

Cite this: *Chem. Sci.*, 2025, 16, 14509

All publication charges for this article have been paid for by the Royal Society of Chemistry

Selective chemical recycling of polyhydroxybutyrate into high-value hydroxy acid using the taurine organocatalyst†

Elena Gabirondo,^{ID a} Ainhoa Maiz-Iginitz,^{ab} Marta Ximenis,^a Katarzyna Świderek,^c Daniel Andrés-Sanz,^{ID b} Vicent Moliner,^{ID c} Luis Cabedo,^d Andrea H. Westlie,^e Eugene Y.-X. Chen,^{ID e} Daniel Alonso Cerrón-Infantes,^{fgh} Miriam M. Unterlass,^{fgh} Fernando López-Gallego,^{ID bi} Agustín Etxebarria^a and Haritz Sardon^{ID *a}

Polyhydroxyalkanoates (PHAs) are receiving significant attention due to their biobased origin, biodegradability, and excellent barrier properties. However, their high cost compared to traditional plastics necessitates the development of recycling technologies to retain their value post-use. Despite being thermoplastics, PHAs are difficult to recycle mechanically due to their narrow processing window, particularly for polyhydroxybutyrate (PHB), and conventional chemical recycling routes often lead to non-selective degradation and dehydration to crotonic acid, yielding complex product mixtures with limited valorization potential. In contrast, this study presents a selective chemical recycling method for PHB that suppresses dehydration pathways by using naturally occurring taurine as an organocatalyst. Taurine outperforms other catalyst families, such as Brønsted acids and bases, in terms of depolymerization yield and selectivity, achieving 98% enantiomerically pure 3-hydroxybutyric acid (HBA) in the optimized process. Density functional theory (DFT) calculations provided insights into the pH-dependent HBA elimination mechanisms demonstrating that taurine does not play a role in this process under very basic nor acidic conditions. A liquid–liquid extraction technique was developed to separate HBA from by-product crotonic acid, successfully maintaining the *R*-enantiomeric form of the recovered HBA. This method is applicable to both synthetic PHB and biological PHB samples, including copolymers and blends. Overall, this taurine-catalyzed PHB depolymerization approach inhibits the formation of dehydrated by-products and offers a promising solution for selective recycling of PHB into valuable chiral building blocks.

Received 21st March 2025
Accepted 4th July 2025

DOI: 10.1039/d5sc02196k

rsc.li/chemical-science

^aPOLYMAT and Department of Polymers and Advanced Materials: Physics, Chemistry and Technology, Faculty of Chemistry, University of the Basque Country UPV/EHU, Donostia-San Sebastián, 20018, Spain. E-mail: haritz.sardon@ehu.es

^bCenter for Cooperative Research in Biomaterials (CIC biomAGUNE), Basque Research and Technology Alliance (BRTA), Paseo de Miramon 182, San Sebastián, Spain

^cBioComp Group, Institute of Advanced Materials (INAM), Universitat Jaume I, 12071 Castellón, Spain

^dPolymers and Advanced Materials Group (PIMA), Universitat Jaume I (UJI), Avenida de Vicent Sos Baynat s/n, 12071 Castellón, Spain

^eDepartment of Chemistry, Colorado State University, Fort Collins, CO 80523-1872, USA

^fFraunhofer Institute for Silicate Research ISC, Neunerplatz 2, 97082 Wuerzburg, Germany

^gChair of Chemical Technologie of Materials Synthesis, Julius Maximilian University of Wuerzburg, Roentgenring 11, 97070 Wuerzburg, Germany

^hCeMM – The Research Center for Molecular Medicine, Austrian Academy of Sciences, Lazarettgasse 14, AKH BT 25.3, 1090 Vienna, Austria

ⁱIKERBASQUE, Basque Foundation for Science, María Díaz de Haro 3, 48013 Bilbao, Spain

† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d5sc02196k>

Introduction

Polyhydroxyalkanoates (PHAs) are a broad class of polyesters produced naturally, biologically, or chemically. They possess diverse properties and show great promise as partial substitutes for conventional non-degradable plastics.^{1,2} Among them, polyhydroxybutyrate (PHB) is the most prominent member and is notable for its excellent barrier properties, outperforming polyethylene terephthalate (PET) in resisting water, oxygen, and carbon dioxide permeation.^{3,4} Therefore, they are considered promising candidates for packaging applications. Moreover, like most aliphatic polyesters, PHB is biodegradable in soil and water, which is crucial if the polymer material accidentally ends up in environments.^{5–7}

PHAs have traditionally been biosynthesized intracellularly as granules *via* polymerization of 3-hydroxy fatty acid monomers by PHA synthase, yielding an enantiomerically pure polymer, with the (*R*)-isomer being the only one reported in nature.⁸ They serve as intracellular reserves of carbon and energy in PHA-producing microorganisms.^{9–11} PHAs can also be



synthesized chemically through copolymerization of epoxides and carbon monoxide or ring-opening polymerization (ROP) of cyclic lactones or diolides.^{12–15} However, it should be noted that these synthetic routes often rely on fossil-derived feedstocks and may involve energy-intensive steps, potentially reducing their overall sustainability. The main limitation of PHB is its high production cost compared to conventional petroleum-based polymers, underscoring the necessity of developing an efficient recycling process to retain material value and enhance sustainability.¹⁶

As PHB is a thermoplastic polyester, several different approaches have been investigated to recycle PHB and PHA-based plastics.¹⁷ In fact, although PHB is a thermoplastic material, mechanical recycling is typically hindered by its narrow processing window. Given that PHA is a polyester, another feasible approach is chemical recycling *via* solvolysis and hydrolysis.^{18,19} While several different chemical recycling mechanisms could be implemented into polyesters, such as methanolysis, hydrolysis, glycolysis, and alcoholysis, hydrolysis is preferred because β -hydroxy acids can potentially be obtained in a single step.^{20–22}

Chiral β -hydroxy acids are important chiral building blocks, used mainly in the pharmaceutical industry, as precursors for the synthesis of specific chemicals, such as antibiotics, vitamins, flavors, fragrances, and pheromones.^{23–25} Specifically, 3-hydroxybutyric acid (HBA) has been used to treat traumatic injuries, including skin burns, myocarditis, cerebral hypoxia, ischemia, and anoxia.^{26,27} Additionally, it has positive effects on the growth of osteoblasts *in vitro* and contributes to osteoporosis reduction *in vivo*.²⁸

The chemical transformation of PHB into HBA has been investigated by using different catalysts such as acids, bases, or enzymes. Prieto *et al.* developed an interesting approach to directly synthesize hydroxy acids by controlling the metabolic states in *Pseudomonas putida* bacteria. This biocatalyst synthesizes PHAs in the cell, however, by deleting the *phaZ* gene and generating differential *phaZ* expression, it can hydrolyze the polymer to obtain hydroxy acids.²⁹ Besides enzymatic catalysis, different acids and bases have been investigated for depolymerizing PHB into HBA.

