Amine-Catalyzed Aldol Addition of Dihydroxyacetone for Bio-Based Flame Retardants

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Abstract: A new catalytic method was developed for synthesizing a sustainable phosphorus-based flame retardant (PFR) from dihydroxyacetone (DHA), a triose derived from hexoses or glycerol oxidation, *e.g.,* for PUR applications. The study first investigates alkyl amine catalysts for self-aldol addition of DHA to form the branched hexose dendroketose. Short-chain, non-functionalized secondary and tertiary amines showed the best balance between aldol activity and branching selectivity. Triethylamine (Et_3N) was chosen for process optimization, enabling scale-up to a 10 L process using 500 g/L DHA and 1 mol% Et_3N, achieving a productivity of 109 g/(L·h)—approximately 7.5 times higher than the current state of the art. The resulting dendroketose was hydrogenated to produce dendroketol, a branched hexitol with three primary alcohol groups suitable for further functionalization. To prevent product loss during hydrogenation due to base-catalyzed retro-aldol addition, various amine neutralization methods were evaluated, with equimolar HCl addition proving most effective and economical. Finally, dendroketol was purified and phosphorylated with P_2O_5 to yield the PFR. Flame-retardant testing, conducted under EU standard BS 7175 (for bedding materials), confirmed compliance, underscoring the industrial potential of the process.

Introduction

Ever since the discovery of polyurethanes (PUR) in 1937 by Otto Bayer, their applications have become widespread in our society *e.g.* in furniture, packaging, coatings, and beddings. However, these compounds were soon identified as highly flammable, burning intensely and completely. This makes them a serious hazard for human life, property, and the environment. Therefore, there has been a focus on producing fire-resistant PUR materials, leading to the discovery of flame-retardant (FR) molecules. Inorganic compounds (*e.g.* hydrated alumina or Sb_2O_3) are sometimes used, but organic compounds are most widely implemented, falling into two major groups: halogen-based flame-retardants (HFRs) or phosphorous-based flame-retardants (PFRs).[1] Initially, HFRs were used predominantly, but were phased out after the discovery of their negative side-effects on humans such as immunotoxicity, endocrine disruption, effects on fetal/child development and being carcinogenic.[2]
The current generation of commercial flame retardants (FRs), such as tris-(2-chloroethylphosphate) (TCEP) and tris-(2-chloroisopropylphosphate) (TCPP), contain both phosphorus and halogens. However, recent efforts have focused on developing halogen-free FRs to avoid toxic and corrosive gases during combustion and to reduce environmental impact during production and PUR recycling. Phosphorus-based FRs are also more efficient,

requiring only 1.5–2 wt.% (relative to PUR) to match the flame-retardant performance of 20–25 wt.% Cl-based or 5–6 wt.% Br-based.[1, 3] Although FRs are typically added after PUR synthesis, studies have shown that migration[3] or degradation can reduce their effectiveness—for example, TCEP's flame-retardant effect was reported to significantly diminish after one year due to hydrolysis.[1] Current research focuses on integrating FRs into the PUR network. One approach is to modify the polyol with halogen or phosphorus groups, making it both a flame retardant and a reactive component in polymerization.[3-4]

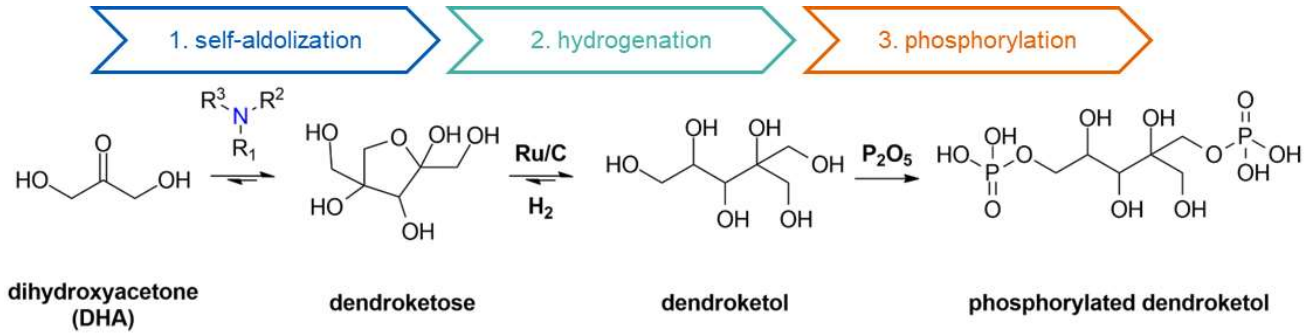
Polyols are typically made by hydrogenating hexoses (*e.g.*, glucose to sorbitol) but an alternative approach involves aldol addition of two carbonyl compounds with α-OHs to form C–C bonds. The resulting α,γ-hydroxy carbonyl product is then hydrogenated to yield the polyol. Currently, most industrial aldol reactions depend on carbonyl compounds derived from fossil feedstocks (*e.g., n*-butanal to 2-ethylhexanol[5-6] or acetaldehyde and formaldehyde to pentaerythritol[7-8]), which raise sustainability concerns.[9-11] With increasing focus on carbon circularity, alternative feedstocks such as lignocellulosic biomass (which provides carbohydrates and lignin)[9-10] or vegetable oils (yielding fatty acids and glycerol) offer more sustainable options for producing polyols.[1, 12-15] A recent review outlines the progress, potential, and challenges of using biomass in aldol addition or condensation reactions.[16]

One specific example in literature of producing a polyol from sustainable biomass is *via* the self-aldol addition of dihydroxyacetone (DHA) in basic aqueous conditions to form a branched hexose, dendroketose.[14, 17-19] Next, dendroketose is hydrogenated to produce dendroketol—a branched hexitol with three reactive primary alcohol groups.[14, 19] These can serve as attachment points for different valorization strategies, such as use as a polyol in polymer synthesis,[15, 20-21] or esterification to produce lubricants[22-24] and emollients.[25-26]

DHA, which is currently produced as a fine chemical through glycerol fermentation[27-30] and used in self-tanning products,[30-33] offers promising prospects for broader applications through increased production from chemocatalytic[30, 34-37] or other oxidative processes.[38] This expanded production could improve the economic and sustainability performance of glycerol-based biodiesel industries, making DHA a valuable precursor for high-value chemicals. The self-aldol addition of DHA has been previously reported using basic anionic exchange resins such as IRA-900[17-18] or Dowex 550A,[19] successfully yielding dendroketose. While aldol additions can be catalyzed by acids[39], they are predominantly conducted using basic catalysts. Basic conditions are preferred because the enolate intermediate is a stronger nucleophile and forms faster than the enol in acidic conditions. This eliminates the need for high temperatures, reducing side reactions like dehydration or the Maillard reaction. Additionally, basic conditions prevent side reactions such as the Mannich reaction with amines. In literature, both homogeneous[40] and heterogeneous[14, 17-19] base-catalyzed aldol additions are widely documented. In these reports, dendroketose is further dehydrated to produce 4-HMF (a potential precursor for pharmaceuticals and materials)[17-18] or hydrodeoxygenated into branched alkanes (a bio-gasoline precursor).[19] Despite the effectiveness of basic resins as aldol catalyst, their high cost (200 – 350 USD/kg), high loading (25 – 100 wt.%), and regeneration complexity make them less suitable for the large-scale production of low-value chemicals or fuels.

