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Abstract: β-lactones are common substructures in a variety of natural products and drugs, and they serve as versatile synthetic intermediates in the production of valuable chemical derivatives. Traditional β-lactone synthesis relies on laborious multi-step synthetic methods that use toxic compounds, sophisticated catalysts, expensive, and/or reactive chemicals. Based on the in-situ electrochemical formation of metal-based nano-clusters, this paper describes the development of a one-step, room temperature electro-catalytic method for the formation of stable β-lactone from CO_2 and olefins. This one-step 'electrosynthesis' method results in the formation of a new class of β-lactone with high selectivity (up to 100 %) and activity (up to 80 percent yields with respect to the reacted diene) by regulating the applied potential and current density. This work paves the way for more sustainable and environmentally friendly reaction pathways based on the in-situ formation of nano-clusters as organic electrosynthesis catalysts.

Introduction

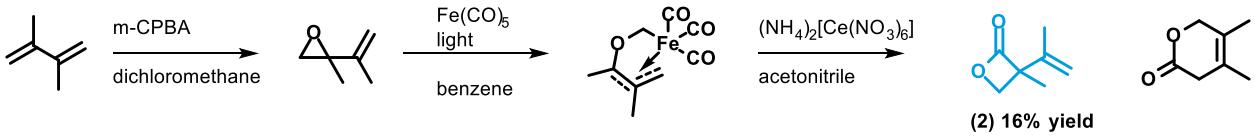
The β-lactones (2-oxetanones) belong to a class of strained four-membered hetero-cycles with highly-reactive electrophilic scaffolds.[1] β-lactones have the same ring strain and reactivity as epoxides (22.8 and 27.2 kcal mol^{-1}, respectively), and the structural characteristics of aldol products. As a result, they can react with a wide variety of nucleophiles via acyl C-O and alkyl C-O bond cleavage.[1-4] Their versatile reactivity, combined with their unusual structural features, increases their potential applications in a wide range of fields. They are a structural motif in a variety of important natural and synthetic bioactive products,[5] as well as anti-obesity, antimicrobial, and anticancer drugs.[1, 6] Furthermore, they are a class of structurally distinct building blocks for a wide range of organic compounds,

making them a versatile building block. Furthermore, because they are a class of structurally distinct building blocks for a wide range of organic compounds, they are a versatile synthetic intermediate with high industrial potential. The β-lactone ring opening can provide access to β-hydroxy carbonic acids with tailored functional groups. As a result, they can be used as building blocks for fine chemicals such as fungicides and herbicides in the agricultural sector.

They can also be used as fragrances, solvents, or surfactants,[1] as well as a monomer for biodegradable polymeric materials based on polyhydroxyalkanoates (PHAs) [7-10] which are used in plastics, clothing, and surgical materials.[11-12] More recently β-propiolactones have been used as an inactivating reagent in the production of inactivated pathogen coronavirus vaccine families.[13-14]

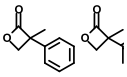
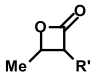
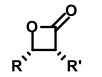
Several catalytic methodologies for the synthesis of -lactones and derivatives have been developed over the last 20 years.[2-3, 15-20] Error! Reference source not found. summarizes the most commonly used synthesis methods for -lactones. Despite their importance, these molecules are still difficult to produce in a selective and high yielding manner, as observed. Current approaches rely primarily on time-consuming synthetic steps involving toxic compounds, sophisticated catalysts, or expensive and/or reactive chemicals.[2-4, 15-17, 19]

It appears that the difficulties of these multistep synthesis preparation methods, which use a number of toxic chemicals or catalysts, inadvertently lead to safety and environmental issues. For the β-lactone synthesis described in this paper, Annis et al. [18] developed a three-step method in 1981 using highly toxic and flammable chemicals such as ironpentacarbonyl and toxic, carcinogenic, or regulated solvents, resulting in the formation of -propiolactones with an overall yield of 16%, as shown in **scheme 1**. There has been no new and less sophisticated synthetic method for these molecules reported in the literature since then.



Scheme 1. Three-step homogeneous catalysed organic synthesis pathways of beta lactones: first step oxidization of a diene with m-chloroperbenzoic acid (m-CPBA) in dichloromethane to a vinyloxirane (7). Second step insertion of CO into the epoxide with the use of ironpentacarbonyl in benzene forming an iron tricarbonyl complex (8) under light irritation. 3rd step synthesises a mixture of β- (2) and δ-lactone by cerium (IV) ammonium nitrate in acetonitrile in an overall yield of 16%.

Table 1. Comparison of different synthesis approaches of β lactones and their toxicity issues

