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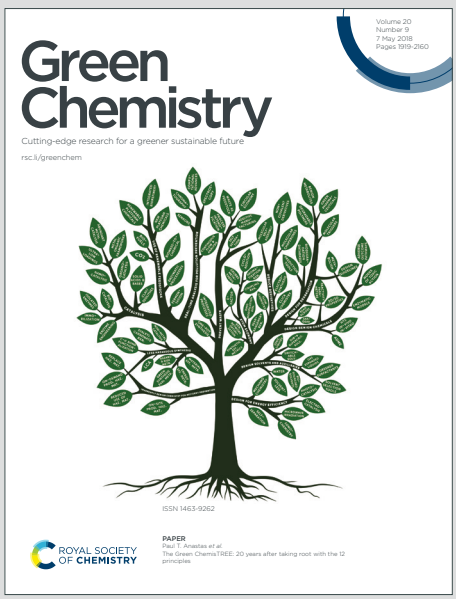

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COMMUNICATION

# A sustainable synthetic route for biobased 6-hydroxyhexanoic acid, adipic acid and ε-caprolactone by integrating bio- and chemical catalysis

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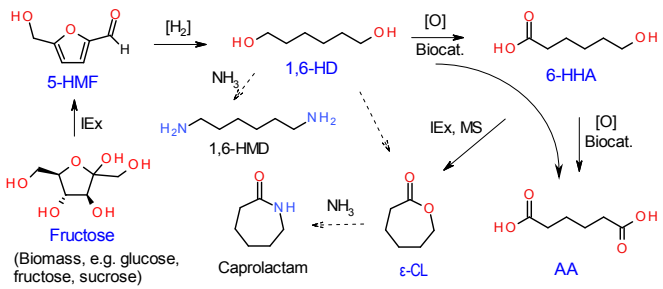
**A green route for production of 6-carbon polymer building blocks 6-hydroxyhexanoic acid, adipic acid and ε-caprolactone from 1,6-hexanediol, a hydrogenation product of biobased 5-hydroxymethylfurfural is reported. *Gluconobacter oxydans* oxidized 1,6-hexanediol completely to adipic acid, and selectively at pH 6-7 to 6-hydroxyhexanoic acid, which was converted to ε-caprolactone by catalytic cyclization.**

Decoupling industrial production from fossil resources is drawing increasing attention as contribution of fossil based greenhouse gas emissions to climate change is becoming a global concern [1-5]. Biobased 5-hydroxymethylfufural (HMF) is projected to be an important platform for functional building blocks for fuel, chemical and polymer industry, thanks to the presence of reactive aldehyde and alcohol groups and the furan ring. Hence, the past decade has seen intensive research in process development for its production from C6-sugar monomers and cellulose [6,7]. Further conversion of HMF to polymer building blocks including 5-hydroxymethylfurancarboxylic acid (HMFCA) and 2,5-furandicarboxylic acid (FDCA) by oxidation, 1,6-hexanediol (1,6-HD) by catalytic hydrogenation [8,9], as well as levulinic acid by hydration, have gained considerable attention [7,10-13].

Production of biobased 1,6-HD allows access to other valuable C6-products like 6-hydroxyhexanoic acid (6-HHA), adipic acid (AA) and ε-caprolactone (ε-CL), with applications both as platform chemicals and as building blocks for important polymers [1,3,14-16] (Scheme 1). Production of 1,6-HD by direct hydrogenations of HMF using double layered catalysts of Pd/$SiO_2$ and Ir–$ReO_x$/$SiO_2$ (with 57.8% yield) [9], and Pd/ZrP (43% yield) [17], and by hydrogenation of a HMF derivative, tetrahydrofuran dimethanol using Pt-$WO_x$/$TiO_2$ (70% yield) [18] have been reported.