Recently, a hydrotalcite catalyst has been shown to catalyze the aldol addition of DHA with high yields of dendroketose at lower loadings (25 wt.%).[14] Moderately basic, hydroxyl-rich hydrotalcite rehydrated under CO_2-free conditions is most effective, while stronger metal oxides promote carboxylic acid formation, causing hydrotalcite dissolution and impurities. These residues hinder the selective hydrogenation of dendroketose to dendroketol. However, the strict synthesis conditions may pose challenges in industrial settings.

Therefore, this study proposes an industrially feasible, biomass-based route to a sustainable PFR as alternative to fossil-based HFRs (see Scheme 1). First, it evaluates cost-effective, commercially available alkyl amine bases to understand their impact on aldol addition rate and product selectivity. Since DHA can isomerize to glyceraldehyde, forming linear sugars and polyols, controlling dendroketose (branching) selectivity is crucial for the process's effectiveness. Second, we will also investigate the impact of residual amines on the subsequent dendroketose hydrogenation and their removal. The optimized synthesis and neutralization protocols were scaled to 10 L to demonstrate industrial feasibility. Lastly, the resulting dendroketol is purified and phosphorylated, and tested as a bio-based flame retardant in mattress fabric as a proof of concept. As the phosphorylated product met the phosphorus content of industrial standards and was tested for flame-retardant properties per BS 7175, it is proposed as an alternative PFR, replacing current industrial harmful HFRs.

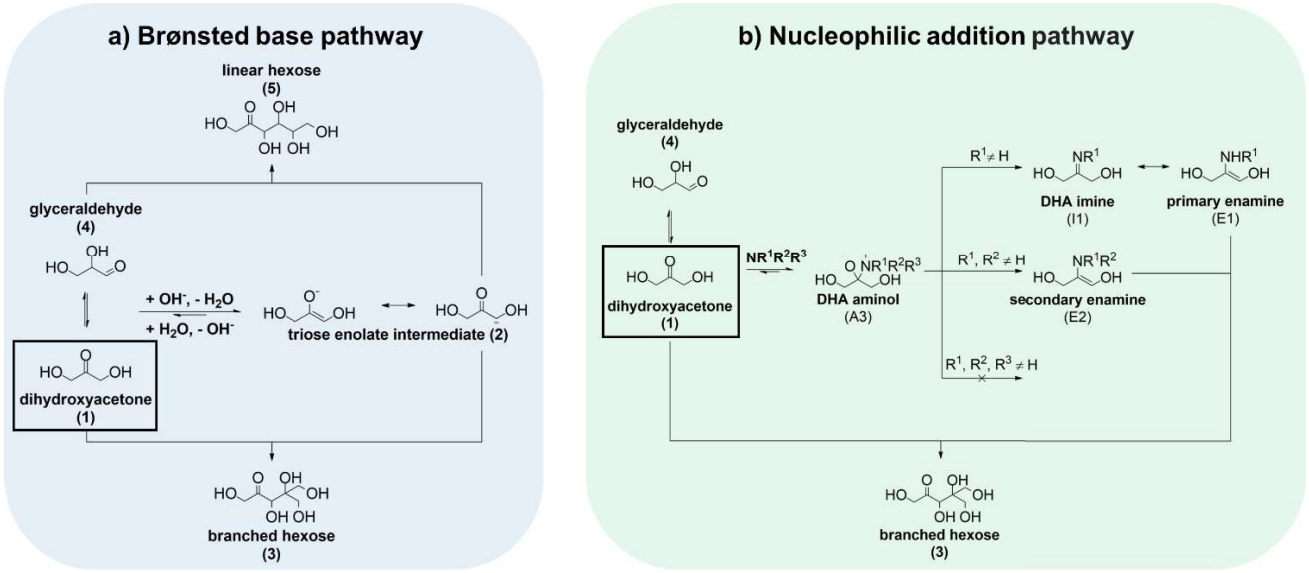


Scheme 1: Overview of the studied valorization of dihydroxyacetone (DHA) into a novel phosphorylated dendroketol, evaluated as a flame-retardant compound, with the different reaction steps.

Results and Discussion

Initial Screening of Soluble Amine Catalysts

The reported self-aldol addition of dihydroxyacetone (DHA, **1**) to form dendroketose proceeds *via* a basic reaction mechanism, simplified in Scheme 2a. Under basic conditions, the process begins with the deprotonation of the α-H of DHA, generating the enolate intermediate (**2**). This enolate performs a nucleophilic attack on the carbonyl group of another DHA molecule, yielding the desired branched hexose (dendroketose, **3**) upon protonation. However, **2** can also isomerize to form glyceraldehyde (GLA, **4**), a competitive side reaction. In aqueous solution, the DHA-GLA equilibrium at room temperature results in a mixture of 60 %– 65% DHA and 35 %– 40% GLA, and this equilibrium is quickly established under basic conditions.[30, 41] The cross-addition of GLA with DHA produces linear hexoses, such as fructose or sorbose (**5**). Due to the higher electrophilicity of aldehydes,[42] these side-products are kinetically favored over the desired self-aldol reaction of DHA.[14, 19]
With amines, a second reaction route to dendroketose *via* DHA-amine adduct formation is simplified in Scheme 2b. A nucleophilic attack of an amine on the electrophilic carbonyl of DHA leads to the DHA aminol intermediary (A3). Based on the degree of substitution, this leads to different intermediaries or routes to dendroketose (see below).



Scheme 2: Overview of the reaction pathway for the aldol addition of dihydroxyacetone (DHA, 1) to form hexoses (3 and 5) under alkaline conditions using organic amines: a) the Brønsted base-catalyzed reaction steps and b) the amine nucleophilic addition pathway.

Initially, twenty-one alkylamines were screened to elucidate the effect of (i) the degree of substitution (primary, secondary, and tertiary), (ii) alkyl chain length, and (iii) functionality (*i.e.*, with or without alcohol; mono- and diamines) on the catalytic performance. This was done to get an insight into how their structural properties affect the reaction performance and to identify a suitable amine catalyst for the basic (self-)aldol addition of DHA, *i.e.* the

amine that exhibits an optimal balance between aldol activity and branching selectivity, viz., dendroketose vs. linear ketose.