When an acidic medium was used (concentrated sulfuric acid, for 5 h at 70 °C), PHB was completely depolymerized, yielding 98% crotonic acid (CA) and 2% HBA (Fig. 1a).³⁰ In acidic media, the elimination of HBA into CA occurs *via* a unimolecular elimination (E1) mechanism, which takes place in a two-step process. In this reaction the alcohol gets protonated, leading to the release of a water molecule and the formation of a double bond. Yu *et al.* studied the hydrolytic depolymerization of PHB in basic media at 70 °C, adjusting the alkaline concentration to evaluate its effect.³⁰ It was observed that at low alkaline concentrations, the depolymerization rate of PHB was low; a solution of 4 M NaOH was required to achieve approximately 75% depolymerization after 4 h. The characterization of the hydrolysis products confirmed the presence of approximately 47% HBA and 27% CA (Fig. 1b).

In basic media, the elimination of HBA follows the E1cB (elimination unimolecular conjugate base) mechanism, where

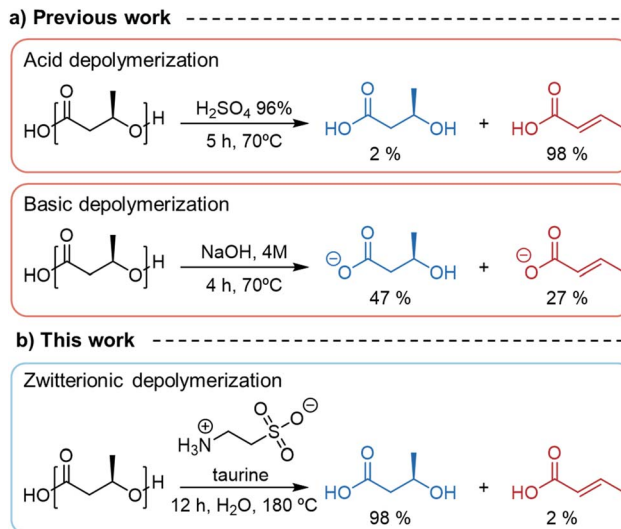


Fig. 1 Outlined three approaches to depolymerize PHB, with the zwitterionic depolymerization described in this work giving the highest (near quantitative) selectivity for the production of HBA.

a carbanion intermediate is formed, eventually leading to the production of CA. While moderate yields have been achieved in some cases, separating HBA and CA is challenging, as HBA readily undergoes elimination at high temperatures. To our knowledge, an efficient separation route has not been reported in the open literature.

The aim of this work is to investigate different depolymerization conditions to maximize the HBA content from PHB depolymerization (Fig. 1c). Different catalysts, temperatures, pH levels, and water/PHB ratios have been evaluated, and we found that the HBA content is highly dependent on both the catalyst and temperature. Indeed, we demonstrate that taurine is a highly efficient catalyst for the depolymerization while also providing high yields of HBA. Moreover, an extraction method to eliminate the undesired CA has been developed. Finally, the suitability of the depolymerization method has been expanded to include some commercial samples and chemically synthesized PHAs, resulting in excellent depolymerization yields.

Results and discussion

Chemical depolymerization of PHB

The hydrolytic depolymerization reaction of PHB was carried out at 180 °C using different catalysts at 10 mol% loadings relative to the monomer repeating unit, and with 15 water equivalents at pH of 5.5 for 12 hours (Fig. 2a). We investigated several catalysts, including organic and inorganic acids, *p*-toluenesulfonic acid (pTSA), methanesulfonic acid (MSA), benzoic acid (BA), hydrochloric acid (HCl), sulfuric acid (H₂SO₄) and acetic acid (AcOH). Additionally, an inorganic base, sodium hydroxide (NaOH), and some naturally occurring catalysts, creatine and taurine that contain both acid and base moieties in their structure were tested (Fig. 2b).

The depolymerization process was followed by the visual disappearance of PHB powder. As observed in the results, the



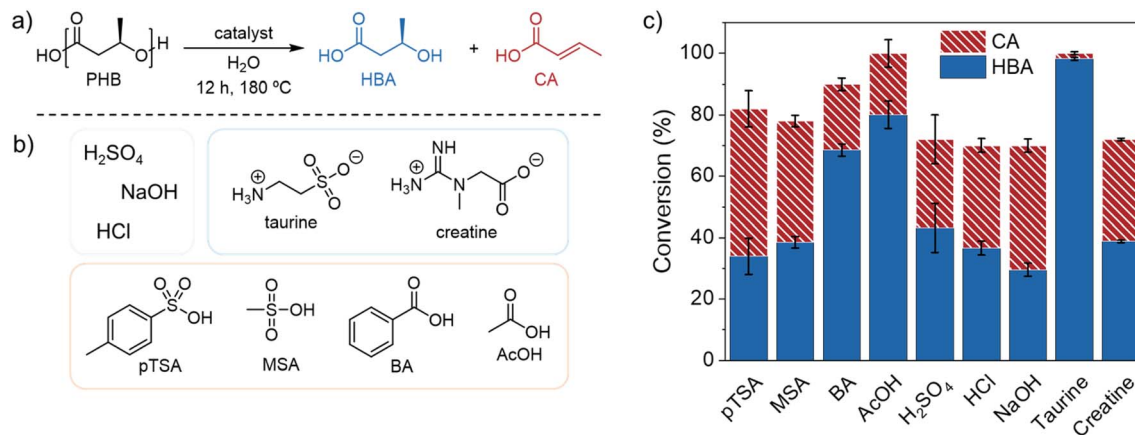


Fig. 2 (a) PHB hydrolytic depolymerization to give HBA and CA. (b) Catalysts employed in the screening process. (c) Conversion of PHB and relative selectivity for HBA and CA formation.

depolymerization reactions were highly dependent on the catalyst (Fig. 2c). If we evaluate the depolymerization rate, AcOH and taurine were able to depolymerize PHB completely in 12 hours, while the other catalysts achieved PHB conversions between 70 and 90% within this timeframe (Table S1†).

Besides the depolymerization degree, we also evaluated the selectivity of the process. As previously mentioned, two main products can be obtained from the depolymerization of PHB: the kinetically favored HBA or the thermodynamically more stable CA. The depolymerization products were monitored by tracking the disappearance of PHB in the reaction medium, and the final products were characterized by ¹H NMR in D₂O (Fig. S1†).