Fossil based AA and ε-CL are already well-established products. AA, the aliphatic dicarboxylic acid is an essential commodity chemical for commercial manufacturing of Nylon-6,6 and polyurethanes, and is now also used as a component in the biodegradable polyester poly(butylene adipate terephthalate) (PBAT). It is produced almost exclusively from cyclohexane, derived from petroleum benzene in an inefficient oxidation process which releases $N_2O$, a potent greenhouse gas (Scheme S1) [19]. A selective synthetic method for AA, 1,6-HD, and 1,6-hexanediamine (1,6-HMD) via adipic aldehyde diacetal obtained by double-n-selective hydroformylation of 1,3-butadiene has been described [15]. Different approaches for producing biobased AA have been reported in recent years. Gilkey et. al. reported up to 89% yield of AA from tetrahydrofuran-2,5-dicarboxylic acid prepared from FDCA, by metal-free selective hydrogenolysis in a propionic acid solvent at 160 °C. Several metabolic engineering approaches have been proposed for production of AA from sugars and lipids, often with low yields [20,21].




**Scheme 1.** An integrated microbial-chemical route for the production of biobased 6-hydroxyhexanoic acid (6-HHA), adipic acid (AA), and ε-caprolactone (ε-CL) via 5-hydroxymethylfurfural (5-HMF) and 1,6-hexanediol (1,6-HD. Biocat: biocatalyst; IEX: ion exchange catalyst. The route can be extended to ε-caprolactam and 1,6-hexamethylenediamine (1,6-HMD) through amination (dotted arrows) [8,15].

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ε-CL, used primarily in the production of biodegradable poly(caprolactone), is industrially produced at a multi-10 000 ton scale per year by the UCC process [16,22,23], in which cyclohexanone is oxidized by using stoichiometric amounts of peracetic acid, with associated drawbacks of toxicity, ecology, and safety [23].

1,6-HD was efficiently transformed to ε-CL using methyl isobutylketone (MIBK) as oxidant and a catalyst system ([{Ru(cymene)$Cl_2$}$_2$] and 1,1'-bis(diphenylphosphino) ferrocene)) by Oppenauer oxidation [8]. However, the stoichiometric amounts of the reduction product of MIBK, 4-methyl-2-pentanol was formed, hence direct dehydrogenation of 1,6-HD to caprolactone without the use of an oxidant would be much preferred, but to date selectivities are too low [8].

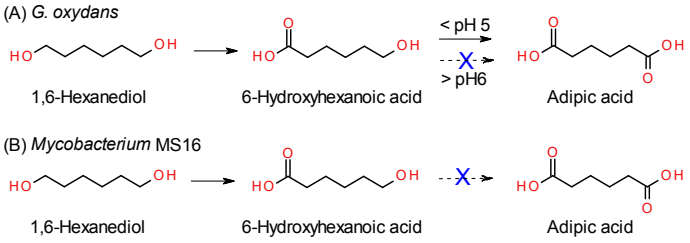
Baeyer–Villiger monooxygenase (BVMO) enzymes including the preferred cyclohexanone monooxygenase (CHMO) from *Acinetobacter calcoaceticus*, catalyse the oxidation of cyclohexanone to ε-CL in the presence of $O_2$ [23,24], however the system suffers from low productivity and stability of the CHMO, which is also subject to substrate and product inhibition [23]. To overcome the inhibition, a direct ring-opening oligomerization of ε-CL by *Candida antarctica* lipase A was reported, which resulted in the formation of more than 20 g/L of oligo-ε-CL from 200 mM cyclohexanol [23].

Kara et al. reported the oxidative lactonization of 1,6-HD to ε-CL with 26% yield catalyzed by horse liver alcohol dehydrogenase in a two-liquid phase system [24]. In a subsequent study, a convergent bi-enzymatic cascade involving BVMO and an alcohol dehydrogenase was designed to produce 3 molar equivalents of ε-CL from cyclohexanone (two equivalents) and 1,6-HD (one equivalent) in one pot process [25]. The BVMO catalysed processes are however still dependent on the petroleum-based cyclohexanone. Buntara et al. have reported a novel process to caprolactam and ε-CL through 1,6-HD from HMF [8].

6-HHA has potential applications in dermopharmaceutical, cosmetic and polymer sectors, especially for the production of poly(caprolactone) [16,26]. The classical synthetic route of 6-HHA includes metal-catalyzed reduction of AA at 523 K with 300 bar $H_2$ [16,27], and is also formed as a by-product by ring opening and oxidation of caprolactone in the AA production [26,28]. Recently, a multi-enzyme cascade reaction for the production of 6-HHA was reported, involving whole cells of *Escherichia coli* co-expressing an alcohol dehydrogenase and a CHMO for oxidation of cyclohexanol to ε-CL, which was ring-opened to 6-HHA using *C. antarctica* lipase B [29]. A route to biobased 6-HHA is via the selective oxidation of 1,6-HD, however the selective oxidation of primary aliphatic diols becomes difficult as the length of the carbon chain between the two hydroxyl groups increases [30].