The rationale for these selections is as follows:

i. Comparing primary, secondary, and tertiary amines helps determine whether deprotonation alone (in the case of tertiary amines, Scheme 2a) or amine adduct formation (*e.g.*, imines for primary and enamines with secondary amines, Scheme 2b) is rate- or selectivity-determining;
ii. Varying the alkyl chains helps elucidate the impact of basicity and steric effects, and
iii. Alcohol groups can further interact with DHA's carbonyl *via* hydrogen bonding, promoting the deprotonation by positioning the active amine site nearer to the substrate.

Practically, adding a heteroatom like oxygen or nitrogen to the amine can improve water solubility and lower vapor pressure, enhancing process safety and sustainability. In contrast, more volatile amines may ease catalyst removal and simplify purification.

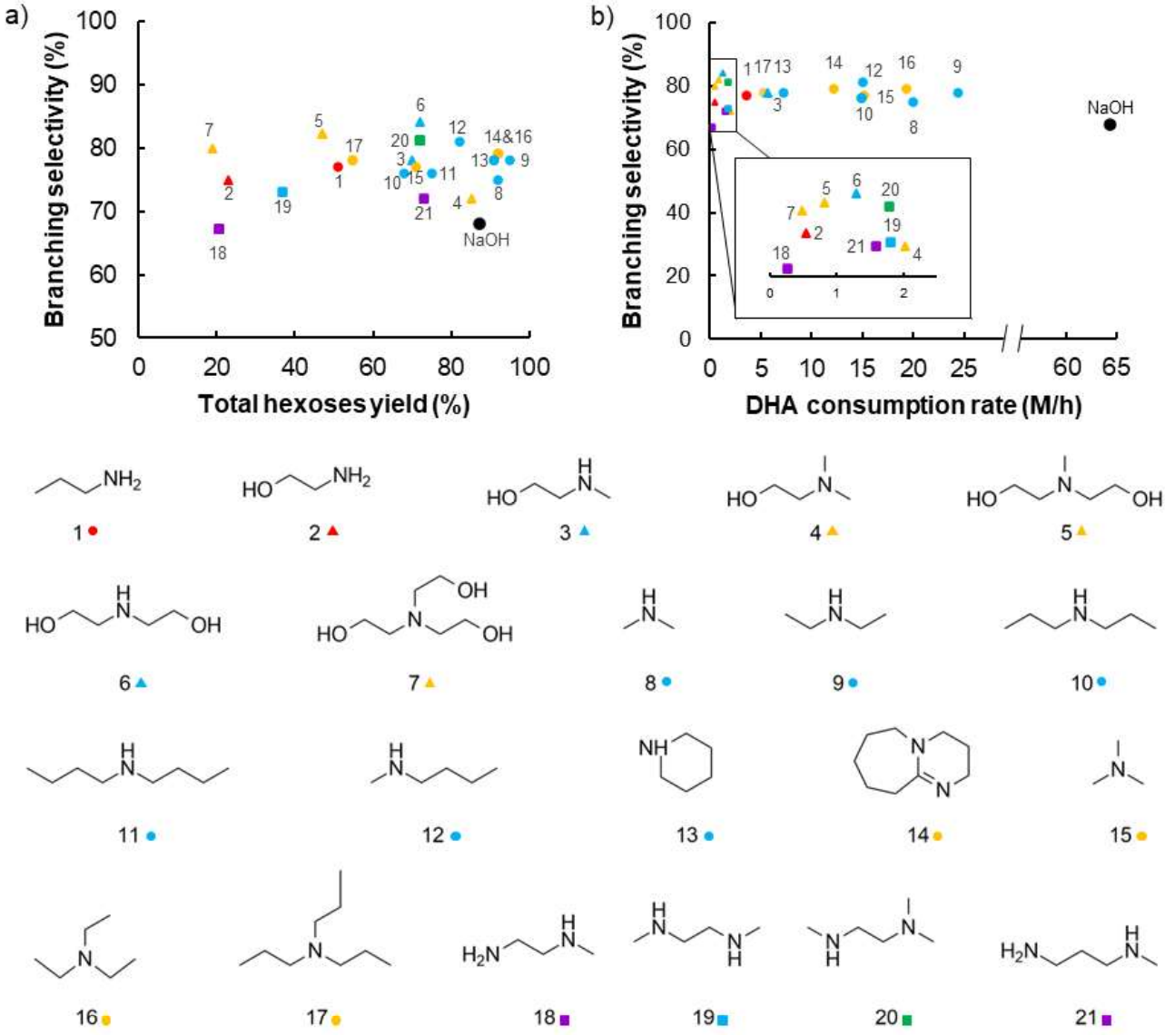


Figure 1: Results from the initial amine screening for the amine catalyzed (self-)aldol addition of dihydroxyacetone (DHA) toward dendroketose with primary (red), secondary (cyan) or tertiary (gold) monoamines with (triangle) or without (circle) alcohol groups on the alkyl chain or primary/secondary (purple), secondary/secondary (cyan) or secondary/tertiary (green) diamines (squares) with a) selectivity toward branched hexose (dendroketose) vs. total hexose yield after 4 h and b) selectivity toward branched hexose (dendroketose) vs. the pseudo first-order DHA consumption rate (in M/h), calculated at a DHA conversion under 15 %. **Reaction conditions**: 200 g/L DHA in mQ water at room temperature with 5 mol % monoamine or 2.5 mol % diamine: 1) propylamine; 2) ethanolamine; 3) 2-(methylamino)ethanol; 4) *N*-dimethylamino ethanol; 5) *N*-methyldiethanolamine; 6) diethanol amine; 7) triethanolamine; 8) dimethylamine; 9) diethylamine; 10) dipropylamine; 11) dibutylamine; 12) *N*-methylbutylamine; 13) piperidine; 14) 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU); 15) trimethylamine; 16) triethylamine; 17) tripropylamine; 18) *N*-methylethylenediamine; 19) *N,N'*-dimethylethylenediamine; 20) *N,N,N'*-trimethylethylenediamine; 21) *N*-methyl-1,3-diaminopropane.

This diverse set of amines aims to establish a structure-activity relationship based on DHA conversion and branching selectivity. Top-performing catalysts will be selected for scale-up and evaluated for their potential in synthesizing the bio-based flame retardant. Figure 1 shows the screened amines and results; additional data are available in Tables S2 and S3.

Figure 1a shows total hexose yield *versus* selectivity after 4 h, ranging from 20% to over 90% yield and 67%–84% branching selectivity. This highlights significant differences in amine catalyst activity and their effect on selectivity. Reorganizing the data presented in Figure 1b, which shows the rate of DHA consumption (determined as the pseudo-first-order rate from kinetic evolution plots under 15% conversion, see Section S1.2 and Table S3), as a function of selectivity, provides a clearer view of the activity differences.

