Lignin-based Bisguaiacol diisocyanate: a green route for the synthesis of biobased polyurethanes

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The synthesis of a new biobased aromatic diisocyanate derived from lignocellulosic raw material, namely guaiacol and vanillyl alcohol, through phosgene-free routes offers the prospect of greener approaches for isocyanate production and the polyurethane industry. Indeed, bisguaiacol F diisocyanate (BGI) was obtained via a three-step process from readily available bisguaiacol F (BGF), involving conversion of aromatic amine into aromatic isocyanate. The unusual metal-free conversion of BGF to bisguaiacol F diamine (BGA) was performed by a two-step approach: a) the Williamson-type alkylation of BGF and then b) the base-promoted Smiles rearrangement of bis O-Alkylated BGF. In order to improve the sustainability of this process, the first step was realized under solvent-free mechanochemical conditions, and the second step was performed using two different activating methods: thermal and microwave. The thermal process provided an isolated BGA yield of ca. 70%. Microwave activation proved to be an interesting alternative, although a lower yield (32%) of the desired BGA was achieved. Finally, the diisocyanate synthesis was performed via a phosgene-free/room temperature protocol using di-tert-butyl dicarbonate in presence of a catalytic amount of 4-dimethylaminopyridine (DMAP). Two polyurethane thermostats were designed and synthesized using the aromatic diisocyanates, biobased BGI and petrochemical-based methylene diphenyl diisocyanate (MDI), by a solvent-free two-step polymerization process, and their thermo-chemical properties were evaluated. These preliminary results suggest that BGI could be potentially used as a fully biobased surrogate for MDI.

Introduction

Within a few decades, polyurethanes have emerged as a powerful class of organic polymers. These materials possess a wide range of industrial applications, ranging from foams to CASE (Coatings, Adhesives, Sealants and Elastomers), owing from the increasing array of polyl and poly-isocyanate monomers available. Until very recently, polyurethane materials were synthesized from petrochemical-based compounds with high toxicity. However, with the growing concerns regarding raw material origin and resource scarcity in the upcoming decades, the design of monomer based on renewable sources is becoming a need. Therefore, both academic and industrial researches have focused on the enhancement of the sustainability in polyurethanes by developing a wide range of new bio-based polyols. On the contrary, bio-based poly-isocyanate monomers have known less development, especially aromatic isocyanates, which have received very little attention. One of the main reasons for this lack of development is the need to use phosgene gas to obtain isocyanate molecules. Indeed, the acute toxicity of phosgene gas is a major hinder to the development of phosgene-based industrial processes. Since 1928, when the first accident related to phosgene occurred in Hamburg, numerous industrial incidents and accidents involving phosgene production and/or use have been reported. Especially, lethal industrial accidents have been reported by DuPont and BASF in the last decade. Henceforth, phosgene is always produced in-situ where isocyanate synthesis occurs and drastic regulations (such as the Seveso directive in the European Union) have been implemented to make sure that the companies that use phosgene possess the appropriate technology and knowledge to avoid such severe accidents. Consequently, phosgene-free routes have been explored to design isocyanate compounds in a greener way. The triphosgenation of amine with bis(trichloromethyl) carbonate (triphosgene) can be explored to synthesize isocyanate compound. This one-step reaction is easy to implement but does not prevent phosgene production during the reaction. Thermalysis of urethanes and reductive carbylation of nitro-compounds are both energy-consuming, requiring high reaction temperatures (>200 °C). Regarding the reductive carbylation reaction, high-pressure of carbon monoxide (85 atm) is used, which severely impacts the sustainability of the process. On the other hand, since the thermalysis of urethane requires a reagent with urethane functions, the synthetic possibilities of this method are limited. Another promising approach is the preparation of isocyanate via the Curtius rearrangement, but the preparation and handling of acyl azide intermediates raises safety concerns, preventing this method from reaching industrial scale-up production. However, recent development in this chemistry using continuous-flow reaction allow for more promising environmental impact.

