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Sustainable bisphenols from renewable softwood lignin feedstock for polycarbonates and cyanate ester resins

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Selective reductive catalytic depolymerisation of softwood lignin (e.g. pine, spruce) yields predominantly 4-npropylguaiacol (4PG; 15-20 wt% on lignin basis), an interesting platform chemical for bio-based chemistry. This contribution specifically shows promising technical, sustainable and environmental advantages of such bio-phenol for various polymer applications. The bisphenolic polymer precursor, 5,5'-methylenebis(4-n-propylguaiacol) (m,m'-BGF-4P), was therefore first synthesized by acid-catalysed condensation, and its synthesis and isolation are compared with shorter chain analogs, viz. 4-methyl- and 4-ethylguaiacol. A thorough GC-GPC/SEC analysis of the crude condensation mixture was developed to assess the purity of the isolated dimers. Isolation is done by a single-step crystallization, yielding 57 wt% of m,m'-BGF-4P in >99% purity. This pure m,m'-BGF-4P bisphenol displays a notably reduced potency to activate human estrogen receptor alpha (hERa; EC₅₀ at 10⁻⁵ M) in comparison to commercial bisphenols, and is therefore useful for future polymer applications. As proof of concept, polycarbonates and cyanate ester resins were prepared from m,m'-BGF-4P and compared to other bisphenols. The polycarbonate had $M_n = 5 \ 182 \ \text{g.mol}^{-1}$, $T_g = 99 \ ^{\circ}\text{C}$, $T_m = 213 \ ^{\circ}\text{C}$, $T_{d.5\%} = 360 \ ^{\circ}\text{C}$, and displayed improved processability in common solvents, as opposed to the methylated and ethylated bisguaiacols. A fully cured resin disk exhibited a T_g = 193 °C, $T_{d.5\%}$ = 389 °C and a water uptake of only 1.18% after being immersed in 85 °C water for four days. These results underscore the potential of the intrinsic functionality of lignin-derived building blocks to transcend the scope of renewability.

Introduction

The transition from a linear to a circular (bio)economy will reduce demands on finite raw materials and input of lignocellulosic feedstock in future bio-refineries, by minimizing waste and closing loops in industrial ecosystems.^{1,2} As a consequence, future thermoplastic polymers and thermosets are preferably bio-renewable and recyclable.^{3,4} This implies a pivotal role for poly(ester)s and poly(carbonate)s, such as succinate),4 poly(butylene poly(hydroxyalkanoates),⁴ poly(ethylene acid),^{5,6} poly(lactic furanoate).7 poly(dihydroferulic acid)⁸ and poly(limonene carbonate).⁹ Ester and carbonate linkages are prone to undergo controlled depolymerization (e.g. via solvolysis^{10,11} or by decarboxylation with carbonate salts¹²) to close the loop towards the original monomeric constituents,¹³ ideally, without considerable losses of carbon. Thermoset recyclability proves to be more challenging, but promising strategies (*e.g.* acid/base-digestion or pyrolytic recycling) are being established.¹⁴⁻¹⁷

Some industrially relevant and chemically recyclable polymers, such as bisphenol A (BPA)-based polycarbonates and epoxy resins, currently lack the perspective of bio-renewability. Poly(BPA carbonate), together with the market for phenolic resins, currently accounts for >77% of the global phenol demand,¹⁸ and is still dependent on traditional cumene-based technology, which relies on volatile benzene markets. Hence, literature has proposed several approaches for benzene-free synthesis of bio-phenol from renewable resources, like glucose,¹⁹ shikimic acid²⁰ and in particular lignin.²¹⁻²³

Bio-phenol synthesis from lignin, the world's largest source of renewable phenolics (*ca.* 40 wt% benzene units),²⁴ remains a foremost challenge. Several pathways to depolymerise lignin streams have been reported.²⁵⁻³⁰ A very appealing *lignin-first* biorefinery concept, simultaneously extracts and disassembles the *proto*lignin from the lignocellulosic matrix, followed by oxidative,³¹⁻³³ redox-neutral^{34,35} or reductive³⁶⁻⁵⁰ stabilization. While many state-of-the-art depolymerization strategies produce a wide variety of products, with a phenol yield limited to *ca.* 5%, the *lignin-first* process converts respectively about 20% and 50% of the softwood and hardwood *proto*lignin -

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values close to the theoretical maximum - into a handful of methoxylated alkylphenols. This allows substantial higher yields of bio-phenol upon catalytic demethoxylation and dealkylation compared to the state-of-the-art single-step processes.⁵¹