It is important to note that dibutylamine (entry 11) has a low water solubility (~4 g/L or 1.3 mol %) at 20°C, resulting in a lower amine concentration compared to the others. As a result, it was excluded from the discussion of initial DHA consumption rates in Figure 1b. However, it was included in the 4-hour results in Figure 1a, as the lower concentration effect is assumed to diminish over time. This is supported by its similar performance to dipropylamine (entry 10) at the higher concentration (1.3 mol % vs. 5 mol %, see Table S3) and after 4 h. Additionally, tests with triethylamine—a more reactive amine—under comparable conditions (200 g/L DHA, 1 mol %) showed equilibrium was reached within 3 h (Figure S8), suggesting that dibutylamine likely reached (near-)equilibrium by 4 h as well.

A closer analysis of the data reveals the following notable trends:

i. Primary amines show much lower catalytic activity than secondary and tertiary amines (*e.g.*, entries 1, 9, and 16), with secondary amines being highly active and slightly faster than tertiary ones.
ii. Among secondary amines, longer alkyl chains (*e.g.*, methyl to ethyl, entries 8 and 9) increase reaction rates, exceeding 20 M/h. While this may relate to base strength (pK_b 3.27 *vs*. 2.91), steric hindrance becomes more significant with larger or cyclic groups (entries 10, 13), suggesting that adduct formation with the amine catalyst is key. Similar but stronger steric effects are seen in tertiary amines when alkyl chains exceed ethyl (*e.g.*, entries 8–9 *vs*. 10; 15–16 *vs*. 17).
iii. Additional functional groups (alcohol or amine) strongly influence activity and selectivity. Amine alcohols impedes the reaction (*e.g.*, entries 6 *vs*. 9 and 7 *vs*. 16), suggesting OH groups and related effects do not impact the rate-determining step. Surprisingly, diamines with secondary methyl amines are much less active than their corresponding monoamines (*e.g.*, entry 8 *vs*. 18, 19 and 21).
iv. There is no correlation between pK_b of homologue amines (*e.g.* 8 – 11 or 15 – 17) and their reaction performance (see Figure S1), highlighting that the Brønsted base pathway Scheme 2a is not the main or predominant dendroketose reaction pathway.

Catalytic Performance Rationalization

As previously mentioned, the reaction activity and branching selectivity of alkylamines are primarily influenced by the degree of alkyl substitution, the length and type of the alkyl chain, and the presence of additional functional groups. These trends likely stem from both DHA and amine properties. All amines act as Brønsted bases, deprotonating α-H of DHA, but they can also act as nucleophiles, forming hemi-aminals with trioses (Scheme 2b). This is especially true for DHA, whose α-OH groups enhance ketone electrophilicity,[43] shifting the equilibrium more toward hemi-aminal formation. Selectivity varies more with the less active catalysts, indicating that slower aldolization allows more isomerization. When aldolization is fast, selectivity remains high (~80%) regardless of the catalyst. Thus, minimizing DHA-to-GLA isomerization is key.

Additionally, side reactions, like Maillard reactions between the amine and DHA, can produce colored by-products.[44-45] In most cases, a faint yellow coloration, indicating product formation, was observed, with its intensity correlating to DHA consumption rates. Darker coloration, suggesting Maillard reactions (orange to brown), occurred mainly after 24+ h for amines with high DHA consumption rates, except for tertiary amines like triethylamine, which do not participate in Maillard reactions.[44]

Degree of substitution

Primary amines form thermodynamically stable imines (**I1** in Scheme 2b) *via* the DHA hemi-aminal intermediate, sequestering a portion of the catalyst. This reduces the concentration of active primary amine, limiting its Brønsted base activity and catalytic efficiency. Although imines can hydrolyze, this occurs slowly under the pH 8–9 reaction

conditions, where imine formation is favored.[46-48] Despite this, a small amount of hexoses can still form from the free primary amines acting as Brønsted bases or *via* an alternative mechanism, as imines resonate with their enamine form, which can also yield hexoses (see Scheme 2b and S1 for more details).

Secondary amines cannot form imines, but they can form iminium ions, which similarly trap the amine, though this is not the dominant species. Instead, the hemi-aminal intermediate equilibrates with the DHA-enamine species (see Scheme S2, intermediate **E2** in Scheme 2b). This enamine, structurally similar to the enolate intermediate in Brønsted-catalyzed pathways, reacts with free DHA, making enamine-mediated aldol addition the primary pathway for secondary amines, rather than α-H deprotonation.[49] The high hemi-aminal formation, due to DHA's increased electrophilicity, and the reactive DHA-enamine species explain why secondary amines exhibit activity similar to tertiary amines, as shown by their comparable hexose yields and pseudo-first-order reaction rates.

These intermediates may also undergo reactions similar to the Mannich reaction (see Schemes S3 & S4), where the DHA enolate attacks DHA imine **I1** (for primary amines) or iminium ions **I2** (for secondary amines), forming β-amino enone derivatives. ^{13}C-NMR analysis of pure DHA and dendroketose (see Figure S11 & S12) and reaction solutions (see Figures S13-S15) of DHA aldolization with propylamine, ethanolamine, and diethylamine (entries 1, 2, and 9) showed no detectable levels of these products, ruling out this side reaction as a cause for the lower hexose yield or dendroketose selectivity.

Tertiary amines, lacking protons on the nitrogen, cannot form imines or enamines and mainly act as Brønsted bases. Being weaker bases than NaOH, they create milder OH^- concentrations, leading to higher branching selectivity and lower isomerization rates at similar hexose yields, reducing product degradation.

Alkyl chain

An optimal alkyl chain length is observed among secondary alkylamines (entries 8–13). As chain length increases from dimethylamine to dibutylamine (entries 8–11), nucleophilicity and basicity rise (see Tables S2 & S3 or Figure S1 for pK_b values). Initially, DHA consumption and hexose yield increase from dimethylamine to diethylamine (entries 8 and 9). However, with longer chains (dipropylamine and dibutylamine, entries 10 and 11), the final yield decreases, falling below dimethylamine levels.

This trend can be explained by two factors. First, while higher nucleophilicity initially promotes aldolization toward dendroketose, further increases may hinder product formation by slowing hydrolysis of aminated dendroketose (D1), the final step in the enamine pathway (see Schemes S1 and S2). Second, bulkier alkyl groups may slow nucleophilic attack, hemi-aminal formation, and hydrolysis of aminated dendroketose, all of which reduce product formation.

This hypothesis is supported by examining other secondary amines. *N*-methylbutylamine (entry 12) reports a similar DHA consumption rate (~15 M/h) and pK_b (~3) to dipropylamine, but a higher hexose yield. This suggests that similar nucleophilicity is hindered by the bulkiness of the latter, which hinders activity over time. Similarly, piperidine (entry 13) with a lower pK_b (~2.8) shows a lower consumption rate than both, supporting the idea that steric hindrance slows the reaction. The secondary amines have an average branching selectivity of 77%, with *N*-methylbutylamine showing the highest selectivity (81%) and total hexose yield (82%).