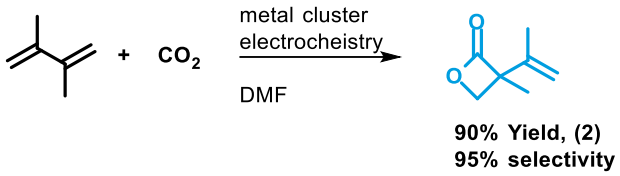
Reference	No. of Steps	Reaction conditions / catalyst	Reactants / Final product	Yield	Chemicals of concern	toxicity	comments
This work	1	RT, 11 to 30 bar / metal clusters	 Olefin, CO_2 /	<90 %	DMF	acute toxicity, inhalation / dermal , possible reprotoxic	Acute (short-term) exposure to DMF has been observed to damage the liver in animals and in humans. Dimethylformamide is embryotoxic in animals;[21] next step will be the replacement of DMF by a more environmental friendly electrochemical solvent
Annis[18]	3, separation	Irradiation / $Pd(PPh_3)_2Cl_2$= complex	olefin, peracid, "CO" (from  $Fe(CO)_5$	16 %	$Fe(CO)_5$	highly toxic	Highly flammable liquid and vapour; fatal if swallowed, in contact with skin or if inhaled
					CH_2Cl_2	possible carcinogen	CH_2Cl_2 is classified as HAP in the US, regulated by EU solvent directive. Suspected of causing cancer. Acute effects consist mainly on nervous system effects. Long-term exposure might target the central nervous system.
					benzene	carcinogen	low flash point (-11℃), very low TLV (0.5 ppm), toxic to humans and environment, strongly regulated in the US (HAP) and the EU. EPA has classified benzene as known human carcinogen for all routes of exposure.[22]
Mulzer[4]	2 step (raw material synthesis) + 2 step complex synthesis	22°C, 62 bar / [Lewis Acid]$^+$[Co(CO)$_4$]$^-$ inert atmosphere, water free	epoxides, CO /  R = alkyl chain (C2 to C6)	63-71 %	epoxide	mutagen	Highly reactive and explosive compounds. The high reactivity makes most epoxides mutagenic.[23-24]
					[Lewis Acid]$^+$[Co(CO)$_4$]	carcino-gen	Many cobalt salts are genotoxic, carcinogen and reprotoxic.[25]
					CO	acute toxicity, inhalation ; reprotoxic	Extremely flammable gas. Toxic if inhaled. May damage the unborn child. Causes damage to organs through prolonged or repeated exposure if inhaled.
					CH_2Cl_2 (raw material synthesis)	possible carcinogen	Classified as HAP in the US, regulated by EU solvent directive. Suspected of causing cancer. Acute effects consist mainly on nervous system effects. Long-term exposure might target the central nervous system.
Kramer[15]	1 + 3 step cat preparation	0-22°C, 1 ATM to 7 bar / Cr complexes (2 mol%), inert atmosphere, water free	epoxides,  CO / R = alkyls, alkenes, ethers, esters R'= H, Me	31-96 %	epoxide	mutagen	Highly reactive and explosive compounds. The high reactivity makes most epoxides mutagenic.[23-24]
					Cr compounds	mutagen, carcinogen	Cr (IV) salts are more toxic than Cr (III) salts. Cr (VI) compounds are carcinogenic to humans and have a mutagenic potential.[26]
					CO	acute toxicity, inhalation ; reprotoxic	Extremely flammable gas. Toxic if inhaled. May damage the unborn child. Causes damage to organs through prolonged or repeated exposure if inhaled.
Zhuang[16]	1	60°C / Pd complex (10 mol%, ligand 20 mol%), t-butyl hydrogen peroxide	aliphatic  acids / R = H, Me, Et R' = alkyl, ether, ...	50-82 %	t-butyl hydrogen peroxide	acute toxic, inhalation , dermal, oral; mutagen	Flammable liquid and vapour. Heating may cause a fire. TBHP is metabolized to free radicals and is a contact irritant affecting skin by the dermal route of exposure.[27] Toxic in contact with skin. Suspected of causing genetic defects. Toxic to aquatic life with long lasting effects
					HFIP	toxic, reprotoxic	Suspected of damaging fertility or the unborn child. May cause damage to organs through prolonged or repeated exposure.
Schneider[3] (example 1[28])	2, insitu + 1 catalyst preparation	-50°C to RT / a triamine complex (10 mol%)	Ketene (from acetyl  bromide), aldehyde /	30 % - 83 %	Hünig's base	toxic if inhaled	Highly flammable liquid and vapour, toxic if inhaled
					dichloro-ethane	acute toxicity oral/inhalation, toxic, carcinogen	Highly flammable liquid and vapour; 1,2-Dichloroethane is classified by EPA in Group B2 as a probable human carcinogen by both the oral and inhalation exposure routes, based on evidence for the induction of several types of tumors in rats and mice.[29]

Reference	No. of Steps	Reaction conditions / catalyst	Reactants / Final product	Yield	Chemicals of concern	toxicity	comments
			R = CH_2R', C≡C-R', ethers		n-hexane (cat preparation)	Aspiration hazard, toxic if swallowed, reprotoxic	n-hexane is a neurotoxin: Short-term exposure to air contaminated with hexane affects the nervous system. Chronic exposure can cause more severe damage to the nervous system.[30]
					CH_2Cl_2	possible carcinogen	CH_2Cl_2 is classified as HAP in the US, regulated by EU solvent directive. Suspected of causing cancer. Acute effects consist mainly on nervous system effects. Long-term exposure might target the central nervous system.
Schneider[3] (example 2[31])	2 step + 1 cat preparation	-78°C / copper(II) - bisoxazoline complexes (20 mol%), inert and dry atmosphere	trimethylsilyl ketene, dicarbonyl compound  / R = H, Me	47 %	dichloroethane	acute toxicity oral/inhalation, toxic, carcinogen	Highly flammable liquid and vapour; 1,2-Dichloroethane is classified by EPA in Group B2 as a probable human carcinogen by both the oral and inhalation exposure routes, based on evidence for the induction of several types of tumors in rats and mice.[29]
					n-hexane (cat preparation)	aspiration hazard, toxic if swal-lowed, reprotoxic	n-hexane is a neurotoxine: Short-term exposure to air contaminated with hexane affects the nervous system. Chronic exposure can cause more severe damage to the nervous system.[30]
Kull[18]	2, insitu + 1 step ligand	-85°C / Al complex with diamine ligands, inert and dry atmosphere	ketenes (from acetyl  bromide, aldehyde4 R = alkyl, alkyl-aromatic, ...	2–80 %	toluene	neurotoxin, reprotoxic	Toluene has been recognized as a neurotoxin that damages cerebral white matter.[32] It is a highly flammable liquid, and specific target organ toxicity following repeated exposure.
					Triethyl-aluminium	toxic	Highly reactive, pyrophoric substance, contact is extremely destructive to the eyes, skin, and mucous membranes. May be fatal if swallowed and enters airways.
					DIBAL	toxic, reprotoxic	DIBAL, like most alkylaluminium compounds, reacts violently with air and water, potentially leading to explosion. May be fatal if swallowed and enters airways, suspected of damaging fertility, May cause damage to organs through prolonged or repeated exposure.
Meier[20]	1 + 4 step ligand preparation	-70°C / Al salen complex (10 mol%), pyridi-nium ligand	acetyl bromide,  aldehyde / R = alkyl, R'= aromatic HBr & pyridine for the / Al salen complex preparation	37 %-69 %	CH_2Cl_2	possible carcinogen	CH_2Cl_2 is classified as HAP in the US, regulated by EU solvent directive. Suspected of causing cancer. Acute effects consist mainly on nervous system effects. Long-term exposure might target the central nervous system.
					Triethyl aluminium	toxic	Highly reactive, pyrophoric substance, contact is extremely destructive to the eyes, skin, and mucous membranes. May be fatal if swallowed and enters airways.
					HBr	toxic	HBr is an extremely irritating, corrosive highly toxic gas with a sharp, irritating odour. Exposure to HBr gas may result in nose and throat irritation, watery eyes, bloody nose, nausea, vomiting, chest pain and/or light-headedness. Immediately or within a few hours after breathing the gas, the lungs can become irritated, causing coughing and/or shortness of breath. In addition, higher exposure can cause swelling and spasms in the airway and a build-up of fluid in the lungs, severe shortness of breath, loss of consciousness, low blood pressure, rapid heartbeat, kidney failure, coma and death.
					Pyridine	possible reprotoxic	Pyridine is regulated by OSHA and cited by ACGIH, DOT, NIOSH. DEP, HHAG, NFPA and EPA. Possible reprotoxic. Long-term effects might include damage of liver and kidneys and effect the brain causing confusion and mental changes.
Ge[21]	2 + 2 step ligand preparation	100°C, 40 bar, Pd catalyst (1 mol%), ligands (6 mol%), inert	CO, alkynols  R^1 = H, alkyl, R^2 =	38 % - 98 %	CO	acute toxicity, inhalation; reprotoxic	Extremely flammable gas. Toxic if inhaled. May damage the unborn child. Causes damage to organs through prolonged or repeated exposure if inhaled.

