.7					
E-factor (no solvent, no IER, no H₂O)	1.8					

This work (p-TSA)^d

	TLA	Oligomers	H ₂ O	p-TSA	Mesitylene	TLD
Mass (g)	0.41	1.49	1.51	1.08	43.20	6.58
Total mass (g)	47.69					6.58
Total mass (no solvent) (g)	4.49					
E-factor	7.2					
E-factor (no solvent)	0.68					
E-factor (no p-TSA, no H₂O)	6.9					
E-factor (no solvent, no p-TSA, no H₂O)	0.29					

^a Assumed 100% conversion. Mass of TLD is based on isolated yield, reaction yields are not available.

^b Based on reaction with product composition as follows: 28.0 % TLD, 67.0 % oligomers with average chain length of 4 TLA units, 5.0 % TLA. Mass of TLD is based on reaction yield determined by ¹H-NMR (Figure 2 (C)).

^c Based on reaction with product composition as follows: 37.9 % TLD, 51.9 % oligomers with average chain length of 2.5 TLA units, 10.2 % TLA. Mass of TLD is based on reaction yield determined by ¹H-NMR (Figure 2 (B)). IER = Amberlyst 36

^d Based on reaction with product composition as follows: 79.3% TLD, 16.6 % oligomers with average chain length of 2.5 TLA units, 4.2 % TLA. Mass of TLD is based on reaction yield determined by ¹H-NMR (Figure 2 (E)).

^e Protonated form of DMAP and excess amount of non-protonated DMAP (DMAP acts as a proton-donating reagent, not as a catalyst)

^f 1-Hydroxybenzotriazole

S2.4 TLD purification

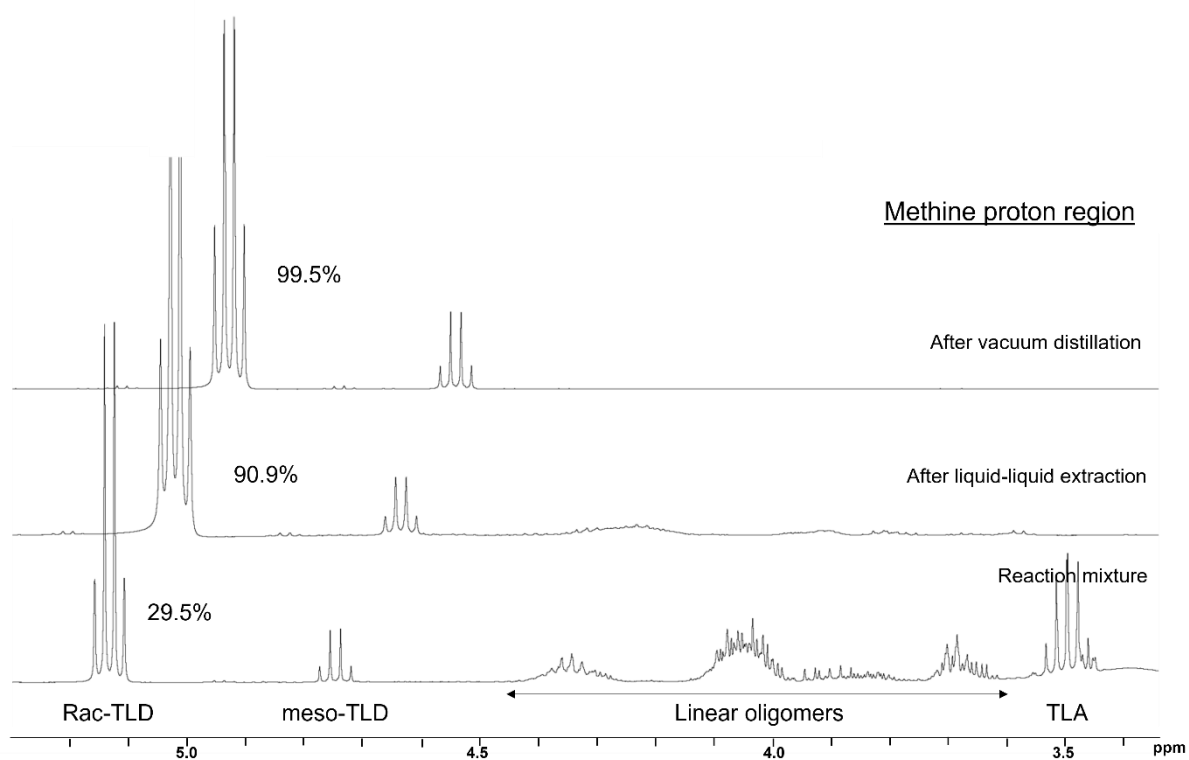


Figure S 23: ^1H -NMR spectra of the methine proton region after different purification steps on the reaction mixture after TLA cyclization to obtain 99.5% pure TLD. Reaction conditions: 0.5 g *rac*-TLA, 0.25 g H-BEA 12.5, 5 ml *o*-xylene, 144°C, 48 h.