Among the tertiary alkylamines (entries 14–17), a similar trend is observed: an increase in reaction rate and hexose yield from trimethylamine to triethylamine (entries 15 & 16), followed by a decrease with tripropylamine (entry 17). The initial increase in alkyl chain length enhances amine basicity, leading to more enolate formation and higher yield. However, the similar pK_b values of triethylamine and tripropylamine (3.25 *vs*. 3.35) suggest that the bulkier alkyl groups of tripropylamine hinder protonation steps, reducing product formation, which has been observed before with the DHA self-aldolization with bulky tertiary amines.[50] The steric effects of tertiary amines suggest they influence selectivity-determining steps, possibly through electrostatic interactions between ionic intermediates, the solvent, and the protonated amine.

Amine functionality

Amines with additional heteroatom functionality generally performed slower and less efficiently. However, there appears to be a trade-off in branching selectivity. The highest branching selectivity was observed for *N*-methyldiethanolamine, diethanolamine, and triethanolamine (entries 5–7), suggesting that while alcohol groups reduce amine reactivity, they enhance selectivity by hydrogen bonding with DHA's ketone. In both amine series 5–

7 and 2–4, secondary amines consistently showed the highest branching selectivity. Three reasons are proposed for the lower activity.

The first explanation involves a catalyst-substrate interaction hypothesis, which accounts for the underperformance of amines with alcohol groups on the alkyl chain (triangle symbols in Figure 1). In these cases, both the amine and alcohol groups interact with the DHA ketone, forming either a hemi-aminal or hemi-ketal. While hemi-ketal formation has minimal impact, hemi-aminal formation can trap the catalyst as cyclic hemi-aminal ethers (oxazolidinone structures). Similar reactions are reported with[51-53] or without catalyst,[54] and a pathway under the slightly basic conditions in this work is proposed (see Scheme S5). For primary amines, the alcohol group may attack the imine, while secondary amines could form a covalent bond between the enamine and alcohol group. These interactions are a major deactivation pathway for proline catalysts.[53] The diamines (square symbols in Figure 1) can follow similar deactivation pathways toward cyclic aminals.

A second hypothesis for slower dendroketose formation is the stabilization of the DHA-amine intermediate through intramolecular complexation between the negatively charged O-atom and the alcohol proton (see Scheme S6). Similar intermolecular complexation after DHA deprotonation may also occur, raising the activation energy and hindering the reaction. Such interactions, which increase energy barriers, are reported in aldol addition reactions with amino acids.[52-53, 55]

The final hypothesis is based on the fact that in all tested cases, the alcohol and amine groups are separated by two carbon atoms, causing the heteroatoms to act as electron-withdrawing groups (EWGs). This reduces the amine's basicity and nucleophilicity, lowering catalytic activity. For example, comparing *N*-methylethylenediamine and *N*-methylpropylene-1,3-diamine (entries 18 and 21) shows that the extra carbon in *N*-methylpropylene-1,3-diamine reduces the EWG effect, lowering the pK_b from 3.85 to 3.40 and leading to a significantly higher hexose yield (46% vs. 21%) and faster DHA consumption rate (1.58 M/h vs. 0.27 M/h). A similar trend is observed in tertiary amines with alcohol groups, such as 2-dimethylaminoethanol, *N*-methyldiethanolamine, and triethanolamine (entries 4, 5, and 7), where increased alcohol groups lead to an increase in pKb, lower hexose yields and DHA consumption rates. A corresponding pattern is noted between 2-(methylamino)ethanol (entry 3) and diethanolamine (entry 6), with the former having a higher DHA consumption rate (5.70 M/h *vs*. 1.28 M/h) despite similar hexose yields.

The ethanolamine series (ethanolamine, *N*-methylethanolamine, and *N*-dimethylaminoethanol, entries 2–4) shows that increasing degree of substitution can reduce the electron-withdrawing effect. Ethanolamine, a primary amine, has low hexose yield (23%) and slow DHA consumption (0.53 M/h) due to its alcohol group. Replacing one hydrogen with a methyl group in *N*-methylethanolamine improves both hexose yield (70%) and DHA consumption rate (5.70 M/h). Adding a second methyl group in *N*-dimethylaminoethanol further increases hexose yield (85%), but at the cost of lower branching selectivity and slower DHA consumption (2.03 M/h). This series demonstrates that adjusting substitution can mitigate the negative effects of EWGs.

Despite the above, *N,N,N'*-trimethylethylenediamine (entry 20) shows competitive hexose yield and dendroketose selectivity. This is due to its secondary and tertiary amines working in tandem to generate the DHA-enamine aldol donor and simultaneously protonate the DHA-acceptor or anionic dendroketose.[56-57] This makes the secondary/tertiary diamine moiety an interesting candidate for further research.

Amine selection and optimization

After excluding primary amines and those with additional functional groups due to low DHA consumption (<3 M/h), ten amines (entries 8–17) remained for optimization. Piperidine, DBU, and tripropylamine (entries 13, 14, 17) were eliminated due to low initial reaction rates (7.21, 12.21, and 5.24 M/h) and productivity. Although dipropylamine, dibutylamine, and *N*-methylbutylamine (entries 10–12) performed well, they were outperformed by dimethylamine and diethylamine (entries 8 and 9), narrowing the focus to two secondary and tertiary amines. Ultimately, dimethylamine (entry 8), diethylamine (entry 9), trimethylamine (entry 15), and triethylamine (entry 16) were selected for further screening and upscaling trials.

After selecting four amines from the initial twenty-one, further experiments were conducted to refine the catalyst choice. Dimethylamine, diethylamine, trimethylamine, and triethylamine were tested at varying DHA concentrations (100–500 g/L) and amine loadings (1, 3, and 5 mol %) to assess their performance (see Table S4). Trimethylamine was eliminated due to low hexose yield (Table S4, entry 3), and dimethylamine was excluded for lower DHA conversion at 3 mol % (Table S4, entry 5). This left diethylamine (Et_2NH) and triethylamine (Et_3N), which performed

similarly. Ultimately, Et_3N was chosen as the optimal catalyst, as it does not catalyze the Maillard reaction[44-45, 58] (see Figure S17), thus ensuring better coloration and selectivity of the final product, and has the lowest vapor pressure between the two (7.2 kPa vs. 25.9 kPa at 20°C), although at a slightly higher operational cost (~2550 USD/MT or 0.258 USD/mol for Et_3N[59] vs. ~2900 USD/MT or 0.212 USD/mol for Et_2NH[60]).
In these screenings (see Table S4), Et_3N showed the best performance at a DHA concentration of 500 g/L and 1 mol % amine loading at room temperature, achieving 95% DHA conversion, 76% dendroketose yield, and a productivity of 109 g/(L·h). These results are compared to the results from the state-of-the-art reported in literature with resins IRA-900[18] and Dowex-55A[19] and the rehydrated hydrotalcite catalyst (RHT-NaOH)[14] in Table 1. Catalyst productivities from other studies were not reported and therefore estimated similarly to this work (see Section S1.2). For IRA-900, lacking a time plot, productivity was calculated over the full reaction, likely underestimating its peak performance. Still, as shown in Table 1, triethylamine (Et_3N) outperformed all systems, with a productivity ~7.5 times higher than the next best (rehydrated hydrotalcite), though values up to ~40 g/L have been reported after optimization. Despite slightly lower branching selectivity, Et_3N's high activity, low cost, and easy implementation make it a strong alternative.

Table 1: Results from the state-of-the-art reported in literature compared with results obtained with triethylamine at similar conditions, comparing dihydroxyacetone (DHA) conversion, dendroketose selectivity and productivity.

Catalyst	X_{DHA} (%)	$S_{dendroketose}$ (%)	Productivity [g/(L.h)]
IRA-900[a]	100	98	2.7
Dowex-550A[b]	85	88	3.5
RHT-NaOH[c]	92	85	14.5
Et_3N[d] (this work)	95	80	109

Reaction conditions: [a] 3.33 g/L DHA in water with equimolar IRA-900 (OH^-) for 12h, calculated after 12h; [18] [b] 2.8 mmol DHA in 9 mL water (28 g/L), 0.05 g Dowex 550A (OH^-) for 24h, calculated at 6h bending point;[19] [c] 100 g/L DHA in EtOH with 20 g/L RHT-NaOH hydrotalcite under Ar for 24h, calculated at 4h bending point;[14] [d] 500 g/L DHA in water with 1 mol % Et_3N for 3h, calculated at 3h bending point (this work).

Investigation of hydrogenation procedure

Next in this study, the Et_3N-catalyzed aldol reaction mixture was hydrogenated to produce dendroketol (Figure 2a). However, direct hydrogenation yielded only 16% dendroketol, with 55% glycerol formed from triose (DHA/GLA) hydrogenation. Since the aldol reaction had >95% conversion, the trioses likely resulted from retro-aldol reactions of hexoses, promoted by the basic pH at the high 110 °C temperature. This highlighted the need to neutralize Et_3N before hydrogenation.

Amine quenching and catalyst reusability

Three methods were tested to remove Et_3N: (i) physical separation, (ii) chemical neutralization, and (iii) adsorption, evaluated for cost, ease, and hydrogenation performance (see Figure 2a and Table S10). Evaporation improved the yield to 79%. Adding equimolar HCl fully neutralized the mixture, achieving ~99% dendroketol yield. Using 1 wt.% Amberlyst-15 gave 92% yield, but full neutralization required 2 wt.%. Due to its simplicity and effectiveness, HCl neutralization was chosen for further experiments. Further analysis showed this method did not induce the formation of new side-products, *e.g.* the formation of organic acids or humins. These pathways are likely impeded due to the hydrogenation reaction being more competitive - hampering organic acid formation - and the reaction conditions too mild for humin formation, which typically require higher temperatures (> 150°C) and acid concentration[61] (pH after neutralization ~7).
Subsequently, the Ru/C hydrogenation catalyst was tested for 4 consecutive runs (see Figure S2). A slight drop in activity was noted (100% to 67% dendroketose conversion) after the first run, stabilizing thereafter (~61% conversion). Different hypotheses (amine poisoning, catalyst oxidation, or catalyst fouling due to product adsorption) were tested experimentally. The amine poisoning hypothesis was negated after achieving a 92% hydrogenation yield (see Figure S3) with Ru/C catalyst stirred in an aqueous 20 mol % Et_3N solution for 4 h, washed

thrice and dried overnight. Reducing the catalyst reactivates its performance up to 95% yield (see Figure S4). Subsequently, different samples (fresh catalyst, spent catalyst after one run, and catalyst reduced after first run) were analyzed via XPS (see Table S5 and Figure S5) and ToF-SIMS (see Tables S6 & S7, and Figures S6 & S7). The XPS results showed 6% of Ru-atoms in fresh catalyst were in metallic form, which increases to 22% after a first run – identical to the reduced catalyst sample – disproving catalyst oxidation as a cause of deactivation. The XPS data additionally shows an increase of C-O & C=O moieties on the catalyst surface after reaction, which is significantly reduced after hydrogenation. Analysis of ToF-SIMS shows a similar trend for ionic species assigned to that of (surface-bound) sugar or polyol, suggesting poisoning by dendroketol or dendroketose, as a possible source of deactivation (see Section S2.2).

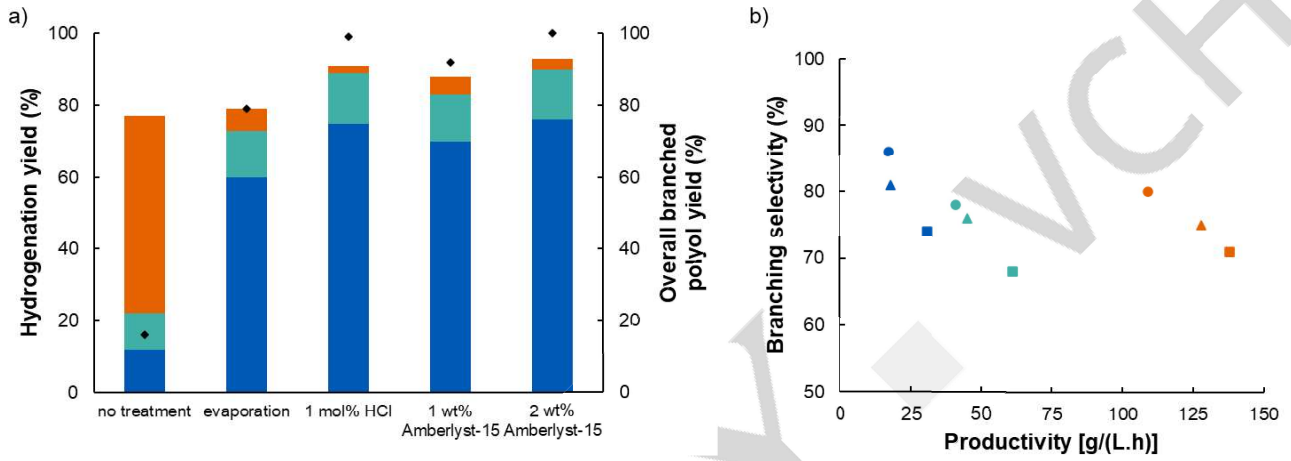


Figure 2: Results from a) hydrogenation of hexose mixture after 500 g/L DHA (self-)aldol addition with 1 mol % triethylamine (Et_3N) after different neutralization techniques, with total dendroketol (navy blue), linear polyol (turquoise) and glycerol (orange) yield, and overall dendroketol yield (black diamonds, secondary axis), b) the screening of different dihydroxyacetone (DHA) and triethylamine (Et_3N) concentrations for the (self-)aldol addition of DHA toward dendroketose with dendroketose selectivity plotted vs. dendroketose productivity, with 100 (navy blue), 200 (turquoise) and 500 (orange) g/L DHA and 1 (circle), 3 (triangle) and 5 (square) mol % Et_3N.

