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Vanillin, a promising biobased building-block for monomer synthesis

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Vanillin was used as a renewable building-block to develop a platform of 22 biobased compounds for polymer chemistry. Vanillin-derived biobased monomers bearing epoxy, cyclic carbonates, allyl, amine, alcohol and carboxylic acid moieties were synthesized. They can be used, among many others, in epoxy, polyester, polyurethanes, and Non-Isocyanate PolyUrethanes (NIPU) polymer synthesis. The epoxy-functionalized compounds were synthesized under solvent-free conditions and are original biobased aromatic epoxy monomers. Cyclic carbonates were prepared through a catalytic reaction between epoxy compounds and CO_2. Thiol–ene reactions allowed the functionalization of allylated compounds with amines, acids and alcohols. The amine-functionalized compounds are, to our knowledge, the first non-aliphatic biobased amine hardeners, usable either in epoxy or NIPU materials.

Introduction

Recent years have witnessed an increasing demand for renewable resource-derived polymers (biobased polymers) owing to increasing environmental concerns and restricted availability of petrochemical resources.[1,2] Some solutions are already industrially available but most of these biobased polymers are aliphatic or cycloaliphatic polymers, for instance derived from cellulose,[1] starch[1] or triglycerides.[3] However, many key commercial chemicals are aromatic compounds, ultimately derived from petrochemical feedstocks.[2]

More recently, great attention was paid to renewable resources-derived thermosetting materials,[4] especially because they are crosslinked polymers and thus cannot be recycled. Also, most of the thermosetting materials contain aromatic monomers, able to confer high mechanical and thermal properties to the network. Moreover, some base chemicals used nowadays have proven harmful and need to be replaced. For instance, bisphenol A is extensively used for the manufacturing of epoxy resins even though it is a reprotoxic substance.[5] Therefore, access to biobased and non-harmful aromatic monomers is one of the main challenges of the years to come.

The three main sources of renewable aromatic compounds available are cashew nutshell liquid, polyphenols and lignin. Even though there have been some very interesting studies based on cardanol[6] or natural flavonoids[7,8] to synthesize promising materials, lignin is the most abundant feedstock.[9] Lignin is an amorphous cross-linked polymer that gives structural integrity to plants, making up 25 to 35% of woody biomass.[10] Thus, depolymerization of lignin is an alluring route to gain access to biobased aromatics needed by the chemical industry. Unfortunately, this route is deceptive. Despite extensive research,[11] there are very few reports on efficient ways of recovering such aromatic products.

The only notable commercial process has been the historical production of vanillin from lignosulfonates contained in the "brown liquor", a by-product of the sulfite pulping paper industry. Even though this process uses cheap and available waste materials, its use declined because of environmental concerns. Nowadays, Solvay dominates the vanillin market using the petroleum-based catechol–guaiacol process. 85% of the vanillin is produced by this method and 15% still from lignin.[12,13]

Most recently, however, lignin-to-vanillin routes regained a lot of interest[12–14] with technical advances in processes[15] as well as waste management. For instance, Borregaard, the second largest vanillin producer in the world and the only one with a vanillin-from-lignin process, employs an ultrafiltration technology, achieving a reduction in waste stream volumes.[16] Therefore, instead of expecting various biobased aromatics from lignin depolymerization, which is not a mature technology, the improvement of lignin-to-vanillin processes and the use of vanillin as a biobased building-block for polymer chemistry seem a better perspective.

Even though the lignin-derived vanillin is becoming relatively easily accessible, still there are only a handful of reports

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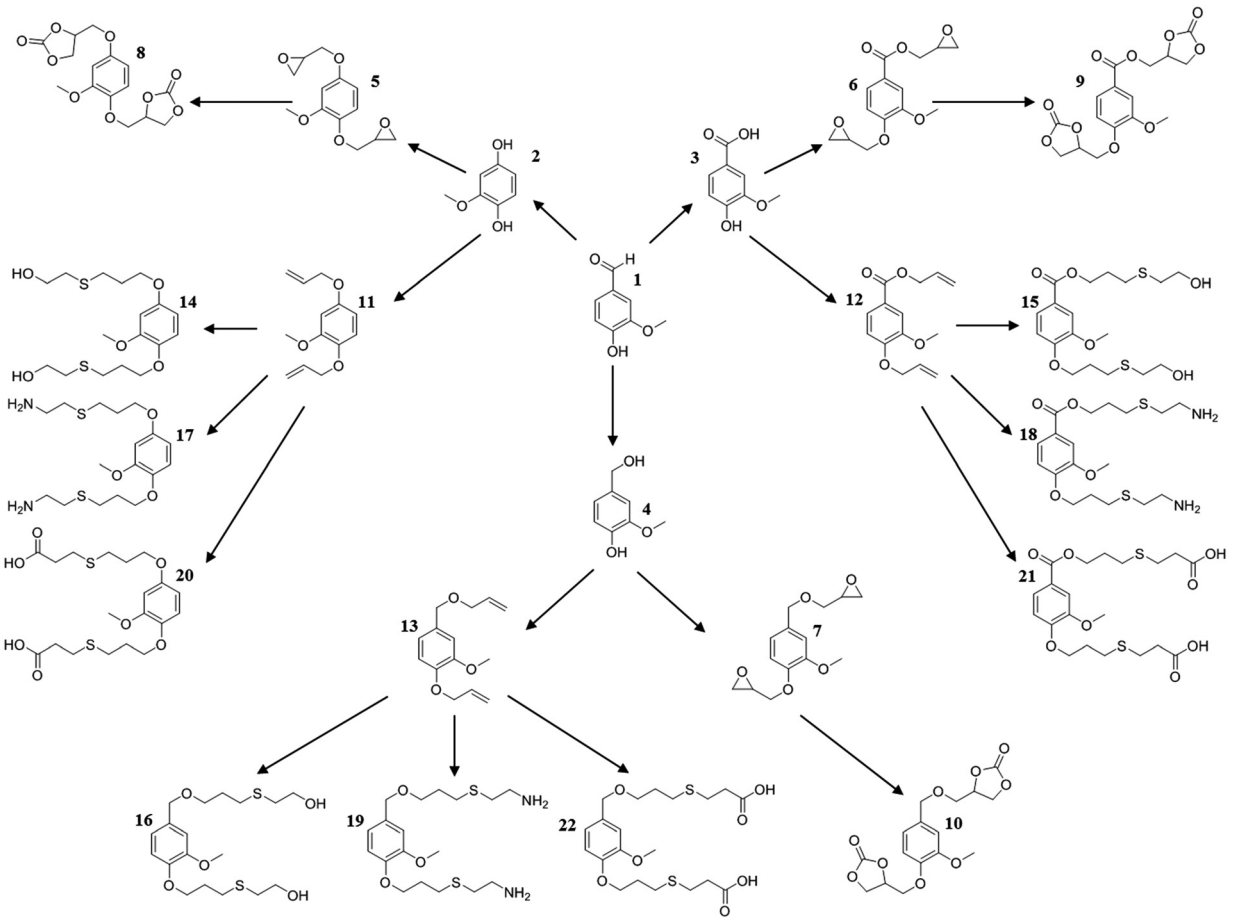
on attempts to utilize vanillin as monomers for biobased polymer synthesis. Amarasekara *et al.* have reported the dimerization and electrochemical reductive polymerization with horseradish peroxidase.[17] The Schiff base synthesized was used for metal ion chelation applications.[18] Schiff bases from vanillin were also prepared by Issam *et al.* and transformed into epoxies in a second step.[19] Concerning epoxy compounds, Aouf *et al.* prepared the allylated vanillic acid and worked on its epoxidation by a chemo-enzymatic process with *Candida antarctica* lipase.[20] Koike described an interesting process allowing the synthesis of an epoxy monomer from vanillin.[21] Other teams reported the synthesis of various biobased polymers from vanillin. Thus, Meier *et al.* reported the synthesis of polymers from vanillin and fatty acids by acyclic diene metathesis (ADMET).[22] Starting from vanillin, Mialon *et al.* synthesized polyesters such as polydihydroferulic acid[23] and polyethylene vanillate.[24] Photoactive liquid crystalline polyesters and polyethers were also prepared from vanillin.[25,26] An original benzoxazine monomer was prepared from vanillin and furfurylamine by Sini *et al.* and then polymerized.[27] Additionally, vanillin was methacrylated and used in the preparation of UV-curable palladium-chelating chitosan derivatives.[28] Vanillin methacrylate also replaced styrene in vinyl-ester resins for composite application.[29] Composites were synthesized directly from vanillin, sorbitol, and pyrogallol with wood flour.[30]

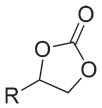
From the few but interesting studies cited, it is clear that vanillin has a huge potential to meet the aforementioned challenge concerning biobased monomers. It is biobased, potentially abundantly available and does not compete with edible resources. Its aromatic structure could provide the desired thermal and mechanical properties to materials and its different substituents led us to consider it to be a versatile biobased platform chemical. Our approach in this work was thus to synthesize from vanillin a wide range of difunctional monomers directly usable in polymer synthesis. These synthesis routes were chosen in order to optimize the yields and with a reduced number of steps, to show the industrial potential of this platform.