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In the 1990s, Knolker reported a very mild method for the preparation of isocyanates.\textsuperscript{14,15} This reaction operates in the presence of 4-dimethylaminopyridine (DMAP) as the catalyst (usually 10 mol%) using cheap and readily available di-tert-butyl dicarbonate (Boc\textsubscript{2}O) as the carbonyl source,\textsuperscript{16-18} in acetonitrile or dichloromethane at 25 °C. The main limitation of this method lies in the choice of the amine starting material, as only anilines and hindered alkyl amines are suitable for this reaction. More nucleophilic primary alkyl amines often yield ureas as the major side-product. We thought that this process could be viewed as a much greener alternative to the phosgene route (room temperature, much less hazardous reagents), especially since Boc\textsubscript{2}O can be synthesized directly from CO\textsubscript{2}.\textsuperscript{18} However, to our great surprise, it has hardly ever been used for the synthesis of isocyanate monomers for the preparation of polyurethanes materials.\textsuperscript{19}

Thus, in our quest to design a greener alternative to methylene diphenyl diisocyanate (MDI), we decided to synthesize a structurally analogous molecule from lignin feedstock using the Boc\textsubscript{2}O route (Erreur Source du renvoi introuvable.B).

Methylene diphenyl diisocyanate (MDI) is a diaromatic diisocyanate with three common isomers (4,4’-MDI, 2,4’-MDI and 2,2’-MDI) produced by a 4 step synthesis starting from aniline.\textsuperscript{20,21} The process for producing MDI (Erreur Source du renvoi introuvable.A) involves the reaction of aniline with formaldehyde in the presence of an acid catalyst to produce a mixture of methylene (diphenylidiamines) (MDA) and polymeric aniline (pMDA).

Further reaction with phosgene provides the corresponding polyisocyanates (step C). Finally, isolation of MDI isomers is performed through distillation (step C).

Aniline, involved in the first step, is classified as highly toxic for human beings and environment, CMR and corrosive.

Formaldehyde is fatal if inhaled and is also classified as highly corrosive, CMR and flammable. Therefore, raw materials for MDI synthesis are highly toxic compounds obtained from petro-based resources. Indeed, aniline is usually obtained from nitration of benzene followed by nitro to amine reduction. Product of the second step is a mixture of MDA isomers and polymeric aniline that is deemed as more toxic than MDI isomers. Finally, in the third step, phosgene gas is used to transform amine into isocyanate. Phosgene is classified by EU as highly toxic material. It has the highest NFPA 704 health rating of 4, “very short exposure could cause death or major residual injury”.\textsuperscript{22}

Since MDI is the most produced diisocyanate with a total European production capacity of 770,000 metric tons in 2020, the design of an analogous bio-based aromatic isocyanate could be of high interest. In addition to use renewable feedstocks, a greener and safer synthetic pathway is proposed in order to avoid the use of lethal compounds such as aniline, formaldehyde and phosgene gas.