Alternatively, the direct use of these methoxylated alkylphenols to design novel BPA monomers could not only lead to bio-renewable and recyclable polymers, but perhaps also to environmentally safer bisphenols.⁵²⁻⁵⁷ BPA, one of the highest-volume chemicals produced worldwide, with an annual production of 5.4 Mt in 2015 and a forecast to reach 7.3 Mt by 2020, has come under close scrutiny when evidence for environmental leaching was found in 1993.58,59 BPA leaching, together with its (long-known) ability to replace natural estrogen, potentially links BPA to health issues upon exposure during critical developmental phases (e.g. puberty, pregnancy). Public awareness, and the negative connotation associated with BPA, now demands a shift towards safer alternatives. Surprisingly, the presence of methoxy functionalities in ortho position relative to the phenolic OHgroup in BPA strongly abates or even abolishes the ability to bind and/or activate estrogen receptors in both alkylphenols,⁶⁰⁻⁶² bisphenols⁶³⁻⁶⁵ and estradiols.⁶⁶ Interestingly, the lignin-first-derived methoxylated alkylphenols naturally possess such a favourable design.

Furthermore, polymer chemistry typically requires highly pure monomers with the degree of purity depending on the type of polymer. For example, the synthesis of thermoplastic poly(BPA carbonate) necessitates a purity of >99% (for the p,p'-isomer), while for BPA-based epoxy resins a purity of >95% is sufficient.^{67,68} As polycarbonate and epoxy resins production accounts for nearly 95% of the global BPA usages, the synthesis and high-purity isolation of bio-renewable and environmental benign bisphenols, which remain functional,⁶⁹ is imperative.

Herein, we disclose a bio-derived bisphenol with substantially (*ca.* 10-100 times) lower estrogenic potency, that is synthesized from 4-*n*-propylguaiacol (4PG), a methoxylated alkylphenol resulting from the *lignin-first* process (in about 15-20 wt% yield based on total lignin, see Table S1 in ESI⁺), and can be isolated in polymer-grade purity (>99%). Finally, the synthesis and characterization of both thermoplastic polycarbonates and cyanate ester thermosets are performed. In all aspects, 4-ethyl-

and 4-methylguaiacol were tested in parallel to provide valuable structure-property relationships (Scheme 1).

Results and discussion

Bisphenol synthesis and in-depth product analysis

To synthesize the bisphenol, 4PG and formaldehyde (i.e. 37 wt% solution in water) were stoichiometrically reacted in a biphasic system in the presence of aqueous hydrochloric acid. Our group very recently demonstrated that also heterogeneous Brønsted acidic zeolites are able to selectively catalyze this reaction.⁷⁰ An in-depth product analysis was performed on the crude condensation mixture after decantation of the aqueous phase. A thorough analysis of this organic phase was acquired by GC and complemented by GPC/SEC analysis (see Experimental). Higher condensation products (such as trimers and tetramers) are further denoted as oligomers, and their yield is calculated from the mass balance (Table 1). Six hours of reaction yields 81 and 13 wt% of total di- and oligomers respectively, at 94% conversion. Besides *m*,*m*'-methylenebis(4-*n*-propylguaiacol) (*m*,*m*'-BGF-4P; 69 wt%), the dimer fraction also comprises o,m'- (12 wt%) and o,o'-isomers (<1 wt%) as confirmed by GC-MS analysis (Fig. S3, see ESI⁺). The selectivity towards the desired m,m'-isomer, expressed as the ratio of m,m'-isomers to the total dimers, equals 85% for 4PG.

To evaluate the steric (and electronic) effect of the alkyl chain length, 4-ethyl- (4EG) and 4-methylguaiacol (4MG) were reacted under similar conditions. On the one hand, shorter 4-alkyl chains result in less *ortho*-coupled dimers (*i.e.* o,m'- and o,o'-isomers; 6-10 wt%) and therefore a somewhat higher m,m'-selectivity (88-93%). On the other hand, shorter alkyl chains limit the total dimer yield (to ca. 81-83%) due to a higher tendency to form oligomers. Overall, even though the propyl chain displays higher steric hindrance, high m,m'-yields (69-75%) are obtained in all cases. As a measure of process efficiency, the total organic phase recovery is also reported in Table 1. This recovery is excellent (≥98%) thanks to a high hydrophobicity in both substrate and product.⁷¹

Both chemo- and regioselectivity are directed by the (*o*-methoxy) substitution in the substrate, as illustrated by comparison of GC and GPC/SEC data for 4-*n*-propylphenol (4PP)

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 Scheme 1. Synthesis, purification and estrogenic activity testing of m,m'-bis(4-n-propylguaiacol) and its potential as precursor to thermoplastic polycarbonates and cyanate
 esters
 thermosetting
 resins.