We designed this platform with three vanillin derivatives as base chemicals, owing to their different oxidation states. This choice was based on the fact that lignin depolymerization often requires harsh oxidative or reductive conditions.[31] Thus, it is mandatory to consider not only vanillin itself, as it is common in the literature, but also its different oxidative states as potentially available. On the one hand, a vanillin **1** oxidation leads to vanillic acid **3** or even to a methoxyhydroquinone **2** in the case of a decarboxylation (strong oxidative and



Scheme 1 Vanillin platform for polymer synthesis.

Table 1 Functions present in the platform and their use in polymer chemistry

Function of monomers	Compounds	Targeted polymers
	**5, 6, 7**	Epoxy resins
	**8, 9, 10**	PolyHydroxyUrethanes (PHUs); polycarbonates
	**11, 12, 13**	Polymers obtained by radical polymerization
	**14, 15, 16**	PolyUrethanes (PUs), polyesters, polyacrylates, polycarbonates
	**17, 18, 19**	Epoxy resins, PHUs, polyimides, polyureas, polyamides
	**20, 21, 22**	Epoxy resins, polyamides, poly(vinyl-esters), polyesters

alkaline conditions[32]). On the other hand, reduction leads to vanillyl alcohol **4**. Our team functionalized these three molecules, transforming them into a number of original biobased monomers bearing well-known polymerizable functions and thus creating the above-mentioned platform shown in Scheme 1. Many of these compounds were prepared for the first time.

The functions introduced in this platform and the types of polymers in which they could be used are summarized in Table 1.

Results and discussion

Platform base chemicals

Among the three platform base chemicals, vanillic acid **3** and vanillyl alcohol **4** are quite common commercial compounds. However, to the best of our knowledge, 2-methoxyhydroquinone **2** is not commercially available. It was thus prepared in 97% yield from vanillin by the Dakin reaction, ultimately leading to one carbon loss. The reaction proceeds *via* the mechanism shown in Scheme 2.

Sodium percarbonate dissociates in solution into H_2O_2 and carbonate anions. As the solution is basic, a hydroperoxide anion can exist. The reaction starts with a nucleophilic addition of this hydroperoxide anion to the aldehyde carbonyl. The final acidification of the mixture is important for two reasons. Firstly, the pH of the solution becomes acidic, and carbonates and hydroperoxide anions no longer exist in solution, thus stopping any further reaction. Secondly, the aqueous phase must be acidic for the phenol form to predominate over the phenolate one in order to perform the extraction efficiently.

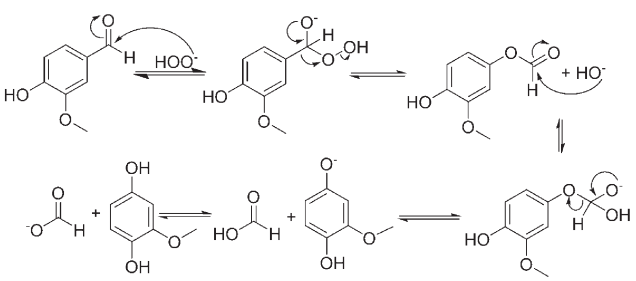
The protocol used[32] is very efficient and the handling simple. Moreover, the oxidation reagent used, sodium percarbonate, has major advantages: it is inexpensive, large-scale available as it is extensively used in the detergent industry as a bleaching agent, easier to handle than a classic H_2O_2 solution and, finally, respects sustainable development principles due to its safety and environmental innocuity.

Glycidylation reactions

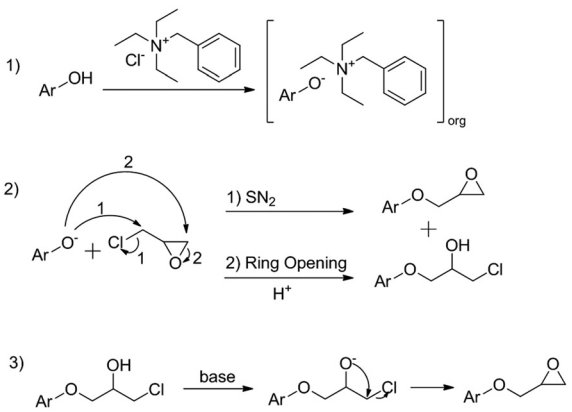
Glycidyl ethers **5**, **6** and **7** were obtained respectively from the three base chemicals **2**, **3**, and **4** in very good yields (≥87%). We are the first, to our knowledge, to synthesize compounds **5** and **7**. In a previous paper, Aouf *et al.* proved that aromatic hydroxyl and acid functions readily react with epichlorohydrin in the absence of a solvent.[33] We adapted this method for the synthesis of **5** and **6**. The reaction mechanism is explained in Scheme 3.

In a first step, a phase transfer catalyst (triethylbenzylammonium chloride – TEBAC) is used to allow the phenolate ion to exist in organic solution. In a second step, this phenolate ion reacts with epichlorohydrin *via* two possible mechanisms, namely SN_2 and ring opening. SN_2 gives the expected glycidylated product and ring opening leads to a chlorinated intermediate. In a third step, this chlorinated intermediate is closed by an intramolecular SN_2 reaction in the presence of an aqueous solution of NaOH and a phase transfer catalyst.

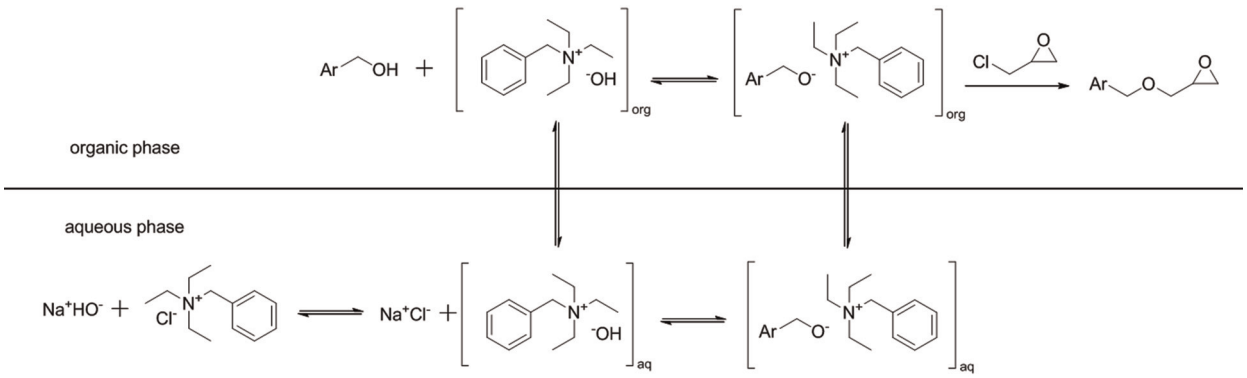
The synthesis of **7** starting from **4** was attempted with this method. **4** possesses both a phenol and a benzyl alcohol. Glycidylation only occurred on the phenol, and not on the benzyl alcohol. This was explained by the fact that protons from



Scheme 2 Mechanism of the vanillin Dakin oxidation.



Scheme 3 Phenol glycidylation mechanism under solvent-free conditions.



Scheme 4 Mechanism of phenol glycidylation by a phase transfer catalysis system.

phenols are more acidic than protons from aliphatic alcohols. Thus, contrary to phenolates, benzyl alcoholates cannot form an ion pair with the phase transfer catalyst to exist in the organic medium. It is worth noting that although this reactivity difference is problematic here, it could be an advantage in another context. In our case, **7** was synthesized using a biphasic phase transfer catalysis system.[34] The mechanism is shown in Scheme 4.