^1H NMR of TLD

(400 MHz, *dms* o -*d* 6): δ 5.13 (q, 2H) (*rac*-TLD), 4.74 (q, 2H) (*meso*-TLD), 1.60 (d, 6H) (*meso*-TLD), 1.34 (d, 6H) (*rac*-TLD)

^{13}C NMR of TLD

(400 MHz, *dms* o -*d* 6): δ 199.4, 48.0, 13.0

S2.5 Ring-opening polymerization of TLD

S2.5.1 $^1\text{H-NMR}$ analysis

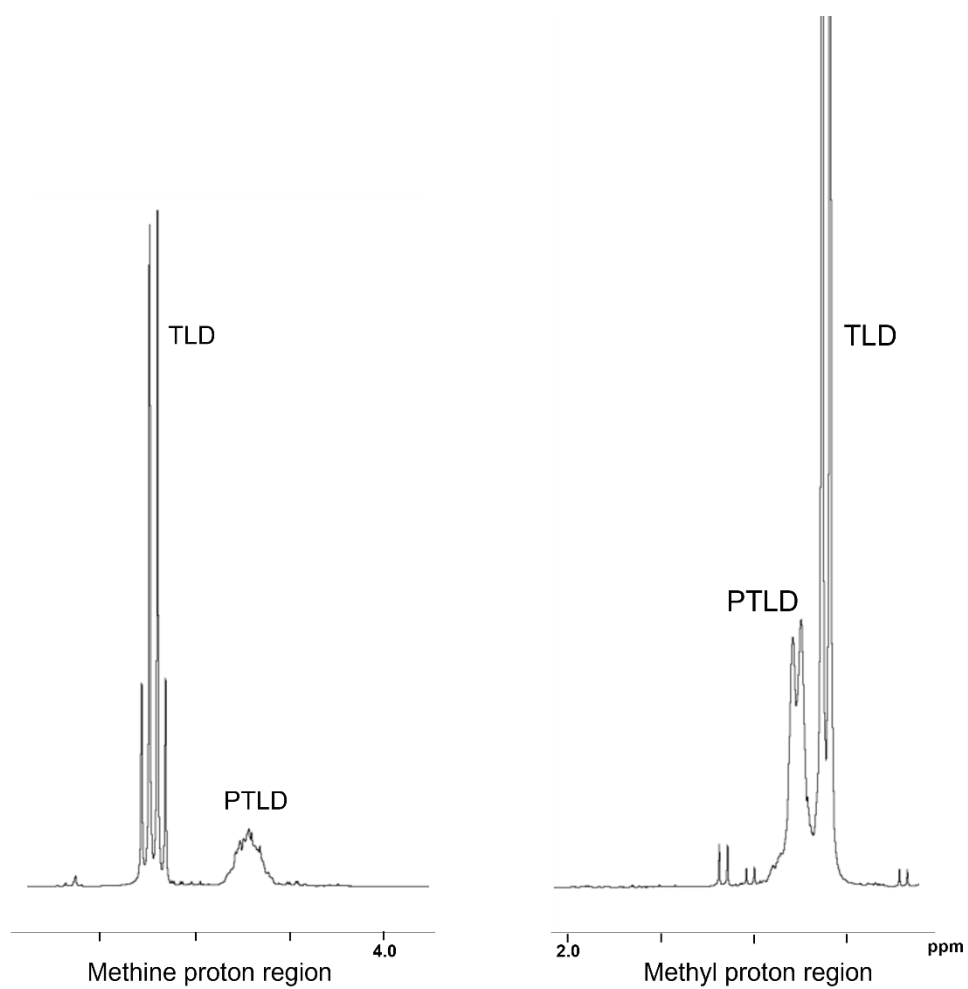


Figure S 24: Typical $^1\text{H-NMR}$ spectrum (400 MHz, CDCl_3) of a reaction mixture after ring-opening polymerization of TLD showing both methine and methyl proton regions of the remaining TLD and its polymer, polythiolactide (PTLD).