The presence of HBA was determined by the signals at 4.1, 2.4, and 1.1 ppm and CA by the signals at 6.9, 5.8, and 1.8 ppm. We found that highly acidic and highly basic catalysts, such as NaOH, pTSA, and MSA, produced more CA than HBA. As enolate formation predominantly occurs under strongly acidic and basic conditions, the presence of these catalysts substantially favored the elimination reaction. In the case of HCl and creatine, a slightly more HBA content was observed.

Carboxylic acids such as BA and AcOH showed significantly higher selectivity compared to other catalysts. Indeed, in the case of BA, up to 90% HBA was achieved. Surprisingly, taurine, a naturally occurring amino acid containing sulfonic acid, showed an outstanding HBA selectivity (98%), along with excellent performance in terms of depolymerization rate.

As taurine is shown to be the best catalyst for the depolymerization of PHB in aqueous media, we studied its structure–property relationship in aqueous media because it contains both an acid and a base site. To do so, the structure of the catalyst was analyzed by ¹H NMR at different pH levels, using a basic medium (in the presence of NaOH), a neutral medium, and an acidic medium (in the presence of HCl) (Fig. S2†).

In basic media (Fig. S2,† red), the main product is the deprotonated taurine, where both amine and sulfonic acid groups exist in their deprotonated forms. In neutral media, the equilibrium is shifted to the structure of the salt, where the amine is protonated and the sulfonic acid is deprotonated (Fig.

S2,† black). Lastly, in acidic media (Fig. S2,† blue), taurine is mainly protonated. In this last case, a stable peak was observed at around 7.7 ppm, which corresponds to the protonated amine.

The relative acidity of the medium also affects the equilibrium: the more acidic the medium, the more protonated the taurine is (Fig. 3a). It was determined that when more equivalents of HCl were added relative to taurine, the signal at 7.7 ppm became more stable, confirming that the equilibrium of taurine was more shifted toward the protonated amine.

After understanding the influence of pH on the taurine structure, we investigated the impact of pH on the depolymerization process in the presence of taurine.

Three pH buffer solutions at pH = 3, 7, and 10 were prepared and compared to the previous sample at pH 5.5 (Fig. S3†). In all cases, the depolymerization rate was similar, achieving 100% conversion. However, pH had a significant impact on the HBA/CA ratio (Fig. 3b and S3†). Among all analyzed pH values, the best result was obtained at pH = 5.5, as it yielded 98% HBA, meaning that almost no elimination reaction occurred. In acidic media, the elimination of the hydroxy group led to CA *via* the E1 mechanism, where the alcohol protonates, leading to water being released (Fig. 3c). In basic media, the formation of CA also occurred, but in this case, the reaction proceeded *via* the E1cB mechanism, where an intermediate carbanion was formed (Fig. 3c).

Computational studies

Computational studies were conducted at the Density Functional Theory (DFT) level, to shed some light on the pH dependence of the elimination reaction of HBA and the role of taurine. As experimental findings suggest, both the mechanisms and the formation of products should be closely linked to the protonation state of the hydroxy acid and taurine. Therefore, multiple reaction pathways were investigated computationally to better understand the elimination mechanism under various pH conditions. In addition, the mechanism for the depolymerization of PHB catalyzed by taurine was also explored.



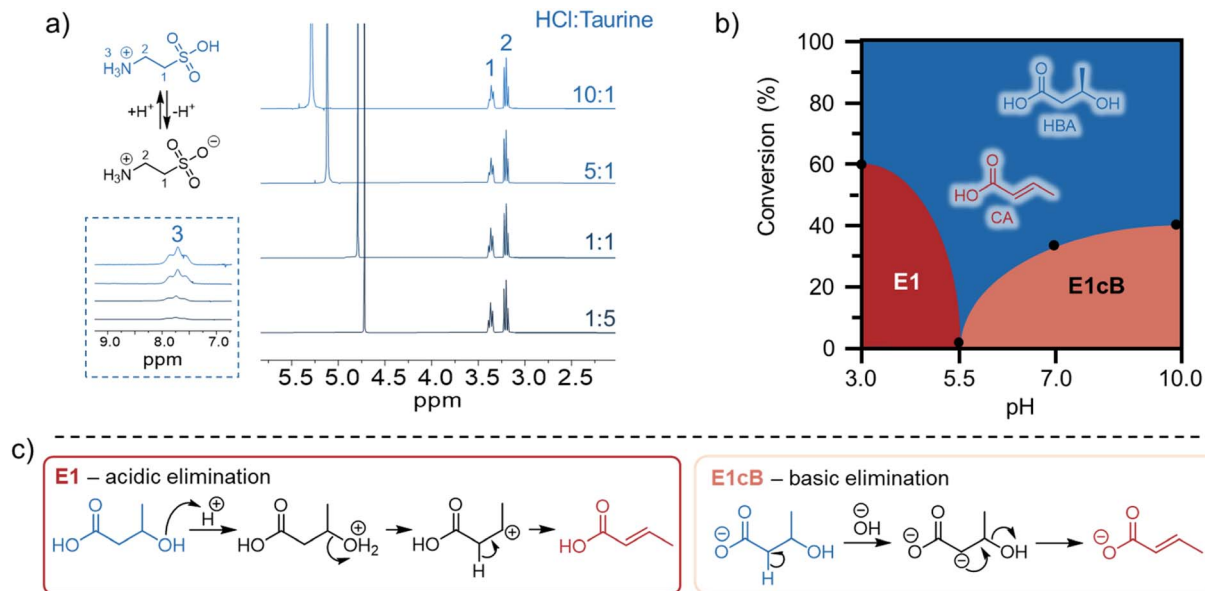


Fig. 3 (a) ¹H NMR study of the taurine structure with different equivalents of HCl. (b) The influence of pH on the HBA/CA ratio (black dots represent experimental points). (c) The proposed mechanism of elimination in acidic or basic media.

Regarding the role of taurine in the elimination reaction of HBA, initial relevant models of the reactive complexes were prepared and optimized at the DFT level, employing the global hybrid functional using M06-2X,³¹ with 54% HF exchange. Then, according to the experimentally determined pK_a values of the functional groups of HBA (4.41 for the carboxyl group and 13.1 for the hydroxyl group)³² and taurine (8.4 for the amino group and 1.0 for the sulfonic acid group),³³ different protonation states of both species were set up (see Table S2[†]).

First, the possible reaction pathways were explored in the absence of taurine, confirming the feasibility of stepwise mechanisms under both acidic and basic conditions, as shown in Fig. 4a and b. The energy barriers support CA formation within the selected experimental conditions, although through different reaction mechanisms (Fig. 4b and c), as anticipated above (Fig. 3).