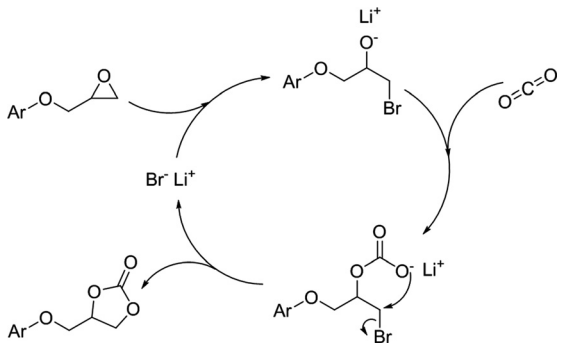
Careful temperature control is mandatory as the reaction is exothermic and any rise of temperature resulted in a colored, crosslinked product.

These reactions do not require organic solvents since epichlorohydrin is used as a reactive solvent. Epichlorohydrin was employed as it is an industrial biobased compound *via* the Epicerol® process from Solvay. Epoxy compounds **5**, **6** and **7** have potential uses in high performance epoxy resins and composites as they are biobased aromatic diglycidyl ethers. Indeed, they are structurally similar to the current petrobased epoxy monomers. They need to be tested as bisphenol A substitutes in terms of safety and material performances.

Carbonation reactions

Cyclic carbonate compounds **8**, **9** and **10** were respectively synthesized from the epoxy compounds **5**, **6**, and **7** previously obtained. Compounds **8** and **10** were obtained quantitatively. In the case of **9**, undetermined side products were detected by ^{1}H NMR, making this synthesis less interesting from an industrial standpoint. However, there is, as far as we know, no other description of compounds **8**, **9** and **10**. These bifunctional cyclic carbonates were obtained by a LiBr-catalyzed CO_2 insertion into the oxirane rings[35] as shown in Scheme 5.

The main advantage of this reaction is the use of CO_2 as reactant. From a sustainable chemistry point of view, two major challenges concern the polyurethane industry. The first one, true for the whole polymer industry, is to switch from petrobased to biobased resources. The second one, more specific to polyurethanes, is to avoid the use of isocyanate compounds since most of them (methylene diisocyanate – MDI, toluene diisocyanate – TDI) are highly toxic or CMR, and are synthesized from phosgene, also highly toxic. Therefore, NIPU (Non-Isocyanate PolyUrethane) systems have received a great deal of interest over the past few years. These systems are actually synthesized by reaction between poly(cyclic carbonates) with polyamines,[35] leading to polyhydroxyurethanes (PHUs). As these systems are shifting from academic studies to industrial use, there is a growing need for bis(cyclic carbonates) monomers and especially aromatic ones in substitution to MDI or TDI for the synthesis of linear polymers. We thus synthesized **8**, **9** and **10** which are biobased, aromatic bis(cyclic carbonates) usable in NIPU systems.



Scheme 5 Cyclic carbonate synthesis from an epoxy compound.

Allylation reactions

Allylated compounds **11**, **12** and **13** were respectively synthesized from base chemicals **2**, **3** and **4**. A method used for the allylation of gallic acid has already been reported by our team.[8] Compounds **11** and **12** were prepared quantitatively using this method. A phenolate (or carboxylate) is first formed by the action of suspended potassium carbonate K_2CO_3. This phenolate (or carboxylate) is then allylated by an easy nucleophilic attack on allyl bromide. As in the case of glycidylation, the benzylic alcohol moiety in **4** is less reactive than phenols or benzoic acids. Compound **4** was thus allylated by using the same phase transfer catalysis system. The mechanism is also the same as the one described in Scheme 4, the only difference being the use of allyl bromide instead of epichlorohydrin. It was found that phase transfer catalysis is a mild and efficient process for the synthesis of **13** (86% yield).

Allyl bromide is not a biobased compound. Since allylated compounds can undergo radical polymerization and thiol–ene click chemistry, compounds **11**, **12** and **13** are therefore essential building blocks to establish our vanillin-based platform for polymer chemistry.

Alcohol functionalization

Alcohol-functionalized compounds **14**, **15** and **16** were obtained in yields ≥90% under solvent-free conditions by thiol–ene "click" addition of mercaptoethanol to allylated compounds **11**, **12** and **13** respectively. This work is the first example, to the best of our knowledge, to report the synthesis of compounds **14**, **15** and **16**.

Click chemistry is a concept now well established and has received a lot of attention lately, especially in the field of sustainable chemistry. Indeed, the click chemistry concepts of efficient, versatile, and safe procedures with high atom economy fit sustainable chemistry principles. Click chemistry reactions are thus increasingly applied to renewable resources.[36]

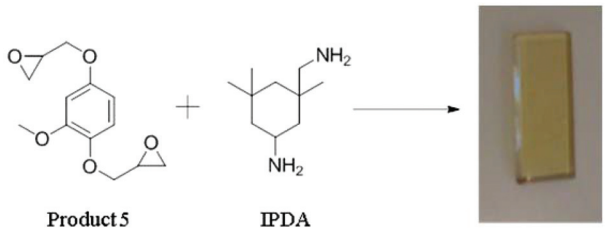
Thiol–ene coupling is considered as a click chemistry reaction and has been extensively used in the polymer field.[37] It consists in the radical addition of a thiol onto a C–C double bond. This coupling was for instance used by our team to synthesize new biobased polyols from vegetable oils. Thiol–ene coupling displays high yields and outstanding functional group tolerance under simple reaction conditions. The reaction can be initiated by either heat or UV irradiation, as in our case.

Molecules **14**, **15** and **16** are alcohol-functionalized biobased compounds bearing an aromatic ring. The aromatic ring provides better thermo-mechanical properties to the material than an aliphatic structure. They also bear primary aliphatic alcohols, making them very reactive. Molecules **14**, **15**, and **16** could therefore bring interesting properties to polyesters or to PU formulations.

Amine functionalization

Amine-functionalized compounds **17**, **18** and **19** were synthesized by thiol–ene addition of cysteamine hydrochloride onto **11**, **12** and **13** respectively in yields ≥88%. Compounds **17**, **18** and **19** are also, as far as we know, described here for the first time. Cysteamine hydrochloride was preferred over cysteamine because the amine moiety catalyzes the formation of disulfide bonds. Interestingly, thiol–ene addition was slower with cysteamine hydrochloride than with mercaptoethanol. Amine-functional compounds were obtained by simple deprotonation of the ammonium in a basic aqueous solution followed by an extraction with an organic solvent.

17, **18** and **19** are of great interest for epoxy thermosets and NIPU manufacturing as they are biobased aromatic compounds bearing two highly reactive primary amines. They can thus react with epoxy and cyclocarbonate moieties. Moreover, hardeners with an aromatic structure will improve thermo-mechanical properties. Concerning epoxy thermosets, good thermo-mechanical properties are one of their characteristic features. As for NIPU systems, tunable properties are needed to fit to the application. These compounds are, to our knowledge, the first non-aliphatic and biobased amine hardeners. They could thus prove very useful from an industrial standpoint.



Scheme 6 Material prepared from **Product 5** and IPDA.

Carboxylic acid functionalization

Acid-functionalized compounds **20**, **21** and **22** were synthesized by thiol–ene addition of 3-mercaptopropionic acid onto **11**, **12** and **13** respectively under solvent-free conditions. To the best of our knowledge, compounds **20**, **21** and **22** are not mentioned in the literature.

In the first place, the reaction was attempted with thioglycolic acid and was much faster but gave rise to unwanted side-products. The literature reports such side-products, especially thioesters, in the case of thioglycolic acid.[38] Thus, the use of 3-mercaptopropionic acid was preferred over thioglycolic acid.

This reaction was slower than the other thiol–ene reactions performed, especially in the case of **11** where only 68% were converted to **20**. **12** and **13** gave good conversions. However, no side-products were detected.

Compounds **20**, **21** and **22** also bear an aromatic ring that may improve the thermo-mechanical properties of materials. They are dicarboxylic acids and can thus be used as epoxy resin hardeners and also as monomers in biobased polyesters.