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Table 1. Composition of the organic product phase after orphasic reaction in aqueous actine medium as quantined by GC-PD.									
Monomeric	t	Recovery ^b	Conversion ^c	Yield dimers ^d [wt%]				Yield oligomers ^e	Selectivity ^f
Substrate	[h]	[wt%]	[%]	o,o'-isomer	o,m'-isomer	<i>m,m'</i> -isomer	total	[wt%]	m,m' [%]
4-n-propylguaiacol	6	>99	94	<1	12	69 (57)	81	13	85
4-ethylguaiacol	6	99	97	-	10	73 (69)	83	14	88
4-methylguaiacol	4	98	>99	-	6	75 (72)	81	19	93

^a reaction conditions: 18 mmol formaldehyde (37 wt% in H₂O), 36 mmol 4-alkylphenol, 50 mL 2.5 M HCl_{av}, 100°C, 1000 rpm. All experiments were performed in duplicate and average values are shown. For photographs of the general lab-scale set-up (Fig. S1) and the reaction mixture before and after reaction (Fig. S2) see ESI⁺, ^b calculated as wt% of theoretical organic phase at full dimer yield. ^c assuming complete insolubility of monomeric substrate in aqueous phase. ^d definition of *x*,*x*⁻ coupling as illustrated in Fig. 1C; values in parentheses are isolated yields. ^e calculated from closing the mass balances, qualitative confirmation by GPC/SEC. ^f defined as percentage *m*,*m*⁻ isomer in total dimer fraction.

and 4PG (Fig. 1). Unsubstituted alkylphenols, such as p-cresol, are typically used to produce novolac-type resins consisting of oligomeric species (up to 10-20 phenolic units). This chemoselectivity also applies to 4PP (tested as reference); under stoichiometric conditions formation of oligomeric species is still substantial (up to 6-7 phenolic units; Fig. 1A and 1B red). However, for guaiacyl analogs, dimer formation clearly predominates and oligomer formation is limited (up to 4 phenolic units; Fig. 1A and 1B blue). The shift in regioselectivity (from ortho to meta coupling) is clarified in Fig. 1A and 1C. For 4PP, the electrons donated by the hydroxy group only direct coupling in ortho position, resulting in undesirable o,o'bisphenols. Unlike para-alkylated phenols, the donating effect of the o-methoxy group in 4-alkylguaiacols strongly reduces the ortho-directing effect of the hydroxyl functionality, preferably steering towards coupling at the meta position. The presence of minor quantities of o,m'-isomers is presumably governed by the bulkiness of the 4-alkyl chain. In conclusion, the intrinsic lignin-functionalities selectively steer towards (i) m,m'-coupling and (ii) dimer formation, hence, m,m'-bis(4alkylguaiacol)s are the main product.

Purification via one-step crystallization

Considering the purity criteria for synthesis of high-molecular weight thermoplastics *via* polycondensation,^{67,68} the presence of *o*,*m*'-dimers and oligomers (which could act for instance as chain-terminators, colouring agents and cross-linkers) is highly unfavorable. Surprisingly, multigram-scale crystallization of the bisguaiacols proves to be simple and enables the isolation of the



Figure 1. Development of substrate-directed selective dimerization from 4-*n*-propylphenol (4PP; top) to 4-*n*-propylguaiacol (4PG; blue) as detected by GC-FID (A) and GPC/SEC (B) with indication of preferred coupling positions (relative to

hydroxy group) in acidic medium (C). For abbreviations and conditions: see ESI†. Standards (P, G and BPF) are not present in GPC/SEC trace.

m,*m*'-dimer in very high purity (>99%). A facile one-step crystallization is achieved by solubilisation of the raw (mono-, di- and oligomer-containing) organic phase in either acetoneheptane or diethyl ether-heptane, followed by gradual evaporation, without prior fractionation by extraction or column chromatography (see ESI⁺). In contrast, classic precipitation yields no crystals (in the case of propyl chains) or impure microcrystals.⁵⁵ These contain residual isomeric and oligomeric impurities, which are poorly detected by NMR due to structural similarity, but are clearly detectable by GPC/SEC, TGA and melting point determination by DSC (Fig. S4, ESI⁺). Selective one-step crystallization of m,m'-bisguaiacols yields large faceted crystals (Fig. 2) in 57-72 wt% (values in parenthesis, Table 1). The larger discrepancy between GC and isolated yield for the propyl derivatives results from their higher solubility in the crystallization medium. The molecular structure of these m,m'-bisguaiacols was unambiguously confirmed by MS, FT-IR and liquid-state ¹H, ¹³C and 2D ¹H-¹³C HMBC NMR spectroscopy (Fig. S3, S5-8, ESI⁺). ¹H and ¹³C NMR data of the asymmetric o, m'-isomers is provided as well (Fig. S9-S11, ESI+).