In this study, we present a new synthetic route for generating biobased 6-HHA, AA and ε-CL from 1,6-HD produced from HMF, by integrating bio- and chemical catalysis (Scheme 1,2). This value chain can be extended further to caprolactam and 1,6-HMD.

The oxidation of 1,6-HD to 6-HHA requires oxidation of only one hydroxyl group to carboxylic acid group via an aldehyde intermediate, while AA is produced as the end product by complete oxidation of both hydroxyl groups (Scheme 2 and S2).




**Scheme 2.** Synthesis of adipic acid by microbial selective oxidation of 1,6-hexanediol via 6-hydroxyhexanoic acid.

In an earlier report, selective oxidation of 1,6-HD to 6-HHA at 81 % yield and 93 % selectivity (with AA as by-product) was achieved by the use of hydrotalcite-supported N,N-dimethyldodecylamine N-oxide (DDAO)-capped bimetallic Au–Pd nanoparticles ($Au_{40}Pd_{60}$-DDAO/HT) as catalyst [26]. Besides the noble metal catalysts, the reaction required the use of an oxidant ($H_2O_2$) and a base. In contrast, biocatalysis can be performed under milder reaction conditions without the use of oxidant and provide higher product selectivity [11,31]. Biotransformation of 1,6-HD to AA using *Gluconobacter oxydans* subsp. *oxydans* has been reported earlier, but only limited information was provided on experimental details and results [32]. The acetic acid bacteria *G. oxydans* are also known for performing selective oxidations [11]. *G. oxydans* DSM 50049 was recently reported to selectively oxidize the aldehyde group of HMF to form 5-hydroxymethylfuran carboxylic acid (HMFCA) under pH control at 7 [11].

The same strain when used for oxidation of 1,6-HD, oxidized both the hydroxyl groups of the diol to carboxylic acid groups to give AA via 6-HHA as intermediate (Figure 1, Figure S1) (Scheme 2A). 1,6-HD at a concentration of 84.6 mM in 100 mM phosphate buffer pH 7 was completely oxidized to AA within 36 hours. Although slower conversions were observed with higher concentration of 1,6-HD, the amounts of AA produced were linearly increased without exhibiting any substrate or product inhibition, which resulted in higher overall oxidation rate and efficiency with the same amount of cells (Figure S1).

Since the aldehyde intermediate was observed in low concentration or not observed at all during the initial reaction time, aldehyde dehydrogenase activity in the bacteria was most likely higher than that of the alcohol dehydrogenase; the risk of biocatalyst inactivation by accumulation of the toxic aldehyde could thus be avoided. During the course of the reaction, pH of the medium was decreased from initial pH 7 to 4.3.