Reference	No. of Steps	Reaction conditions / catalyst	Reactants / Final product	Yield	Chemicals of concern	toxicity	comments
		atmosphere	alkyl (cyclic)				

In this work we developed a simple electrochemistry method that provides a new reaction pathway for the synthesis of these specific propiolactone derivatives. This method is particularly interesting not only because it is mild and selective, but also because it is based on the use of and the formation of nano-clusters in situ. It not only reduces the number of process steps, waste, and catalyst recovery, but it also provides an appealing approach to converting CO_2, a greenhouse gas, into value-added products.[33-35]

The electro-carboxylation of unsaturated hydrocarbons, with butadiene as the prototype substrate, is one of the most fundamental applications of electro-organic synthesis.[36-43] 1,3-dienes are widely used in the synthesis of valuable compounds because they are readily available commodity chemicals. Based on the work of Li et al.,[43] we demonstrated in a previous paper that it is electrochemically possible to synthesize dicarboxylic acids such as 3,4-dimthylhex-3-enedioici acid with up to 45 percent yields from dienes or olefins with CO_2.[42] In this work, we developed a single-step, room temperature method for selectively forming a new class of β-lactones from CO_2 and olefins with up to 100% selectivity and more than 80% yields with respect to the diene. This very selective and simple single step electrochemical approach described in this work is depicted in **Scheme 2.**



Scheme 2. electrochemical single step synthesis pathway of the formation of β-lactones

This is accomplished simply by modifying the electrochemical reaction conditions for di-acid formation and employing an in-situ electrosynthesis method, which is commonly used in the literature for nano-cluster formation (**Figure 1a, b**). We show that by using a very low current density (below 2 mA/cm^2) and a small amount (0.001-0.005 M) of $NiBr_2$ or $FeBr_2$ as a source of M^{2+} in the solution to form nano-clusters, it is possible to promote CO_2 C2 attack rather than C1 attack of terminal olefin methyl groups with high selectivity and activity. This provides a new one-pot reaction pathway for β-lactone synthesis that allows for easier catalyst recovery and reutilization.

It clearly shows how an electrochemical method can provide a real sustainable advantage over all of the methods listed in Error! Reference source not found.. Furthermore, while the use of in-situ nano-cluster formation is applied to a specific class of materials in this paper as a proof of concept, it may pave the way for their future application in the formation of other electrochemical reactions.

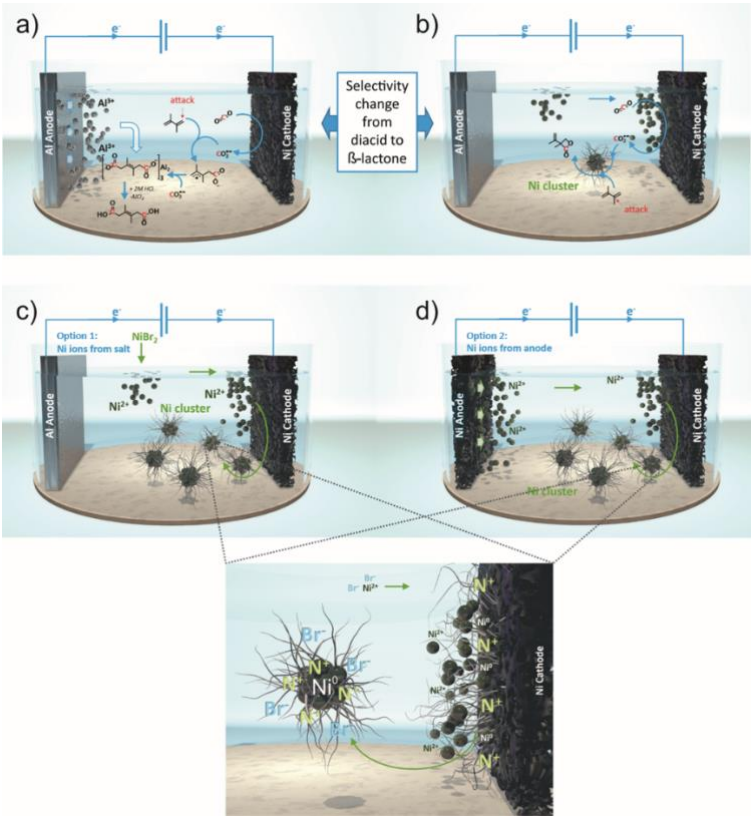


Figure 1. Schematic electrochemical steps of synthesis of the a) diacid and b) β-lactone, a) diacid formation mechanism: consisting of dissolution of the sacrificial anode to Al^{3+}, reduction of CO_2 at the cathode and the attack of C1 position of dienes, carboxylate anions complex with metal cations (Al^{3+}) and can be collected by precipitation from organic solvents. b) β-lactone formation mechanism: Consisting of c) dissolution of metal salt or d) the sacrificial anode i.e, in this case by oxidation of Ni to Ni^{2+}, metal ion migration to the cathode, leading to reductive metal adatom formation at the cathode and aggregation and stabilization by 'self-organization' of the ammonium ions around the metal core, and finally favouring the C2 attack of dienes by CO_2 and formation of β-lactone. The hairy lines in the schematic represent the butyl groups of the tetrabutylammonium cation.

Results and Discussion

As a first step in our investigation, we modified the process used for electrocarboxylation of conjugated dienes for lactone synthesis. In this process, Ni foam serves as the cathode and Al sacrificial electrodes serve as the anode. The reaction takes place in a single compartment home-built high pressure electrochemical reactor **(Figure S1),** with a polar, aprotic solvent DMF, n-Bu4N Br as a supporting salt, and very low electrochemical potentials (-2 to -2.5 V vs SHE).