Thus, according to computational findings, under acidic conditions, the abstraction of HBA's hydrogen by a water molecule is accompanied by the transfer of a proton from the hydronium ion to the oxygen of HBA's carboxyl group. This transformation is followed by proton transfer to the hydroxyl group, leading to the departure of a water molecule and CA formation. This second step becomes the rate-determining step (rds) with an energy barrier of 22.8 kcal mol⁻¹ (Fig. 4c). Interestingly, despite the energy barriers can be just slightly modified after adding thermal corrections at 180 °C, which is the temperature used in the experiments, the shape of the energy profiles is not qualitatively modified. In contrast, rate constants are highly sensitive to temperature—a behavior quantitatively captured by the exponential dependence on temperature in the Eyring equation. For example, the energy barrier of 22.8 kcal mol⁻¹ leads to rate constant values of 1.18 × 10⁻⁴ s⁻¹ at 25 °C and 3.75 × 10² s⁻¹ at 180 °C, as estimated using transition state

theory. When the model simulates basic conditions, the reaction proceeds *via* the E1cB mechanism discussed earlier: HBA's hydrogen is initially abstracted by hydroxide, and a carbanion intermediate is formed. In the second step, the intermediate is converted into CA through the departure of the hydroxide group. The reaction pathway under basic conditions presents a slightly higher energetic barrier (27.3 kcal mol⁻¹), which may explain the lower conversion to CA observed in this experiment (Fig. 3b) as well as previously by Yu *et al.*³⁰

As expected, under neutral pH conditions, the elimination process would occur much slower, with an rds energy barrier of 42.3 kcal mol⁻¹ (see ESI[†] for details).

Next, several scenarios were considered with taurine actively involved in the elimination process (Table S2[†]). Similar to HBA, different protonation states were assigned based on taurine's experimentally determined pK_a values. Specifically, the sulfonic group was assumed to be protonated below pH 1, while the amine group was considered protonated below pH 8.8.³³ To construct the molecular models, these protonation states of taurine were combined with the appropriate protonation states of CA at different pH levels. Consequently, the potential reaction mechanisms for taurine-catalyzed elimination were explored under four possible pH ranges: basic (pH > 8.4), moderate (4.41 < pH < 8.4), acidic (1 < pH < 4.41), and highly acidic conditions (pH < 1): ①, ②, ③ and ④, respectively, as shown in Fig. 4d.

As schematically summarized in Fig. 4d, among the various possibilities (concerted or stepwise, as detailed in the ESI[†]), the most favorable mechanism under highly acidic conditions resulted in an activation-free energy significantly higher than that of the previously studied reaction in the absence of taurine (32.8 vs. 22.8 kcal mol⁻¹, respectively). This finding indicates that the protonated form of taurine does not participate in the



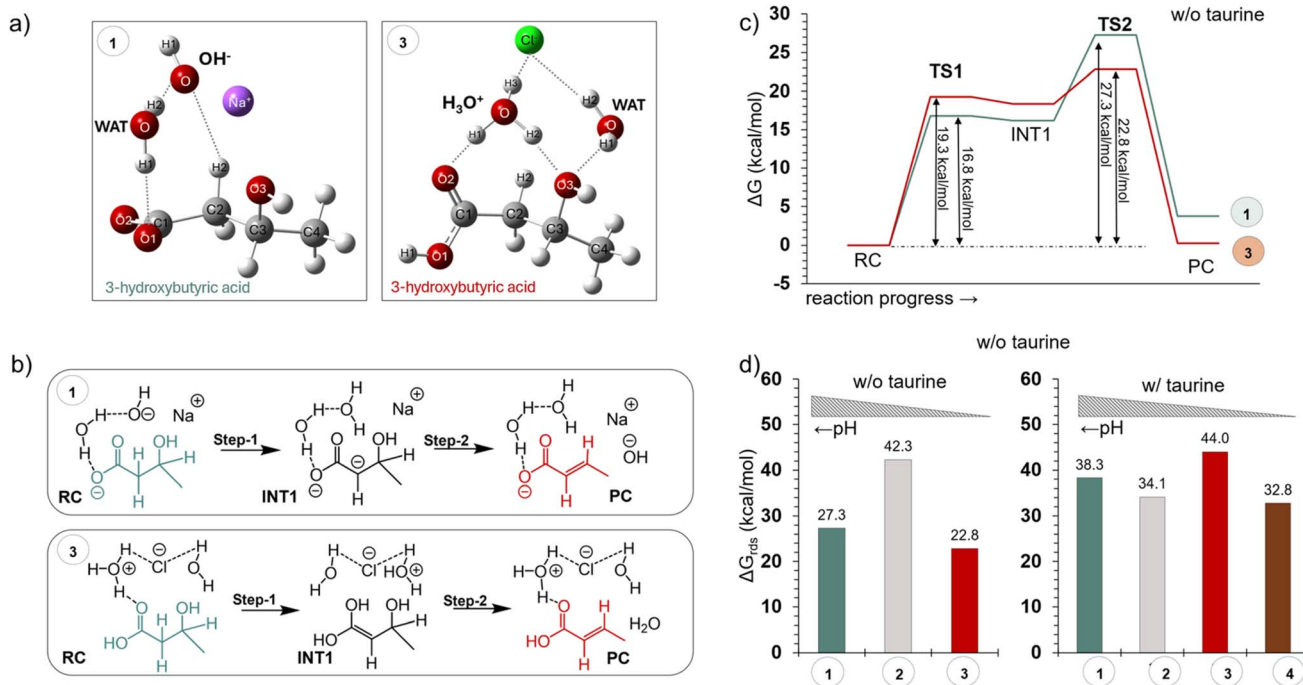


Fig. 4 (a) Structures of initial models used to explore the most energetically favorable mechanisms. (b) Reaction mechanism revealed computationally for the elimination process taking place in the absence of taurine under basic ① and very acidic ③ conditions. (c) Energy profile for the elimination reaction of HBA under basic ① and acidic ③ conditions. All reported energy values for products, intermediates, and transition state structures are referenced to the reactant complex. (d) Energy barriers of the rds computed for all explored elimination mechanisms without (w/o) and with (w/) the participation of taurine under basic ①, neutral ②, acidic ③, and highly acidic ④ conditions: basic (pH > 8.4), moderate (pH 4.1 < pH < 8.4), acidic (pH 1 < pH < 4.41), and highly acidic conditions (pH < 1), respectively. Energies in panels c and d represent potential energy plus zero-point vibrational energy and thermal corrections at 180 °C.

HBA elimination under very highly acidic conditions, since the presence of H₃O⁺ molecules can act as a better catalyst than the fully protonated taurine. Similarly, exploration of the process under very basic conditions, with deprotonated sulfonic and ammonia groups of taurine, provided a reaction mechanism with an activation-free energy barrier higher than the corresponding process in solution when the concentration of OH⁻ species can act as a basic catalyst (38.3 vs. 27.3 kcal mol⁻¹, respectively). The results suggest a residual participation of taurine in the elimination mechanism of HBA under very basic or very acidic conditions, when the reaction appears to be catalyzed by H₃O⁺ or OH⁻ from the medium.