**Results and discussion**

Our initial idea was to use bisguaiacol F (BGF) as the starting material. Indeed, BGF can be easily synthesized by acid-mediated Friedel-Crafts-type alkylation\textsuperscript{23,24} of guaiacol with vanillyl alcohol, which are both bio-based and readily available lignin-derived phenols. We selected the procedure of Periyasamy et al.\textsuperscript{23} (1:1 ratio on both bio-based phenol, sulfuric acid, ETOH, 100 °C) for multi-gram synthesis of BGF.\textsuperscript{23} Using these conditions, we were able to obtain 125 g of BGF in an approximately 3:1 mixture (p,p'-BGF : o,p'-BGF ratio) of isomers (Scheme 2). We then turned our attention to the transformation of BGF 3 into the corresponding diamine 6 (BGA). However, the direct amination of phenol derivatives, although very attractive, is usually difficult and requires harsh conditions and expensive transition-metal catalysts to achieve
effective dearomatic “hydrogen-borrowing strategy” (scheme 3A). Therefore, we decided to synthesize 6 via a two-step sequence: a) the Williamson-type alkylation of BGF 3 and b) the base-promoted Smiles rearrangement/amide hydrolysis of bis O-alkylated BGF 5 (Scheme 4). The alkylation of BGF was first carried out in DMSO at 50 °C for 24 h using K₂CO₃ as a base and KI as a catalyst. Surprisingly, incomplete conversion (89%) was obtained. Moreover, the high solubility of 5 in water made its purification difficult, since a substantial amount of product (>50%) was lost when attempting to remove DMSO from the mixture via aqueous work-up. When switching the reaction solvent to acetonitrile, incomplete conversion was observed at 50 °C (68%), but full conversion of BGF was observed at 80 °C after 24 h, and pure compound 5 was isolated in nearly quantitative yield (94%) after evaporation of acetonitrile followed by filtration on silica gel. To further improve this synthetic step in which using a solvent was found to be problematic, we turned our attention to solvent-free ball-milling.37–39

Scheme 2 Synthesis of BGF according to literature procedure.23

Moreover, the substrate scope of such transformations is somewhat limited, especially when using ammonia as the nitrogen nucleophile.26,27 Alternatively, the alkylation of phenols via transition-metal-free Smiles rearrangement has also been described (scheme 3B).31–34 The reaction operates via a three-step process, first a Williamson-type O-alkylation of the phenolic substrate, then the subsequent base-promoted Smiles rearrangement of the pendant amide moiety, followed by the base-promoted amide cleavage. Such a rearrangement is highly kinetically disfavoured, owing from the loss of aromaticity in the Meisenheimer-type intermediate (especially when using a phenol substituted with electron-donating groups), and therefore high temperatures (>100 °C) are usually required. In addition, it also seems that the formation of the Meisenheimer intermediate is accelerated by Thorpe-Ingold effect, as highlighted by the superior reactivity of secondary aryl ethers (R₂ = Me or Ph) versus primary ones (R₂ = H).31 Interestingly, this method features a broad scope of phenol derivatives, even for the formation of unsubstituted anilines.32 Another advantageous feature of the reaction is the possibility to perform the two-step sequence in one-pot31–33 as the conditions used for the O-alkylation are very close to the ones required for the Smiles rearrangement / amide cleavage. Therefore, we settled for a strategy based on the metal-free Smiles rearrangement of bisguaiaicol F. Initial attempts using bisguaiaicol F 3 and 2-bromopropionamide 4 as the amination reagent in a one-pot process in DMSO under previously reported conditions26,35,36 resulted in very low yields (< 10%) of bisguaiaicol diamine 6.

Thus, we decided to synthesize 6 via a two-step sequence: a) the Williamson-type alkylation of BGF 3 and b) the base-promoted Smiles rearrangement/amide hydrolysis of bis O-alkylated BGF 5 (Scheme 4). The alkylation of BGF was first carried out in DMSO at 50 °C for 24 h using K₂CO₃ as a base and KI as a catalyst. Surprisingly, incomplete conversion (89%) was obtained. Moreover, the high solubility of 5 in water made its purification difficult, since a substantial amount of product (>50%) was lost when attempting to remove DMSO from the mixture via aqueous work-up. When switching the reaction solvent to acetonitrile, incomplete conversion was observed at 50 °C (68%), but full conversion of BGF was observed at 80 °C after 24 h, and pure compound 5 was isolated in nearly quantitative yield (94%) after evaporation of acetonitrile followed by filtration on silica gel. To further improve this synthetic step in which using a solvent was found to be problematic, we turned our attention to solvent-free ball-milling.37–39