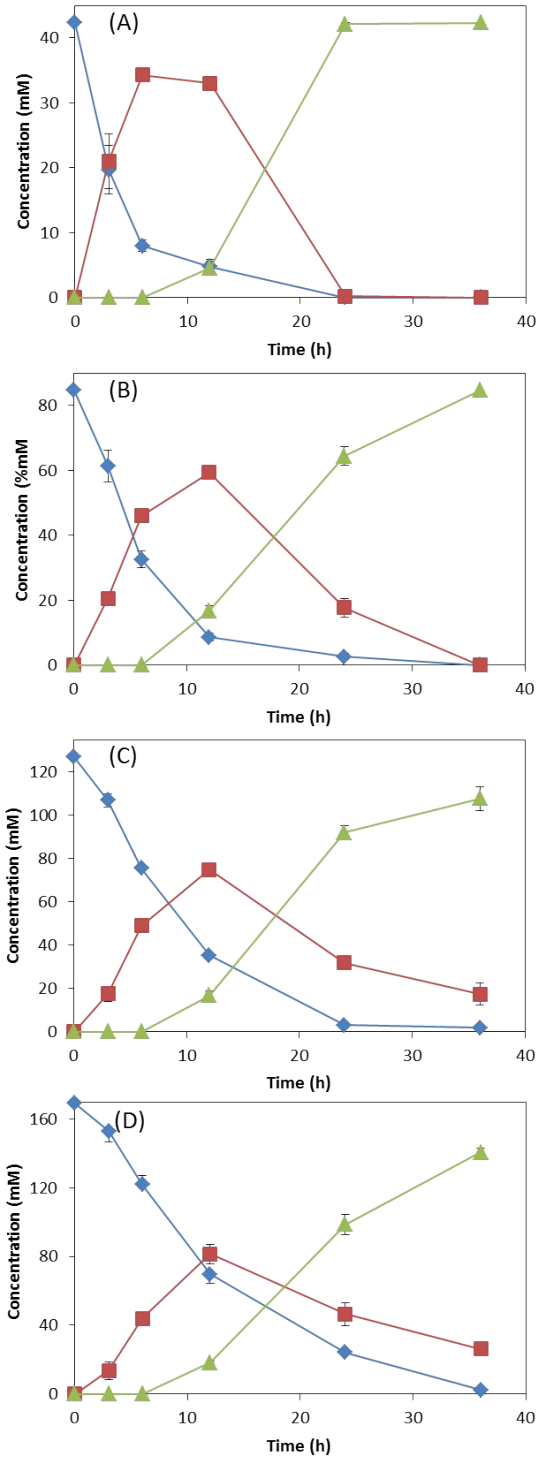



**Figure 1.** Oxidation of (A) 42.3 mM, (B) 84.6 mM, (C) 126.9 mM and (D) 169.2 mM 1,6-hexanediol to adipic acid via 6-hydroxyhexanoic acid by *G. oxydans* 50049 at 30 °C. The initial pH of the reaction was 7. The symbols indicate conversion (%) of 1,6-HD (♦), and content (%) of 6-HHA (■) and AA (▲) in the reaction.

Meanwhile, selective (incomplete) oxidation of 1,6-HD to 6-HHA was achieved by *Mycobacterium* sp. MS16 (Scheme 2B) (Figure 2); 100% conversion of 42.3 mM 1,6-HD at initial reaction pH of 7, was achieved with 100% product selectivity. However, with increasing concentration of 1,6-HD, the conversion rate and product amount were significantly decreased although still maintaining the selectivity (Figure 2). The enzymes involved are most likely subject to substrate inhibition, hence bioprocess engineering such as fed batch mode of reaction and *in situ* recovery of product could be the solution to reduce the inhibition and to improve the productivity.

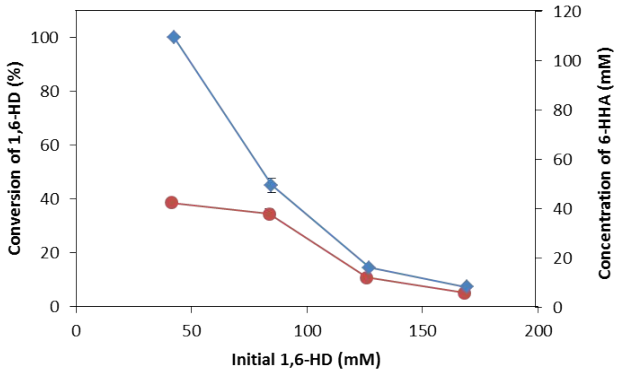



**Figure 2.** Selective oxidation of 1,6-HD to 6-HHA at 30 °C by *Mycobacterium* sp. MS16. Conversion of 1,6-HD (%, ♦) at initial diol concentrations of 42.3, 84.6, 126.9 and 169.2 mM, respectively, and content of 6-HHA (mg/mL, ●) formed at 36 h reaction time.

Since the oxidative activity of the responsible enzymes in *G. oxydans* and *Mycobacterium sp.* might depend on the reaction pH, the degree of substrate conversion and product profiles were also determined with initial pH at 5 instead of pH 7 (Figure 3). *G. oxydans* oxidized 1,6-HD to AA via 6-HHA, while *Mycobacterium sp*. exhibited very low activity with 18% conversion mainly to AA with 6-HHA as a minor product. It seems therefore that the lower pH is more favourable for adipic acid formation in both cases. While the reaction efficiency seems to be slightly increased at pH 5 with *G. oxydans* cells as catalyst, both the reaction efficiency and the product profiles were altered in case of *Mycobacterium* sp. Especially the oxidation of 1,6-HD was negatively affected in the latter case.