Under moderately acidic conditions, where taurine is present in its zwitterionic form, computational studies for the elimination reaction of protonated and unprotonated HBA variants resulted in a slow process with rds barriers of 44.0 and 34.1 kcal mol⁻¹, respectively (see ESI† for details). Interestingly, the latter value is lower than the one obtained for the reaction in the absence of taurine (42.3 kcal mol⁻¹). Overall, after exploring all possible mechanistic scenarios, both with and without taurine's active participation in the elimination process, it was found that taurine does not play a role under very basic or acidic conditions. However, the activation energy barriers in the pH range between 4.41 and 8.4, where taurine exists in its zwitterionic form and the hydroxy acid molecule is deprotonated, are slower than those in the absence of taurine (34.1 vs. 42.3 kcal mol⁻¹, respectively). However, considering these high values, it

cannot be assured that taurine can promote elimination at this pH range.

With respect to the involvement of taurine in PHB depolymerization, a detailed reaction profile was computed under neutral conditions, assuming the zwitterionic form of taurine—its predominant form at physiological pH, where it is expected to act as a catalyst (Tables S14, S15 and Fig. S17†). According to the results, the PHB depolymerization catalyzed by taurine proceeds *via* a two-step mechanism, with active participation of a water molecule. In the first step, a solvent water molecule attacks the carbonyl carbon of the ester bond, accompanied by two proton transfers: one from the water molecule to the sulfonic oxygen of taurine, and another from the amino group of taurine to the carbonyl oxygen of PHB. In the second step, the C–O ester bond is cleaved, facilitated by a double proton transfer: from the protonated sulfonic group of taurine to the scissile oxygen atom of PHB, and from the protonated carbonyl group of PHB to the amino group of taurine, thereby restoring the initial protonation state of the catalyst. The rate-determining step (TS1) of the computed free energy profile shows a moderate activation barrier (~18.7 kcal mol⁻¹), while the second step features a negligible barrier from the intermediate (Fig. S17†).

Overall, the computational results confirms that taurine plays an active catalytic role in the depolymerization of PHB but it is not responsible for the elimination reaction of HBA.



Optimization of depolymerization conditions

As taurine was confirmed to be the best catalyst for this process among the ones investigated, we evaluated the depolymerization process in more detail. Since the hydrolysis of PHB yields HBA and CA, we aimed at determining whether both products formed simultaneously at the initial stage of depolymerization or whether CA formation could be avoided. For this purpose, depolymerization kinetics were followed by ^1H NMR analyzing the formation of HBA and CA as a function of time, using 10 mol% of taurine, 15 equivalents of water, 180 °C and pH of 5.5 (Fig. S4†). Up to six hours into the depolymerization reaction, HBA was the only product detected; however, beyond this point, HBA began converting into CA. Indeed, the production of CA seems to increase gradually, more probably due to an increase in the acidity of the medium.

Once the depolymerization of PHB was successfully achieved, additional reaction conditions were examined to maximize HBA formation while reducing depolymerization time and temperature, thereby preventing the formation of thermodynamically favored CA. Initially, the reaction was performed at 160 °C, while maintaining the other conditions (Fig. S5a†). No depolymerization was observed by ^1H NMR, likely due to the T_m value of PHB (168.5 °C), and its high crystallinity (melting enthalpy (ΔH_m) = 86 J g $^{-1}$). Under these conditions, the catalyst was unable to interact effectively with PHB to initiate the depolymerization (Fig. S5b†).

When increasing the temperature from 180 to 200 °C, the depolymerization rate was enhanced but at the same time, the amount of CA increased considerably (Fig. S5a†). Moreover, insoluble species were observed in the reaction medium, suggesting other side reactions. It is noteworthy that thermogravimetric analysis of PHB indicates degradation in a single-step weight-loss process under a nitrogen atmosphere at approximately 200 °C so it could be that the polymer is suffering some chemical decomposition together with hydrolytic depolymerization (Fig. S5c†).

Different catalyst loadings were also investigated using 5, 7.5, 10, 15, and 20 mol% of taurine relative to the repeating unit of PHB (Fig. S6†). Results indicate that catalyst concentration significantly impacts the HBA content. Optimal HBA yield was achieved with 10 mol% taurine. Higher catalyst concentrations decreased the PHB depolymerization and also increased the CA formation.

Besides investigating the impact of the catalyst content and temperature, we also investigated the effect of concentration on the depolymerization process. To determine the optimal quantity of water for depolymerization reactions, several different conditions were investigated, employing 5, 10, 15, 20, and 30 equivalents relative to PHB's repeating unit (Fig. S7†). While a minimum amount of water was necessary for complete depolymerization, excessive water content significantly reduced the HBA yield, from 98% to 40%, when increasing the water content from 15 to 30 equivalents.

After identifying the best conditions for maximizing the yield of HBA, we addressed its purification. Separating HBA from CA is not a facile process as they have similar physical properties.

Initially, when ethanol was added to the mixture, taurine precipitated and could be removed completely from the reaction media.

Once the catalyst was removed, different approaches were tried for the separation of HBA and CA. Neither crystallization nor distillation provided efficient purification, as harsh conditions favored HBA elimination, leading to CA formation (Fig. S8†). After several attempts, we found that liquid-liquid extraction with diethyl ether successfully separated HBA from CA. HBA remained in the aqueous phase, while CA migrated to the organic phase (diethyl ether). The aqueous phase was then subjected to rotary evaporation to remove all water and obtain pure HBA.

The ^1H NMR analysis (Fig. S9†) and MALDI-TOF spectroscopy of the pure HBA revealed a small amount of the dimer (4%), suggesting that some monomer converted into the dimer during the evaporation process (Fig. S10†). MALDI-TOF spectroscopy confirmed the presence of HBA with an exact mass of 104.05 g mol $^{-1}$, along with another species corresponding to the dimer, 190.08 g mol $^{-1}$.

More significantly, the enantiopurity of the obtained HBA from the depolymerization of (*R*)-PHB was measured by GC-FID chromatographic analysis, comparing the purified sample with *R* and *S* standards (Fig. S11†). The hydrolytic depolymerization process preserved the *R* nature of the repeating unit, obtaining 100% (*R*)-HBA. This result validates the depolymerization process as an effective method for obtaining chiral HBA.