It has been demonstrated that electrochemical methods can be used to create metal colloids based on Fe, Cu, Ni, etc., in the nanometre range with novel catalytic properties.[44] These nanoparticles can be made by electrochemical reduction of metal salts using a simple two-electrode setup with either a sacrificial anode made of the bulk metal to be transformed into metal clusters or the corresponding metal salt used instead of the sacrificial anode (**Figure 1 c, d**). The particle size can be easily controlled by varying the current density. [45] Stabilizers such as

tetraalkylaminonium salts are used to prevent unwanted agglomeration. Tetraalkylammonium salt can thus act as both a supporting electrolyte and a cluster stabilizer.

We prepare in-situ Ni-clusters for the conversion of olefin and CO_2 based on the literature,[45] . $NiBr_2$ was added to the standard diene solution as a source of Ni^{2+}. After the addition of all reactants and CO_2 pressure stabilization in the solution and prior to electrochemical synthesis, chronoamperometry (CA) was performed at potentials between -2 and -2.5 V vs SHE at an average current density of -1.9 mA/cm^2 for 1500 s. The reaction was then stabilized for 5000 s at open circuit voltage prior to the electro-organic synthesis step. The effect of current and potential on the selectivity and yield of the compound using $NiBr_2$ as a metal source, with or without the Ni cluster step preparation, was investigated (**Figure 2**).

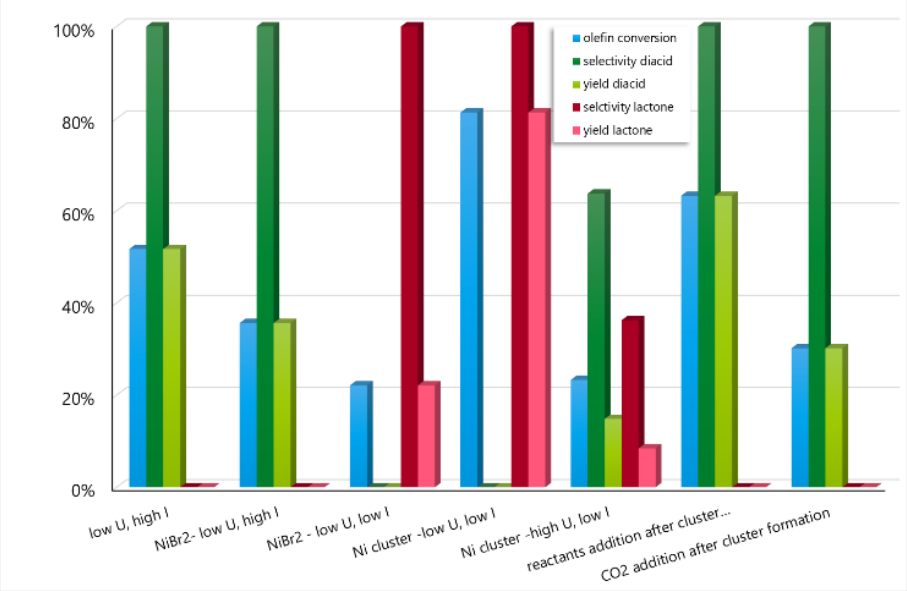


Figure 2. The selectivity and calculated yields of diacid and lactones as function of current and potential.

The selectivities reported are based on olefinic raw materials. However, some of the excess of CO_2 will be converted into CO_2-based by-products such as inorganic carbonate, oxalate, and formate.

Without the Ni-cluster preparation step, according to NMR analysis and as shown in **Figure 2**, when high current density > 5 mA/cm^2 and low voltage < -2 V are applied (Error! Reference source not found.**, entry 1**), dienes are converted to diacids with good yields and selectivity[42] (52% isolated yield with respect to the reacted diene). This process is well known.[36-43]

It has been demonstrated that at current densities ranging from 5 to 8 mA/cm^2, diacid could be formed primarily at very low reduction potentials (-2 V vs SHE), corresponding to the reduction of CO_2 to CO_2 radical anion [$CO_2^{\bullet-}$].

$$CO_2 + e^- \leftrightarrow CO_2^{\bullet-} \quad (E° = -2V \text{ versus SHE})\ ^{46} \qquad \text{eq.1}$$

The $CO_2^{\bullet-}$ radical or the dienyl radical is formed in the first rate-limiting step.[42-43] The radical then reacts at the C1 position with an olefin or CO_2 molecule to form an allyl radical intermediate. This intermediate This intermediate is

then fast reacting with a second CO_2 molecule. The dimerization of two [$CO_2^{\bullet-}$] radicals results in the formation of oxalic acid from oxalate in all reactions as a trace product (eq.2).

$$2\ CO_2^{\bullet-} \leftrightarrow C_2O_4^{2-}\ \text{(oxalate production)} \quad \text{eq. 2}$$

Table 1. The Conversion and selectivities of β-lactone and diacid from 2,3-dimethyl -1,6-butadiene by using different parameters

entry	Parameters	U[V]	J [mA/cm^2]	conversion of olefin	Selectivities [%]		Yields* [%]	
				[%]	diacid	lactone	diacid	lactone
1	no addition of $NiBr_2$ low U, high I	-2.5	6.3	52	100	0	52	0
2	no addition of $NiBr_2$ - low U, low I	-2.5	1.5	77	100	0	77	0
3	addition of $NiBr_2$ - low U, high I	-2.2	5	36	100	0	36	0
4	addition $NiBr_2$ - low U, low I	-2.0	1.9	22	0	100	0	22
5	In-situ cluster formation -> low U, low I	-2	2.1	81	0	100	0	81
6	In-situ cluster formation -> high U, low I	-1	2.1	23	64	36	15	8
7	In-situ cluster formation -> reactants addition-low U, low I	-2.0	1.8	63	100	0	63	0
8	In-situ cluster formation --> CO_2 addition -low U, low I	-2	0.9	30	100	0	30	0

The addition of $NiBr_2$ to solution (**Table 1**, **entry 3**) has no effect on the selectivity for dicarboxylic acids. However, as shown in **Figure 2**, lowering the current density below 3 mA/cm^2 (**Table 1**, **entry 4**), results in a complete switch (up to 100%) from di-acid formation to the formation of a 4-member ring -lactone known as 3-methyl-3-(prop-1-en-2-yl)oxetan-2-on (2).

Using the pre-step Ni-cluster preparation and a current density of around 2 mA/cm^2 (and a potential of -2 V vs SHE) (**Table 1**, **entry 5**), we observed an increase in conversion, resulting in an 81% yield (relative to the reacted diene) of this 4-member ring β-lactone. However, for similar low current density when potential is higher than -1.3 V vs SHE (**Table 1, entry 6**), a mixture of diacid and lactone is observed. This underlines the importance of potentials ~-2 V vs SHE, enabling the formation of [$CO_2^{\bullet-}$] radicals, for the lactone synthesis.