{Scheme 3 Strategies for the amination of phenol derivatives

Indeed, this approach already gave excellent results in our hands for monomer or polymer synthesis.40–42 Gratifyingly, using a 20 mL stainless steel milling jar with a 1 cm diameter stainless steel ball agitated at a frequency of 30 Hz, in a vibratory ball-mill, we obtained an excellent yield (90%) of 5 after only 90 minutes of milling. The yield of the transformation was even improved to nearly quantitative (>99%), when running the reaction for 3 h in the presence of potassium iodide catalyst.43 It is worth noting that under these mechanochemical conditions, the reaction can be carried out with similar success (96% conversion) in the absence of potassium iodide as catalyst. The purified product 5 was fully characterized by ¹H NMR, 13C NMR, FTIR, LC/MS and DSC analysis (see supplementary information).

With these alkylation conditions in hand, we then moved to the optimization of the Smiles rearrangement of bis-amide 5 to yield the desired diamine 6. We first examined the feasibility of such a rearrangement under thermal activation (140 °C) in DMSO and we observed that decreasing the amount of potassium hydroxide from 10 to 2.2 equiv. resulted in the increase of the yield of 6. We attributed this result to the potential irreversible hydrolysis of the starting di-amide in 5 at high hydroxide anion concentrations. However, at 140 °C using 2.2 equiv. of KOH, 6 was isolated in yields ranging from 34 to 47%. Decreasing the reaction temperature resulted in lower yields of the desired diamine and increasing the reaction time at 140 °C allowed the degradation of the desired product.
Concerned by the reproducibility issues at 140 °C, we decided to run the reaction using dry DMSO, hypothesizing that an inconsistent amount of water in the reaction mixture might be detrimental to the effectiveness of the Smiles rearrangement. Using dried DMSO, we obtained compound 6 in an improved 67% isolated yield, and more importantly, with an enhanced reproducibility, obtaining differences in yields within the range of experimental error. The purified product 6 was fully characterized by ¹H NMR, ¹³C NMR, FTIR, LC(MS), GC(MS) and DSC analysis (see supplementary information). Next, we examined the possibility of performing the Smiles rearrangement using microwaves activation. After prior optimization, we found that 4 equiv. of KOH at 200 °C for 30 minutes (50 W) was the optimal set of conditions. However, in DMSO, very low yield of 6 was obtained (13%). The use of polar co-solvents was found to be beneficial for the yield of rearrangement product in that case, with NMP being the best co-solvent (21-32%). The yield could be slightly increased when increasing the reaction time to 1 h (29-35%). Once again, reproducibility issues prompted us to explore the use of anhydrous solvents, but under microwave activation, these conditions did not improve the efficiency of the process (32%).

After having optimized the Smiles rearrangement conditions, we finally carried out the isocyanate synthesis using phosgene-free conditions (Scheme 5). Inspired by the work of Knöker, we synthesized the bisguaiacol F diisocyanate 7 from the corresponding diamine 6. We first tried the described set of conditions using catalytic amount of DMAP (10 mol%) along with a slight excess of di-tert-butyl dicarbonate (2.2 equiv.) in dry acetonitrile. Full conversion into the diisocyanate was observed by GCMS after 2 h, but the crude product was found to contain a substantial amount (ca. 15%) of Boc₂O. Therefore, we isolated BGF diisocyanate by flash column chromatography on silica gel. However, fast column chromatography with less polar solvents was found to be critical to obtain good yield of the diisocyanate, as 7 decomposes rapidly on silica gel. In these conditions, the desired BGF diisocyanate 7 was successfully isolated as a white solid with an isolated yield of 70%. A greener solvent, 1,3-dioxolane, was also used in substitution of acetonitrile and showed promising results (90%). Noteworthy, diisocyanate 7 possesses a calculated biomass degree of 88% against a biomass degree of 0% for MDI. Finally, the chemical structure of product 7 was ascertained by ¹H NMR, ¹³C NMR, and FTIR, spectroscopy, while LC(MS) and GC(MS) confirmed the good purity of the isolated product.