Example of the material synthesized

Each type of compound is currently evaluated for the synthesis of materials, especially NIPUs and epoxy polymers. These studies will be reported in detail in future articles. However, as an example of the potential use of these compounds, we chose to prepare an epoxy material (Scheme 6) from **Product 5**. The amine hardener chosen was the one most reported in the literature, IsoPhorone DiAmine (IPDA).

Preliminary DSC results indicate a T_g of 117 °C for this material. By improving the formulation and the process, the T_g could reach a value close to the one of the epoxy polymer prepared from DiGlycidylEther of bisphenol A (DGEBA) and IPDA, namely 158 °C.[39] This material is the one most described in the literature and the one most used in industry. However, DGEBA is derived from bisphenol A, a reprotoxic substance,[5] and thus needs to be replaced. The material prepared from **Product 5** is a high-T_g, biobased alternative to the DGEBA–IPDA system that will be investigated in future studies.

Experimental

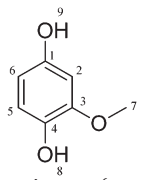
Materials and methods

Vanillin (99%) and vanillic acid (99%) were purchased from ABCR. Vanillyl alcohol (98%), sodium percarbonate $Na_2CO_3{\cdot}1.5H_2O_2$ (available H_2O_2 20–30%), triethylbenzylammonium chloride (TEBAC) (99%), LiBr (99%), mercaptoethanol (>99%), thioglycolic acid (>99%), 3-mercaptopropionic acid (>99%), potassium carbonate K_2CO_3 (>99%), allyl bromide (99%), IPDA (>99%), anhydrous sodium sulfate Na_2SO_4 (99%) and HCl (37.5 wt%) and all solvents used (>99.5%) were purchased from Sigma-Aldrich. Cysteamine hydrochloride (>97%) and epichlorohydrin (>99%) were purchased from Fluka. Sodium hydroxide, NaOH (99%), was purchased from Fisher. All reactives were used as received.

^{1}H and ^{13}C (APT mode) NMR spectra were recorded on a 400 MHz Brucker Aspect Spectrometer at room temperature. Deuterated solvents used are given for each molecule. Chemical shifts are in ppm. Silica gel flash chromatography was performed on a Grace Davison Reveleris device. UV irradiation was performed in a Rayonet RPR-200 UV reactor equipped with a cooling fan and 16 lamps of 35 W each with λ_{max} = 254 nm. A 50 mL Paar autoclave equipped with an overhead stirrer was used for carbonation reactions. MS measurements were performed on a Waters Synapt G2-S High Resolution Mass Spectrometer (HRMS) equipped with an ESI ionization source. DSC analyses were carried out on a NETZSCH DSC200 calorimeter at 20 °C min^{-1}.

Synthesis of methoxyhydroquinone 2 from vanillin 1

A two-necked round-bottomed flask was charged with a solution of vanillin (0.25 mol L^{-1}, 1.0 eq.) in THF. Deionized water (40% vol.) was added. The mixture was degassed with nitrogen. Sodium percarbonate ($Na_2CO_3{\cdot}1.5H_2O_2$, 1.1 eq.) was then added by portions under nitrogen and agitation. The reaction was conducted for 3 hours at room temperature. Portions of a HCl solution (0.1 mol L^{-1}) were added to the mixture under vigorous stirring until pH = 3 to quench the reaction. THF was evaporated and the aqueous phase was extracted with ethyl acetate. The organic phases were collected, washed with brine, dried on anhydrous Na_2SO_4 and ethyl acetate was removed under reduced pressure.



Product 2: methoxyhydroquinone (97%, m.p. 88 °C).

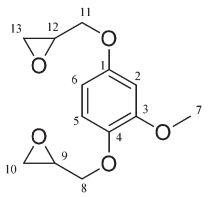
^{1}H NMR (400.1 MHz, acetone-d_6, ppm) δ: 3.77 (s, 3H, H_7); 6.27 (dd, $^3J_{H_6H_5}$ = 8.4 Hz, $^4J_{H_6H_2}$ = 2.6 Hz, 1H, H_6); 6.46 (d, $^4J_{H_2H_6}$ = 2.6 Hz, 1H, H_2); 6.63 (d, $^3J_{H_5H_6}$ = 8.4 Hz, 1H, H_5); 6.86 (broad s, 1H, H_8); 7.73 (broad s, 1H, H_9).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 56.38 (s, C_7); 101.40 (s, C_2); 107.64 (s, C_6); 116.13 (s, C_5); 140.71 (s, C_4); 149.07 (s, C_3); 151.82 (s, C_1).

HRMS (m/z, AP+): calculated: 140.0473; found: 140.0473.

Procedures for glycidylation (5, 6, 7)

This protocol was used for the preparation of **5** and **6** from **2** and **3**. A round-bottomed flask was charged with **2** or **3** (1.0 eq.) and TEBAC (0.1 eq.). Epichlorohydrin (10.0 eq.) was added and the mixture was stirred for 1 hour after reaching 80 °C. The solution was then cooled down to room temperature. An aqueous solution of TEBAC (0.1 eq.) and NaOH (4.0 eq., 5.0 mol L^{-1}) was added and the mixture was stirred for 30 minutes at room temperature. Ethyl acetate and deionized water were then added. The mixture was stirred and the aqueous phase was extracted with ethyl acetate. Organic phases were combined, rinsed with brine and dried on anhydrous Na_2SO_4. Ethyl acetate and epichlorohydrin excess were removed using a rotary evaporator. Further purification was achieved by silica gel flash chromatography using a hexane–ethyl acetate gradient as an eluent.

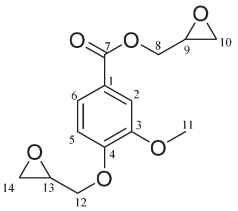


Product 5: 2,2′-(((3-methoxy-1,4-phenylene)bis(oxy))bis(methylene))bis(oxirane) (87%, m.p. 87 °C).

^{1}H NMR (400.1 MHz, acetone-d_6, ppm) δ: 2.66 (m, 2H, H_{10a}, H_{13a}); 2.81 (m, 2H, H_{10b}, H_{13b}); 3.27 (m, 2H, H_9, H_{12}); 3.81 (m, 2H, H_{8a}, H_{11a}); 3.81 (s, 3H, H_7); 4.23 (m, 2H, H_{8b}, H_{11b}); 6.43 (dd, $^3J_{H_6H_5}$ = 8.8 Hz, $^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.63 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.88 (d, $^3J_{H_5H_6}$ = 8.8 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 44.91 (s, C_{10}, C_{13}); 51.16 (s, C_{12}); 51.32 (s, C_9); 56.63 (s, C_7); 71.09 (s, C_{11}); 72.89 (s, C_8); 102.57 (s, C_2); 105.90 (s, C_6); 117.37 (s, C_5); 144.29 (s, C_4); 152.51 (s, C_3); 155.66 (s, C_1).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 253.1079; found: 253.1076.



Product 6: oxiran-2-ylmethyl 3-methoxy-4-(oxiran-2-ylmethoxy)-benzoate (95%, m.p. 77 °C).

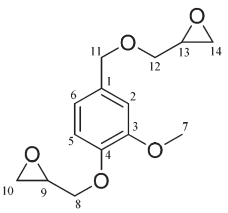
^{1}H NMR (400.1 MHz, $CDCl_3$, ppm) δ: 2.72 (m, 1H, H_{14a}); 2.77 (m, 1H, H_{10a}); 2.91 (m, 2H, H_{10b}, H_{14b}); 3.34 (m, 1H, H_{13}); 3.40 (m, 1H, H_9); 3.92 (s, 3H, H_{11}); 4.09 (m, 2H, H_{8a}, H_{12a}); 4.34 (dd,

1H, H_{12b}); 4.64 (m, 1H, H_{8b}); 6.94 (d, $^3J_{H_5H_6}$ = 8.4 Hz, 1H, H_5); 7.57 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.69 (dd, $^3J_{H_6H_5}$ = 8.4 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ: 44.68 (s, C_{10}); 44.78 (s, C_{14}); 49.52 (s, C_9); 49.90 (s, C_{13}); 56.04 (s, C_{11}); 65.37 (s, C_8); 69.86 (s, C_{12}); 112.29 (s, C_5); 112.63 (s, C_2); 122.85 (s, C_1); 123.65 (s, C_6); 149.05 (s, C_3); 152.16 (s, C_4); 165;92 (s, C_7).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 281.1025; found: 281.1025.