Two additional experiments were carried out in order to elucidate the mechanism of β-lactone formation. Ni clusters were first prepared without the presence of CO_2 and diene in the solution (**Table 1**, **entry 7**), or only in the presence of diene without the presence of CO_2 pressures (**Table 1**, **entry 8**). Missing reagents were added after the Ni-cluster pre-formation step. **Figure 2** shows that only dicarboxylic acids are formed in both cases, with no traces of β-lactone detected. These results clearly demonstrate that not only [$CO_2^{\bullet-}$] radicals are required to get 100% selectivity towards β-lactone, but also the presence of diene and CO_2 during cluster formation is required to tune the selectivity from di-acid to β-lactone.

Characterization of β-lactones

IR (**Figure S2**), TGA, DSC (**Figure S3**), ^{1}H NMR, and ^{13}C NMR (**Figure S4, S5**) were used to characterize the isolated β-lactone product. According to these results, the synthesized molecule is 3-methyl-3-(prop-1-en-2-yl)oxetan-2-on (2). This isolated β-lactone, is a brown to purple liquid that is soluble at least in DMF, acetonitrile, DMSO and chloroform. The presence of β-lactones is clearly visible in the NMR analysis of the reaction solution prior to workup (**Figure S6)**. Based on DSC and TGA analysis of the isolated product, this β-lactone begins to decompose at around 209°C and has a boiling point between 150 and 200°C. Furthermore, despite the fact that most lactones are reported to open in acidic solutions, the product appears to be relatively stable in 2 M HCl for at least 6 h, as it remains largely intact during the acidification process of workup.

Impact of electrodes

Using a nickel anode instead of an Al anode may eliminate the need for an additional metal catalyst, simplifying the process. First, we replaced the aluminium anode with a nickel anode (Error! Reference source not found.**, entry 9**), (Table 3, entry 9), without adding $NiBr_2$ and using the previous synthesis conditions for the formation of Ni-clusters and β-lactones.

Table 2: The Conversion and selectivities of β-lactone and diacid from 2,3-dimethyl -1,6-butadiene using different catalyst precursors

entry	Parameters	U [V]	J [mA/cm^2]	conversion of olefin [%]	Selectivities [%]		Yields* [%]	
					diacid	lactone	diacid	lactone
9	Ni electrodes, cluster formed from electrode	-2.6	2.0	79	7	93	6	73
10	Pt counter electrode	-2.2	2.4	48	0	100	0	48
11	$FeBr_2$	-2.0	2.4	83	0	100	0	83

*Yields are calculated by olefin conversion multiplied by selectivity

As shown in Error! Reference source not found.**,** it results in the formation of the β-lactone as well as a small amount of diacids. As the ion source, a small amount of $NiBr_2$ added to the previous solution provides complete conversion of olefin to β-lactone product. Along with all of the advantages of these sacrificial anodes, the gradual consumption of the anode material is a significant disadvantage for industrial applications. As a result, a platinum anode with NiB_{r2} salts was also tested (Error! Reference source not found.**, entry 10**), resulting in 100 percent β-lactone selectivity but lower yield (Error! Reference source not found.).Replacing nickel by an economic and environmentally friendly catalyst source such as iron (Error! Reference source not found., **entry 11**), is another way to improve the sustainability of this process. The potential of Fe was also assessed by replacing $NiBr_2$ salts by $FeBr_3$ salts in the solution. Based on NMR characterisations, Fe-nano-clusters also lead to the formation of -lactone in nearly the same yield and selectivity as Ni, as shown in Error! Reference source not found..

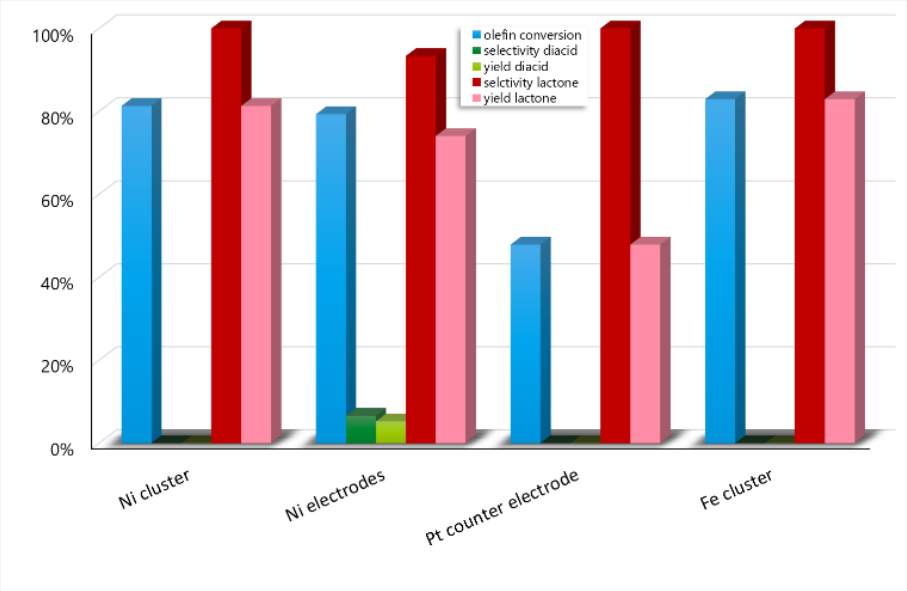


Figure 3. The impact of the electrode materials and clusters on the selectivity and calculated yields of diacid and lactones

Assessment of other olefins

We expanded the scope to other dienes that underwent β-lactonization using these optimized and convenient conditions. For that the optimized process for 3-methyl-3-(prop-1-en-2yl)oxetan-2-on (2) formation using $NiBr_2$ salt (Error! Reference source not found., **entry 12**) was used with isoprene, α-methyl styrene and myrcene as substrates (**Figure 3**, Error! Reference source not found.**).**

Table 3: The Conversion and selectivities of β-lactone and diacid by using different olefins as starting materials and at different electrochemical parameters

entry	Parameters,	U [V]	J [mA/cm^2]	conversion of olefin	Selectivities [%]		Yields* [%]	
				[%]	diacid	lactone	diacid	lactone
12	2,3-dimethyl-1,3-butadiene	-2.0	2.3	95	5	95	5	90
13	α-methyl styrene	-3.0	2.2	39	0	100	0	39
14	isoprene	-3.4	2.7	84	75	25	63	21
15	myrcene	-1.7	0.9	14	51	0	7	0

*Yields are calculated by olefin conversion multiplied by selectivity

As a result, α-methyl styrene (Error! Reference source not found.**, entry 13**), with a single double bond underwent β-lactonization showing so far the best performance. The reaction presents 100% selectivity and more than 80% diene to lactone yields, leading to 39% yield and 39% conversion. Even though our model compound 1,3-dimethylbutadiene contains a conjugated double bond, this functional group is not required for lactone formation. The analytical results from isoprene (Error! Reference source not found.**, entry 14**) show that in this case a mixture of dicarboxylic acid and β-lactone is formed. In the case of myrcene (Error! Reference source not found.**, entry 15**) the conjugated double bond reacts with CO_2, whereas the isolated double bond remains unreacted, resulting in the

formation of diacids. Experiments with isoprene and myrcene clearly show that only olefins with a methyl group on the 2 position of terminal olefins can form β- lactones.