S2.5.2 Ring-opening polymerization kinetics

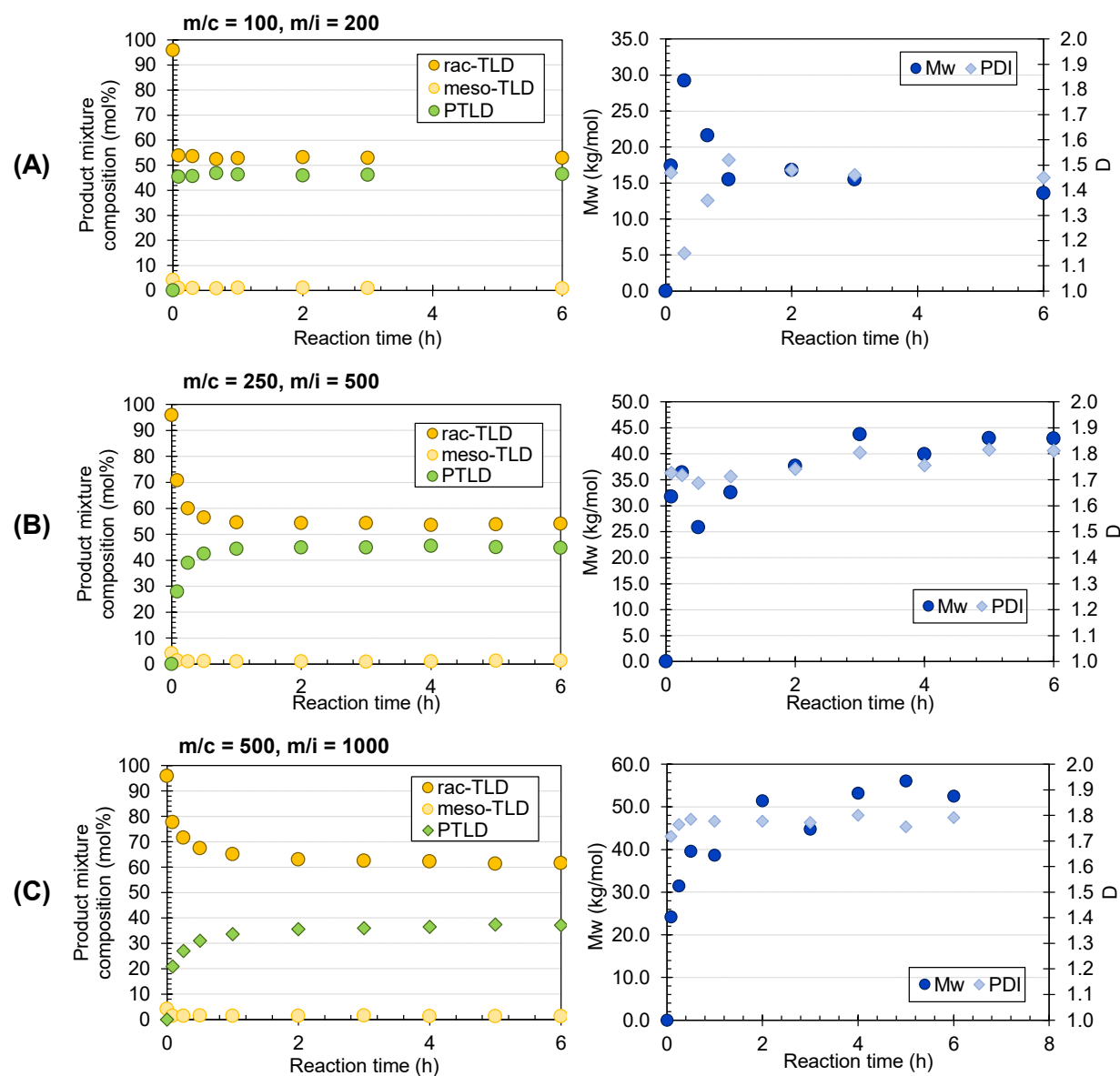


Figure S 25: Reaction mixture composition ($^1\text{H-NMR}$ (400 MHz, CDCl_3), mol%) over reaction time (h) of *rac*-TLD, *meso*-TLD and PTLD, and weight-average molecular weight (M_w , kg/mol) and polydispersity index (D) as measured by GPC obtained via ring-opening polymerization of TLD (monomer (m)). Reaction conditions: solution ROP (25 M TLD in DCM), room temperature (21-27°C), 5 min – 6 h, catalyst (c) = triethylamine, initiator (i) = benzyl alcohol. (A) $m/c = 100$, $m/i = 200$, (B) $m/c = 250$, $m/i = 500$, (C) $m/c = 500$, $m/i = 1000$.

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