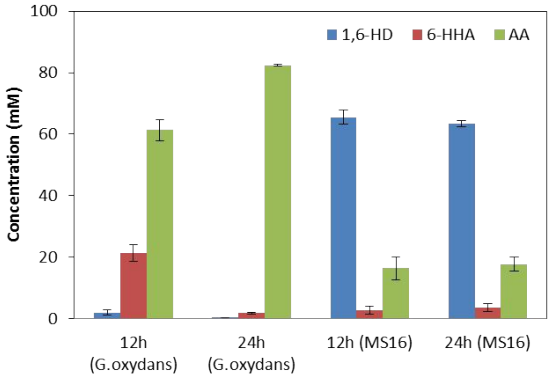



**Figure 3.** Comparison of pH effect on the oxidation of 84.6 mM 1.6-HD at 12 h and 24 h at pH 5 by *G. oxydans* DSM 50049 and *Mycobacterium sp*. MS16, respectively.

These observations provide the basis for a unique approach for controlling the selectivity of the microbial oxidation reaction using *G. oxydans* by simple switching of pH, one of the key parameters in biotransformation. In further investigations, reactions with shorter and longer aliphatic diols will be run to determine if their oxidation to the corresponding hydroxyl-carboxylic acids and di-acids could be achieved by controlling the reaction pH.

Further studies with oxidation of 1,6-HD using *G. oxydans* revealed shift in the selectivity from AA to 6-HHA by controlling the pH at 6-7 (Scheme 2A). As seen in Figure 4, addition of 1,6-HD in a fed-batch mode (total amount 250 mg) over a period of 100 hours led to quantitative production of 6-HHA while showing no product inhibition (Figure 4). Comparing with the productivity (4.39 mmol $h^{-1}$ $mg_{dcw}^{-1}$) in the selective oxidation of the aldehyde group in HMF (16 mg/L, 126.8 mM) to form HMFCA under similar conditions (about 4 mg/mL cell dry weight and 6 h reaction time) [11], lower productivity (1.34 mmol $h^{-1}$ $mg_{dcw}^{-1}$) was observed in the oxidation of 1,6-HD (10 mg/mL, 84.6 mM) to 6-HHA at 6 h of reaction (Figure 4). This is most likely due to the higher substrate concentration and the two-step oxidation of alcohol to acid via aldehyde in the present work. The extremely high selectivity of the reaction provides a definite advantage over the metal catalysed oxidation of 1,6-HD reported earlier [26].

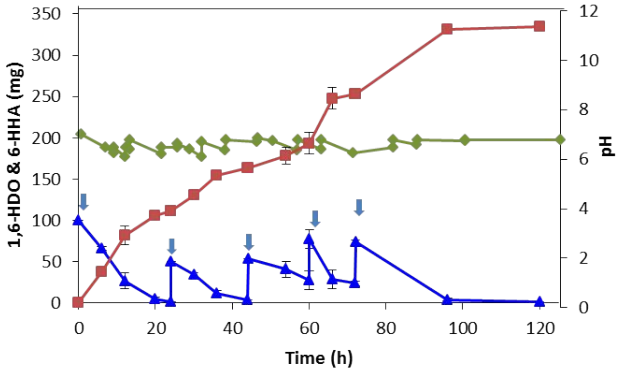



**Figure 4.** Continuous selective oxidation of 1,6-HD to 6-HHA by *G. oxydans* DSM 50049 at 30 °C with pH control at pH 6.5-7 in a reaction volume of 10 mL in a 50 mL bioreactor. Symbols: accumulated 6-HHA amount (mg, ■), 1,6-HD content (mg, ▲), and pH (♦). Arrows indicate addition of 50 mg 1,6-HD at 0, 24, 44, 60 and 72 h, respectively.