The latter possesses a melting point of 82.5 °C as determined by DSC analysis. As an example of the different applications of BGI as a monomer, we decided to synthesize BGI- and MDI-based polyurethane thermosets. Since BGI and MDI are solid compounds, a two-step method was used to design these materials. This method consists in synthesizing an isocyanate-terminated prepolymer followed by the formation of a 3D network though the addition of a trifunctional chain extender (Scheme 6).

Thereby, the selected isocyanate was heated up above its melting point (∼90 °C) and the system was purged with nitrogen in order to avoid side reactions. Velvetol® H500, which is a fully bio-based difunctional hydroxyl-terminated poly(1,3-propanediol) with an approximate molecular weight of 500 g/mol, was slowly added to the system. An excess of diisocyanate (2.5 equiv.) was used to react with Velvetol® H500 (1 equiv.) in order to control the system stoichiometry and to

form an isocyanate-terminated prepolymer. The prepolymer structure was confirmed by ¹H NMR (Figures S22 and S27). Finally, the obtained prepolymer was poured in a polypropylene flask and the appropriate amount of glycerol was added. The
mixture was stirred and cured into a silicon mould at 90 °C for 24 h in an oven. The BGI- and MDI-based thermosets (Erreur ! Source du renvoi introuvable.) properties were determined by FTIR, TGA and DSC methods and compared. FTIR (ATR) spectra of cured materials made with BGI and MDI monomers are displayed in Figures S23 and S28 (see supplementary information). In both cases, a broad band between 3600 and 3300 cm⁻¹, corresponding to the N-H bond of the urethane groups, is observed. A sharp peak around 1700 cm⁻¹, corresponding to C=O function of urethane groups, is also observed in both spectra.

Figure 1  Picture of MDI-based thermoset (left) and BGI-based thermoset (right)

Table 1  Thermal and chemical properties of MDI- and BGI-based thermosets

<table>
<thead>
<tr>
<th>Unit</th>
<th>T₅₀% (°C)</th>
<th>T₅₀% (°C)</th>
<th>T₈5% (°C)</th>
<th>Tg</th>
<th>SI</th>
<th>GC</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDI-based thermoset</td>
<td>287</td>
<td>380</td>
<td>487</td>
<td>34</td>
<td>100</td>
<td>99</td>
</tr>
<tr>
<td>BGI-based thermoset</td>
<td>287</td>
<td>391</td>
<td>428</td>
<td>15</td>
<td>290</td>
<td>75</td>
</tr>
</tbody>
</table>

Moreover, the absence of a band around 2300-2200 cm⁻¹ corresponding to isocyanate bond in Figure S28 shows that the conversion of isocyanates was fully reached in the case of the MDI-based thermoset. In contrast, BGI-based thermoset displays a small signal at 2245 cm⁻¹, indicating the presence of residual isocyanate groups in the cured material. The thermal stability of each cured materials was studied by TGA measurements under nitrogen atmosphere (Erreur ! Source du renvoi introuvable.). Both materials have quite similar degradation profiles. The BGI-based thermoset tends to be slightly less thermally resistant compared to the MDI-based thermoset. Moreover, the BGI-based material exhibits a lower Tg value (15 °C) compared to the MDI-based material (34 °C) (Erreur ! Source du renvoi introuvable.). This can be explained by the presence of unreacted isocyanate functions in BGI-based cured material that provides lower thermal properties, although it can also partially result from the presence of a neighbouring methoxy group in the BGI-based material. Finally, gel content were measured and (Erreur ! Source du renvoi introuvable.) indicate that the material synthesized with BGI possesses a lower crosslink density than the one synthesized with MDI, which is expected since the FTIR spectrum of the BGI-based material shows the presence of unreacted isocyanate functions. This can also be observed by comparing the swelling index of both materials since the MDI-based thermoset has a much lower swelling index (100%) than the BGI-based thermoset (290%). However, the formation of a crosslinked material was confirmed since the BGI-based thermoset features a 75% of insoluble fraction.