Industrial scalability

After selecting Et_3N as the main catalyst and optimizing its neutralization for full sugar hydrogenation, the focus shifted to scaling up the process. DHA (100–500 g/L) and Et_3N (1–5 mol %) concentrations were screened to determine optimal conditions (Figure 2b). For industrial relevance, results were evaluated based on dendroketose selectivity (purity) and productivity (g/(L·h)), measured when dendroketose formation plateaued (see Table S8-S9 and Figures S8-S10). As shown in Figure 2b, higher initial DHA concentrations improved dendroketose productivity. Dendroketose productivity rose sharply with increasing DHA concentrations, by 2–2.5 times at 200 g/L and 6–6.5 times at 500 g/L, depending on amine loading. This boost stems from the second-order dependence on DHA concentration. However, it also increases GLA formation, slightly lowering selectivity. Since linear sugars form faster than dendroketose, productivity gains are limited to just above the concentration increase. A similar trend occurs at higher amine levels, where the triose isomer equilibrium is reached faster due to higher pH.
The optimal upscaling conditions for DHA aldol addition were set at 500 g/L DHA and 1 mol % Et_3N, balancing productivity, selectivity, and purity with minimal catalyst use. This also reduced waste, especially the amine salts, an important factor since acidic neutralization was used before hydrogenation. Table 2 compares DHA aldolization and hydrogenation across scales, showing minimal differences in DHA conversion, dendroketose, and linear sugar yields. This consistency underscores the benefit of homogeneous catalysts in avoiding diffusion limitations during scale-up. The hydrogenation procedure showed consistent dendroketol yields across all scales, with a slight increase in linear polyol yield at the 1 and 10 L scales, likely due to longer reaction times. These results demonstrate the industrial feasibility of the process, with the aldolization reaction performing similarly at both lab (10 mL) and larger (1–10 L) scales.

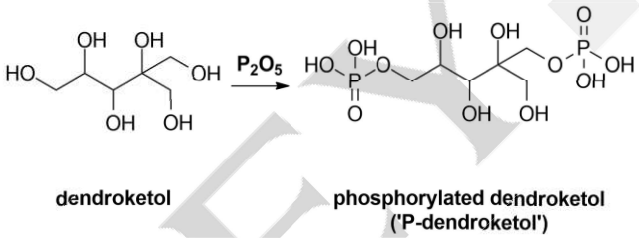
Table 2: Results at different lab scales for the DHA (self-)aldol addition and subsequent dendroketose hydrogenation at 600 mL scale to highlight industrial scalability.

	DHA aldol addition[a]				Dendroketose hydrogenation[b]		
Scale	X_{DHA} (%)	$Y_{dendroketose}$ (%)	$Y_{linear\ sugars}$ (%)	Productivity [g/(L.h)]	$X_{dendroketose}$ (%)	$Y_{dendroketol}$ (%)	Ylinear polyol (%)
10 mL	95	76	14	95	100[c]	75[c]	5[c]
1 L	98	78	15	98	98[d]	78[d]	15[d]
10 L	92	74	15	93	100[d]	80[d]	16[d]

Reaction conditions: [a] 500 g/L DHA, 1 mol % Et_3N in H_2O at 600 RPM and R.T. for 4h, and [b] 110 °C, 50 bar H_2 at [c] 800 RPM for 4h and [d] 600 RPM for 6h

Flame retardant application

This research demonstrates the first application of dendroketol, exploring its conversion into a flame retardant using a traditional phosphorylation method with phosphorus pentoxide (P_2O_5) and a co-solvent (Scheme 3). The process achieved an average total phosphate ester yield of 62%–65% after four iterative reactions, demonstrating a consistent and reliable synthesis of phosphorylated polyols.



Scheme 3: Reaction procedure for the phosphorylation of the novel branched hexitol, dendroketol, towards the sustainable phosphorylated dendroketol ('P-dendroketol') with phosphorous pentoxide (P_2O_5).

Titration was used to estimate the degree of phosphorylation (DoP), with an average DoP value between 1 and 2, corresponding to a phosphorus content of 7.2% P, consistent with industrial compounds. After synthesis, the resulting compounds, termed 'P-dendroketol,' were applied to mattress fabric and subjected to rigorous flame-retardant testing according to the BS 7175 standard (as detailed in the Experimental Section). Remarkably, the mattress ticking fabric treated with the phosphorylated polyol passed the test at both application levels, including the stringent 15 wt.% (relative to fabric mass) application rate (Figure 3). This demonstrates the effective flame-retardant properties of the synthesized compound and suggests its potential for use in fire safety applications. These findings provide a promising foundation for further research into the compound's viability as an industrial flame retardant, such as using P-dendroketol as a polyol in PUR polymerization, thereby incorporating the PFR into the PUR chemical network, as suggested in the literature.[1, 3-4]

Future work should focus on optimizing the synthesis process, refining application techniques, and conducting washability tests to assess the durability and long-term performance of the flame-retardant properties. These improvements will be essential for establishing this new flame retardant as a competitive alternative in industrial sectors where fire safety is a critical priority.

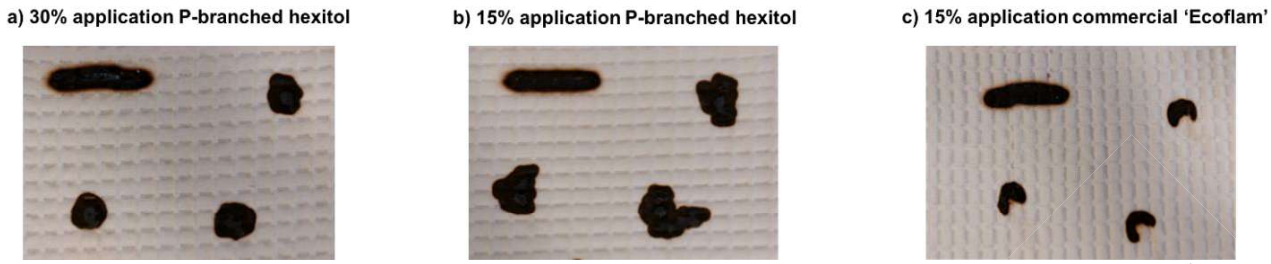


Figure 3*:* Results from the flame-retardant results (according to standard BS 7175 test) for a) the 30 wt% and b) 15 wt% application level of the novel phosphorylated dendroketol 'P-dendroketol, c) compared to the commercially available 'Ecoflam' flame retardant of Devan as reference. Both application levels of the novel bio-based flame retardant report a 'pass' rating after extinguishing a flame induced by a 35 mm torch, identical to the commercial flame-retardant.