For the preparation of **7** from **4**, a phase transfer catalysis system was used. A round-bottomed flask was charged with **4** (1.0 eq.) and TEBAC (0.1 eq.). Epichlorohydrin (10.0 eq.) was added and the mixture was stirred for 4 hours until obtention of a limpid pink solution. This solution was cooled down to 0 °C with an ice bath. A NaOH solution (33 wt%, 15.0 eq.) in deionized water was prepared and poured into the cold mixture under vigorous stirring. The reaction was conducted overnight at room temperature (the ice bath was left to melt over time). Deionized water was added to the mixture to dilute 4 times the NaOH solution. An equal volume of ethyl acetate was added. The mixture was stirred and the aqueous phase was extracted 2 more times with ethyl acetate. Organic phases were combined, rinsed with brine and dried on anhydrous Na_2SO_4. Ethyl acetate and epichlorohydrin excess were removed using a rotary evaporator. Further purification was achieved by silica gel flash chromatography using a hexane–ethyl acetate gradient as an eluent.



Product 7: 2-((3-methoxy-4-((oxiran-2-ylmethoxy)methyl) phenoxy)methyl)oxirane (89%, m.p. 53 °C).

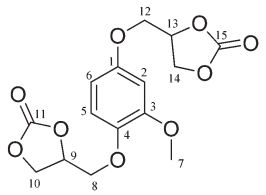
^1H NMR (400.1 MHz, acetone-d_6, ppm) δ: 2.53 (dd, 1H, H_{14a}); 2.69 (m, 2H, H_{10a}, H_{14b}); 2.81 (m, 1H, H_{10b}); 3.10 (m, 1H, H_{13}); 3.30 (m, 2H, H_9, H_{12a}); 3.73 (dd, 1H, H_{12b}); 3.82 (s, 3H, H_7); 3.87 (dd, 1H, H_{8a}); 4.28 (dd, 1H, H_{8b}); 4.47 (d, 2H, H_{11}); 6.86 (dd, $^3J_{H_6H_5}$ = 8.0 Hz, $^4J_{H_6H_2}$ = 1.6 Hz, 1H, H_6); 6.94 (d, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5); 6.98 (d, $^4J_{H_2H_6}$ = 1.6 Hz, 1H, H_2).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 44.16 (s, C_{14}); 44.49 (s, C_{10}); 50.76 (s, C_9); 51.28 (s, C_{13}); 56.16 (s, C_7); 71.39 (s, C_8); 71.82 (s, C_{12}); 73.42 (s, C_{11}); 112.91 (s, C_5); 114.76 (s, C_2); 120.99 (s, C_6); 132.93 (s, C_1); 148.86 (s, C_4); 150.75 (s, C_3).

HRMS (m/z, ASAP$^-$, [M$^-$]): calculated: 266.1153; found: 266.1154.

Procedures for carbonation (8, 9, 10)

Epoxy-functionalized compound **8**, **9** or **10** (1.0 eq.) and LiBr (0.05 eq.) were stirred in acetone (35 mL) and introduced into the autoclave. The atmosphere was replaced with CO_2 (P = 12 bar), and then the solution was heated at 80 °C with continuous stirring for 12 hours. The solvent was distilled under vacuum (P = 0.01 bar) at 60 °C. Deionized water was added and the aqueous phase was extracted with ethyl acetate. The organic phase was washed with brine, dried on anhydrous Na_2SO_4 and ethyl acetate was removed using a rotary evaporator.

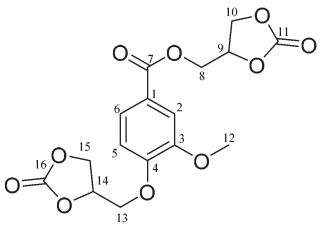


Product 8: 4,4′-(((3-methoxy-1,4-phenylene)bis(oxy))bis(methylene))bis(1,3-dioxolan-2-one) (100%, m.p. n.d.).

^1H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 3.76 (s, 3H, H_7); 4.16 (m, 4H, H_8, H_{12}); 4.39 (m, 2H, H_{10a}, H_{14a}); 4.61 (q, 2H, H_{10b}, H_{14b}); 5.11 (m, 2H, H_9, H_{13}); 6.47 (dd, $^3J_{H_6H_5}$ = 8.8 Hz, $^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.63 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.93 (d, $^3J_{H_5H_6}$ = 8.8 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 55.77 (s, C_7); 65.95 (s, C_{14}); 66.00 (s, C_{10}); 67.91 (s, C_{12}); 69.73 (s, C_8); 74.88 (s, C_{13}); 75.12 (s, C_9); 101.25 (s, C_2); 104.76 (s, C_6); 116.29 (s, C_5); 142.08 (s, C_4); 150.53 (s, C_3); 153.57 (s, C_1); 154.87 (s, C_{11}, C_{15}).

HRMS (m/z, ASAP$^+$, [M + H$^+$]): calculated: 341.0871; found: 341.0873.

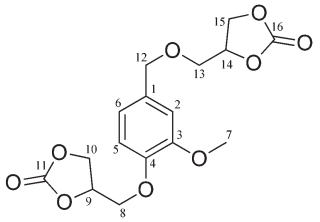


Product 9: (2-oxo-1,3-dioxolan-4-yl)methyl 3-methoxy-4-((2-oxo-1,3-dioxolan-4-yl)methoxy) benzoate (50%, m.p. n.d.).

^1H NMR (400.1 MHz, acetone-d_6, ppm) δ: 3.87 (s, 1H, H_{12}); 4.42 (m, 2H, H_{13a}, H_{13b}); 4.58 (m, 4H, H_{8a}, H_{8b}, H_{10a}, H_{15a}); 4.75 (m, 2H, H_{10b}, H_{15b}); 5.26 (m, 2H, H_9, H_{14}); 7.13 (d, $^3J_{H_5H_6}$ = 8.4 Hz, 1H, H_5); 7.55 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.62 (dd, $^3J_{H_6H_5}$ = 8.4 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 56.44 (s, C_{12}); 65.08 (s, C_8); 66.76 (s, C_{10}); 67.29 (s, C_{15}); 69.59 (s, C_{13}); 75.29 (s, C_9); 75.65 (s, C_{14}); 113.76 (s, C_5); 114.32 (s, C_2); 123.87 (s, C_1); 124.23 (s, C_6); 150.45 (s, C_3); 153.27 (s, C_4); 155.62 (s, C_{11}); 155.74 (s, C_{16}); 165.93 (s, C_7).

HRMS (m/z, ES+, [M + Na$^+$]): calculated: 391.0549; found: 391.0549.



Product 10: 4-((2-methoxy-4-(((2-oxo-1,3-dioxolan-4-yl)methoxy)-methyl)phenoxy)methyl)-1,3-dioxolan-2-one (100%, pale yellow liq.).

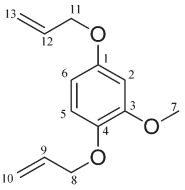
^{1}H NMR (400.1 MHz, $CDCl_3$, ppm) δ: 3.62 (dd, 1H, H_{13a}); 3.72 (dd, 1H, H_{13b}); 3.86 (s, 3H, H_7); 4.23 (dd, 2H, H_8); 4.40 (dd, 1H, H_{15a}); 4.60 (t, H_{15b}); 4.54 (s, 2H, H_{12}); 4.61 (d, 1H, H_{10a}); 4.63 (s, 1H, H_{10b}); 4.83 (m, 1H, H_{14}); 5.02 (m, 1H, H_9); 6.82 (dd, $^3J_{H_6H_5}$ = 8.0 Hz, $^4J_{H_6H_2}$ = 1.2 Hz, 1H, H_6); 6.90 (d, $^4J_{H_2H_6}$ = 1.2 Hz, 1H, H_2); 6.91 (d, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ: 55.84 (s, C_7); 66.15 (s, C_{10}); 66.19 (s, C_{19}); 68.67 (s, C_{13}); 69.22 (s, C_8); 73.17 (s, C_{12}); 74.48 (s, C_9); 75.05 (s, C_{14}); 111.78 (s, C_2); 116.13 (s, C_5); 120.14 (s, C_6); 132.27 (s, C_1); 147.10 (s, C_4); 150.36 (s, C_3); 154.76 (s, C_{11}); 154.98 (s, C_{16}).