Assessment of the melting temperature reveals a marked influence of chain elongation. m,m'-BGF-4P melts at 78°C, which is about 50-60°C lower than that of the corresponding ethyl (129°C) and methyl (138°C) bisguaiacols and at least 80°C lower than that of conventional BPA (158-159 °C) and bisphenol F (BPF; 163 °C). Thermal degradation, as measured by TGA, takes place at similar ($T_{d,max} \ge 244$ °C; methyl) or higher temperatures (ethyl and propyl) in comparison with standard BPA and BPF. All thermal characteristics are summarized in Table S2, ESI[±]. Advantageous from an industrial point of view, lower melting temperatures combined with similar or higher thermal stabilities provide a broader liquid state processing window, that is especially notable for 4PG-derived bisguaiacols.

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Figure 2. High-purity (>99%) faceted crystals obtained by a facile one-step crystallization of the crude condensation mixture. Left to right: m,m'-methylenebis(4-ethylguaiacol) and m,m'-methylenebis(4-n-propylguaiacol).

Human estrogen receptor α (hER α) activity

Before evaluating the potential polymeric properties, novel bisphenol monomers should undergo preliminary toxicity tests, as to obey the concept of 'safety by design'.^{72,73} Suitable monomers are expected to exhibit less or no estrogen receptor (binding) activity. Thereto, purified bisguaiacols were assessed in an estrogen-responsive reporter assay in a human MCF-7 breast cancer cell line stably transfected with the estrogen responsive gene ERE-βGlob-Luc-SVNeo (MELN assay), 74,75 benchmarked against 17β -estradiol and commercial bisphenols (i.e. BPF, BPE and BPA) (Fig. 3). In general, 4alkylated m,m'-bisguaiacols display a significantly lower relative estrogenic induction (% vs. vehicle control) at higher concentration (log₁₀ M), which makes them less potent for binding to the estrogen receptor. Whereas the sigmoidal response of *m*,*m*'-bis(4-methylguaiacol) still closely resembles the response for bisphenols, the relative induction for ethyl and propyl derivatives substantially decreased, up to a factor two. Meanwhile, potencies (expressed as EC₅₀ values) shift to ca. 10-100 times lower values (see also ESI⁺, Table S3). To illustrate the strong influence of the substitution type and pattern, as a proof-of-concept, 4,4'-methylenebis(5methylguaiacol) (p,p'-BGF-5M) was synthesized in an analogous manner (Fig. S12-13, ESI⁺) and an even lower potency was achieved (Fig. 3 dark brown). This together with the fact that bisguaiacols typically display a lower solubility (~10⁻⁴ M; in water with 0.1 vol% DMSO at 25 $^{\circ}$ C) than conventional bisphenols (~10⁻³ M in water at 25 $^{\circ}$ C) will likely reduce the environmental impact for lignin-derivable bisphenols, regarding their endocrine disrupting potential. Future research should however also evaluate possible agonistic and antagonistic interactions with other members of the human nuclear receptor family, such as the androgen and thyroid hormone receptor. Furthermore, besides in vitro whole cell activity assays, progression towards whole animal assessment (e.q. fish, amphibian and mammalian) is indispensable and necessary to consider all of the possible sites of action and mechanisms of endocrine disruption.^{72,76}



Figure 3. *In vitro* screening of the estrogenic potency of bis(4-alkylguaiacol)s via an estrogen-responsive reporter assay in human MCF-7 cells (MELN-assay). Three zones of sigmoidal responsiveness are indicated for reference estrogen (blue), commercial bisphenols (magenta) and bisguaiacols (green). The individual test compounds: E2 (blue, •), BPF (dark mag., \diamond), BPA (light mag., **a**), 4-methyl- (light green, ∇), 4-ethyl- (dark green, \circ), 4-*n*-propyl- (light brown, \Box) and 5-methyl- (dark brown, **a**) bisguaiacols.