Conclusions

In summary, we have developed an efficient synthetic strategy to produce a greener lignin-based surrogate of MDI with a biobased content of 88%. This approach involves a 4-step synthesis from lignin-based, readily available guaiacol and vanillic alcohol. Unlike the MDI synthesis, our strategy relies on a metal-free and phosgene-free route to afford the biobased aromatic diisocyanate BGI, avoiding the use of very toxic and environmentally harmful compounds such as aniline, formaldehyde and phosgene. BGI was found to be a convincing alternative to MDI for the preparation of cross-linked polyurethanes, as similar thermal properties were obtained for both MDI and BGI based materials. Lately, chemical companies such as BASF⁴⁵ are actively working on the development of biobased MDI from biobased aniline, highlighting once more the urgent need for the design of more sustainable aromatic isocyanates monomers. In this study, we offer a possibility to avoid the risks associated with the conventional preparation of MDI and to valorise greenhouse gas through Boc₂O synthesis. In particular, we believe that bypassing the use of phosgene is a significant advance in the design of greener isocyanate monomers, and further studies using phosgene-free isocyanate monomers are currently underway in our laboratory.

Conflicts of interest

There are no conflicts to declare.

Notes and references


7 Explosion of phosgene gas at Hamburg, The National Archives, 1928.


22 Codes and Standards of the NFPA retrieved from www.nfpa.org.


General information

2-methoxyphenol (guaiacol, ≥99%), 4-Hydroxy-3-methoxybenzyl alcohol (vanillyl alcohol, 98%), sulfuric acid (H₂SO₄, 99.99%), potassium carbonate (K₂CO₃, ≥99%) potassium iodide (KI, ≥99%), 2-bromopropionamide (99%), hydroxide potassium (KOH, ≥85%), triethylamine (≥99.5%), di-tert-butyl dicarbonate (Boc₂O, 99%), 4-(dimethylamino)pyridine (DMAP, ≥99%), methylene diphenyl diisocyanate (MDI, 98 %), 1,3,5-trimethoxybenzene (≥99%), d-chloroform (CDCl₃, 99.5 % D) were supplied by Sigma-Aldrich (Darmstadt, Germany) and used as received. Velvetol® H500 was kindly supplied by WeylChem International GmbH (Frankfurt am Main, Germany) and used as received. Glycerol (≥99.5%) was purchased by Prolabo (Paris, France) and used as received.

Silica gel plates (GF254, coating thickness 0.2-0.25 mm) were employed for thin-layer chromatography (TLC), and 200-300 mesh silica gel was used for flash column chromatography. ¹H and ¹³C NMR spectra were recorded on a Bruker Advance™ 400 spectrometer at ambient temperature with CDCl₃ as solvent. Chemical shifts were reported in ppm with tetramethylsilane as an internal standard. The Fourier transform infrared (FTIR) spectra were recorded using attenuated total reflection (ATR) in transmission mode with a ThermoScientific Nicolet iS50 FT-IR Flex Gold spectrometer. High resolution mass spectrometry (HRMS) data were obtained on a LC-TOF mass spectrometer (micrOTOF-Q) using electrospray ionization (ESI) in positive or negative mode. GCMS were analyzed by electrospray ionization (ESI) using Chimaedu QP2010SE mass spectrometer. Thermogravimetric analyses (TGA) of the cured polyurethanes were performed on a Netzsch STA 449 F1 TGA. The protective gas used was nitrogen with a 20 mL·min⁻¹ flow. Approximately 10 mg of sample was placed in an alumina crucible and heated from room temperature to 800 °C with a 10 °C·min⁻¹ heating ramp. Differential scanning calorimetry (DSC) analyses were carried out using a Netzsch DSC 3500 Sirius calorimeter. Nitrogen was used as the purge gas at 40 mL·min⁻¹. Approximately 10 mg of sample was placed in pierced aluminum pans. The melting temperatures were recorded between room temperature and 150°C at 20 °C·min⁻¹. The thermal properties of the thermoset materials were recorded between −100 and 200 °C at 20 °C·min⁻¹ to observe the glass transition temperature.