HRMS (m/z, ES+, [M + Na^+]): calculated: 377.0854; found: 377.0849.

Procedures for allylation (11, 12, 13)

A first protocol was used for the preparation of **11** and **12** from **2** and **3**. A two-necked round-bottomed flask was charged with **2** or **3** (1.0 eq.). Ethanol was added to obtain a 0.5 mol L^{-1} solution. The solution was cooled with an ice bath and K_2CO_3 (4.0 eq.) was added. After 10 minutes, allyl bromide (4.0 eq.) was added dropwise using a syringe. The solution was stirred for 30 minutes at 0 °C and then at room temperature for seven days. Deionized water was added and the aqueous phase was extracted with pentane. The organic phase was washed with brine, dried on anhydrous Na_2SO_4 and pentane was removed using a rotary evaporator. Further purification was achieved by silica gel flash chromatography using a pentane–dichloromethane gradient as an eluent.

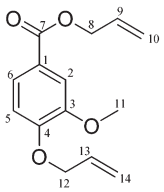


Product 11: 1,4-bis(allyloxy)-3-methoxybenzene (100%, pale yellow liq.).

^{1}H NMR (400.1 MHz, acetone-d_6, ppm) δ: 3.80 (s, 3H, H_7); 4.48 (m, 4H, H_8, H_{11}); 5.20 (m, 2H, H_{10a}, H_{13a}); 5.38 (m, 2H, H_{10b}, H_{13b}); 6.05 (m, 2H, H_9, H_{12}); 6.42 (dd, $^3J_{H_6H_5}$ = 8.6 Hz, $^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.60 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.85 (d, $^3J_{H_5H_6}$ = 8.6 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 56.68 (s, C_7); 70.27 (s, C_{11}); 71.98 (s, C_8); 102.73 (s, C_2); 106.03 (s, C_6); 117.24 (s, C_5); 117.57 (s, C_{10}); 117.71 (s, C_{13}); 135.61 (s, C_{12}); 136.02 (s, C_9); 144.09 (s, C_4); 152.56 (s, C_3); 155.41 (s, C_1).

HRMS (m/z, ES+, [M + H^+]): calculated: 221.1178; found: 221.1178.



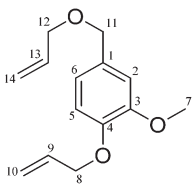
Product 12: allyl 4-(allyloxy)-3-methoxybenzoate (100%, brown liq.).

^{1}H NMR (400.1 MHz, $CDCl_3$, ppm) δ: 3.93 (s, 3H, H_{11}); 4.68 (dt, 2H, H_{12}); 4.81 (dt, 2H, H_8); 5.30 (m, 2H, H_{10a}, H_{14a}); 5.42 (m, 2H, H_{10b}, H_{14b}); 6.06 (m, 2H, H_9, H_{13}); 6.89 (d, $^3J_{H_5H_6}$ = 8.4 Hz, 1H, H_5); 7.58 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.68 (dd, $^3J_{H_6H_5}$ = 8.4 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, $CDCl_3$, ppm) δ: 56.02 (s, C_{11}); 65.50 (s, C_8); 69.69 (s, C_{12}); 111.95 (s, C_2); 112.40 (s, C_5); 118.04 (s, C_{10}); 118.49 (s, C_{14}); 122.81 (s, C_1); 123.44 (s, C_6); 132.44 (s, C_9); 132.54 (s, C_{13}); 148.95 (s, C_3); 152.04 (s, C_4); 166.01 (s, C_7).

HRMS (m/z, ES+, [M + H^+]): calculated: 249.1126; found: 249.1127.

As in the case of the glycidylation of a benzyl alcohol moiety, a phase transfer catalysis system was used for the preparation of **13** from **4**. A round-bottomed flask was charged with **4** (1.0 eq.) and TEBAC (0.1 eq.). NaOH (5.0 eq.) was dissolved in water to obtain a 20 wt% solution. This solution was poured into the flask and the suspension was stirred for 10 minutes while heating to 50 °C. Allyl bromide (4.0 eq.) was then added to the mixture and the reaction was conducted for 5 hours. Deionized water was added and the mixture was extracted with pentane. The organic phase was washed with brine, dried on anhydrous Na_2SO_4 and pentane was removed using a rotary evaporator. Further purification was achieved by silica gel flash chromatography using a pentane–dichloromethane gradient as an eluent.



Product 13: 4-(allyloxy)-1-((allyloxy)methyl)-3-methoxy benzene (86%, pale yellow liq.).

^{1}H NMR (400.1 MHz, acetone-d_6, ppm) δ: 3.81 (s, 3H, H_7); 3.98 (m, 2H, H_{12}); 4.43 (s, 2H, H_{11}); 4.55 (m, 2H, H_8); 5.11–5.16 (m, 1H, H_{14a}); 5.20–5.25 (m, 1H, H_{10a}); 5.25–5.32 (m, 1H, H_{14b}); 5.38–5.45 (m, 1H, H_{10b}); 5.94 (m, 1H, H_{13}); 6.08 (m, 1H,

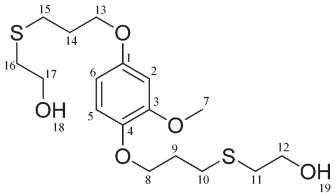
H_9); 6.84 (dd, $^4J_{H_6H_2}$ = 2.0 Hz, $^3J_{H_6H_5}$ = 8.0 Hz, 1H, H_6); 6.91 (dd, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5); 6.96 (dd, $^3J_{H_2H_6}$ = 2.0 Hz, 1H, H_2).

^{13}C NMR (100.6 MHz, acetone-d_6, ppm) δ: 56.7 (s, C_7); 70.9 (s, C_8); 71.9 (s, C_{12}); 73.0 (s, C_{11}); 113.4 (s, C_2); 115.2 (s, C_5); 116.9 (s, C_{14}); 117.8 (s, C_{10}); 121.4 (s, C_6); 133.3 (s, C_1); 135.6 (s, C_9); 136.9 (s, C_{13}); 149.2 (s, C_4); 151.3 (s, C_3).

HRMS (m/z, ASAP$^-$, [M − H$^+$]): calculated: 233.1180; found: 233.1178.

Procedures for alcohol functionalization (14, 15, 16)

Allylated compound **11**, **12** or **13** (1.0 eq.) and mercaptoethanol (6.0 eq.) were mixed without adding any solvent. The solution was irradiated in the UV reactor. The reactions were monitored by ^{1}H NMR.

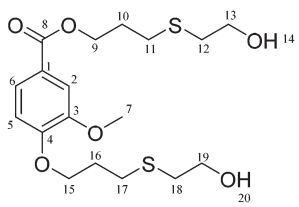


Product 14: 2,2′-((((3-methoxy-1,4-phenylene)bis(oxy))bis(propane-3,1-diyl))bis(sulfanediyl))diethanol (92%, pale yellow liq.).

^{1}H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.91 (m, 4H, H_9, H_{14}); 2.57 (dt, 4H, H_{11}, H_{16}); 2.65 (dt, 4H, H_{10}, H_{15}); 3.53 (dt, 4H, H_{12}, H_{17}); 3.74 (s, 3H, H_7); 3.93 (t, 2H, H_8); 3.97 (t, 2H, H_{13}); 4.76 (m, 2H, H_{18}, H_{19}); 6.40 (dd, $^3J_{H_6H_5}$ = 8.8 Hz, $^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.56 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.84 (d, $^3J_{H_5H_6}$ = 8.8 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 27.95 (s, C_{10}, C_{15}); 29.12 (s, C_{14}); 29.29 (s, C_9); 33.90 (s, C_{16}, C_{11}); 55.54 (s, C_7); 60.86 (s, C_{12}, C_{17}); 66.33 (s, C_{13}); 67.86 (s, C_8); 101.02 (s, C_2); 104.28 (s, C_6); 115.03 (s, C_5); 142.10 (s, C_4); 150.26 (s, C_3); 153.41 (s, C_1).

HRMS (m/z, ES+, [M + Na$^+$]): calculated: 399.1277; found: 399.1276.