Synthesis of thermoplastic polycarbonates

Encouraged by the low estrogen activity of m,m'-BGF-4P, a first exploratory synthesis of the corresponding aromatic poly(carbonate)s and aromatic cyanate ester resins was pursued to demonstrate its potential in material applications. First, the corresponding poly(carbonate)s were evaluated and synthesized by reacting the m,m'-bis(4-alkylguaiacol)s with triphosgene (i.e. a solid phosgene substitute) via a standard lab scale procedure (Scheme 1; see details in ESI⁺). Three quasi-white powders were obtained in >60 wt% yield under non-optimized conditions (Fig. S14, ESI⁺). Phosgene and derivatives (*i.e.* di- and triphosgene)^{77,78} were selected here, as they remain to play a pivotal role in industrial polycarbonate synthesis (i.e. 80-90% of total PC synthesis in 2007).79 Nevertheless, more sustainable CO₂-based non-phosgene procedures (e.g. Asahi-Kasei process) exist on an industrial scale as well.80

The molecular structures of these poly[methylene bis(4alkylguaiacol) carbonate]s were confirmed by ¹H and ¹³C NMR in deuterated trifluoroacetic acid (TFAA-d) (Fig. S15-16, ESI⁺) and FT-IR spectroscopy (Fig. S17, ESI⁺) and are shown in Figure 4A. The molecular weight (distribution) for these novel types of polycarbonate was evaluated by both ¹H NMR end-group analysis (see details in ESI⁺) and GPC/SEC analysis (Fig. 4B). End-

group analyses provide number-average molecular weights (M_n) of 2503, 4783 and 5182 g.mol⁻¹ for methyl-, ethyl- and propyl-substituted polycarbonates respectively. GPC/SEC analyses in hexafluoroisopropanol (HFIP) against a commercial poly(BPA carbonate) (PC-BPA, $M_w = 64,000 \text{ g.mol}^{-1}$) standard, reveal broad bimodal mass distributions (9.0 – 13.0 min). Similar bimodal distributions were found in a previous study on the interfacial polycondensation of BPA with triphosgene catalyzed by triethylamine, yielding mixtures of cyclic and OH-terminated polycarbonates.^{81,82} Furthermore, these bimodal distributions partially overlap the standard (9.6 – 11.8 min), indicating that favorable molecular weights are attainable, in particular for propyl-chained polycarbonates. These results

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motivate a follow-up study to attain higher molecular weight poly[methylene bis(4-alkylguaiacol) carbonate]s.



Figure 4. Molecular structure of poly[methylene bis(4-alkylguaiacol) carbonate]s as confirmed by FT-IR and NMR in TFAA-d (A), and analysis of their molecular weight (distribution) by GPC/SEC in HFIP against a known standard (B).

Commercial PC-BPA are typically amorphous and well known for their optical transparency. In the solid state their molecular structure is random and disordered, the long chain molecules all being entangled.⁸³ Suitable replacements therefore ideally share this amorphous nature with poly(BPA carbonate). Yet, a recent study showed that polycarbonate made from m,m'bis(4-methylguaiacol) was highly crystalline and quasiinsoluble, despite the favorable thermal properties ($T_g = 122$ and $T_{\rm m} = 314^{\circ}$ C).⁵⁶ To combat this tendency for crystallization, we envisioned that especially the longer 4-propyl chain could be used as a bio-inherent tool to inhibit alignment and promote the required disorder and entanglement. Hence, the initial crystallinity of the precipitated polycarbonates was inspected by powder X-ray diffraction (PXRD; Table 2 and Fig. S18 in ESI⁺). Remarkably, upon 4-alkyl chain elongation, the highly crystalline nature fades out and a more amorphous character appears. This trend is confirmed by DSC data, which shows the loss of both hot and cold crystallization exotherms for propyl-substituted polycarbonate (Table 2 and Fig. S19, ESI⁺).

Extension of the 4-alkyl chain affects not only (i) the crystallinity, but also (ii) the glass transition temperature (T_{e}) , (iii) the melt temperature (T_m) and (iv) the solubility. The propyl-substitution displays a T_g of 99 °C, which is 17 and 26 °C lower than the ethyl (116 °C) and methyl analog (125 °C), respectively. A similar trend is observed for the $T_{m_{\ell}}$ which drops from about 299 to 213 °C. A concise overview is given in Table 2. Next, chain elongation proves to be beneficial for the solubility of the polycarbonates. Especially the propylsubstitution displays improved solubility in CHCl₃, DCM and THF, which may be beneficial for interfacial polymerization strategies. Finally, the thermal stability of the polycarbonates was determined by thermogravimetrical analysis (TGA; Table 3 and Fig. 5). Single-stage degradation was observed for all samples with an onset of degradation ($T_{d,5\%}$) between 345-375 $^{\circ}$ C and a maximum weight loss ($T_{d,max}$) around 425 $^{\circ}$ C (under

nitrogen). Though no clear trend was observable, both ethyl and propyl substituents seem to result in slightly higher thermal stabilities compared to methyl groups. In theory, proper end-capping of free reactive phenolic groups could result in even higher thermal stabilities.⁸⁴ In general, it must be taken into account that aforementioned properties correlate with the molecular weight of the polycarbonates.⁸⁵ For example, a PC-BPA with a similar M_n as the novel propylsubstituted polycarbonate (~5000 g.mol⁻¹) would display a T_g of 125 °C, about 20-25 °C lower than high molecular weight PC-BPA (145-150 °C).

Table 2. PXRD and DSC data of poly[methylene bis(4-alkylguaiacol) carbonate]s.						
Type of polycarbonate ^a	Initial crystallinity ^b	Tendency to crystallize ^c	T _{g, hot} (DSC) ^d	T _m (DSC)		
PC1 (4-methyl) ^e	high	fast (hot/cold)	125	292-305		
PC2 (4-ethyl)	medium	slow (cold)	116	236-273		
PC3 (4-n-propyl)	low	slow	99	205-220		

^a literature values reported for PC-BPA are T_g = 145-150 and T_m = 225°C. ^b estimated from PXRD and DSC. ^c based on the presence of a crystallization exotherm in DSC, see Fig. S19. ^d measured upon heating/cooling at 20 °C.min⁻¹. ^e literature values reported by Chen et al.⁵⁶ are T_e = 122 and T_m = 314 °C.

Type of	<i>T</i> _{d,5%} in N ₂ (air)	T _{d,10%} in N ₂ (air)	T _{d,max} in N ₂ (air)
polycarbonate ^a	°C	°C	°C
PC1 (4-methyl) ^b	346 (311)	373 (345)	422 (411)
PC2 (4-ethyl)	376 (329)	392 (352)	429 (398)
PC3 (4-n-propyl)	360 (341)	376 (359)	424 (414)

^a literature values reported by Dong *et al.*⁸⁶ for PC-BPA in N₂ (air) are $T_{d.5\%}$ = 445 (436) and $T_{d.max}$ = 504 (505) ^oC. ^b literature values reported by Chen *et al.*⁵⁶ are $T_{d.5\%}$ = 382, $T_{d,10\%}$ = 392 and $T_{d,max}$ = 420 °C.





Synthesis of cyanate ester thermosets

Cyanate ester resins are a relatively new class of highperformance thermosets that have been studied extensively over the last decades.^{87,88} The combination of low water uptake, high T_{g} 's , excellent electrical properties, reduced firesmoke-toxicity (FST) and outstanding mechanical properties makes them attractive alternatives to standard BPA-based epoxy resins. Recently, several novel aromatic cyanate esters were constructed from renewable bio-phenols, such as anethole,^{89,90} resveratrol,^{91,92} creosol (*i.e.* 4MG),¹⁶ eugenol,^{93,94} vanillin95 and carvacrol.96 Both the properties of the cyanate Published on 27 April 2017. Downloaded by Fudan University on 27/04/2017 11:47:20.

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ester monomer (*e.g.* T_m , cure exotherm, processing window) as well as the polymer network (*e.g.* T_g , water uptake) can be fine-tuned by the choice of substituents on the bisphenolic precursor.⁹⁷

To evaluate the influence of the propyl chain, the corresponding bis(cyanate ester)s were first synthesized by reaction of the *m*,*m*'-bis(4-alkylguaiacols) with cyanogen bromide (CNBr) (Scheme 1; see procedure in ESI[†]). The cyanate esters were obtained in excellent yield (\geq 97%) and their molecular structure was confirmed by ¹H and ¹³C NMR and FT-IR spectroscopy (Fig. S20-23, ESI[†]).

Subsequently, these cyanate ester monomers were used to study the effect of the propyl chain on (i) the cure chemistry, (ii) the thermal properties (T_g , T_d and char yield) and (iii) the water uptake. Insight into the cure chemistry of the resins was probed by DSC (Fig. 6 and Table 4). The propyl- and ethyl-substituted monomers melted cleanly at about 108-109°C and both display a cure exotherm maximum at 309°C with a cure enthalpy of about 130-121 kJ.mol⁻¹ or 65-61 kJ.(mol OCN)⁻¹. This presence of a broad processing window, *i.e.* the difference between T_m and onset of cure (ca. 110-115 °C), for the molten resins renders them highly suitable for the fabrication of composites. The melting temperature of the bis(cyanate ester) with 4-methyl chains lies 15-17 °C higher (at 125 °C) and has a peak cure



Figure 6. DSC traces of (a) 4-methyl-, (b) 4-ethyl- and (c) 4-n-propyl-substituted bis(cyanate ester)s from first (solid) and second (dashed) heating cycle at 10° C.min⁻¹. Values for (a) and (b) are offset with 6 and 3 W.g⁻¹ respectively.