Finally, conversion of 6-HHA to ε-CL was investigated. In general, lactonization to a ring of more than 7-carbons from ω-hydroxy acids or esters is not efficient, since inter-molecular esterification occurs as the main reaction [33]. Lactonization of ethyl 6-hydroxyhexanoate to ε-CL with quantitative yield was achieved in a flow reactor with a fixed-bed catalyst hydrous zirconium (IV) oxide at 250 °C [33], while direct lactonization of the acid form, 6-HHA is still rare. We made use of molecular sieves (4Å, zeolites composed of sodium aluminosilicate) and acidic ion exchange resin for performing the catalytic lactonization of 6-HHA in dimethylformamide (DMF) at 130-160 °C (Table 1). Molecular sieves (zeolites) and cation exchange resins may be considered as recyclable and "green" Brönsted and/or Lewis acid heterogeneous catalysts [34-36]. Based on Lewis versus Brönsted contributions, Friedel Crafts reactions are better performed with zeolites, whereas the etherification of alkenes with light alcohols is essentially performed with cation exchange resins in the $H^+$ form. Although the two catalysts could individually convert 6-HHA to ε-CL and also a by-product ε-formyloxyhexanoic acid (ε-FOHA), (Table 1), the combination of two catalysts enhanced the formation of cyclic product, ε-CL with 74.4% selectivity at 98.3% 6-HHA conversion (Table 1, Entry 11).

This method provides a useful approach for the direct lactonization of ω-hydroxy acid without activation of acid to ester or anhydrous form. With both the catalysts, the conversion of 6-HHA and selectivity of cyclization to ε-CL increased with increasing amount of molecular sieves (Figure S2). The molecular sieves most likely promote the cyclization process through scavenging of $H_2O$ resulting from the dehydration. In our previous report, we have successfully demonstrated the use of molecular sieves for cyclization of polyols including 1,3-type diols such as 1,3-propanediol and 2-methyl-1,3-propanediol, and trimethylolpropane in reaction with dimethylcarbonate to form cyclic carbonates [37]. ε-FOHA could be formed by the reaction between formyl group of DMF and hydroxyl group of 6-HHA in the acidic environment. The formation of ε-FOHA was increased with decrease in the amount of molecular sieves, and the highest amount was formed when no molecular sieves were used (Table 1, entry 2).

**Table 1.** One-pot cyclization and esterification of hydroxyhexanoic acid (6-HHA) to ε-caprolactone (ε-CL) by combination of two acidic heterogeneous catalysts. Reaction conditions: 0.38 mmol 6-HHA in 1.5 mL DMF at 140 °C using given amounts of molecular sieves (MS) and cation exchange resin DR-2030. ε-Formyloxyhexanoic acid (ε-FOHA) was formed as a byproduct (Figure S5). [a] Analyzed by GC. [b] Overall isolated yield (mol/mol) from 1,6-HD through 6-HHA by integrating bio- and chemical catalysis.

| Entry | MS (g) | IEx (mg) | Time (h) | Conversion (%) [a] | Selectivity (%) [a] | |
|---|---|---|---|---|---|---|
| | | | | | ε-CL | ε-FOHA |
| 1 | 0.5 | 0 | 20 | 77.9 | 43.5 | 14.0 |
| 2 | 0 | 50 | 20 | 50.5 | 47.4 | 46.3 |
| 3 | 0.25 | 25 | 20 | 60.3 | 51.0 | 30.3 |
| 4 | 0.5 | 50 | 20 | 86.6 | 61.3 | 17.4 |
| 5 | 0.5 | 100 | 9 | 90.0 | 51.3 | 18.4 |
| 6 | 0.5 | 100 | 20 | 88.9 | 53.9 | 22.8 |
| 7 | 0.75 | 75 | 9 | 90.5 | 64.1 | 15.8 |
| 8 | 0.75 | 75 | 20 | 90.8 | 63.1 | 17.8 |
| 9 | 1 | 50 | 9 | 94.6 | 62.2 | 12.2 |
| 10 | 1 | 100 | 9 | 97.0 | 73.1 | 15.5 |
| 11 | 1.5 | 50 | 6 | 98.3 | 74.4 (67.2)[b] | 12.5 |

Interestingly, the synthesis of ε-FOHA is rare, and its formation as a co-product has been reported during production of 6-HHA from the peroxides of cyclohexanone, formed by reaction of cyclohexanone with hydrogen peroxide, using concentrated

formic acid with a small amount of a mineral acid [38,39]. Further investigation may be of interest to improve the yield of ε-FOHA, and for formylation of ω-hydroxy acids in organic synthesis and catalysis.