The milling reactions were carried out in a vibratory Retsch Mixer Mill 400 (vbm) operated at up to 30 Hz. The microwave reactions were carried out in an Anton Paar Monowave 300 microwave reactor using standard 5 mL glass vials.

1. Experimental section

1.1 General procedure for the synthesis of bis O-Alkylated guaiacol F

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\begin{align*}
\text{conditions} \rightarrow \quad & \quad \text{Bisguaiacol F (1 equiv., 1.92 mmol, 5 g), potassium iodide (0.1 equiv., 0.19 mmol, 0.32 g), potassium carbonate (3 equiv., 5.77 mmol, 7.96 g) and 2-bromopropionamide (2 equiv., 3.84 mmol, 5.80 g) were}
\end{align*}
\]

- Thermal procedure

Bisguaiacol F (1 equiv., 1.92 mmol, 5 g), potassium iodide (0.1 equiv., 0.19 mmol, 0.32 g), potassium carbonate (3 equiv., 5.77 mmol, 7.96 g) and 2-bromopropionamide (2 equiv., 3.84 mmol, 5.80 g) were
taken in a 500 mL round bottomed flask equipped with a magnetic stirrer and a reflux condenser. To the stirring mixture, 150 mL of acetonitrile was added. Then, the reaction mixture was heated to reflux for 24 h, cooled to room temperature, filtrated and concentrated under reduced pressure. The crude product was purified through flash column chromatography on silica gel with dichloromethane-methanol as eluent. After evaporation of the eluent, the isolated bis O-Alkylated bisguaicol F was obtained as a white to yellowish powder with a yield of 94%.

- **Mechanochemical procedure**

A 20 mL stainless steel milling jar was loaded with bisguaicol F (1 equiv., 0.81 mmol, 0.212 g), potassium iodide (0.1 equiv., 0.08 mmol, 0.014 g), potassium carbonate (3 equiv., 2.41 mmol, 0.333 g), 2-bromopropionamide (2 equiv., 1.62 mmol, 0.245 g) and one 1 cm stainless steel ball. The reactor was then sealed and subjected to vibratory milling at 30 Hz for the set amount of time. The reaction mixture was then dissolved in acetonitrile, filtrated and concentrated under reduced pressure. The obtained bis O-Alkylated bisguaicol F was obtained as a white to yellowish powder with a full conversion.

**1.2 General procedure for the synthesis of bisguaicol F diamin (BGA)**

- **Thermic procedure**

Bis O-Alkylated bisguaicol F (1 equiv., 12.4 mmol, 5 g) and potassium hydroxide (85% purity, 2.4 equiv., 29.8 mmol, 1.67 g) were taken in a 100 mL round bottomed flask equipped with a magnetic stirrer. The reaction mixture was dissolved in 50 mL of dry DMSO and heated at 140 °C for 18 h. The solution was then cooled to room temperature and diluted in water, extracted three times with ethyl acetate. The combined organic layers were washed one time with sat. brine solution and finally dried over MgSO₄. The crude product was purified through flash column chromatography on silica gel with cyclohexane/ethyl acetate as eluent containing (0.2% v of triethylamine). After evaporation of the solvents, the obtained bisguaicol F diamin was obtained a light brown powder with a yield of 66%.

- **Microwave procedure**

Bis O-Alkylated bisguaicol F (1 equiv., 1.24 mmol, 0.500 g), potassium hydroxide (85% purity, 5.2 equiv., 6.46 mmol, 0.380 g) and 5 mL of solvent were added in a microwave reactor consisting in a 10 mL vessel tube, a pressure monitor system and a fiber optic temperature probe. The system was irradiated under microwave conditions at different temperature and during different periods. Reaction conversion was monitored by GCMS analysis using 1,3,5-trimethoxybenzene as internal standard.
1.3 General procedure for the synthesis of bisguaiacol F diisocyanate (BGI)

A solution of di-tert-butyl dicarbonate (2.2 equiv., 8.52 mmol, 1.86 g), DMAP (0.1 equiv., 0.39 mmol, 0.047 g) in 10 mL of dry acetonitrile was prepared in a 50 mL round bottomed flash equipped with a magnetic stirrer. A solution of bisguaiacol F diamine (1 equiv., 3.87 mmol, 1 g) in 10 mL of dry acetonitrile was then slowly added to the previous solution. The reaction mixture was stirred at room temperature for 2 h and then concentrated under reduce pressure. The product was additionally dried under vacuum during 1 h. The obtained bisguaiacol F diisocyanate was obtained a brown viscous liquid with a purity around 95% and a total conversion.

1.4 General procedure for the synthesis of polyurethane thermosets through a two-step method

As a representative example, 2.40 g of BGI (2.5 equiv., 0.77 mol) was introduced in a 10 mL two necks round-bottom flask, equipped with a mechanical stirrer. The system was purged with nitrogen for 10 min and then heated up to 90 °C. Afterwards, 1.60 g of Velvetol® H500 (1 equiv., 2.72 mmol) were added with a syringe driver for one hour. The mixture was mechanically stirred for 4 h at 90 °C. Finally, 2.60 g of the obtained prepolymer was poured into a PP flask, and 0.187 g of glycerol was added. The mixture was mixed at 2500 rpm for 3 mins in a PP flask with a SpeedMixer™, poured into a silicon mould, and cured at 90 °C for 24 h in oven.
2. Characterization of the products

2.1 O-bis Alkylated BGF characterizations

S1. Molecular structure assignment of O-bis Alkylated BGF

S2. $^1$H NMR spectrum of O-bis Alkylated BGF (in CDCl$_3$)

S3. $^{13}$C NMR spectrum of O-bis Alkylated BGF (in CDCl$_3$)
S4. FTIR spectrum of O-bis Alkylated BGF

S5. (LC)-HRMS of O-bis Alkylated BGF
S6. DSC thermogram of O-bis Alkylated BGF
2.2 BGF diamine characterizations

Figure S7. Molecular structure assignment of BGF diamine

S8. $^1$H NMR spectrum of BGF diamine

S9. $^{13}$C NMR spectrum of BGF diamine
S10. FTIR spectrum of BGF diamine

Figure S11. (LC)-HRMS of BGF diamine
Figure S12. (GC)-MS of BGF diamine

Figure S13. DSC thermogram of BGF diamine
2.3 BGF diisocyanate characterizations

Figure S14. Molecular structure assignment of BGF diisocyanate

S15. $^1$H NMR spectrum of BGF diisocyanate

S16. $^{13}$C NMR spectrum of BGF diisocyanate
S17. FTIR spectrum of BGF diisocyanate

Figure S18. (LC)-HRMS of BGF diisocyanate
Figure S19. (GC)-MS of BGF diisocyanate

Figure S20. DSC thermogram of BGF diisocyanate
2.4 MDI-based material characterization

Figure S21. Molecular structure assignment of MDI-based prepolymer

S22. $^1$H NMR spectrum of MDI-based prepolymer

S23. FTIR spectrum of MDI-based thermoset
Figure S24. TGA thermogram of MDI-based thermoset

Figure S25. DSC thermogram of MDI-based thermoset
2.5 BGI-based prepolymer characterization

Figure S26. Molecular structure assignment of BGI-based prepolymer

S27. $^1$H NMR spectrum of BGI-based prepolymer

S28. FTIR spectrum of BGI-based thermoset
Figure S29. TGA thermogram of BGI-based thermoset

Figure S30. DSC thermogram of BGI-based thermoset