Extending the scope of the depolymerization process

Although PHB is naturally produced by bacteria, PHB with high crystallinity and molecular weight can also be obtained synthetically.¹⁴ To explore the full potential of this process, we investigated the depolymerization of PHB synthesized *via* ROP of an eight-membered cyclic diolide.^{14,15} One of the advantages of this process in comparison to the PHB prepared from bacteria is its ability to prepare polymers with narrow dispersities and excellent stereochemical control. After 12 h of depolymerization reaction of the synthetic PHB, 90% of the polymer was depolymerized and the ^1H NMR spectrum indicated the formation of 99% HBA, with the rest 1% being CA (Fig. S12†).

Homopolymer PHB exhibits high crystallinity, which results in poor mechanical properties (being extremely brittle). To address this limitation, PHB is often copolymerized with other monomers to reduce crystallinity and improve ductility. One of the most common PHA copolymers is PHBV (polyhydroxybutyrate-*co*-hydroxyvalerate), which contains low percentages of hydroxyvalerate. The addition of hydroxyvalerate significantly enhances the mechanical properties of PHBV, making it more suitable for various applications.

The optimized reaction conditions were applied in all cases, including 10 mol% taurine, pH 5.5, 15 equivalents of water, 180 °C, and 12 h of reaction time. For the PHBV sample (Fig. 5a), ^1H NMR results determined that the depolymerization process was successful, yielding HBA (88%) and CA (10%), with minor



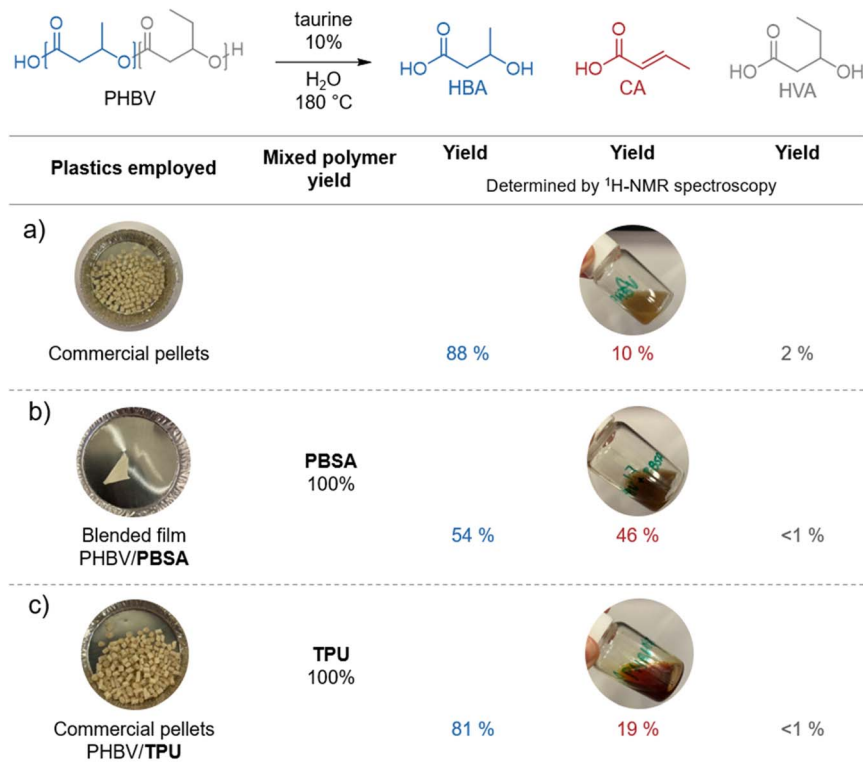


Fig. 5 Depolymerization process of commercial PHB-based samples (a) PHBV, (b) PHBV + PBSA and (c) PHBV + TPU.

amounts of hydroxyvaleric acid (HVA), which constituted only 2% of the polymer (Fig. S13[†]).

Another approach to tune the properties and make suitable materials out of PHB is to blend it with other polymers. PHBV is often blended with other commodity polymers, such as poly(*n*-butylene succinate-*co*-adipate) (PBSA) and thermoplastic polyurethanes (TPU) to enhance their performance. To assess the versatility of taurine as a catalyst for depolymerizing different PHB-based commercial samples, PHBV, PHBV + PBSA and PHBV + TPU have been tested (Fig. 5). When the polymer mixture PHBV + PBSA was subjected to the depolymerization process (Fig. 5b), only PHBV underwent depolymerization into HBA and CA, while PBSA remained unchanged. This selective depolymerization of PHBV was confirmed by ¹H NMR results, which showed that PHBV was completely depolymerized, whereas PBSA remained unaltered before and after the process (Fig. S14[†]). Similarly, in the case of the polymer mixture PHBV + TPU (Fig. 5c), selective depolymerization was observed, yielding HBA, CA and intact TPU (Fig. S15[†]). These results demonstrate the suitability and selectivity of taurine as a catalyst for depolymerizing PHB-based commercial copolymers or blends.

Conclusion

This study presents a promising method for the production of high-value HBA from chemical recycling of biological or synthetic PHB *via* hydrolytic depolymerization. Screening of different types of catalysts was performed to determine their efficiency and selectivity in the depolymerization reaction and

optimize the HBA-to-CA ratio. The results concluded that taurine is the most effective catalyst, fully depolymerizing PHB to HBA in 98% selectivity.

Both pH and temperature were found to be critical factors in the depolymerization reaction. pH 5.5 was identified as the ideal condition, as it minimized elimination reactions and thus suppressed the side-product (CA) formation; lower or higher pH values promoted E1 or E1cB eliminations, respectively. Additionally, the depolymerization reaction needs to be performed above the T_m (180 °C) of PHB, as no reaction was observed below this temperature. Computational studies further supported that taurine, in its natural zwitterionic form, does not promote elimination but effectively catalyzes the depolymerization process.

Finally, this selective depolymerization method was successfully extended to PHB-based commercial copolymers and blends, achieving promising results in all cases. To the best of our knowledge, this perhaps is the first study to achieve selective depolymerization of PHB into HBA in near quantitative (98%) selectivity, accompanied by only a very small amount of CA formation. Overall, the simplicity of this one-step process makes it a feasible method for producing HBA in large quantities.

Data availability

The data that support the findings of this study are available from the corresponding author H. S. upon reasonable request.