Application of zeolites in industrial processes is well established in mature technologies such as fluid catalytic cracking, hydrocracking or alkylation of aromatics [34], while acidic ion exchange resin has been widely exploited in various types of reactions such as esterification, hydrolysis, condensation, dehydration, carbonylation, hydrogenation, and also catalytic dehydration of fructose to HMF and levulinic acid [7,11,36]. Furthermore, the solvent, DMF was also a crucial factor in the dehydration and cyclization of 6-HHA; other solvents like DMSO and toluene resulted in only low yield (below 5%, data not shown) of ε-caprolactone under the same conditions. Further investigations for each step are required to find optimal processes.

## Conclusions

We have demonstrated a new facile process to produce industrially important 6-carbon chemicals such as 6-HHA, AA and ε-CL from renewable resources, and which can be further valorized to caprolactam and 1,6-HMD, and their polymers. The biobased synthetic route, highly selective and controlled oxidation of diol to ω-hydroxy acid or dicarboxylic acid, and catalytic cyclization of ω-hydroxy acid can be a valuable model for an environmentally friendly synthetic process for chemicals and polymers by integrating biotechnology and chemical synthesis.

## Conflicts of interest

There are no conflicts to declare.

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## Notes and references

[1] R. Hatti-Kaul, L.J. Nilsson, B. Zhang, N. Rehnberg, and S. Lundmark, *Trends Botechnol.,* 2020, 38, 50-67.
[2] Y. Zhu, C. Romain, and C.K. Williams, *Nature*, 2016, *540*, 354-362.
[3] T. Iwata, *Angew. Chem.*, 2015. *54*, 3210-3215.
[4] A.K. Mohanty, S. Vivekanandhan, J.M. Pin and M. Misra, *Science*, 2018, *362*, 536-542.
[5] A.J. Straathof, S.A. Wahl, K.R. Benjamin, R. Takors, N. Wierckx, and H.J. Noorman, *Trends Biotechnol.,* 2019, 37, 1042-1050.
[6] K.M. Iris, and , D.C., Tsang, *Bioresource technology*, 2017, *238*, 716-732.
[7] S.H. Pyo, M. Sayed and R. Hatti-Kaul, *Org. Process Res. Dev.*, 2019, *23*, 952-960.
[8] T. Buntara, S. Noel, P.H. Phua, I. Melián-Cabrera, J.G. de Vries and H.J. Heeres, *Angew. Chem.*, 2011, *50*, 7083-7087.
[9]. B. Xiao, M. Zheng, X. Li, J. Pang, R. Sun, H. Wang, X. Pang, A. Wang, X. Wang and T. Zhang, *Green Chem.*, 2016, *18,* 2175-2184.
[10] D.R. Vardon, N.A. Rorrer, D. Salvachúa, A.E. Settle, C.W. Johnson, M.J. Menart, N.S. Cleveland, P.N. Ciesielski, K.X. Steirer, J.R. Dorgan and G.T. Beckham, *Green Chem.*, 2016, *18*, 3397-3413.
[11] M. Sayed, S.H. Pyo, N. Rehnberg and R., Hatti-Kaul, *ACS Sustain. Chem. Eng.*, 2019, *7*, 4406-4413.
[12] X. Tang, J. Wei, N. Ding, Y. Sun, X. Zeng, L. Hu, S. Liu, T. Lei and Lin, L., *Renew. Sustain. Energy Rev.*, 2017, *77*, 287-296.
[13] S.M. McKenna, S. Leimkühler, S. Herter, N.J. Turner and A.J. Carnell, *Green Chem.*, 2015, *17*, 3271-3275.
[14] B. Agarwal, K. Kailasam, R.S. Sangwan, and S. Elumalai, *Renew. Sustain. Energy Rev.,* 2018, *82*, 2408-2425.
[15] J. Mormul, J. Breitenfeld, O. Trapp, R. Paciello, T. Schaub and P. Hofmann, *ACS Catal.,* 2016, *6*, 2802-2810.