Table 4. DSC data of uncured and cured bis(cyanate ester)s.					
Type of alkyl chain	4-n-propyl	4-ethyl	4-methyl		
T _m (standard) ^a / ^o C	108-110	107-108	123-126		
<i>T</i> _m (DSC) / ^{<i>o</i>} <i>C</i>	109.4	107.7	124.7 ^b		
parent $T_m / {}^oC$	78-79	128-129	138-139		
Cure exotherm / max. °C	309	309	272		
Processing window / °C	~110	~115	~75		
Cure enthalpy / kJ. (mol OCN) ⁻¹	65	61	88		
Degree of cure / %	<70	<65	<90		

 a as determined with sealed capillaries in melting point apparatus. b literature value reported by Meylemans et $al.^{16}$ is 125.4 $^\circ C$

exotherm at 272 °C, reducing its stable molten temperature range to *ca.* 75 °C. Here, the enthalpy change for the cure was 88 kJ.(mol OCN)⁻¹. Overall, chain elongation (from methyl to propyl) brings about a wider stable processing window, but

results in a slower curing. This is indicated by the cure enthalpy values, which typically lie at about 100 kJ.(mol OCN)^{-1,16} and is confirmed by the weight loss profile of uncured bis(cyanate ester)s during TGA (Fig. S24, ESI⁺).

To determine the glass transition (T_g) of the thermoset network, oscillatory thermomechanical analyses (TMA) were performed, which involves measuring flexing of a polymer specimen upon exposure to heat.⁹² Bulk samples were cured in a silicone mold by heating under 'standard cure' conditions (1 h at 150 °C followed by 210 °C for 24 h). Previous reports showed that this standard curing schedule was not sufficient to completely polymerize the monomers.^{91,92} To obtain complete cure, samples were 'post-cured' at 280 °C for 4 h. The preparation of homogeneous, void-free thermoset discs was achieved in all cases (Fig. S25, see method in ESI⁺). The propyl chain proves to have a clear effect on the T_{g} . Whereas methyl and ethyl substitutions show similar $T_{\rm g}$ values (~231 °C), the TMA thermogram of a fully cured propyl substituted sample shows a T_g of about 193 °C in the storage modulus curve, which is about 35-40 °C lower (Fig. S23, ESI⁺). Although this T_{g} value is lower than a typical BPE and BPA-derived cyanate ester (post-cure T_g of 289-305 °C),⁸⁹ the value is comparable to high performing epoxy resins (T_q of 150-200 °C). The thermal stability and char yield of the polycyanurates after post-curing was studied by TGA (Table 5 and Fig. 7). No ble 5. TGA data of post-cu

Tuble 5. Tel tatta of post curca cyanate ester mermosets.						
Type of	T _{d,5%} in N ₂ (air)	T _{d,10%} in N ₂ (air)	T _{d,max} in N ₂ (air)	Char yield		
alkyl chain	°C	°C	°C	% ^a		
4-methyl ^b	375 (380)	383 (389)	396 (400)	30 (28)		
4-ethyl	389 (387)	392 (391)	401 (401)	26 (28)		
4-n-propyl	389 (389)	393 (394)	411 (411)	22 (22)		
^a at 850 °C in N ₂ (air). ^b literature values reported by Meylemans et al. ¹⁶ for T_{d} s						

 $T_{d,10\%}$ and char yield are 360 (357), 366 (362) °C and 35% respectively





significant differences could be observed for heating in nitrogen versus air. Chain elongation results in slightly higher thermal stabilities with maximum values attained for propyl-substituted resins. Here, the degradation starts at 389 °C ($T_{d,5\%}$) and reaches a maximum loss at 411 °C ($T_{d,max}$), which is about 10-15 °C higher

than methyl-substituted resins. Unlike earlier reports,¹⁶ the char yield (measured at 850 °C) was quasi similar under nitrogen and air. The char yield ranged from 22-30% with the lowest value obtained for propyl chains, which might be