Author contributions

E. G. and H. S. conceived and initiated the study. E. G. and A. M. conducted the depolymerization experiments and characterization. D. C. and M. U. supervised the optimization experiments. K. S. and V. M. performed the theoretical calculations. D. A. and F. L. conducted the GC-FID chromatogram analysis. A. E. carried out the NMR characterization. L. C., A. W. and E. C. synthesized and provided the synthetic material and blends. E. G., A. M. and H. S. motivated and supervised the research. E. G., A. M., M. X. and H. S. drafted the initial manuscript. All authors discussed the results and worked on the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgements

The authors acknowledge the Spanish Ministry of Science and Innovation: PID2022-138199NB-I00 funded by MCIU/AEI/10.13039/501100011033, as well as the funding of the State Research Agency (AEI) with numbers TED2021-129852B-C21 and TED2021-129852B-C22 and the Basque Government with number GC IT-1667-22. EG thanks the Basque Government for the Postdoctoral fellowship (POS_2022_1_0040). VM gratefully acknowledges financial support from grant PGC2018-094852-B-C21 funded by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe", and from grant PROMETEO CIPROM/2021/079 of Generalitat Valenciana. KŚ thanks the Spanish Ministerio de Ciencia, Innovación y Universidades for the Ramon y Cajal fellowship (RYC2020-030596-I) and Grant to Encourage Research Consolidation (CNS2024-154238). The authors acknowledge ERC-Co (METACELL-818089), IKERBASQUE for sponsoring him. DAS thanks the Basque Government's Predoctoral Programme (PRE_2022_2_0138). The work done at Colorado State University was supported by the U.S. National Science Foundation (NSF-1955482). The authors acknowledge the assistance of ChatGPT (GPT-4) in refining the English language and improving the clarity of this manuscript.

References

- Z. Li, J. Yang and X. J. Loh, Polyhydroxyalkanoates: Opening Doors for a Sustainable Future, *NPG Asia Mater.*, 2016, **8**(4), e265, DOI: [10.1038/am.2016.48](#).
- V. Sharma, R. Sehgal and R. Gupta, Polyhydroxyalkanoate (PHA): Properties and Modifications, *Polymer*, 2021, **212**, 123161, DOI: [10.1016/J.POLYMER.2020.123161](#).
- D. Z. Bucci, L. B. B. Tavares and I. Sell, PHB Packaging for the Storage of Food Products, *Polym. Test.*, 2005, **24**(5), 564–571, DOI: [10.1016/J.POLYMERTESTING.2005.02.008](#).
- A. Sangroniz, J. B. Zhu, X. Tang, A. Etxeberria, E. Y. X. Chen and H. Sardon, Packaging Materials with Desired Mechanical and Barrier Properties and Full Chemical Recyclability, *Nat. Commun.*, 2019, **10**(1), 1–7, DOI: [10.1038/s41467-019-11525-x](#).
- B. Hazer and A. Steinbüchel, Increased Diversification of Polyhydroxyalkanoates by Modification Reactions for Industrial and Medical Applications, *Appl. Microbiol. Biotechnol.*, 2007, **74**(1), 1–12, DOI: [10.1007/S00253-006-0732-8](#).
- J. Kim, N. S. Gupta, L. B. Bezek, J. Linn, K. K. Bejagam, S. Banerjee, J. H. Dumont, S. Y. Nam, H. W. Kang, C. H. Park, G. Pilania, C. N. Iverson, B. L. Marrone and K. S. Lee, Biodegradation Studies of Polyhydroxybutyrate and Polyhydroxybutyrate-co-Polyhydroxyvalerate Films in Soil, *Int. J. Mol. Sci.*, 2023, **24**(8), 7638, DOI: [10.3390/IJMS24087638](#).
- N. Altaee, G. A. El-Hiti, A. Fahdil, K. Sudesh and E. Yousif, Biodegradation of Different Formulations of Polyhydroxybutyrate Films in Soil, *SpringerPlus*, 2016, **5**(1), 762, DOI: [10.1186/s40064-016-2480-2](#).
- B. H. A. Rehm, Polyester Synthases: Natural Catalysts for Plastics, *Biochem. J.*, 2003, **376**(1), 15–33, DOI: [10.1042/BJ20031254](#).
- B. Laycock, P. Halley, S. Pratt, A. Werker and P. Lant, The Chemomechanical Properties of Microbial Polyhydroxyalkanoates, *Prog. Polym. Sci.*, 2013, **38**(3–4), 536–583, DOI: [10.1016/J.PROGPOLYMSCI.2012.06.003](#).
- A. Anjum, M. Zuber, K. M. Zia, A. Noreen, M. N. Anjum and S. Tabasum, Microbial Production of Polyhydroxyalkanoates (PHAs) and Its Copolymers: A Review of Recent Advancements, *Int. J. Biol. Macromol.*, 2016, **89**, 161–174, DOI: [10.1016/J.IJBIOMAC.2016.04.069](#).
- A. V. Samrot, R. B. Avinesh, S. D. Sukeetha and P. Senthilkumar, Accumulation of Poly[(R)-3-Hydroxyalkanoates] in Enterobacter Cloacae SU-1 during Growth with Two Different Carbon Sources in Batch Culture, *Appl. Biochem. Biotechnol.*, 2011, **163**(1), 195–203, DOI: [10.1007/S12010-010-9028-7](#).
- H. Li, R. M. Shakaroun, S. M. Guillaume and J. F. Carpentier, Recent Advances in Metal-Mediated Stereoselective Ring-Opening Polymerization of Functional Cyclic Esters towards Well-Defined Poly(Hydroxy Acid)s: From Stereoselectivity to Sequence-Control, *Chem.-Eur. J.*, 2020, **26**(1), 128–138, DOI: [10.1002/CHEM.201904108](#).
- A. H. Westlie, E. C. Quinn, C. R. Parker and E. Y. X. Chen, Synthetic Biodegradable Polyhydroxyalkanoates (PHAs): Recent Advances and Future Challenges, *Prog. Polym. Sci.*, 2022, **134**, 101608, DOI: [10.1016/J.PROGPOLYMSCI.2022.101608](#).
- X. Tang and E. Y. X. Chen, Chemical Synthesis of Perfectly Isotactic and High Melting Bacterial Poly(3-Hydroxybutyrate) from Bio-Sourced Racemic Cyclic Diolide, *Nat. Commun.*, 2018, **9**(1), 1–11, DOI: [10.1038/s41467-018-04734-3](#).
- X. Tang, A. H. Westlie, E. M. Watson and E. Y. X. Chen, Stereosequenced Crystalline Polyhydroxyalkanoates from Diastereomeric Monomer Mixtures, *Science*, 2019, **366**(6466), 754–758, DOI: [10.1126/science.aax8466](#).
- N. A. Manikandan, K. Pakshirajan and G. Pugazhenthii, Techno-Economic Assessment of a Sustainable and Cost-Effective Bioprocess for Large Scale Production of



- Polyhydroxybutyrate, *Chemosphere*, 2021, **284**, 131371, DOI: [10.1016/J.CHEMOSPHERE.2021.131371](https://doi.org/10.1016/J.CHEMOSPHERE.2021.131371).
- 17 D. H. Vu, D. Åkesson, M. J. Taherzadeh and J. A. Ferreira, Recycling Strategies for Polyhydroxyalkanoate-Based Waste Materials: An Overview, *Bioresour. Technol.*, 2020, **298**, 122393, DOI: [10.1016/J.BIORTECH.2019.122393](https://doi.org/10.1016/J.BIORTECH.2019.122393).
- 18 C. Jehanno, J. W. Alty, M. Roosen, S. De Meester, A. P. Dove, E. Y. X. Chen, F. A. Leibfarth and H. Sardon, Critical Advances and Future Opportunities in Upcycling Commodity Polymers, *Nature*, 2022, **603**(7903), 803–814, DOI: [10.1038/s41586-021-04350-0](https://doi.org/10.1038/s41586-021-04350-0).
- 19 J. B. Mensah and P. C. A. Buijninckx, Polyhydroxyalkanoate Valorization beyond Bioplastics: Opportunities as a Circular Carbon Feedstock, *Curr. Opin. Green Sustainable Chem.*, 2022, **37**, 100656, DOI: [10.1016/J.COCS.2022.100656](https://doi.org/10.1016/J.COCS.2022.100656).
- 20 I. Vollmer, M. J. F. Jenks, M. C. P. Roelands, R. J. White, T. van Harmelen, P. de Wild, G. P. van der Laan, F. Meirer, J. T. F. Keurentjes and B. M. Weckhuysen, Beyond Mechanical Recycling: Giving New Life to Plastic Waste, *Angew. Chem., Int. Ed.*, 2020, **59**(36), 15402–15423, DOI: [10.1002/ANIE.201915651](https://doi.org/10.1002/ANIE.201915651).
- 21 A. Dhaini, V. Hardouin-Duparc, A. Alaeddine, J. F. Carpentier and S. M. Guillaume, Recent Advances in Polyhydroxyalkanoates Degradation and Chemical Recycling, *Prog. Polym. Sci.*, 2024, **149**, 101781, DOI: [10.1016/J.PROGPOLYMSCI.2023.101781](https://doi.org/10.1016/J.PROGPOLYMSCI.2023.101781).
- 22 A. L. Merchan, T. Fischöder, J. Hee, M. S. Lehnertz, O. Osterthun, S. Pielsticker, J. Schleier, T. Tiso, L. M. Blank, J. Klankermayer, R. Kneer, P. Quicker, G. Walther and R. Palkovits, Chemical Recycling of Bioplastics: Technical Opportunities to Preserve Chemical Functionality as Path towards a Circular Economy, *Green Chem.*, 2022, **24**(24), 9428–9449, DOI: [10.1039/D2GC02244C](https://doi.org/10.1039/D2GC02244C).
- 23 D. Seebach, M. Albert, P. I. Arvidsson, M. Rueping and J. V. Schreiber, From the Biopolymer PHB to Biological Investigations of Unnatural β - and γ -Peptides, *Chimia*, 2001, **55**(4), 345, DOI: [10.2533/chimia.2001.345](https://doi.org/10.2533/chimia.2001.345).
- 24 Q. Ren, K. Ruth, L. Thöny-Meyer and M. Zinn, Enantiomerically Pure Hydroxycarboxylic Acids: Current Approaches and Future Perspectives, *Appl. Microbiol. Biotechnol.*, 2010, **87**(1), 41, DOI: [10.1007/S00253-010-2530-6](https://doi.org/10.1007/S00253-010-2530-6).
- 25 Q. Ren, A. Grubelnik, M. Hoerler, K. Ruth, R. Hartmann, H. Felber and M. Zinn, Bacterial Poly(Hydroxyalkanoates) as a Source of Chiral Hydroxyalkanoic Acids, *Biomacromolecules*, 2005, **6**(4), 2290–2298, DOI: [10.1021/BM050187S](https://doi.org/10.1021/BM050187S).
- 26 L. Massieu, M. L. Haces, T. Montiel and K. Hernández-Fonseca, Acetoacetate Protects Hippocampal Neurons against Glutamate-Mediated Neuronal Damage during Glycolysis Inhibition, *Neuroscience*, 2003, **120**(2), 365–378, DOI: [10.1016/S0306-4522\(03\)00266-5](https://doi.org/10.1016/S0306-4522(03)00266-5).
- 27 K. Tieu, C. Perier, C. Caspersen, P. Teismann, D.-C. Wu, S.-D. Yan, A. Naini, M. Vila, V. Jackson-Lewis, R. Ramasamy and S. Przedborski, D- β -Hydroxybutyrate Rescues Mitochondrial Respiration and Mitigates Features of Parkinson Disease, *J. Clin. Invest.*, 2003, **112**(6), 892–901, DOI: [10.1172/jci18797](https://doi.org/10.1172/jci18797).
- 28 Y. Zhao, B. Zou, Z. Shi, Q. Wu and G. Q. Chen, The Effect of 3-Hydroxybutyrate on the in Vitro Differentiation of Murine Osteoblast MC3T3-E1 and in Vivo Bone Formation in Ovariectomized Rats, *Biomaterials*, 2007, **28**(20), 3063–3073, DOI: [10.1016/j.biomaterials.2007.03.003](https://doi.org/10.1016/j.biomaterials.2007.03.003).
- 29 M. T. Manoli, J. Nogales and A. Prieto, Synthetic Control of Metabolic States in *Pseudomonas Putida* by Tuning Polyhydroxyalkanoate Cycle, *mBio*, 2022, **13**(1), e01794, DOI: [10.1128/MBIO.01794-21](https://doi.org/10.1128/MBIO.01794-21).
- 30 J. Yu, D. Plackett and L. X. L. Chen, Kinetics and Mechanism of the Monomeric Products from Abiotic Hydrolysis of Poly [(R)-3-Hydroxybutyrate] under Acidic and Alkaline Conditions, *Polym. Degrad. Stab.*, 2005, **89**(2), 289–299, DOI: [10.1016/j.polymdegradstab.2004.12.026](https://doi.org/10.1016/j.polymdegradstab.2004.12.026).
- 31 Y. Zhao, N. E. Schultz and D. G. Truhlar, Design of Density Functionals by Combining the Method of Constraint Satisfaction with Parametrization for Thermochemistry, Thermochemical Kinetics, and Noncovalent Interactions, *J. Chem. Theory Comput.*, 2006, **2**(2), 364–382, DOI: [10.1021/CT0502763](https://doi.org/10.1021/CT0502763).
- 32 J. A. Dean, Proton-Transfer Reactions of Inorganic Materials in Water at 25 °C, in *Lange's handbook of chemistry*, McGraw Hill Book Company, New York, NY, 1985, pp. 5–16.
- 33 A. P. Smith and C. Williams, Amino Acid and Peptide Ionization Constants in Aqueous Solutions: The pK_a Values of Taurine, *J. Am. Chem. Soc.*, 1977, **99**(8), 2601–2606.