[16] M. Labet and W. Thielemans, *Chem. Soc. Rev.,* 2009, *38*, 3484-3504.
[17] J. Tuteja, H. Choudhary, S. Nishimura, and K. Ebitani, *ChemSusChem*, 2014, *7*, 96-100.
[18] J. He, S.P. Burt, M. Ball, D. Zhao, I. Hermans, J.A. Dumesic, G.W. Huber, 2018. *ACS Catalysis*, 2018, *8,* 1427-1439.
[19] M.J. Gilkey, A.V. Mironenko, D.G. Vlachos and B. Xu, *ACS Catal.,* 2017, *7*, 6619-6634.
[20] N.S. Kruyer, P. Peralta-Yahya, *Curr. Opin. Biotechnol.*, 2017, 45, 136-143
[21] E. Skoog, J.H. Shin, V. Saez-Jimenez, V. Mapelli, L. Olsson, *Biotechnol. Adv.*, 2018, 36, 2248-2263
[22] K. Weissermel and H. -J. Arpe, *Industrial Organic Chemistry*, 4th ed., Wiley-VCH, Weinheim, 2003.
[23] S. Schmidt, C. Scherkus, J. Muschiol, U. Menyes, T. Winkler, W. Hummel, H. Gröger, A. Liese, H.G. Herz and U.T. Bornscheuer, *Angew. Chem.*, 2015, *54*, 2784-2787.
[24] S. Kara, D. Spickermann, J.H. Schrittwieser, A. Weckbecker, C. Leggewie, I.W. Arends, F. Hollmann, *ACS Catalysis*, 2013, 3, 2436-2439.
[25] A. Bornadel, R. Hatti-Kaul, F. Hollmann and S. Kara, *ChemCatChem*, 2015, *7*, 2442-2445.
[26] J. Tuteja, S. Nishimura, H. Choudhary and K. Ebitani, *ChemSusChem*, 2015, *8*, 1862-1866.
[27] R. H. Fischer, R. Pinkos, F. Stein, Method for producing 1,6-hexanediol and 6-hydroxycaproic acid or their esters, US Patent 6426438 B1, 2002.
[28] Y. Usui and Sato, K., *Green Chem.*, 2003, *5*, 373-375.
[29] V.S. Srinivasamurthy, D. Böttcher and U.T. Bornscheuer, *Z. Naturforsch. C*, 2019, *74*, 71-76.
[30] M.S. Ide and R.J. Davis, *J. Catal.*, 2013, *308*, 50-59.
[31] M. Sayed, T. Dishisha, W.F. Sayed, W.M. Salem, H.M. Temerk and S.H. Pyo, *Process Biochem.*, 2017, *63*, 1-7.
[32] M. Faber, Process for producing adipic acid from biomass. U.S. Patent 4,400,468, 1983.
[33] H. Kuno, M. Shibagaki, K. Takahashi, I. Honda and H. Matsushita, *Chem. Lett.*, 1992, *21*, 571-574.
[34] C. Martínez and A. Corma, *Coord. Chem. Rev.*, 2011, *255*, 1558-1580.
[35] G. Gelbard, *Ind. Eng. Chem. Res.*, 2005, *44*, 8468-8498.
[36] V.M. Bhandari, L.G. Sorokhaibam and V.V. Ranade, *Industrial Catalytic Processes for Fine and Specialty Chemicals*, 2016, 393-426, Elsevier.

View Article Online
DOI: 10.1039/D0GC01454K

[37] S.H. Pyo and R. Hatti-Kaul, *Adv. Synth. Catal.*, 2016, *358*, 834-839.
[38] E.G.E. Hawkins, 1969. Reactions of organic peroxides. Part XV. Conversion of cyclohexanone into hexan-6-olide. J. Chem. Soc. C: 1969, *20*, 2691-2697.
[39] A. Isard, F. Weiss, U. Kuhlmann, Method for producing derivatives of 6-hydroxy caproic acid. U.S. Patent 3,784,567, 1974

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# A sustainable synthetic route for biobased 6-hydroxyhexanoic acid, adipic acid and ε-caprolactone by integrating bio- and chemical catalysis





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Green synthetic route and possible utilization of biobased 6-carbon polymer building blocks 6-hydroxyhexanoic acid, adipic acid and ε-caprolactone from biomass via 1,6-hexanediol, a hydrogenation product of biobased 5-hydroxymethylfurfural.