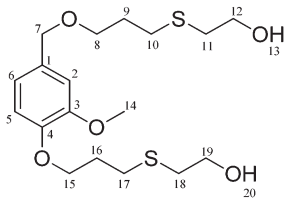


Product 15: 3-((2-hydroxyethyl)thio)propyl-4-(3-((2-hydroxyethyl)thio)propoxy)-3-methoxybenzoate (96%, pale yellow liq.).

^{1}H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.97 (m, 4H, H_{10}, H_{16}); 2.58 (2*t, 4H, H_{12}, H_{18}); 2.66 (2*t, 4H, H_{11}, H_{17}); 3.52 (m, 4H, H_{13}, H_{19}); 3.81 (s, 3H, H_7); 4.11 (t, 2H, H_{15}); 4.30 (t, 2H, H_9); 4.87 (broad m, 2H, H_{14}, H_{20}); 7.07 (d, $^3J_{H_5H_6}$ = 8.4 Hz, 1H, H_5); 7.45 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.57 (dd, $^3J_{H_6H_5}$ = 8.4 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 27.78, 27.97 (2*s, C_{11}, C_{17}); 28.85, 28.54 (2*s, C_{10}, C_{16}); 33.83, 33.89 (2*s, C_{18}, C_{12}); 55.59 (s, C_7); 60.82, 60.87 (2*s, C_{13}, C_{19}); 63.22 (s, C_8); 66.87 (s, C_{15}); 111.95, 112.10 (2*s, C_2, C_5); 121.97 (s, C_1); 123.14 (s, C_6); 148.54 (s, C_3); 152.20 (s, C_4); 165.47 (s, C_7).

HRMS (m/z, ES+, [M + K$^+$]): calculated: 443.0962; found: 443.0964.



Product 16: 2-((3-(4-(3-((2-hydroxyethyl)thio)propoxy)-3-methoxybenzyl)oxy)propyl)thio)ethan-1-ol (100%, pale yellow liq.).

^{1}H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.76 (m, 2H, H_9); 1.93 (m, 2H, H_{16}); 2.56 (m, 6H, H_{10}, H_{11}, H_{18}); 2.66 (t, 2H, H_{17}); 3.45 (t, 2H, H_8); 3.52 (m, 4H, H_{12}, H_{19}); 3.75 (s, 3H, H_{14}); 4.00 (t, 2H, H_{15}); 4.36 (s, 2H, H_7); 4.77 (m, 2H, H_{13}, H_{20}); 6.81 (dd, $^3J_{H_6H_5}$ = 8.0 Hz, $^4J_{H_6H_2}$ = 1.2 Hz, 1H, H_6); 6.90 (d, $^4J_{H_2H_6}$ = 1.2 Hz, 1H, H_2); 6.91 (d, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5).

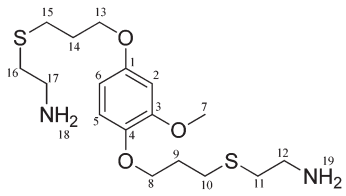
^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 28.08 (s, C_{17}); 28.43 (s, C_{10}); 29.31 (s, C_{16}); 29.84 (s, C_9); 35.25 (s, C_{18}); 35.29 (s, C_{11}); 55.93 (s, C_{14}); 60.30 (s, C_{19}); 60.34 (s, C_{12}); 67.38 (s, C_{15}); 68.34 (s, C_8); 72.89 (s, C_7); 111.65 (s, C_5); 113.27 (s, C_2); 120.32 (s, C_6); 131.36 (s, C_1); 147.80 (s, C_3); 149.56 (s, C_4).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 391.1611; found: 391.1613.

Procedures for amine functionalization (17, 18, 19)

Allylated compound **11**, **12** or **13** (1.0 eq.) and cysteamine hydrochloride (6.0 eq.) were dissolved in a minimum of methanol. The solution was irradiated in the UV reactor. The reactions were monitored by ^{1}H NMR.

When the reaction was complete, the resulting mixture was dissolved in water and K_2CO_3 was added to reach pH = 9. The solution was then extracted with ethyl acetate, dried on anhydrous Na_2SO_4 and ethyl acetate was evaporated under reduced pressure.



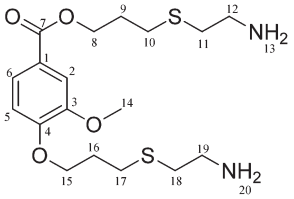
Product 17: 2,2′-((((3-methoxy-1,4-phenylene)bis(oxy))bis(propane-3,1-diyl))bis(sulfanediyl))diethanamine (96%, pale yellow liq.).

^{1}H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.90 (m, 4H, H_9, H_{14}); 2.45–2.70 (m, 12H, H_{10}, H_{11}, H_{12}, H_{15}, H_{16}, H_{17}); 3.72 (s, 3H, H_7); 3.94 (m, 4H, H_8, H_{13}); 6.39 (dd, $^3J_{H_6H_5}$ = 8.8 Hz,

$^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.54 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.83 (d, $^3J_{H_5H_6}$ = 8.8 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 27.50 (s, C_{15}); 27.52 (s, C_{10}); 29.14 (s, C_{14}); 29.30 (s, C_9); 35.23 (s, C_{16}); 35.25 (s, C_{11}); 41.55 (s, C_{17}); 41.57 (s, C_{12}); 55.56 (s, C_7); 66.34 (s, C_{13}); 67.85 (s, C_8); 101.00 (s, C_2); 104.26 (s, C_6); 114.98 (s, C_5); 142.12 (s, C_4); 150.27 (s, C_3); 153.42 (s, C_1).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 375.1779; found: 375.1776.

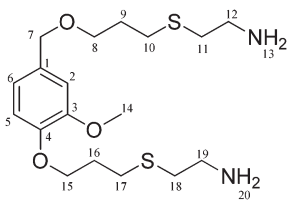


Product 18: 3-((2-aminoethyl)thio)propyl-4-(3-((2aminoethyl) thio) propoxy)-3-methoxybenzoate (93%, pale yellow liq.).

^1H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.97 (m, 4H, H_9, H_{16}); 2.52 (2*t, 4H, H_{11}, H_{18}); 2.63 (2*t, 4H, H_{10}, H_{17}); 2.68 (t, 4H, H_{12}, H_{19}); 3.82 (s, 3H, H_{14}); 4.11 (t, 2H, H_{15}); 4.30 (t, 2H, H_8); 7.09 (d, $^3J_{H_5H_6}$ = 8.6 Hz, 1H, H_5); 7.45 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.58 (dd, $^3J_{H_6H_5}$ = 8.6 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 27.28 (s, C_{10}); 27.47 (s, C_{17}); 28.52 (s, C_9); 28.83 (s, C_{16}); 35.14, 35.16 (2*s, C_{11}, C_{18}); 41.52 (s, C_{12}, C_{19}); 55.59 (s, C_{14}); 63.19 (s, C_{15}); 66.87 (s, C_8); 111.94 (s, C_5); 112.09 (s, C_2); 121.95 (s, C_1); 123.13 (s, C_6); 148.55 (s, C_3); 152.20(s, C_4); 165.44 (s, C_7).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 403.1721; found: 403.1725.



Product 19: 2-((3-((4-(3-((2-aminoethyl)thio)propoxy)-3-methoxybenzyl)oxy)propyl)thio)ethan-1-amine (88%, pale yellow liq.).

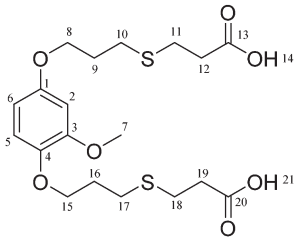
^1H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.76 (tt, 2H, H_9); 1.94 (tt, 2H, H_{16}); 2.52 (m, 3H, H_{10}, H_{11}, H_{18}); 2.66 (m, 3H, H_{12}, H_{17}, H_{19}); 3.46 (t, 1H, H_8); 3.75 (s, 3H, H_{14}); 4.01 (t, 1H, H_{15}); 4.36 (s, 2H, H_7); 6.81 (dd, $^3J_{H_6H_5}$ = 8.0 Hz, $^4J_{H_6H_2}$ = 1.2 Hz, 1H, H_6); 6.90 (d, $^4J_{H_2H_6}$ = 1.2 Hz, 1H, H_2); 6.91 (d, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 27.41 (s, C_{17}); 27.78 (s, C_{10}); 29.10 (s, C_{16}); 29.57 (s, C_9); 35.19 (s, C_{18}); 35.26 (s, C_{11}); 41.54 (s, C_{12}, C_{19}); 55.49 (s, C_{14}); 66.91 (s, C_{15}); 67.88 (s, C_8); 71.77 (s, C_7); 111.72 (s, C_5); 113.11 (s, C_2); 119.93 (s, C_6); 131.25 (s, C_1); 147.33 (s, C_4); 148.96 (s, C_3).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 389.1932; found: 399.1933.