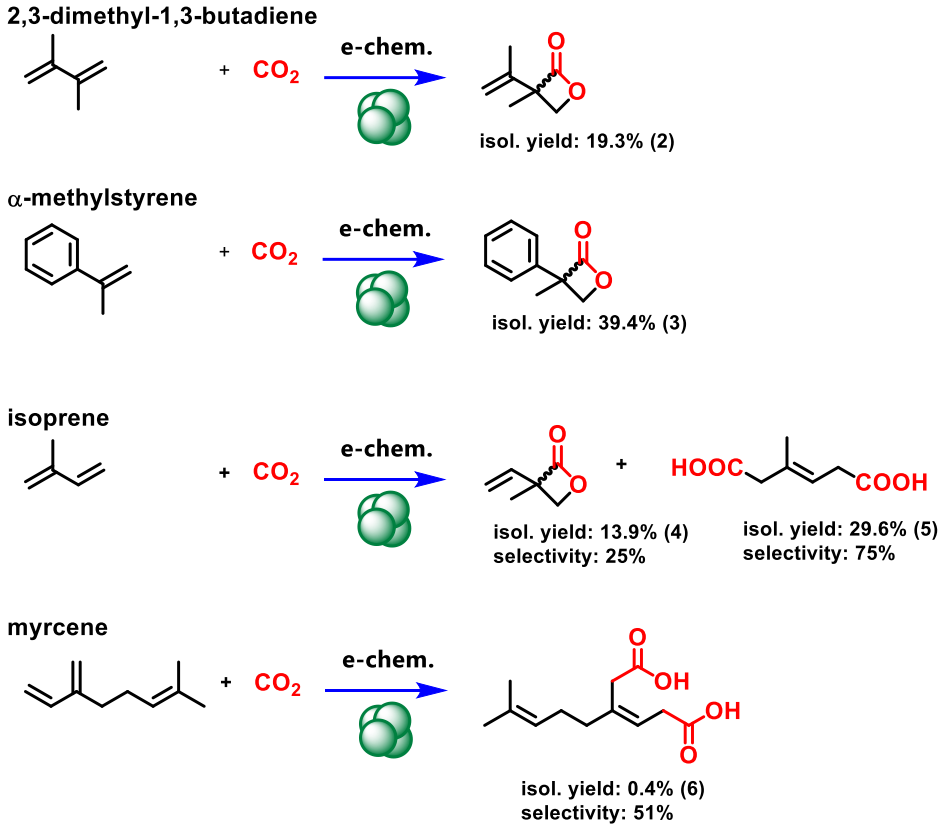


Figure 3. The observed coupling products in lactone synthesis conditions with different olefins as starting materials. While the 2,3-dimethyl-1,3-butadiene and α-methylstyrene mainly formed the β-lactone with olefin conversion of 95% with 95% selectivity and 39.% conversion with 100% selectivity, respectively, the reaction with isoprene (conversion 84%) resulted in both the diacid (selectivity 75%) and the β-lactone (selectivity 25%). Myrcene did not produce a lactone. The diacid selectivity was 51% with a conversion of 14%

Reaction mechanism

The reaction mechanism of lactone formation was investigated using density functional theory computations to understand how the combination of the applied synthesis method of nano-cluster formation and low current density enabled the β-lactonization of dienes. Due to the system's complexity, only thermodynamic data in the solution phase has been determined. A first assessment of the thermodynamics reveals that the formation of β-lactones from alkenes and CO_2 is endergonic by 27 kcal/mol. As a result, the reaction cannot occur in the absence of an external driving force. Furthermore, the overall reaction is an "electro-neutral," rather than a Faradaic reaction.

The most plausible reaction mechanism that we have identified is the following: For simplicity, the nickel cluster is here simulated as a Ni(0) complex, with its coordination sphere saturated with CO, i.e., derived from the well-known nickel tetracarbonyl complex $Ni(CO_4)$. The diene is adsorbed on the Ni nano-cluster through a formal oxidative addition (see **Figure 4**), a step that is slightly exergonic (-5.9 kcal/mol). CO_2 is then activated at the cathode at reductive potentials (-2.4 V vs SHE), forming a radical anion. This CO_2 radical anion is stabilized by -9.1 kcal/mol

via the interaction with the nickel cluster. The next step is the C-C bond formation via a reductive elimination, leading to an “open” intermediate, resembling the Ni-lactones discussed in homogeneous, mono-nuclear Ni catalysis.[47] The Ni-lactone bonds are very strong in homogeneous reactions, making catalytic reaction nearly impossible, even though coupling to electrochemistry has also been shown to be able to harness these intermediates. In our case, the reactant atoms could be interacting with sterically bulky Ni-clusters rather than just one metal centre, weakening the bonds. This “open” intermediate can then lose an electron at the anode (potential of 0.5 V vs SHE) and form the C-O bond leading to the closed lactone. The reaction mixture being stirred and the catalyst suspended in solution, this is a plausible scenario. Furthermore, this is consistent with the experimental observation of small current densities required for electrochemical β-lactone formation. Finally, the lactone desorbs into the solution (-1.8 kcal/mol), restoring the nickel catalyst. This catalytic cycle has, of course, a competitive branch that leads to dicarboxylic acids. However, this branch is completely independent of the nano-clusters (**Figure 4**) as it occurs on the solid electrode. Moreover, due to the competition between lactone and di-acid formation, high current densities favour the electrochemical reaction leading to the thermodynamically much more stable di-acid.