Conclusion

This study tested twenty-one amine catalysts for the basic-catalyzed self-aldolization of dihydroxyacetone (DHA) to identify a cost-effective alternative to resin-based catalysts. Primary amines showed poor performance due to imine formation, limiting their ability to act as Brønsted bases. Amine catalysts with additional heteroatoms exhibited reduced basicity and nucleophilicity, leading to suboptimal performance. However, amines with alcohol groups showed the highest branched selectivity, likely due to hydrogen bonding between the alcohol and DHA's ketone. Secondary and tertiary alkylamines performed best, achieving selectivities between 70% and 80%, with hexose formation rates ranging from 70% to 90%, often exceeding 80%.
A notable trend was observed in the activity of these non-functionalized alkylamines: initially, increasing the alkyl chain length enhanced the reactivity of both secondary and tertiary amines. However, as the chain length increased further, reaction rates and product formation declined. For secondary amines, longer alkyl chains likely reduced product formation due to slower hydrolysis rates toward dendroketose. In contrast, tertiary alkylamines seemed to be more negatively affected by increased bulkiness, which caused steric hindrance, but showed no product coloration, thus avoiding Maillard reactions.

Overall, selectivity variation is more pronounced for less active catalysts, indicating that slower aldolization rates lead to increased isomerization. When aldolization occurs quickly, selectivity is typically around 80%, regardless of the amine base. Preventing DHA to GLA isomerization is crucial, which can be achieved using less sterically hindered secondary amines or tertiary amines with lower pK_b values.
Triethylamine (Et_3N) was identified as the optimal catalyst, showing high branched selectivity and efficient hexose formation at 500 g/L DHA with 1 mol % catalyst loading. The subsequent hydrogenation highlighted the need to neutralize the mixture to prevent retro-aldol reactions at elevated temperatures (110°C) caused by the presence of amine. Neutralization with 1 mol % HCl proved simplest and most effective, achieving a 99% hydrogenation yield. Both the DHA aldolization and hydrogenation reactions were tested at 10 mL, 1 L, and 10 L scales, with consistent results, demonstrating the process's industrial potential.
The resulting dendroketol was phosphorylated to create a bio-based alternative to halogenated flame retardants. These novel compounds passed rigorous BS 7175 flame ignition tests for both cigarette and torch ignition at application levels of 30 and 15 wt.%, matching the performance of the commercially available "Ecoflam" reference sample. These results demonstrate the potential of the synthesized compound as a sustainable, bio-based flame retardant for industrial applications, paving the way for further research in fire safety materials.

Experimental Section

Aldol addition procedure

One gram of DHA dimer (96%, TCI Europe) was dissolved in 2, 5 or 10 mL milliQ water, depending on the targeted DHA concentration. The mixture was stirred (600 RPM) at room temperature to promote the DHA dissolution prior

to the addition of the amine in a catalytic amount (1 – 5 mol % relative to DHA). The reaction was stirred at room temperature for a specified reaction time (in the range of 4-18 h). More information about utilized reagents, their purity and suppliers is provided in Table S1.

Sugar mixture hydrogenation
The aldol addition reaction mixture was neutralized with an equimolar amount of HCl (compared to amine loading, *i.e.* 1 – 5 mol %) and then transferred to a stainless steel 15 mL Parr reactor with 5 wt.% (relative to starting DHA concentration) of commercial 5 wt.% Ru/C (Sigma-Aldrich) and a magnetic stirring bar. The reactor head was sealed and purged three times with N_2 gas before being pressurized with 50 bar H_2. The reaction was held at 110°C and stirred at 800 RPM, starting the reaction time (4 h).

Hydrogenation catalyst recycling experiments
To test the recyclability of the Ru/C catalyst, the first experiment was run as described above. The spent catalyst was collected and separated from reaction mixture *via* centrifugation. The catalyst was then washed with deionized water and separated again, this process was repeated three times. The catalyst was then collected and dried overnight (18 h) *via* N_2-flow and used for the following run without fresh catalyst added. For the regeneration *via* reduction experiment, the catalyst was collected after the 2nd run and reduced at 250°C for 2.5 h at 50 mL/min H_2. After completion, the catalyst was stored under N_2 atmosphere.

Reaction mixture quantification
Both the aldol addition and the hydrogenation reaction mixtures were analyzed on an Agilent 1200 series HPLC system with a Varian MetaCarb 67C column (30 x 0.65 cm). Reaction samples were diluted with milli-Q water by a factor of 20 and filtered, of which 5 µL was injected. The separation was carried out at 85°C at a flow rate of 0.5 mL/min with milli-Q water as mobile phase and analyzed by a RID detector, with an elution time of 30 min. Calculations regarding conversion (%), yield (%), and selectivity (%), as well as the DHA consumption rate (M/h) and dendroketose productivity [g/(L.h)], are described in Section S1.2.

Upscaling methodology
After the amine screening and selection, and the reaction condition optimization on lab scale (2 – 10 mL), both the DHA aldolization and subsequent reaction mixture hydrogenation were performed at larger scales at the facilities of Oleon. The DHA aldolization was performed under identical conditions at 1 and 10 L scale, while the subsequent hydrogenation was performed at 110°C in a 600 mL Parr reactor in different conditions (800 RPM for 4 h at lab scale vs. 600 RPM for 6 h at larger scale).

Textile treatments with phosphorylated polyols
The synthesized phosphorylated polyols were applied to mattress ticking fabric made of polyester/viscose by padding with an aqueous solution containing varying concentrations of the phosphorylated polyols (15 wt.% and 30 wt.%), maintaining a pH of 4–5. The fabric is passed through the bath, where it absorbs the product from the solution, and then squeezed between two rolls at a pressure of 4 bar. Following this, the fabric is dried and cured in a stenter at 140°C.

Thermal degradation testing of treated textiles
After the incorporation of the produced phosphorylated polyols, the flame-retardant tests were performed using standard BS 7175 (fire test for bedcovers and pillows), according to EU standards for this type of fabric. The material was ignited by a smoldering and flaming ignition source at different flame-retardant application levels (15 wt.% and 30 wt.% incorporation relative to mattress fabric) and evaluated based upon set criteria by the standard.

Supporting Information

Experimental details, additional information on reaction mechanism, additional figures supporting results and discussion can be found in supporting information. The authors have cited additional references within the Supporting Information. [62-70]

Acknowledgements

This work was performed in the framework of the Catalisti cluster ICON project POLYFLAM ("Polyol based Flame retardants and lubricants", HBC.2018.0482), with the financial support of VLAIO (Flemish Agency for Innovation and Entrepreneurship).

Keywords: aldol reaction • amines • biomass • homogeneous catalysis • sustainability

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