Procedures for acid functionalization (20, 21, 22)

Allylated compound **11**, **12** or **13** (1.0 eq.) and 3-mercaptopropionic acid (6.0 eq.) were mixed without adding any solvent. The solution was irradiated in the UV reactor. The reactions were monitored by ^{1}H NMR.

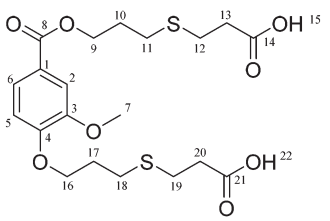


Product 20: 3,3′-((((3-methoxy-1,4-phenylene)bis(oxy))bis-(propane-3,1-diyl))bis(sulfanediyl))dipropionic acid (68%, pale yellow liq.).

^1H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.91 (q, 4H, H_9, H_{16}); 2.51 (m, 4H, H_{13}, H_{20}); 6.66 (m, 8H, H_{10}, H_{11}, H_{17}, H_{18}); 3.73 (s, 3H, H_7); 3.93 (t, 2H, H_8); 3.96 (t, 2H, H_{15}); 6.39 (dd, $^3J_{H_6H_5}$ = 8.8 Hz, $^4J_{H_6H_2}$ = 2.8 Hz, 1H, H_6); 6.56 (d, $^4J_{H_2H_6}$ = 2.8 Hz, 1H, H_2); 6.84 (d, $^3J_{H_5H_6}$ = 8.8 Hz, 1H, H_5); 12.28 (broad s, 2H, H_{14}, H_{21}).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 26.36, 26.39 (2*s, C_{11}, C_{18}); 27.59, 27.62 (2*s, C_{10}, C_{17}); 28.92, 29.08 (2*s, C_9, C_{16}); 34.45, 34.49 (2*s, C_{12}, C_{19}); 55.55 (s, C_7); 66.33 (s, C_8); 67.85 (s, C_{15}); 101.04 (s, C_2); 104.31 (s, C_6); 115.06 (s, C_5); 142.11 (s, C_4); 150.30 (s, C_3); 153.44 (s, C_1); 172.66 (s, C_{13}, C_{20}).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 433.1357; found: 433.1355.

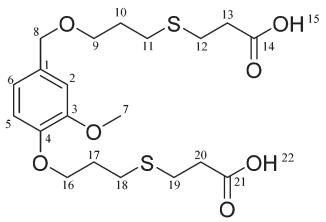


Product 21: 3-((3-((4-(3-((2-carboxyethyl)thio)propoxy)-3-methoxybenzoyl)oxy)propyl)thio)propanoic acid (92%, m.p. 68 °C).

^1H NMR (400.1 MHz, (DMSO-d_6, ppm) δ: 1.97 (m, 4H, H_{10}, H_{17}); 2.51 (m, 4H, H_{13}, H_{20}); 2.67 (m, 8H, H_{11}, H_{12}, H_{18}, H_{20}); 3.81 (s, 3H, H_7); 4.10 (t, 2H, H_{16}); 4.29 (t, 2H, H_9); 7.06 (d, $^3J_{H_5H_6}$ = 8.6 Hz, 1H, H_5); 7.45 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 7.58 (dd, $^3J_{H_6H_5}$ = 8.6 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6).

^{13}C NMR (100.6 MHz, (DMSO-d_6, ppm) δ: 26.31, 26.34 (2*s, C_{12}, C_{19}); 27.39, 27.63 (2*s, C_{11}, C_{18}); 28.34, 28.64 (2*s, C_{10}, C_{17}); 34.42, 34.46 (2*s, C_{13}, C_{20}); 55.60 (s, C_7); 63.22 (s, C_9); 63.8 (s, C_{16}); 111.94, 112.09 (2*s, C_5, C_2); 121.99 (s, C_1); 123.18 (s, C_6); 148.57 (s, C_3); 152.20 (s, C_4); 165.49 (s, C_7); 173.03 (s, C_{14}, C_{21}).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 461.1302; found: 461.1304.



Product 22: 3-((3-((4-(3-((2-carboxyethyl)thio)propoxy)-3-methoxybenzyl)oxy)propyl)thio)propanoic acid (90%, liq.).

^{1}H NMR (400.1 MHz, DMSO-d_6, ppm) δ: 1.76 (quint., 2H, H_{10}); 1.93 (quint., 2H, H_{17}); 2.51 (m, 6H, H_{11}, H_{13}, H_{20}); 2.66 (m, 6H, H_{12}, H_{18}, H_{19}); 3.45 (t, 2H, H_9); 3.75 (s, 3H, H_7); 4.00 (t, 2H, H_{16}); 4.36 (s, 2H, H_8); 6.81 (dd, $^3J_{H_6H_5}$ = 8.0 Hz, $^4J_{H_6H_2}$ = 2.0 Hz, 1H, H_6); 6.90 (d, $^4J_{H_2H_6}$ = 2.0 Hz, 1H, H_2); 6.91 (d, $^3J_{H_5H_6}$ = 8.0 Hz, 1H, H_5).

^{13}C NMR (100.6 MHz, DMSO-d_6, ppm) δ: 26.32, 26.42 (2*s, C_{12}, C_{19}); 27.52, 27.91 (2*s, C_{11}, C_{18}); 28.91, 29.39 (2*s, C_{10}, C_{17}); 34.46, 34.51 (s, C_{13}, C_{20}); 55.49 (s, C_7); 66.87 (s, C_{16}); 67.88 (s, C_9); 71.82 (s, C_8); 111.67 (s, C_2); 113.04 (s, C_5); 119.99 (s, C_6); 131.25 (s, C_1); 147.32 (s, C_3); 148.96 (s, C_4); 173.09 (s, C_{14}, C_{21}).

HRMS (m/z, ES+, [M + H$^+$]): calculated: 447.1505; found: 447.1511.

Material preparation

Epoxy compound **5** (1.20 g, 2.0 eq.) was molten at 100 °C. IPDA (0.81 g, 1.0 eq.) was quickly added and the mixture was vigorously stirred for 1 min at 100 °C. The liquid and homogeneous mixture was then poured into a rectangular silicon mold. The formulation was cured in an oven for 1.5 hours at 100 °C. The polymer obtained was then cooled down to room temperature and post-cured at 160 °C for 1 hour. A DSC analysis was performed and showed a complete reticulation and a T_g of 117 °C.

Conclusions

Vanillin was used as a building block to develop a platform of biobased compounds usable in the polymer field. The lack of biobased aromatic monomers necessary to reach good thermo-mechanical properties was the major identified challenge. Vanillin was chosen as the starting point of the platform as it is one of the few monoaromatic biobased compounds that are abundantly available. Indeed, vanillin is already industrially produced by lignin depolymerization.

Three vanillin derivatives in different oxidation states were chosen as starting materials to take into account differences in lignin depolymerization processes and the possible resulting products. These chemicals were functionalized with epoxy, cyclic carbonates, allyl, amine, alcohol and carboxylic acid moieties. Original biobased monomers useful for epoxy, polyester, PU, and NIPU polymer synthesis were obtained. The epoxy-functionalized compounds could be tested as biobased substitutes for bisphenol A-based epoxy resins. The amine-functionalized compounds are, to our knowledge, the first non-aliphatic biobased amine hardeners, useful either in epoxy or NIPU materials. The cyclic carbonate-functionalized compounds could be useful to tune NIPU properties.

Products from the vanillin-derived methoxyhydroquinone are especially interesting and versatile. Industrialization is possible thanks to clean and straightforward syntheses and there is no fragile bond on the methoxyhydroquinone that could impact polymer properties.

In future studies, compounds from this platform should be used in polymer formulations and thermo-mechanical properties of the corresponding materials should be tested.

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