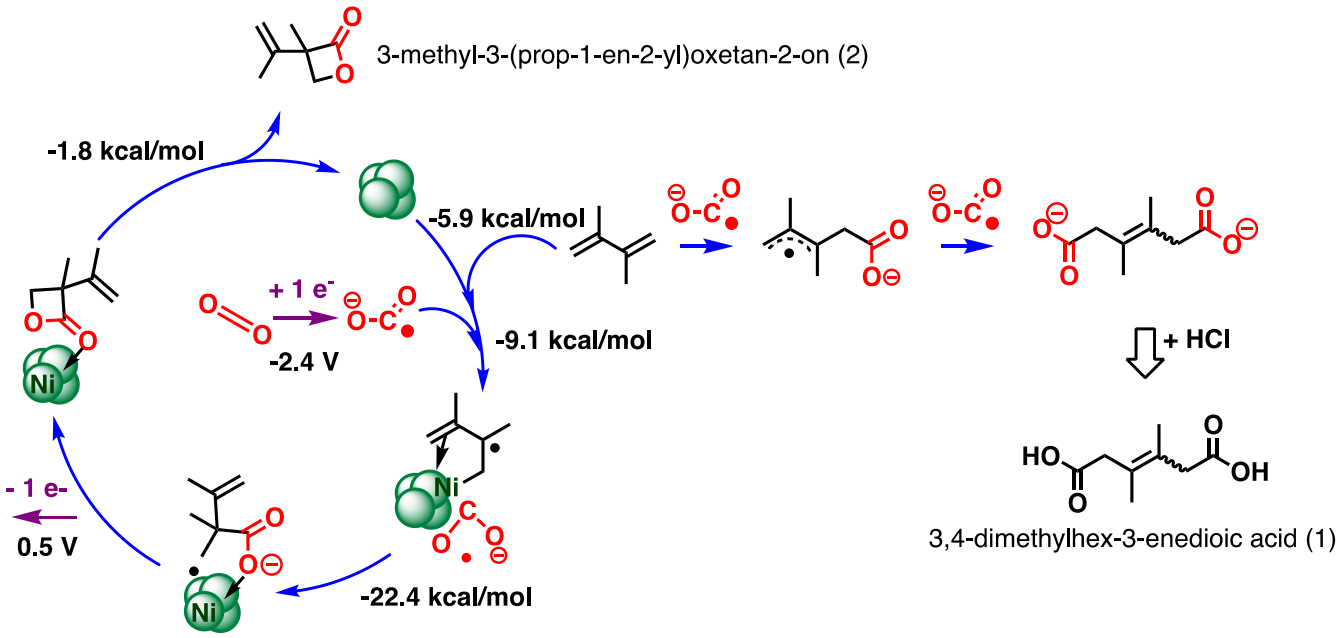


Figure 4. Schematical electrochemical mechanism for the synthesis of the diacid or β-lactone from CO_2 and diene based on the in-situ formation of Ni-nano-clusters. All free energies and potentials are computed at the M06-2X/def2-TZVP level of theory in an implicit solvent and default settings of Gaussian 09

It should be noted that the only explanation for the occurrence of the otherwise endergonic lactone formation is the electrochemical potential difference between reduction and oxidation. The large (2.9 V) electrochemical potential difference between the reduction (CO_2) and oxidation (formation of the neutral intermediate) is at the origin of the

driving force for the lactone formation: The endergonic reaction requires 27 kcal/mol to take place. The remaining 40 kcal/mol are converted into heat. Given the slow conversion rates, this electrochemical heating is not an issue. The preparation of nano-clusters without the addition of diene and/or CO_2 revealed only selectivity towards dicarboxylic acids regardless of the applied current. This finding implies that the "open" intermediate formation could only occur in the presence of reduced diene and/or CO_2 during the in-situ preparation of nano-clusters. In other words, the catalyticly active size and shape of the nano-clusters for forming the active sites appear to be produced only when the clusters are formed in the presence of CO_2 and dienes.

The overall lactonization procedure can be considered as a molecular assembling process in which three distinct individual species, a terminal olefin with a methyl group on its 2 position, carbon dioxide, and nano-clusters, are used in a well-controlled manner to build a complex organic molecule. Similarly, the formation of a quaternary centre as well as the incorporation of both a dioxide and a carboxyl group required for ring closure can be achieved in a single synthetic procedure.

Conclusions

A promising method for the formation of a specific class of β-lactones is developed in this work, which is based on a one-step room temperature and selective electro-catalytic synthesis method directly from olefins with a methyl group on the two positions of terminal olefins and CO_2. As demonstrated, the activity and selectivity of electrocatalytic reactions towards dienes or β-lactones can be modulated and optimized by varying the applied potential and current.

Aside from demonstrating an original, simple synthetic pathway that leads to the formation of a new class of stable β-lactones, the in-situ formation of Ni-clusters exhibits intriguing mechanistic differences from the related di-acid synthesis. Although the precise reaction mechanism of these β-lactone molecules remains unknown, this one-step and novel procedure allows for the highly selective preparation of β-lactones from CO_2 and available substrates, which has never been reported before. It has the potential to open new electrochemical pathways based on abundant materials, thereby shortening the synthetic steps and paving the way for "green chemistry." This method can be applied to other valuable organic reactions in the future.

Experimental

Chemicals and materials

Dry DMF (J&K Chemicals, 99.8%), 2,3-dimethyl-1,3-butadiene (J&K Chemicals, 98%), isoprene (Aldrich, 99%), α-methylstyrene (TCI, 99%), styrene (Sinopharm, 99,0%), and myrcene (Aldrich, >70%) were used as received. Tetrabutylammonium bromide (n-Bu4NBr) from J&K (purity >99+%) was dried in vacuum at 60 °C for 24 h. In order to minimize the introduction of water to the system a 0.24 mg/ml n-Bu4NBr stock solution in DMF was prepared in order to be able to add fast and under controlled atmosphere the desired amount. The cluster precursors $NiBr_2$ (J&K, 99.99%), Bis(1,5-cyclooctadiene)nickel(0) ($Ni(COD)_2$, Aldrich), Copper(I) bromide (Aldrich, 99%), and Co(II) acetate (Aldrich, 99.99%) were stored under Ar in a Schlenk flask in order to minimize the impact of air. Electrodes: Ni foam (battery grade, Shandong Heze Tianyu Technology Development Co., Ltd.), Al sheet (99.9%, Shenzheng Kejing Star Technology Company), Pt wire (99.99%, Goodfellow Cambridge Limited).