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explained by the lower aromatic/aliphatic carbon ratio and the fact that aliphatic groups are more prone to oxidative degradation. $^{96}\,$

Finally, the fully cured resin discs were exposed to hot water (85°C) for four days to determine their water uptake. It was hypothesized that the hydrophobic character of the propyl chains could significantly reduce moisture uptake. Indeed, a propyl substituted resin displays an uptake of only 1.18%, in comparison with respectively 1.36 and 1.75% for ethyl and methyl groups. This value is lower than for BPE and BPA-based based resins (respectively 1.75 and 1.34%).⁸⁹ Hence, the presence of propyl chains has a favourable impact on the hydrophobicity of the thermosetting material, broadening its applicability to humid conditions.

Conclusions

We demonstrate the production of bio-renewable m,m'bisguaiacols from methyl-, ethyl- and propylguaiacols, the latter being abundantly available in the reductive catalytic biorefinery (in 15-20 wt% on lignin basis from softwood). The effect of the propyl (vs. ethyl and methyl) chain was systematically examined for (i) the acid-catalysed synthesis of the m,m'-bisphenols, (ii) the purification via crystallization, (iii) the estrogenic potency, as well as for (iv) the final properties of aromatic polymers.

The original substitution pattern of the guaiacols directs the selectivity to primarily m,m'-coupled bisguaiacols, while undesired oligomer formation is restricted for steric reasons, being most pronounced for the propyl-substituted guaiacols. Despite the unusual m,m'-regioselectivity, highly pure crystals (devoid of o,m'-isomers and oligomers) are easily formed upon controlled crystallization in all cases. From the m,m'-isomers, especially the propyl-substituted bisguaiacol (m,m'-BGF-4P) displays strongly reduced in vitro estrogenic receptor (binding) activity and are therefore the most sustainable bisphenol alternatives for the synthesis of novel aromatic polymers, like polycarbonates and cyanate ester resins. In thermoplastic polycarbonates, the propyl chain (i) lowers the tendency to crystallize, and (ii) improves its solubility in common solvents, which facilitates downstream processing. Propyl-substituted cyanate ester thermosetting resins on the other hand benefit from (i) a broad processing window (ca. 110 $^{\circ}$ C) during resin synthesis, and (ii) reduced water uptake (1.18%). Both type of polymers exhibited a high thermal stability (>360 °C) that is not compromised by the presence of the aliphatic propyl chain. From a more conceptual point-of-view, this work highlights the benefits gained from deliberately exploiting nature's intrinsic functional groups, present for instance in lignin.

Experimental

Chemicals, materials and methods

For a complete list of all used chemicals and materials as well as a more detailed description of all experimental methods and procedures, the reader is kindly referred to the ESI⁺.

Reaction procedure

Reactions were conducted as previously described with minor modifications.⁵⁵ In a typical reaction, to alkylphenol or - guaiacol (36 mmol) in a 100 mL Duran[®] laboratory bottle with screw cap, 37 wt% formaldehyde (18 mmol) and concentrated HCl (50 mL, 2.5 M in Milli-Q H₂O) were added, as well as a magnetic stirring bar (45 mm). At the start of the reaction, the bottle is partially (2/3) submerged in a pre-heated stirred temperature-controlled oil bath. The bath is held at 100 °C under continuous stirring (1000 rpm) for the indicated time. Once at room temperature, the aqueous acidic phase was decanted and the resulting 'organic phase' analysed.

Reaction product analysis

The 'organic phase' contains dimers, oligomers, unreacted monomers and trace amounts of the aqueous acidic phase (<3 wt%). To avoid overestimation of 'total organic phase recovery', underestimation of product yields or damaging the column, this 'organic phase' was dissolved in acetone or diethyl ether and dried with MgSO4. After filtration, the solvent was removed by rotary evaporation (150 mbar at 80 °C for 1 h) yielding a semi-solid or viscous oil. This 'dried organic phase' was analysed by both GC and GPC/SEC (see ESI+) for determining product yields and monomer conversion. Due to the high chemical similarity between reagent and products, the dimer yield and monomer conversion can only be measured accurately by GC. Due to the limited volatility of (derivatized) higher oligomers, the use of GC is excluded for their quantification. To confirm their presence, GPC/SEC measurements were performed. The 'total organic phase recovery' is calculated from the ratio of the weight of the 'dried organic phase' and the weight of the 'theoretical organic phase at full dimer yield' (cf. n mol dimer, resulting from the ideal stoichiometrical reaction between the initial n mol formaldehyde and 2n mol methoxylated phenols without oligomer formation).

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