Instrumentation

A custom-made high-pressure stainless steel electrochemical reactor allows running electrochemical synthesis under inert conditions **(Figure S1).** The electrochemical measurements and synthesis were carried out with Biologic VSP-300 multichannel potentiostat/galvanostat. NMR spectra were measured with a BRUKER 300 MHz instrument. IC measurements were carried out in a DIONEX ICS-3000 with AS11-HC column. The IR spectrum was measured with a PerkinElmer Spectrum Version 10.5.1 and the TGA/DSC obtained by SDT Q600 V20.9 Build 20 instrument. The carbonate content of the reaction residue was determined using a burette apparatus for CO_2 capture as described in Pile et al.[48]

Electrochemical procedure

The reaction was carried out in a single compartment homemade high pressure electrochemical reactor that was equipped with a nickel foam working electrode (cathode), aluminium sacrificing anode and a Pt wire as reference **(Figure S1).** DMF was used as solvent and tetrabyutylammonium bromide ($n\text{-}Bu_4N$ Br) as supporting salt with a salt conzentration of about 4.2 %. Before the chemicals are filled in, the reactor is sealed and dried at 50 °C in vacuum for 12 h. 67 ml DMF and 13 ml $n\text{-}Bu_4N$ Br solution are added and degassed with Ar (0.06 gr/ml, 0.13 mol/L). Then 0.07 to 0.09 M 2,3-dimethyl-1,3-butadiene is introduced, the reactor is closed and the pressure is increased by adding CO_2. Pressure is varied between 20 and 30 bar. Once the pressure is stable and the reactor cooled down to 25 °C, the electrodes are connected to the potentiostat. Cyclic voltammetry experiments were carried out before and after electrochemical synthesis. Scan rate was 50 mV/s. Chronopotentiometric experiments were carried out at a potential between -2.2 V and -1V. The current density was set in a range between 1 and 10 mA/cm^2. In order to be able to achieve the low current needed for the cluster synthesis while keeping the required potential, a tunable resistor of about 100 Ω is placed between the working electrode and potentiostat. After synthesis, DMF was removed under vacuum and a burette apparatus for CO_2 capture determined the carbonate content. The

residue was acidified with 2 M HCl for 6 h. Oxalic acid and formic acid were measured by IC measurements before the product was extracted with dimethyl ether and dried over Na_2SO_4. After filtration and removing of the ether, the composition of the organic phase is evaluated by ^1H and ^{13}C NMR in DMSO.

Besides the diacid and lactone products, other observed side products are formic acid due to traces of water, oxalic acid and inorganic carbonate. Monocarboxylated acids were never observed.

Nano-cluster formation

$NiBr_2$ is used as a source of metal cation. After the addition of all reactants and CO_2 pressure stabilization at 20 barg in the solution and prior to electrochemical synthesis, chronoamperometry (CA) was performed at potentials between -2 and -2.5 V at an average current density of -1.9 mA/cm^2 for 1500 s. The clusters are then stabilized during 5000 s at the open circuit voltage prior to the electro-organic synthesis step. The so prepared Ni-cluster reaction-solution is directly used for electrochemical lactone synthesis.

Characterization of Reactants and Products by NMR

2,3-dimethyl-1,3-butadiene: ^{1}H-NMR (300 MHz, DMSO-d6): δ 5.04 (d, J = 20.2 Hz, 4H), 1.87 (s, 6H); $^{13}C\{1H\}$ NMR (300 MHz, DMSO-d6): δ 142.7, 113.2, 20.1.

3,4-dimethyl-3-hexene-1,6-dioic acid (1): ^{1}H-NMR (300 MHz, DMSO-d6): δ 12.1 (s, 2H), 2.98 (s, 4H), 1.68 (s, 6H); $^{13}C\{1H\}$ NMR (300 MHz, DMSO-d6): δ 173.0, 125.7, 41.2, 19.4.

3-methyl-3-(prop-1-en-2-yl)oxetan-2-on (2) : ^{1}H-NMR (300 MHz, DMSO-d6): δ 5.0 (d, J = 13.4 Hz 2H), 4.38 (ABq, J = 33.1 Hz, 8.5Hz , 2H), 1.77 (s, 3H), 1.56 (s, 3H); $^{13}C\{1H\}$ NMR (300 MHz, DMSO-d6): δ 154.06, 143.85, 112.00, 84.82, 73.18, 23.29, 17.86.

α-methyl styrene: ^{1}H-NMR (300 MHz, DMSO): δ 7.48 (m, 2H), 7.35 (m, 3H), 5.42 (1H), 5.09 (s, 1H), 2.10 (s, 3H).

3-methyl-3-phenyloxetan-2-one (3): ^{1}H-NMR (300 MHz, DMSO): δ 7.35 to 7.23 (m, 5H), 2.91 (ABq, J=79.5 Hz, 16.4 Hz, 2H), 1.57 (s, 3H); $^{13}C\{1H\}$ NMR (300 MHz, DMSO-d6): δ 162.8, 144.0, 128.9, 127.2, 126.1, 47.9, 43.3, 23.9.

Isoprene: ^{1}H-NMR (300 MHz, DMSO): δ 6.44 (dd, J = 17.3 Hz, J = 11.1 Hz, 1H), 5.15 (dd, 2H), 5.02 (s, 2H), 1.79 (s, 3H); $^{13}C\{1H\}$ NMR (300 MHz, DMSO-d_6): δ 141.8, 117.2, 114.3, 17.6.

3-methyl-3-vinyloxetan-2-one (4): ^{1}H-NMR (300 MHz, DMSO): δ 6.0 (dd, 1H), 5.1 (d, 1H), 5.04 (d, 1H), 4.83 (d, 2H), 1.27 (s, 3H).

3-methylhex-3-enedioic acid (5): ^{1}H-NMR (300 MHz, DMSO): δ 5.38 (y, 1H), 2.98 (d, 2H), 2.95 (s, 2H), 1.62 or 1.71 (s, 3H).

Myrcene: ^{1}H-NMR (300 MHz, DMSO): δ 6.37 (dd, J = 7.6 Hz, J = 10.7 Hz, 1H), 5.25 (d, J = 17.6 Hz, 1H), 5.08 (d, J = 10.7Hz, 2H), 5.03 (d, J = 8.8 Hz, 2H), 2.15 (m, 4H), 1.65 (s, 3H), 1.56 (s, 3H); ^{13}C{1H} NMR (300 MHz, DMSO-d_6): δ 145.4, 138.7, 131.0, 124.0, 116.2, 113.5, 30.9, 26.2, 25.5, 17.5.

3-(4-methylpent-3-en-1-yl)hex-3-enedioic acid (6): ^{1}H-NMR (300 MHz, DMSO): δ 5.07 (t, J = 7.1 Hz, 1H), 4.72 (t, J = 4.8 Hz, 1H), 3.05 (d, 2H), 3.00 (s, 2H), 2.9 (m, 4H), 1.63 (s, 3H), 1.55 (s, 3H).

Keywords: CO_2 valorisation • β-lactone • electrochemistry • in-situ nano-cluster formation

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Graphical abstract: