Study into alternative (biobased) polar aprotic solvents

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Colophon

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Executive Summary

This report is the second part of the project 'Verkenning aprotische oplosmiddelen'. The goal of this project, which is a collaboration between Wageningen Food and Biobased Research (WFBR) and the National Institute for Public Health and the Environment (RIVM), is to identify new biobased alternatives to the currently disputed polar aprotic solvents (PAS) NMP, DMAc and DMF, which are suspected to be reprotoxic.

The first objective of this desk study is to present an overview of both emerging and existing biobased chemicals (and materials), and to identify potential (side) streams of 'new' biobased chemicals that will (need to) be valorised in the near future. The description 'new' biobased chemicals relates to the fact that these substances are not (yet) commercially available in significant quantities, despite the fact that many of them have been known for more than a century. For example, substances like ethanol, lactic acid and citric acid are not considered new as they have already been produced by industrial scale fermentation for a long time. Furthermore, chemicals like bio succinic acid are not considered new, as they are currently still mostly produced from petrochemical feedstocks. Examples of substances that are considered as new in this study are for instance furandicarboxylic acid, levulinic acid and itaconic acid.

While the information thus obtained is already interesting by itself from a regulatory perspective, the second objective of this study is to evaluate the replacement potential of these new biobased substances with regard to the PAS NMP, DMAc and DMF. Since many biobased chemicals are (highly) polar, the increasing availability of 'new' substances with unique chemical structures and properties could be the solution to finding safe alternatives to disputed PAS.

For most of the existing and emerging biobased product streams 'new' substances have been identified, which has resulted in a list of substances (or classes of substances) that are likely to reach a significant production volume in the coming decades. This list has been prioritised according to criteria like feedstock availability, level of (industrial) development, whether or not a substance is already commercially produced, and its potential as alternative polar aprotic solvent. Based on these criteria, nineteen substances and substance classes have been identified as potential alternatives for the currently disputed PAS.

Toxicological analysis should give more insight into the feasibility of these substances as safe alternatives for the currently disputed polar aprotic solvents. Next, the technical and economic feasibility should be determined for these substances in various key applications by the relevant stakeholders (industry, knowledge institutes, government). This also implies that synthesis and production of substances that are not yet readily available should be developed further. Due to the rather diffuse nature of the solvents market, with both many (potential) producers and end-

users, as well as a myriad of applications, a proactive role of the government in stimulating and facilitating the development of these new biobased solvents and chemicals is strongly advised. Next to e.g. matchmaking events and 'green deals', a specific R&D program involving a broad number of stakeholders, (potential) solvent producers and users, and knowledge institutes (comparable to e.g. the Biobased Performance Materials program) is recommended in order to accelerate the introduction and acceptance of new, safe biobased solvents.

Content

1 Introduction

In 2014 Wageningen Food & Biobased Research conducted a quick-scan for the Dutch National Institute for Public Health and the Environment (RIVM) with the aim to identify potential biobased alternatives to substances of very high concern (SVHC). The report concluded that the substance class of polar aprotic solvents (PAS) was of special interest. These solvents, more specifically NMP (N-methyl pyrolidone), DMAc (dimethylacetamide) and DMF (dimethylformamide), are suspected reprotoxic and are under increasing regulatory pressure. While biobased chemicals offer potential alternatives (given the highly polar character of many biobased feedstocks like carbohydrates), there were also concerns that short term restriction of the use of NMP, DMF and DMAc could be prohibitive to the development of a biobased economy. Since most biobased feedstocks and chemicals contain significantly more oxygen (and water) than their petrochemical counterparts, common industrial petrochemical processes based on distillation and high temperature gas phase reactions are not feasible, due to too high boiling points and thermal instability. Hence, more often solvents need to be used for biomass pretreatment and downstream chemical conversions. Whereas water and alcohols are highly preferred from an environmental and safety point of view, also the use of PAS is often required. Hence, in the first part of the project 'Verkenning aprotische oplosmiddelen' emphasis was placed on identifying whether short term restrictions in the use of NMP, DMF and DMAc would have detrimental effects on the development of biomass pretreatment processes. The conclusions from this first part were that this is not the case, due to the large scale of these processes and the (too) high costs associated with the use of non-aqueous solvents. The goal of the second part of the project is to identify new biobased alternatives to the currently disputed PAS by means of a desk study.

The first objective of this desk study is to present an overview of both emerging and existing biobased chemicals (and materials), and to identify potential (side) streams of 'new' biobased chemicals that will (need to) be valorised in the near future. The description 'new' biobased chemicals relates to the fact that these substances are not (yet) commercially available in significant quantities, despite the fact that many of them have been known for more than a century. For example, substances like ethanol, lactic acid and citric acid are not considered new as they are already produced by industrial scale fermentation for a long time. Furthermore, chemicals like bio-succinic acid are not considered new, as they are currently still mostly produced from petrochemical feedstocks. Examples of substances that are considered as new in this study are for instance furandicarboxylic acid (FDCA), levulinic acid and itaconic acid. Another reason to focus on new biobased solvents is that most of the existing biobased solvents (unique or drop-in) such as ethanol, ethyl acetate, or ethyl lactate are unsuitable as functional alternatives to NMP, DMAc and DMF in the majority of their applications.

The second objective of this study is to evaluate the replacement potential of these new biobased substances with regard to NMP, DMAc and DMF. Since many biobased chemicals are (highly) polar, the increasing availability of 'new' substances with unique chemical structures and properties could be the solution to finding safe alternatives to disputed PAS.

2 Methods & Terminology

For this report use has been made of several literature search methods:

- Reaxys
- SciFinder
- Google Scholar
- Espacenet

Furthermore, several WFBR and external experts in the field of biobased chemicals and building blocks have been consulted (see chapter 6).

Definitions

- In this report a substance is considered as a 'new' biobased chemical if it is not (yet) currently commercially available in significant quantities, yet has already attained a TRL (technological readiness level) of ≥ 5 (EC definition), meaning that it has already achieved a pilot (5-6) or demo level (7) of development. Biobased substances that are already produced on an industrial scale such as lactic acid or citric acid are also not considered as 'new' in this report. Mind that non-commercial derivatives of such substances, like certain lactic acid esters, are considered as 'new'. Furthermore, biobased substances that are produced either via existing or emerging biobased processes, that have known existing petrochemical counterparts, such as ethanol and succinic acid, are also not considered as 'new". Such substances are defined as 'drop-in'.
- Drop-in: Substance that is chemically identical to substance that is currently produced from petrochemical feedstocks. It can be used directly in existing downstream and conversion processes: e.g. biobased ethylene obtained from bio ethanol, is a drop-in chemical in the production of polyethylene.
- Near drop-in: Substance that is chemically similar but not identical to substance that is currently produced from petrochemical feedstocks. Application/implementation of this substance in downstream and conversion processes will require development, reformulation and possibly registration. For example, methylsuccinic acid obtained from itaconic acid versus existing succinic acid.

Methodology

- Assessment of TRL levels of the 'new' biobased substances described in this report are based on qualitative information, such as industry press releases, company websites, personal communications, and feedback from experts in the field. Since little public information exists mentioning actual TRL levels, they were not used in this report as such, as it would imply an unrealistic level of accuracy.

- PAS assessment: The suitability of a ‘new’ biobased chemical as potential PAS replacement, as given in table 1, is based on qualitative assessment of factors such as (expected) low melting point (the substance should be liquid over a wide temperature range), (expected) boiling point (preferably high enough not to qualify as volatile organic compound (VOC)), polarity (based on presence of polar chemical functionalities, such as oxygen containing ether, ester of ketone groups) and absence of reactive substituents (e.g. hydroxyl or amine groups).

- Process Feasibility, as used in table 1: The process feasibility is based on qualitative assessment of the publically available information on required number of unit operations, yields and selectivities, required reagents, waste production and energy demand.

Notes

Note 1: Since industrial development cannot guarantee commercial success, this report does not include projections on market volumes or time-to-market of emerging biobased processes and chemicals.

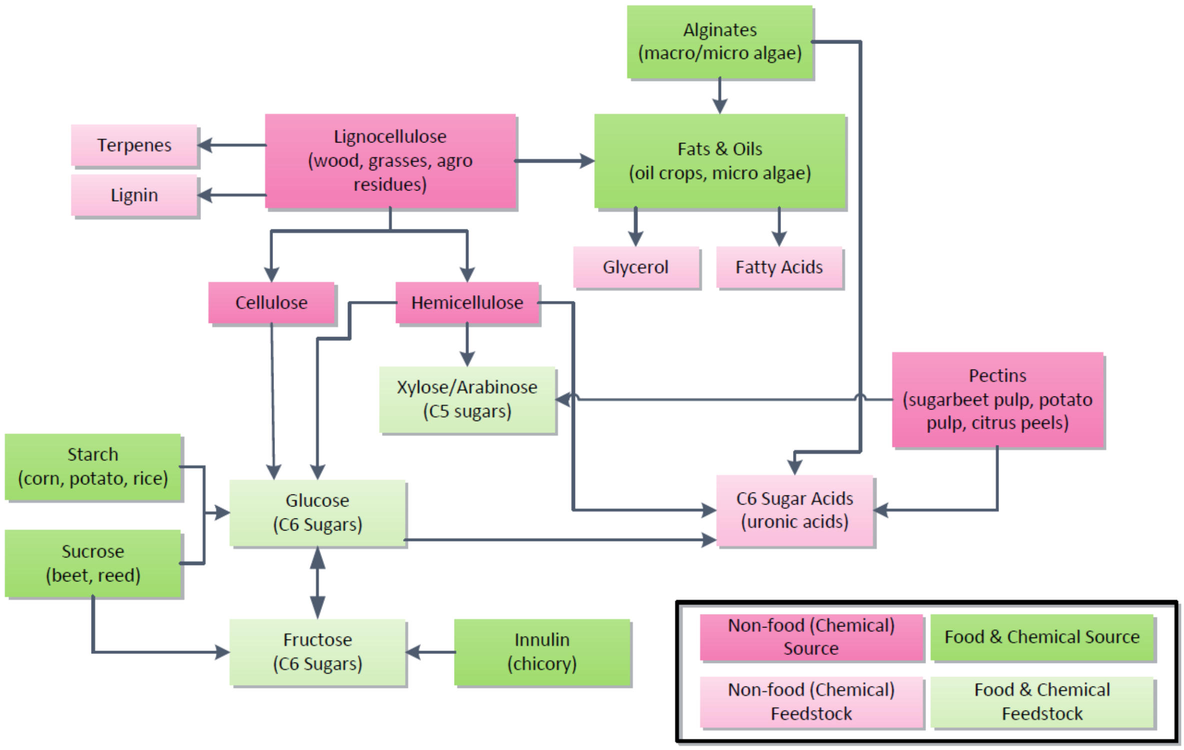
Note 2: In this report company names are only used when publically available information (from scientific publications, press releases or company websites) was used, and are not to be considered as endorsement.

Note 3: When the toxicity of certain substances is mentioned in this report, it is based on existing scientific literature, with the intention to identify potential issues with the use of these substances. When no mention is made of toxicity of substances this does not imply that these substances are non-toxic, yet that there is currently no, or not sufficient information available in the literature and sources used for this report with regard to toxicity.

3 Results & Discussion

3.1 Biobased resources and chemicals

Biobased, renewable resources are the oldest resources known to man for providing food, feed, materials and chemicals. Hence it is difficult to make sharp distinctions between food and non-food applications of renewable feedstocks. The same applies to the definition of new biobased substances or chemicals many of which have been known for more than a century, since most of 19th century organic chemistry started with biobased feedstocks. In scheme 1 a, by no means complete, overview is given of various important biobased chemical feedstocks and intermediates and the biobased raw materials that they are derived from. Mind that proteins have not been included in this report due to their predominant use in food and feed.



Scheme 1: Schematic overview of major flows of biobased feedstocks, chemicals and intermediates; legend: bottom right corner.

In this scheme vegetable sources (including the plants they are extracted from) are shown in straight rectangles, differing between non-food sources such as lignocellulose, which is the major part of wood, grasses and various agro residues (e.g. straw, sugar-cane bagasse) and food sources like starch. The latter finds use as a major food source, yet is also used for the production of biobased chemicals (e.g. 1st gen. bio ethanol) and is also applied in a diverse range of industrial materials, such as adhesives and thickeners. This means that especially for existing, traditional biobased sources and products (such as starch and vegetable oils) various food, feed, materials and chemicals applications exist simultaneously. In scheme 1 products derived from these biobased sources are considered as either pure chemical feedstocks with no significant direct food or feed outlets (such as terpenes), or mixed food & chemical feedstocks, which is mainly limited to sugars.

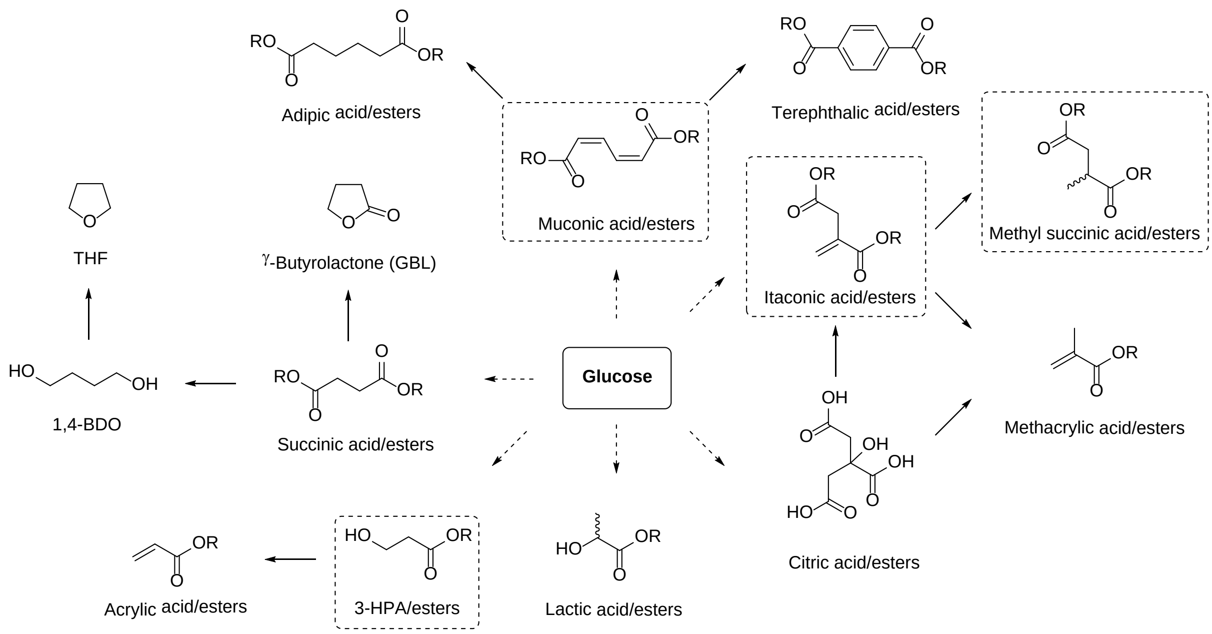
- Glucose and fructose, which are C6 sugars, are obtained from various sources, such as non-food lignocellulose, or food components such as starch, sucrose or inulin.
- C5 sugars, mainly xylose and arabinose, can be obtained from non-food sources like hemicellulose and pectins.
- C6 sugar acids can be obtained directly from C6 sugars like glucose, but are also found in significant quantities in non-food pectins, alginates, and hemicelluloses.
- Vegetable oils and animal fats are the main source of fatty acids and glycerol, which has been the basis for the traditional oleochemical industry as well as biodiesel production.
- The broad class of lignocellulosic materials (wood, straw, grasses, corn stover, sugar cane bagasse) can also be a source of lignin, fats and oils, and terpenes.

In the following sections these biobased chemical intermediates, and their (potential) down-stream products will be discussed in more detail. In order to give a relevant overview various downstream products will be discussed, yet the emphasis will be on 'new' emerging biobased substances. At the end of each section a list is given of 'new' biobased substances (or classes of substances) that are potentially interesting as PAS replacement.

3.2 Glucose derived acids

Glucose is the most predominant sugar in nature as it is the building block for e.g. cellulose and starch. It is also a very important biobased intermediate for the production of a wide range of chemicals. In this section we focus on (di/tri)acids that can be obtained from glucose, most of which are obtained by fermentation (scheme 2).

- Glucose can be fermented to muconic acid, which in turn can be used to obtain the existing petrochemicals terephthalic acid and adipic acid (and related downstream products).[1-4] Muconic acid and derivatives are currently not produced on large scale, yet could become more widely used (see also sections 3.6 and 3.8).



Scheme 2: overview of industrially relevant carboxylic acids (and esters) that can be obtained from glucose, either by fermentation (dashed arrow) or by bio/chemocatalysis (plain arrow); substances in dashed boxes are “new”.

- Itaconic acid can be obtained by direct fermentation of glucose or by chemocatalytic conversion of citric acid.[5,6] Although itaconic acid itself is not a new chemical, various derivatives are being developed (e.g. esters) for e.g. coating and unsaturated polyester resin applications.[7] Commercialisation of itaconic acid is amongst others pursued by Itaconix corporation.[8] Also methyl succinic acid, which is obtained by catalytic hydrogenation of itaconic acid, is an interesting derivative that is attracting attention, in e.g. polymer applications.
- Citric acid is already produced on large scale by fermentation of glucose.[9] Also many derivatives, such as citrate esters have been known for many decades, and are used as e.g. safe plasticisers for PVC.[10] Chemocatalytic conversion of either citric acid or itaconic acid to drop-in methacrylic acid is also becoming more feasible.[11-13]
- Like in the case of citric acid, also the fermentation of glucose to lactic acid is a very old process, generating lactic acid for food applications, but also for the production of the biopolymer polylactic acid (PLA).[14,15] As a result of increasing lactic acid production also the development of lactic acid esters, e.g. as biobased solvents, is increasing.[16] Companies like Corbion are active in this field.[17]
- Another hydroxyacid that can be obtained by fermentation of glucose is 3-hydroxypropionic acid (3-HPA).[18] While 3-HPA can be polymerised to obtain a biobased polyester, it is also an intermediate for the production of biobased acryl acid and acrylates[19], which are currently still produced from petrochemical feedstocks. Companies like Perstorp, BASF, Cargill, Dow Chemical and Metabolix are preparing commercialisation of 3-HPA and biobased acrylic

acid.[18] Polyacrylates are the main components used in the production of water borne paints and coatings, as well as super absorbents for hygienic products. Since the production of 3-HPA is expected to grow, it is reasonable to assume that also more derivatives of 3-HPA will be developed.

- The biotechnological production of drop-in succinic acid is attracting significant attention with various (large) companies and joint ventures entering the market; e.g. Myriant, BioAmber, Reverdia.[18,20-22] Most outlets are directed at the biopolymer polybutylene succinate (PBS) and 1,4-butanediol (14BDO), all of which have historically been produced from petrochemical feedstocks.[23] The same holds for tetrahydrofuran (THF) and ɣ-butyrolactone, which are used as solvents and building blocks for polymers. Nevertheless, with growing production volumes of bio succinic acid, also new outlets are being explored, such as succinate esters and amides.

'new' Biobased substances with PAS replacement potential:

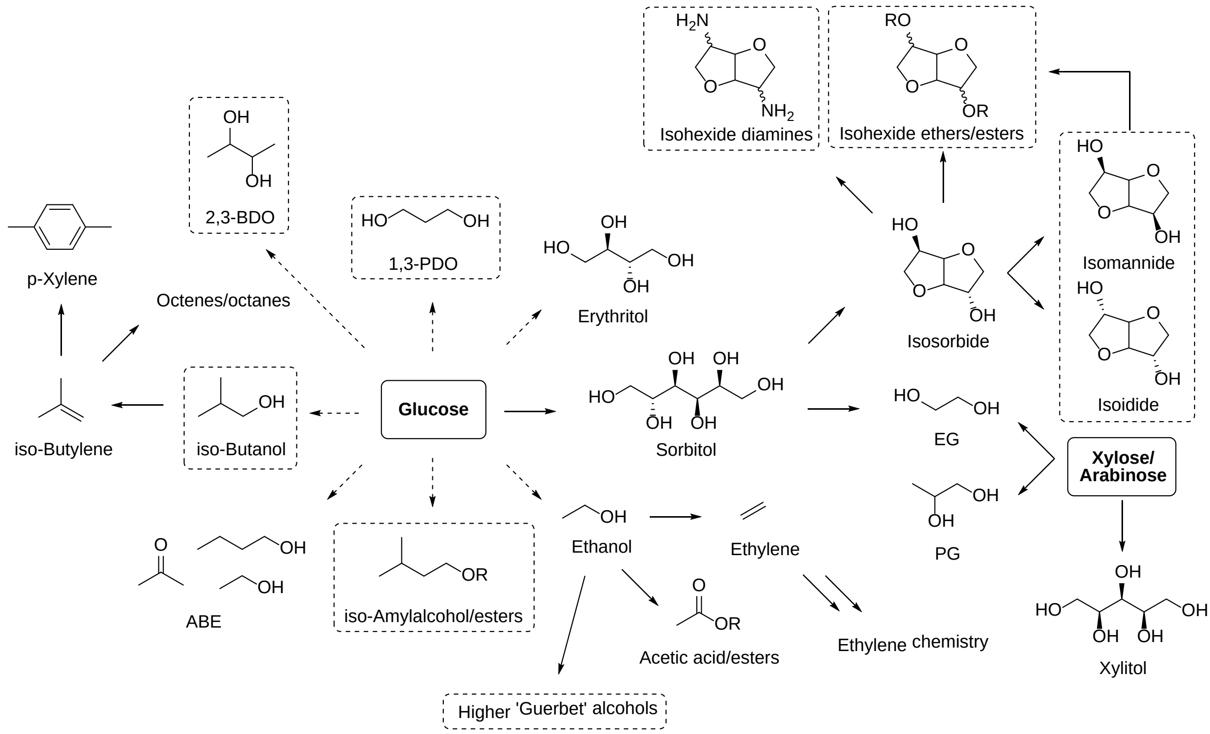
- Itaconic acid and derivatives; growing production from various sources, need for additional outlets
- 3-Hydroxypropionic acid (3-HPA) and derivatives; growing production, need for additional outlets
- Lactic acid derivatives; growing production, need for additional outlets
- Succinate esters and amides; growing production, need for additional outlets

3.3 Sugar derived alcohols

Next to acids also a wide range of alcohols, diols and polyols is produced from glucose. Scheme 3 gives an overview of some of the most import ones. In the case of alcohols both fermentation and bio/chemocatalytic conversion are used to a large extent.

- Glucose can be fermented to several types of diols, including 2,3-butanediol (2,3-BDO) and 1,3-propanediol (1,3-PDO). While the biobased version of the former is still being developed[24-26], mainly for application in polyesters, the latter has been commercial since 2000, and finds application in the polyester polytrimethylene terephthalate, aka Sorona® from DuPont, which is mainly used in textile and carpet fibre applications.[18,27]
- Catalytic hydrogenation of glucose yields the natural polyol sorbitol, which is produced on large scale (up to 1 million tons annually worldwide) by[28] companies like ADM and Roquette.[18,29] Applications of sorbitol are as diverse as low calorie sweetener to ingredient for personal care products. Catalytic cyclisation of sorbitol yields the rigid bicyclic diol isosorbide, which is being developed as building block for polyesters (e.g. SK chemical's Ecozen[30]), polycarbonates (e.g. Mitsubishi Chemical's Durabio[31]), and toner resins. Major players in the isosorbide market are again ADM and Roquette.[18,28,29]
- Recently chemocatalytic conversion of easily obtainable isosorbide to the less common isomers isomannide and isoidide has been developed[32,33], opening up opportunities for these

substances, either for direct applications in e.g. polymers, or as feedstock for further derivatisation. Isosorbide dimethyl ether[34] has been commercial for decades as solvent in pharmaceutical and personal care products [e.g. Arlasolve™ DMI from Croda[35]], while isosorbide diesters are being developed as alternative plasticisers for e.g. PVC [36]. Furthermore, isosorbide acrylates and diglycidyl esters are being developed as reactive diluents or as (co)monomer in respectively polyacrylate or epoxy resins.[37-40] Also the bio- and chemocatalytic transformation of isosorbide to the corresponding diamines is being developed, directed at applications in polyurethanes, either as diamine or as diisocyanate.[41-43]



Scheme 3: overview of industrially relevant alcohols that can be obtained from glucose (and C5 sugars), either by fermentation (dashed arrow) or by bio/chemocatalysis (plain arrow); substances in dashed boxes are "new".

- Catalytic hydrogenolysis and hydrodeoxygenation of sorbitol (and C5 sugars) yields ethylene glycol (EG) and propylene glycol (PG), both of which are bulk chemicals produced by the petrochemical industry for predominantly application in polymers (PET, polyurethanes). Currently the only producer of bio-EG is India glycols[44], while biobased PG is (amongst others) produced by US based Archer Daniels Midland (ADM)[45]. Catalytic hydrogenation of the C5 sugar xylose yields xylitol (as e.g. produced by Dupont subsidiary Danisco, and by Roquette), which is mainly used as low calorie sweetener.[28,46]
- The production of bioethanol is currently the largest industrial application of fermentation technology. While the majority of bioethanol is produced for use as bio-fuel, it can also be

the starting point for the production of a broad range of chemicals. Dehydration of ethanol gives bio-ethylene, which opens up opportunities for the production of e.g. bio-polyethylene and bio-PVC as for instance developed by Braskem.[47] Not shown in scheme 3 is the conversion of ethanol to 1,3-butadiene (for the production of e.g. SBR rubber or ABS) via the Lebedev and Ostromislenski processes developed in world war 2, and currently being 'rediscovered'.[48,49] Oxidation of bioethanol yields acetic acid, and ethyl acetate, which are already produced on large scale from fossil feedstocks. Conversion of ethanol to higher alcohols via the so called Guerbet reaction is developed with the aim to produce improved bio-fuels (less hydrophilic) as well as longer chain alcohols that are currently used in e.g. plasticisers or acrylates.[50]

- Although bioethanol production is quite efficient and selective, higher alcohols are formed in small quantities. Due to the large scale of ethanol fermentation, the distillation residue, so called fusel oil, is also becoming available in larger quantities (0.1-1 vol% of ethanol).[51] Fusel oil is a mixture of alcohols, but contains predominantly isoamyl alcohol (40-80%), which increasingly finds use as solvent by itself and in a variety of esters.[52]
- The ABE fermentation of glucose yields mainly Acetone, Butanol and Ethanol, all of which are currently produced on large scale either from fossil (acetone, butanol) or renewable feedstock (ethanol).
- The fermentation of glucose to isobutanol is a key step in a possible route towards bio terephthalic acid, as is e.g. pursued by US company Gevo.[53] Dehydration of isobutanol to isobutene, followed by dimerization gives either mixtures of octenes or para-xylene; the precursor to terephthalic acid.

'new' Biobased substances with PAS replacement potential:

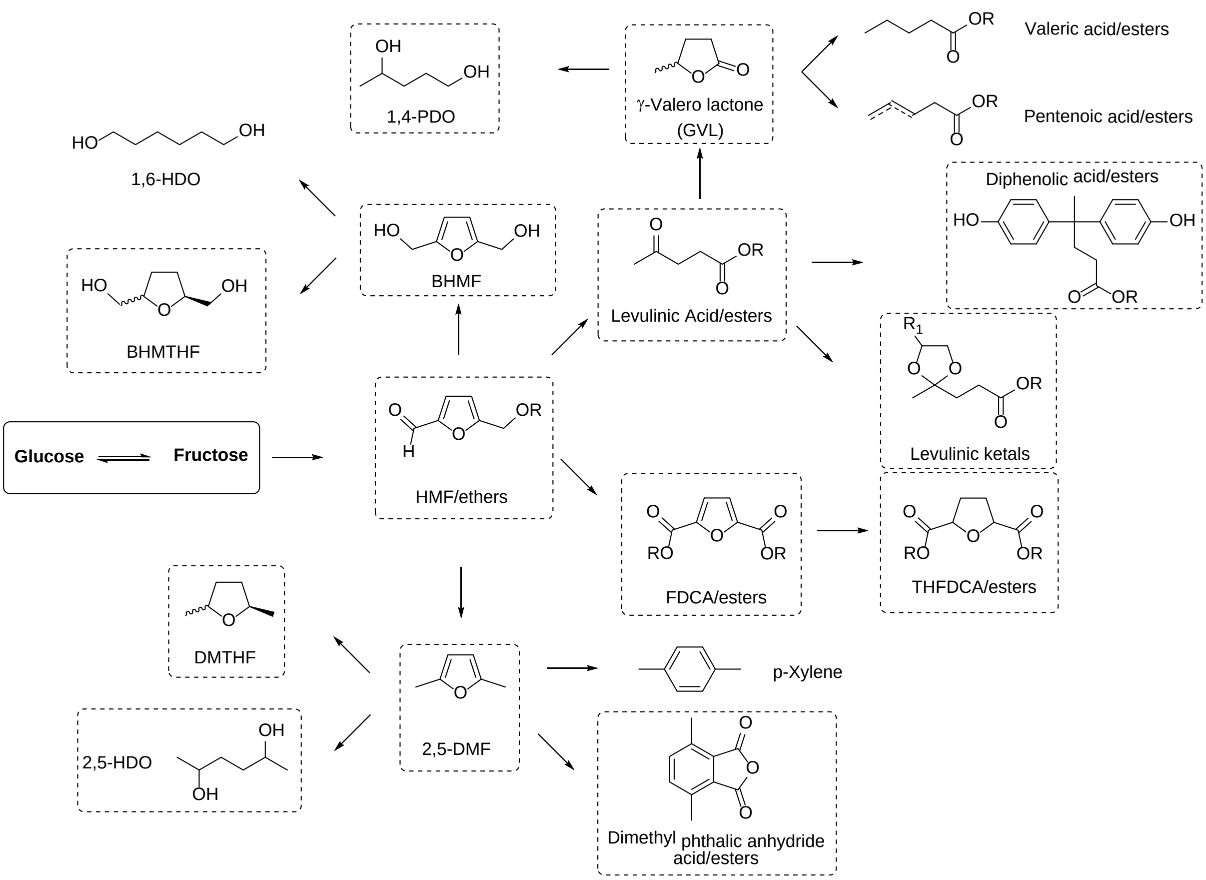
- 1,3-Propanediol and derivatives; growing production, need for additional outlets.
- 2,3-Butanediol and derivatives; still in demo phase.
- Isohexides and derivatives; growing production, need for additional outlets.
- Isoamyl derivatives; growing ethanol production, need for additional outlets.
- Iso-butanol and derivatives; depends on positive business cases.

3.4 Hexose derived furanics and aromatics

A class of substances that is increasingly growing in importance are furan derivatives. Since polysaccharides are the most abundant group of biobased substances, they are the most investigated types of feedstock for the production of chemicals. Although cellulose and starch can be used as materials themselves (with or without derivatisation), their limited thermal and hydrolytic stability have sparked a search for more robust carbohydrate based chemicals and materials. When heated in the presence of acid catalysts, sugars in general will convert to furan derivatives.

- C6 sugars, mainly glucose and fructose, will convert to 2-hydroxymethyl-2-furaldehyde (HMF).[54,55] Since HMF is highly reactive, it is considered a platform chemical, from which a broad family of biobased chemicals and building blocks can be made.
- Currently, the main (potential) outlet for HMF (and HMF ethers) is the production of furan-2,5-dicarboxylic acid (FDCA).[56-59] FDCA is widely advocated as biobased alternative for terephthalic acid, for instance in polyesters like polyethylene terephthalate (PET).[60,61] The FDCA analogue PEF is highly comparable to PET, with superior gas barrier properties[62,63], making it a very interesting material for food packaging applications, such as bottles. Since the current annual production volume of terephthalic acid exceeds 80 million tons[64], it can be expected that FDCA production will increase to significant volumes in the coming decade. Various companies are already involved in HMF (e.g. Swiss based Ava-Biochem[65]), and FDCA production (Synfina, the joint venture between Avantium and BASF; Ava-Biochem, Corbion, as well as a collaboration between ADM and Dupont).[66-69] Next to its use as building block for polyester resins FDCA is also an excellent platform for the development of phthalate-free plasticisers for e.g. PVC.[70-73]
- Ring hydrogenation of FDCA yields THFDCA, which is currently only evaluated at low TRL levels. However, if THFDCA should prove to have beneficial properties in specific applications, it can be expected that this substance will become a downstream product of FDCA production.
- FDCA synthesis via HMF results in significant coproduction of levulinic acid and/or its esters.[74] Levulinic acid can also be directly produced from e.g. glucose or cellulose, as currently developed by GF Biochemicals.[75]
- Levulinic ketals are developed as biobased solvents by the company Segetis.[76] Similarly levulinic acid esters themselves (e.g. methyl- or ethyl levulinate) are developed as biobased solvents, amongst others by Avantium.[77]
- By reacting levulinic acid with phenols, the bisphenol derivative diphenolic acid can be obtained, which is promoted as potential replacement for bisphenol A (BPA).[78]
- Reductive cyclodehydration of levulinic acid yields ɣ-valerolactone (GVL), which is promoted as fuel, solvent, and building block for polymers.[79]
- Hydrolysis of GVL yields 4-hydroxypentanoic acid, which can be converted into pentenoic acid and valeric acid.[78,79]
- Hydrogenation of GVL can yield the asymmetrical 1,4-pentanediol, which is a potential building block for e.g. unsaturated polyester resins and polyurethanes.[80]
- Selective hydrodeoxygenation of HMF yields 2,5-dimethylfuran (DMF), which is promoted as biofuel.[81-84] Furthermore, it is an essential building block for the production of aromatics by means of sequential Diels-Alder addition, and aromatisation, giving different types of products depending on the type of dienophile used.[85,86] In the case of ethylene, the major product is para-xylene, the drop-in precursor to terephthalic acid.[87-90] Mind that DMF is a suspected toxic compound.[91]

- Ring hydrogenation of DMF yields dimethyl-THF, which is developed as a biobased solvent.[83,84]
- Hydrogenolysis of DMF results in 2,5-hexanediol, which is a potential building block for polyesters and polyurethanes. Mind that this substance is known to be potentially neurotoxic.[92-94]



Scheme 4: overview of industrially relevant furans and aromatics that can be obtained from glucose and fructose; substances in dashed boxes are "new".

- Hydrogenation of the aldehyde group in HMF yields bishydroxymethyl furan (BHMF).[95] Although this substance is mentioned in many scientific papers (and patents) as potential building block for polyesters, in practice this substance is highly sensitive to heat and acid catalysis, giving uncontrolled resinification.
- Ring hydrogenation of BHMF results in bishydroxymethyl tetrahydrofuran (BHMTHF), which is a potential building block in polyesters and polyurethanes.[96-98] Although usually cis/trans mixtures are obtained by hydrogenation, the reaction is mainly selective towards the cis isomer (90/10), which could be prohibitive for application in high temperature engineering polymers due to unfavourable polymer chain configurations.

'new' Biobased substances with PAS replacement potential:

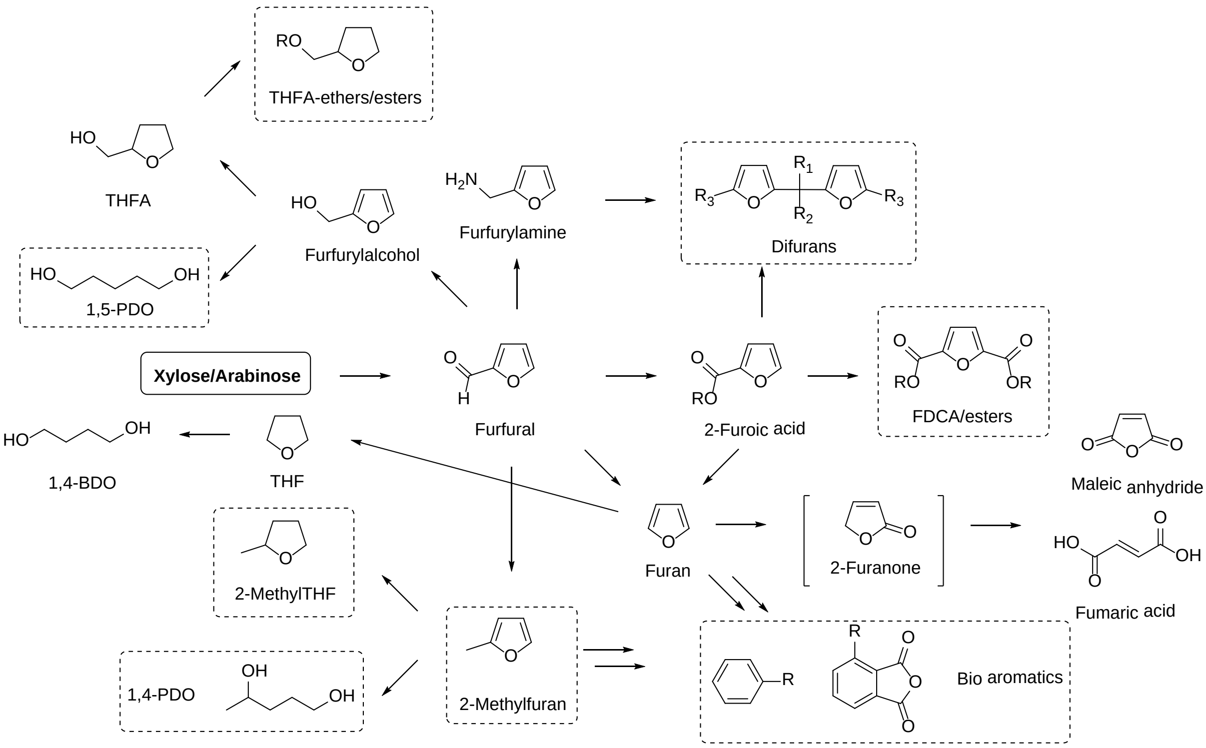
- HMF derivatives; growing production, need for additional outlets.
- FDCA derivatives; growing production, need for additional outlets.
- THFDCA derivatives; could become downstream product from FDCA production.
- Levulinic acid derivatives; side stream of HMF/FDCA production; outlets required.
- GVL; coupled to increased Levulinic acid production.
- 1,4-PDO and derivatives; coupled to increased Levulinic acid production.
- 2,5-DMF; driven by demand for biobased aromatics, coupled to increased HMF production.
- DMTHF; coupled to increased HMF production.
- BHMTHF; coupled to increased HMF production.

3.5 Pentose derived furanics and aromatics

Xylose and arabinose are C5 sugars predominantly found in hemicellulose and pectin fractions of agro-residues like wheat straw, sugarcane bagasse or sugar beet pulp, and are also precursors to furan derivatives (scheme 5).

- Acid catalysed cyclodehydration of C5 sugars yields 2-furaldehyde or furfural.[99-101] This substance has been produced on industrial scale, mainly starting from sugarcane bagasse, since the 1920's.[99-101] While furfural has direct applications in petrochemicals refining (extraction of aromatics from lubricant oils), it also serves as feedstock for a wide range of furan derivatives, many of which are used in the pharmaceutical and fine chemical industries.[102]
- Hydrogenation of the aldehyde group of furfural yields furfuryl alcohol, which is the major component in furan thermoset resins, which in turn are mainly used in foundry sand binders. Belgium based Transfuran Chemicals (TFC) is a major player in this field.[103]
- Hydrogenation of furfuryl alcohol yields the tetrahydro derivative which can be further derivatised.[99-101] THfurfuryl ethers have been reported as useful solvents in paint stripping formulations (combined with NMP).[104]
- Selective hydrogenolysis of furfuryl alcohol can yield 1,5-pentanediol (1,5-PDO), an interesting building block for polyesters and polyurethanes.[99] [99-101]
- Reductive amination of furfural yields furfuryl amine (currently used as e.g. pharmaceutical intermediate), while oxidation yields 2-furoic acid. Both can be used for the production of substituted difurans. Although industrial interest in these substances has been around since the 1950's, they have never been commercialised in any significant scale. However, with the growing demand for biobased chemicals and fuels, combined with increased supply of starting material such as furfural, it is likely that there will be renewed interest in difurans, especially in the area of thermoset resins.[105,106]
- Various routes exist to convert 2-furoic acid into FDCA, although most of them are still at a low TRL level.[107,108]

- Decarboxylation of 2-furoic acid or decarbonylation of furfural yields furan.[83] While furan itself is toxic (hepatocarcinogen in rodent studies)[91,109,110], like e.g. benzene it is a valuable intermediate for producing a number of high value chemicals.
- Hydrogenation yields the solvent THF, while hydrogenolysis yields 1,4-BDO, a building block for the production of polyesters like PBS and PBT.[111]
- Diels-Alder addition to furan, followed by aromatisation, is a convenient route for the production of a myriad of aromatic substances such as benzene and phthalic anhydride, most of which are now produced from fossil feedstocks.[64,86,112,113]
- Oxidation of furan yields maleic anhydride (MA) or fumaric acid.[114,115] These substances are currently produced from fossil feedstocks by selective oxidation of butane. Major current applications are unsaturated polyester resins, but can also include the production of biobased aromatics by Diels-Alder addition to furan (*vide supra*).
- An intermediate in the route from furan to MA is 2-furanone, which after hydrogenation yields ɣ-butyrolactone (see also section 3.2).



Scheme 5: overview of industrially relevant furans and aromatics that can be obtained from xylose or arabinose; substances in dashed boxes are “new”.

- 2-Methyl furan, obtained by hydrodeoxygenation of furfural, can be converted to methyl substituted aromatics, such as toluene. Mind that 2-methyl furan is a suspected toxic substance.[91]

- Hydrogenation of 2-methyl furan yields the solvent 2-methyl tetrahydrofuran, a widely advocated alternative to THF.[116] Hydrogenolysis yields 1,4-pentanediol, a potentially interesting building block for polyesters and polyurethanes.[80]

'new' Biobased substances with PAS replacement potential:

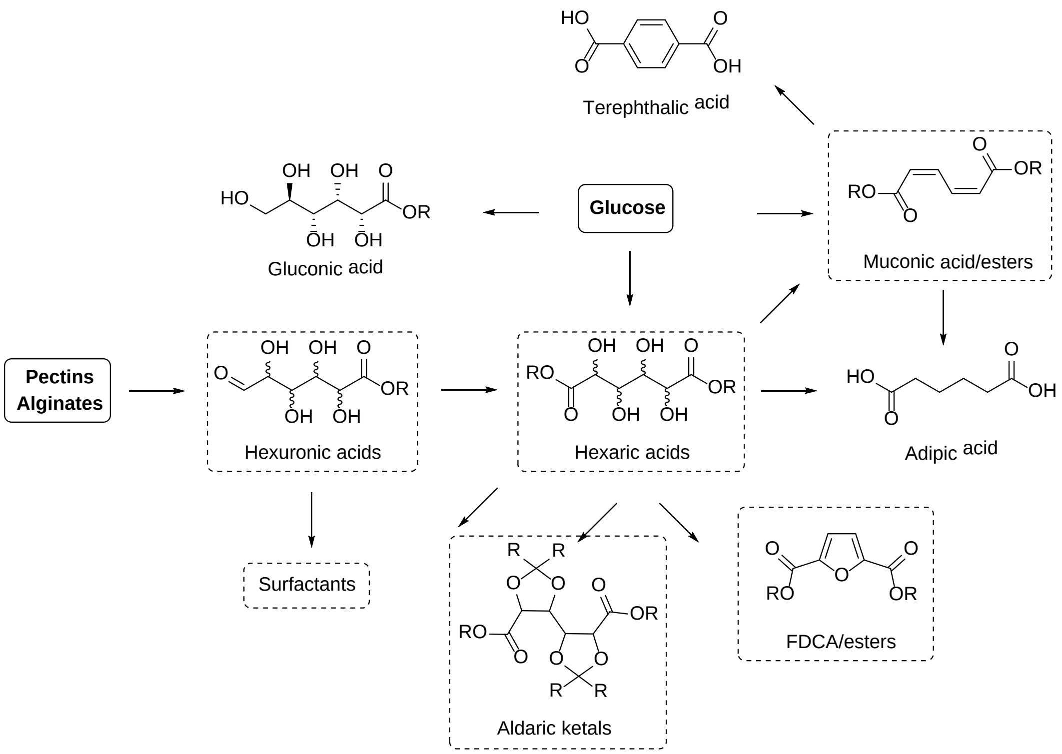
- THfurfuryl ethers and esters; coupled to increased furfural production.
- FDCA derivatives; see section 3.4.
- Difurans; coupled to increased furfural production.
- Near-drop in bioaromatics; driven by demand for biobased aromatics.
- 2-Methylfuran; driven by demand for biobased aromatics.
- 2-Methyltetrahydrofuran; driven by demand for polar biobased solvents.
- 1,4-PDO and derivatives: coupled to increased furfural production.
- 1,5-PDO and derivatives: coupled to increased furfural production.

3.6 Uronic acids and derivatives

Uronic acids, i.e. sugars with a carboxylic acid group at C6, are major constituents of polysaccharides like pectins (as can be found in e.g. fruit peels, sugar beet pulp and potato pulp) and alginates (as can be found in seaweeds).[117] Sugar acids based on C6 sugars, such as glucose and arabinose, are called hexuronic acids. Scheme 6 is an overview of chemicals based on hexuronic acids.

- Increased sugar beet production and (potentially) growing sea weed production are expected to result in an increased supply of hexuronic acids (D-galacturonic acid, and D-mannuronic/L-guluronic acid respectively). Direct application of uronic acids can be found in e.g. biobased surfactants.
- Oxidation of uronic acids yields aldaric acids.[118-120] In the case of C6 sugar acids, this produces hexaric acids. Galactaric acid can be obtained from sugar beet pulp derived galacturonic acid, as is currently being developed by Royal Cosun.[121] In contrast, glucaric acid is currently produced by the US company Rivertop Renewables by nitric acid oxidation of glucose.[122]Another US based company, i.e. Rennovia, is developing a route from glucose to adipic acid, *via* glucaric acid.[123] Aldaric acids can be used as metal sequestering agent, corrosion inhibitor, or as a starting material for surfactants and polymer building blocks.[120]
- Also the conversion of aldaric acids to muconic acid *via* deoxydehydration is the subject of increasing interest[124,125] Muconic acid can subsequently be hydrogenated to adipic acid, or can be a feedstock for the production of biobased terephthalic acid.[3,4]
- Hexaric acids can also be used as feedstock for the production of furan-2,5-dicarboxylic acid or FDCA.[58] When starting from sugar beet pulp derived galactaric acid, this would result in 2nd generation, non-food based FDCA.

- Furthermore, there are continuing developments of (derivatives of) aldaric acid ketals as rigid building blocks for polyesters and polyamides.[126-128]



Scheme 6: overview of industrially relevant chemicals based on hexuronic acids; substances in dashed boxes are "new".

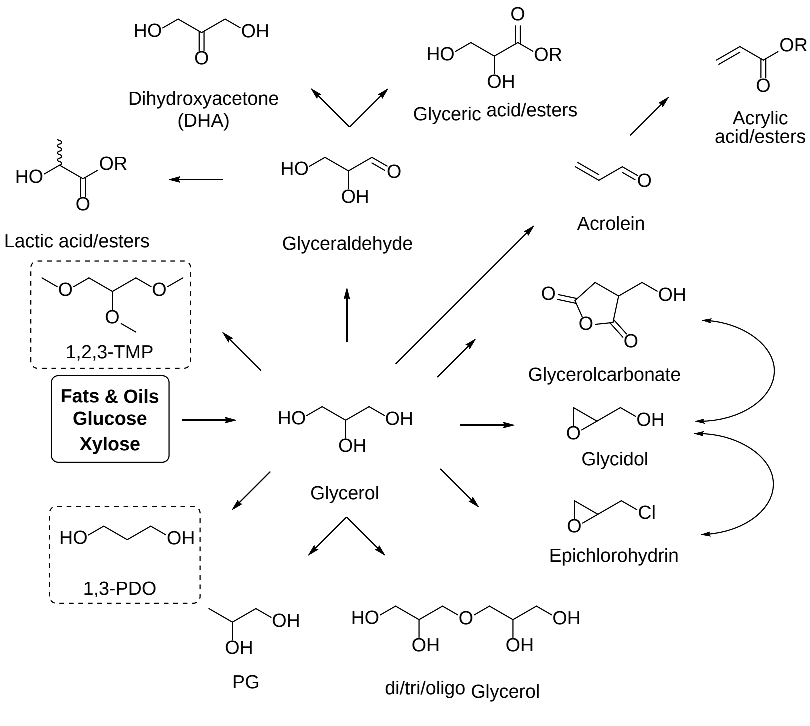
'new' Biobased substances with PAS replacement potential:

- Hexuronic acid derivatives, mainly galacturonic acid; side stream of increasing sugar beet production.
- Hexaric acid derivatives; Galactaric acid derivatives; depending on galacturonic acid production; Glucaric acid derivatives from glucose; driven by demand for biobased corrosion inhibitors etc.
- FDCA derivatives; see section 3.4.
- Muconic acid derivatives: see section 3.2.
- Aldaric ketals; depending on aldaric acid production.

3.7 Glycerol and oleochemicals

Oleochemistry is based on the conversion of vegetable and animal fats and oils. This includes vegetable oils obtained from dedicated (food) oil crops such as sun-flowers, palm, rapeseed or micro algae, but also side stream products such as tall oils from the pulping industry of waste fats from animal sources. Hydrolysis of vegetable oils (i.e. triglycerides) yields fatty acids and glycerol (approx. 10 wt%). Alcoholysis of vegetable oils yields esters, such as fatty acid methyl esters or FAME's, which are mainly used as 1st generation biodiesel. Especially the biodiesel industry has been responsible for flooding the existing market for glycerol, which was originally produced by traditional oleochemistry. Due to this surplus (several million tons world-wide) various initiatives were taken to valorise this glycerol, with an emphasis on the conversion to drop-in chemicals, such as lactic acid, dihydroxyacetone, glyceric acid, acrylic acid, 1,3-propanediol (PDO), propylene glycol (PG) and oligo glycerols (mainly diglycerol). Mind that glycerol can also be produced by hydrogenolysis of C6 and C5 sugars, e.g. from lignocellulose sources.

- The French chemical company Arkema is involved in the development of biobased acrylic acid from glycerol.[129] Epichlorohydrin (ECH) is an existing, toxic, bulk chemical used for the production of epoxy-resins, which is based on fossil propylene. Solvay is currently producing a biobased ECH, which is based on renewable glycerol.[130]
- Both from ECH and glycerol, glycidol can be obtained, which can be converted to glycerol carbonate (alternatively this substance can also be obtained directly from glycerol), which is currently marketed by Huntsman as a non-toxic, green solvent and reactant.[131] Due to the presence of the hydroxyl group and the cyclic carbonate group, glycerol carbonate cannot be used as alternative to PAS for many of the current applications where low (or no) reactivity is required.



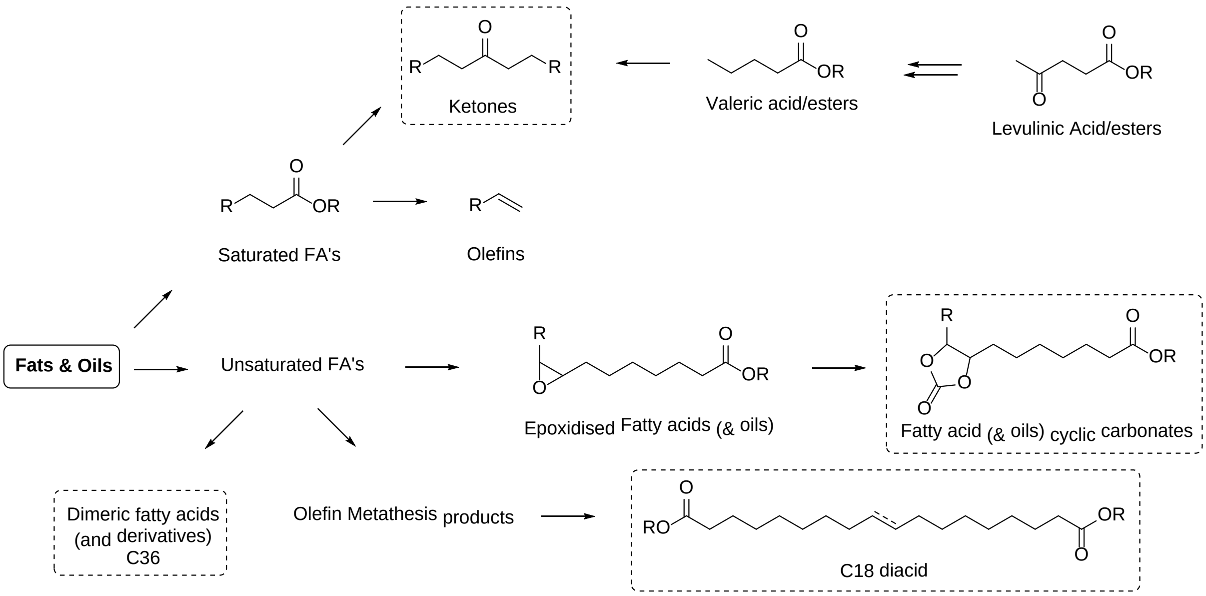
Scheme 7: overview of industrially relevant chemicals that can be obtained from glycerol.

- 1,3-propanediol can be obtained from glycerol by selective hydrogenolysis of glycerol or by fermentation[132]. However, the current commercial fermentation process for 1,3-PDO is still more effective.
- 1,2,3-Trimethoxy propane (or glycerol trimethyl ether, GTME), and related glycerol ethers, are interesting highly polar liquid chemicals that have been developed as alternative fuels and fuel additives, and have been shown to have interesting solvent properties combined with positive toxicity profiles.[34,133-135] The actual feasibility as solvent will to a large extent depend on costs resulting from crude glycerol purification, and alkylation technology.

Although oleochemistry is already a very old and established means of producing bio based chemicals, various developments in fatty acid chemistry are leading to 'new' products (re)entering the market. Since most vegetable oils contain unsaturated fatty acids (e.g. oleic acid), many 'new' derivatives are based on chemical conversion of these functional fatty acids.

- As mentioned previously treatment of fats and oils with alcohols gives esters, with FAMES (Fatty Acid Methyl Esters) begin the most predominant ones. While the major application of FAMES (mixtures of saturated and unsaturated C18-C14 fatty acid methyl esters) is biodiesel, FAMES can also be used as solvent or lubricant, yet only in applications where apolar, lipophilic solvents are required.
- Triglycerides, fatty acids and fatty esters can be hydrodeoxygenated to paraffins like the Finish company Neste is doing in its NExBTL process, yielding (after isomerisation of the n-paraffin) a superior quality 2nd generation biodiesel.[136]
- Another approach is catalytic decarboxylation or decarbonylation, optionally yielding α-olefins, which are interesting feedstocks for the production of polyolefins and surfactants.[137]
- High temperature dimerisation of saturated fatty acids by means of ketonisation gives ketones, such as the lubricant stearone from stearic acid.[138,139] Ketonisation is also investigated with the aim to produce high octane bio-gasoline from Short Chain Fatty Acids (C4-C10), which can be obtained by fermentation of waste water[140,141] or from glucose *via* levulinic acid[142,143].
- Epoxidised sunflower (ESO) or linseed oil (ELO) have been known for many years, and have found many applications.[144]
- More recently conversion of these epoxides to cyclic carbonates has opened up possibilities for non-isocyanate polyurethanes (NIPU's) based on fatty acids.[145]
- Olefin methathesis of e.g. oleic acid produces a C18 diacid than can be used in the production of polyamides and polyesters.[146-148]
- Direct dimerisation of unsaturated fatty acids produces dimeric fatty acids (and related diols, diamines and diisocyanates), as produced by companies like Croda , Oleon and BASF (formerly Cognis).[149,150]
- Other 'new' developments (no included in the scheme) with regard to unsaturated fatty acid chemistry are selective hydration/hydroxylation and hydroformylation, introducing respectively hydroxyl and aldehyde/acid groups on the fatty acid chain. Although this will

increase the polarity of the fatty acid derivatives, the resulting substances will still lack the polarity required for PAS alternatives.[151]



Scheme 8: overview of industrially relevant chemicals based on fats and oils; substances in dashed boxes are "new".

Driven by legislation, vegetable oil based biodiesel production (mainly FAME's) has led to a significant increase in the production of fatty acid derivatives (mainly esters). Although demand for biodiesel is expected to remain high for quite some time (in order to meet e.g. EU legislation), biofuels, and especially biodiesel are considered by many to be a transitional phenomenon, eventually to become obsolete by e.g. electrification. This means that if the current biodiesel production capacity remains active, more fatty acid derivatives will become available for the production of chemicals and materials.

'new' Biobased substances with PAS replacement potential:

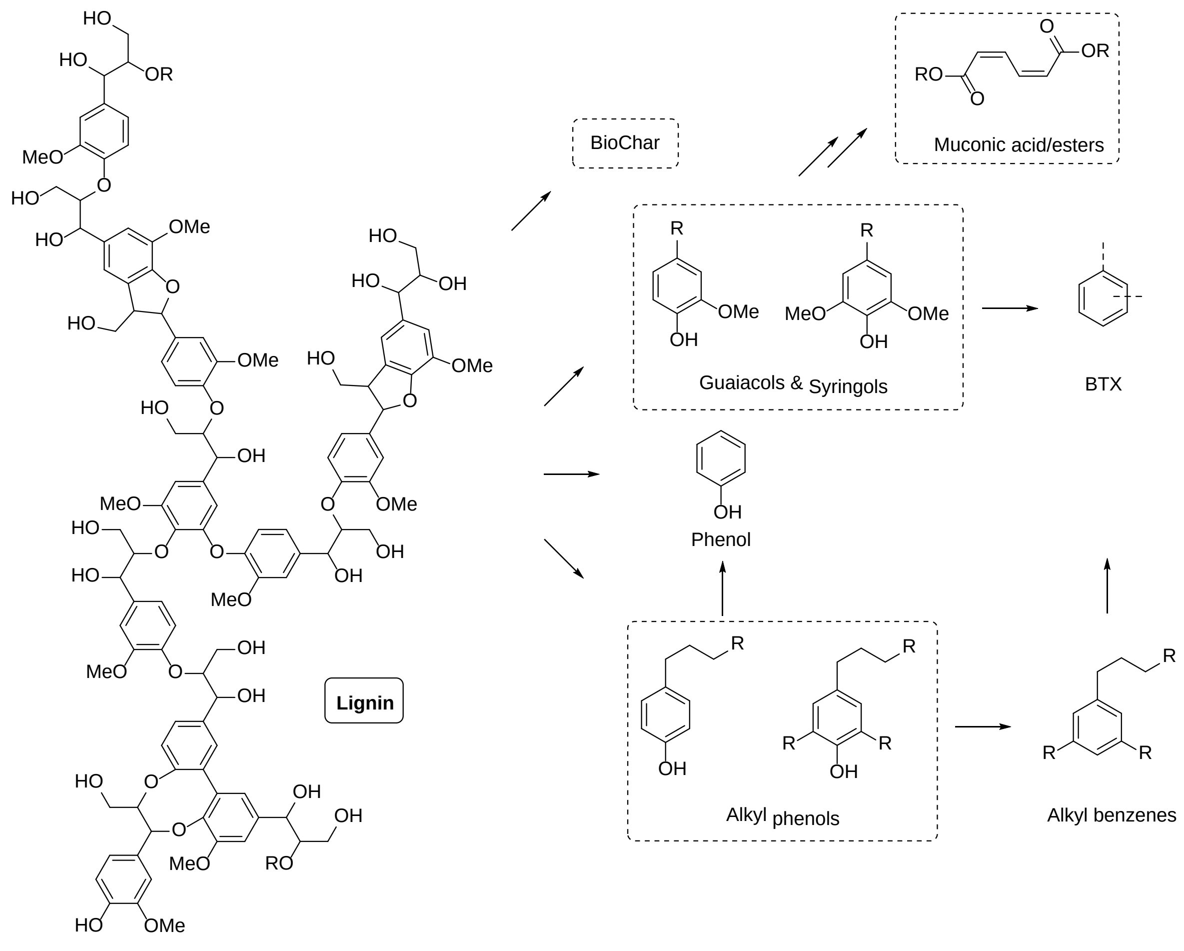
- 1,3-PDO; see section 3.3.
- 1,2,3-Trimethoxy propane.

3.8 Lignin derived chemicals

Lignin is potentially the largest renewable source of aromatic chemicals. Lignin is found in lignocellulosic materials such as woody biomass and grasses. It is a complex, recalcitrant polyphenolic polymer that differs in composition according to plant species, as well as growing season and geographical origin.[152,153] Currently most technical lignins are produced as by-products from the paper pulping industry, and predominantly serve as energy source for the paper mills.

However, it is expected that increasing production of e.g. bioethanol from lignocellulosic biorefineries will result in a concomitant increase in lignin side streams (20-30 wt% of dry matter in-take).

- Many efforts are being spent on producing aromatic chemicals from lignin. Especially those developments directed at producing base aromatics, such as benzene, toluene, xylene (BTX) and phenol are of interest to the chemical industry.
- Given the complexity and recalcitrance of lignin it is likely that the primary products of a lignin refinery will be substituted phenolics and alkylbenzenes, which can be further processed by traditional petrochemical industry. As a consequence it can be expected that in time alkylated phenols and oxygenated phenols will become more available, also for alternative applications, such as thermoset resins or as solvents.
- Guaiacol and syringol derivatives can be interesting with regard to solvent properties, and have been suggested as solvents for lignin depolymerisation. Broader use of these substances in solvent applications will depend heavily on their (eco)toxicity.



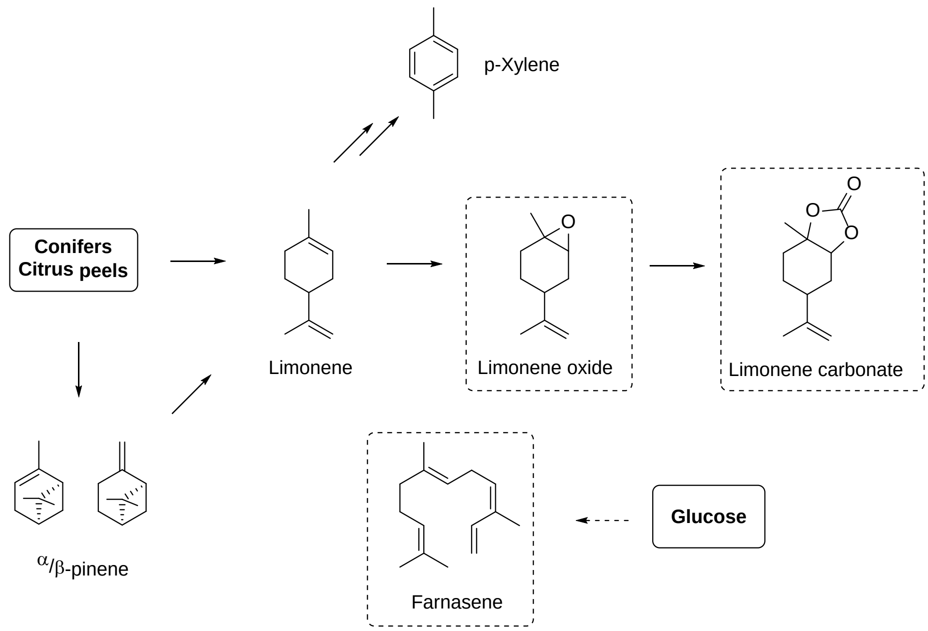
Scheme 9: overview of industrially relevant chemicals based on lignin; substances in dashed boxes are “new”.

- Furthermore, oxidation of substituted catechols and phenols, such as guaiacol and syringol, is known to yield muconic acid derivatives, which are potential intermediates for the production of adipic acid or terephthalic acid.[3,4]

'new' Biobased substances with PAS replacement potential:
- Guaicols and syringols; depending on (eco) toxicity, and efficiency of downstream processing of lignin deconstruction process used.
- Muconic acid derivatives: see section 3.2.

3.9 Terpenes and derivatives

Terpenes are hydrocarbons based on the isoprene motif, and are predominantly found in coniferous trees, such as pine (pinene), and in citrus peels (limonene). Monoterpenes have already been industrially used for a long time, amongst others as solvents.[154]
- Although various initiatives towards the production of *p*-xylene from terpenes such as limonene have been reported, the limited availability of the required specific terpenes makes this approach highly unpractical.[64]
- More polar terpene derivatives, such as limonene oxide and limonene carbonate, are increasingly explored as monomer for the synthesis of novel biobased polymers.[155,156]



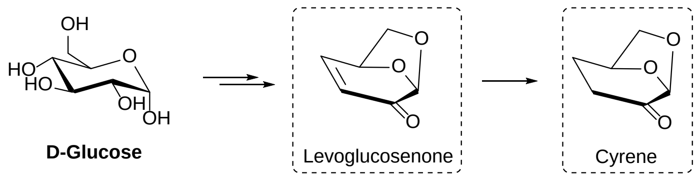
Scheme 10: overview of industrially relevant chemicals based on terpenes; substances in dashed boxes are "new".

- Whereas alpha and beta pinene are the most commonly found terpenes, their specific chemical structure (lack of polar functionalities) makes them unsuitable for polar solvents.[157] Nevertheless, derivatisation and conversion to e.g. limonene is possible.[157]
- In a different approach, the American company Amyris is developing trans-β-Farnesene, a sesquiterpene, as a renewable hydrocarbon building block and solvent by direct fermentation from glucose.[154,158] This approach could open up possibilities for obtaining terpenes with industrially interesting properties that are now difficult to obtain in sufficient purity and quantities. Thus far Amyris has focussed on products based on (partial) hydrogenation or dimerisation of farnesene, yielding low polarity chemicals. Polar functionalisation could yield interesting products with PAS replacement potential.

'new' Biobased substances with PAS replacement potential:
- Limonene derivatives; depending on increase in availability of cheap terpenes.
- Farnesene derivatives; not yet developed.

3.10 Miscellaneous

The Australian/UK company Circa is developing products based on levoglucosenone, which is obtained from glucose (scheme 11). The novel solvent Cyrene, i.e. hydrogenated levoglucosenone, is currently being developed as potential alternative to NMP.[159,160]

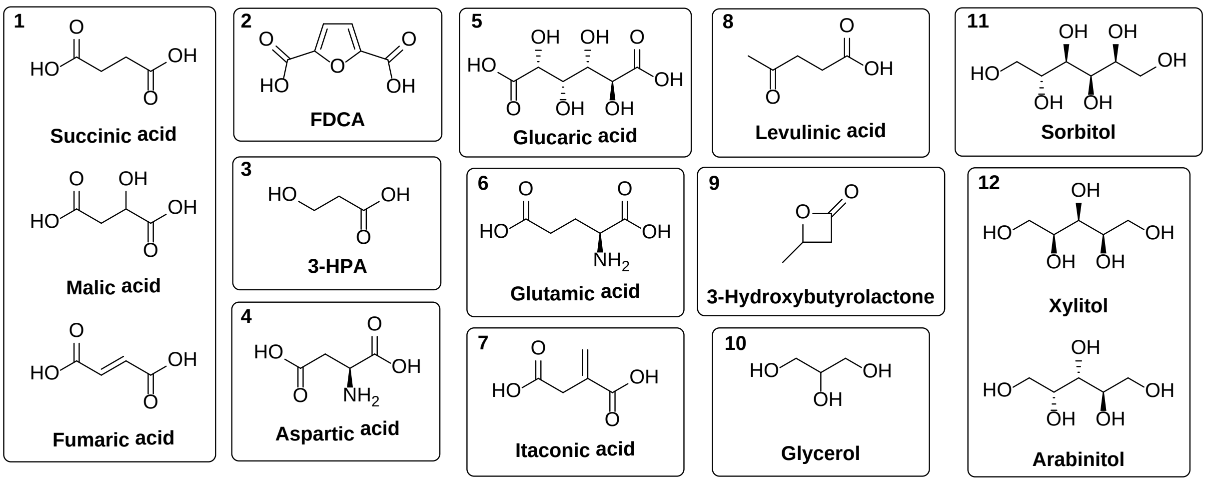


Scheme 11: from glucose to levoglucosenone and derivatives.

'new' Biobased substances with PAS replacement potential:
- Cyrene; depending on availability of cheap levoglucosenone

3.11 Comparison with DOE list of top value added chemicals from biomass.

In 2006 the US Department of Energy (US-DOE) initiated a study that resulted in a now famous report entitled 'Top Value Added Chemicals from Biomass'.[161] This report described a top 12 of biobased chemicals that 'can be produced from sugars via biological or chemical conversions, and that subsequently can be converted to a number of high-value bio-based chemicals or materials'.[161] The chemicals of the 2006 top twelve are shown in scheme 12. While several of the substances of the top 12 list are also identified as substances of interest in the preceding sections of the current report (e.g. FDCA, 3-HPA, glucaric acid, itaconic acid, levulinic acid), there are several distinct differences. Whereas the DOE report merely lists biobased substances that can be made from sugars, the main focus of the current report is on 'new' biobased substances that have not reached (full) industrial production scale and that have no fossil based counterpart. Substances like succinic acid, glycerol, sorbitol and xylitol do not meet these criteria. The main differences with the current report are malic acid, 3-hydroxybutyrolactone and the amino acids aspartic acid and glutamic acid, as these substances have not reached any successful commercial status since 2006.



Scheme 12: overview of the DOE top 12 added value chemicals from biomass.

In 2010 Bozell and Petersen, the original authors of the DOE report, published a follow-up paper, where they scored the original top 12 against a list of 9 criteria that was used to identify the actual break-through potential of these substances (see scheme 13).[162]

Table 2 Criteria used in evaluating biobased product opportunities from carbohydrates

1. ***The compound or technology has received significant attention in the literature.*** A high level of reported research identifies both broad technology areas and structures of importance to the biorefinery.
2. ***The compound illustrates a broad technology applicable to multiple products.*** As in the petrochemical industry, the most valuable technologies are those that can be adapted to the production of several different structures.
3. ***The technology provides direct substitutes for existing petrochemicals.*** Products recognized by the chemical industry provide a valuable interface with existing infrastructure and utility.
4. ***The technology is applicable to high volume products.*** Conversion processes leading to high volume functional equivalents or utility within key industrial segments will have particular impact.
5. ***A compound exhibits strong potential as a platform.*** Compounds that serve as starting materials for the production of derivatives offer important flexibility and breadth to the biorefinery.
6. ***Scaleup of the product or a technology to pilot, demo, or full scale is underway.*** The impact of a biobased product and the technology for its production is greatly enhanced upon scaleup.
7. ***The biobased compound is an existing commercial product, prepared at intermediate or commodity levels.*** Research leading to production improvements or new uses for existing biobased chemicals improves their utility.
8. ***The compound may serve as a primary building block of the biorefinery.*** The petrochemical refinery is built on a small number of initial building blocks: olefins, BTX, methane, CO. Those compounds that are able to serve an analogous role in the biorefinery will be of high importance.
9. ***Commercial production of the compound from renewable carbon is well established.*** The potential utility of a given compound is improved if its manufacturing process is already recognized within the industry.

Scheme 13: List of criteria as used by Bozell and Petersen.[162]

This exercise resulted in a revised list of carbohydrate based opportunities, named the Top 10+4, shown in scheme 14.

Table 4 Ranking of compounds against criteria in Table 2[a]

Compound	1. Extensive recent literature	2. Multiple product applicability	3. Direct substitute	4. High volume product	5. Platform potential	6. Industrial scaleup	7. Existing commercial product	8. Primary building block	9. Commercial biobased product
Ethanol	+++	+++	+++	+++	+++	+++	+++	+++	+++
Furfural	+++	++	+	++	+	+	+++	++	+++
HMF	+++	++	+	+	++	+	+	++	+
FDCA	+++	+	+	+++	++	+	+	+	+
Glycerol/derivatives	+++	+++	+++	+++	+++	+++	+++	+++	+++
Isoprene	+++	++	+++	+++	+	+++	+++	+	+
Biohydrocarbons	+++	++	+++	+	+	+	+	++	+
Lactic acid	+++	+++	+	+++	++	+	++	+	+
Succinic acid	+++	+++	+	+	+++	+++	+	+	+
HPA	+++	+	+++	+++	++	+	+	+	+
Levulinic acid	+++	++	+++	++	+++	+++	+	+++	+
Sorbitol	+++	+++	+++	+++	+++	+++	+++	+++	+++
Xylitol	+++	+++	+	+	+++	+	++	+++	++

[a] +++ = Good performance against criterion; ++ = emerging performance against criterion; + = lower performance against criterion.

Scheme 14: Revised Top 10+4 as suggested by Bozell and Petersen.[162]

Apparently, malic acid, 3-hydroxybutyrolactone, aspartic acid, glutamic acid, as well as glucaric acid did not meet the criteria shown in scheme 13, and were deleted from the original top 12 list. With the exception of glucaric acid, this is in agreement with the list of substances defined in the current report. Also interesting are the additional substances that were included in the revised list, i.e. furanics (furfural, HMF), lactic acid and biobased hydrocarbons, which again agrees well with the current analysis. Note that the current report contains a much broader selection of substances than the adapted Top 10+4 list.

The 2010 paper by Bozell and Petersen shows that even for experts that are well integrated in the biobased sector, it is difficult to make accurate predictions about the potential of 'new' substances.

Whereas the DOE study and follow up were mainly focused on the biobased feedstocks and chemicals themselves, listing a wide array of potential markets and applications, the current report is focussed on the application potential as (precursors to) high polarity solvents. This will be addressed in the next section.

4 Significance for replacement of polar aprotic solvents (PAS)

Since this study aims to identify potential biobased alternatives for the polar aprotic solvents NMP, DMAc and DMF, the biobased substances thus far identified as 'new' and emerging with PAS replacement potential, are summarised in table 1. The substances have been qualitatively ranked according to four criteria, in a similar fashion as Bozell and Petersen presented in their paper (scheme 14).[162]

- All new substances have been ranked according to their PAS replacement potential (qualitatively based on polarity only): resulting in three main groups, high, medium and low polarity. Obviously (very) apolar substances such farnesene have a negative replacement potential. The second group contains substances that are (relatively) polar, yet in most cases can only be used in the form of derivatives, which will reduce the polarity. For instance, while FDCA is highly polar, it cannot be applied in the diacid form (solid). FDCA esters based on short chain alcohols (methanol, ethanol, etc.) are also highly polar, yet are also solids at room temperature. In contrast, long chain alcohol esters (C8-12) of FDCA are liquids at room temperature, yet have become too lipophilic to be sued as PAS substitute. They are however highly suitable as plasticisers in e.g. PVC.[70-73] Similarly, since 1,3-PDO is diprotic, it can only be used in derivatives form such as e.g. ethers and esters, whereby the choice of conjugate acid determines the overall polarity.[163] Thus were derivatives are mentioned in the table, in practice it will be limited to methyl or ethyl ethers, and acetate esters. Highly polar substances such as Cyrene, isohexide- and levulinic acid derivatives, GVL and lactates are potential PAS substitutes. These substances (both generic classes and specific substances) warrant further investigation with regard to their (eco) toxicological profiles. Furthermore, these potential PAS alternatives require further development, e.g. by preparing and testing new derivatives, as well as further application testing of known and already available derivatives, such as for instance Cyrene, dimethyl isosorbide, and methyl levulinate.
- The potential availability of substances is qualitatively based on feedstock availability (e.g. high for starch, cellulose and glucose, and low for terpenes) as well as process feasibility (estimated required number of unit operations, yields and selectivities, required reagents, waste production and energy demand).
- Industrial scale indicates whether substances are or have already been produced on demo-, small- or full industrial scale (based on publicly available information).
- Commercial production indicates whether a substances is actually commercially produced. (Mind that the difference between industrial and commercial production is not trivial. Especially in start-up companies, demo or small scale industrial production, although technically feasible, often results in failure to reach commercial production due to financial problems or adverse market conditions)

Table 1: Overview of emerging biobased substances (and derivatives), ranked according to their potential for substitution of polar aprotic solvents (PAS).[a]

Substance[b]	**PAS substitute**[c]	**(potential) Availability**[d]	**Industrial scale**[e]	**Commercial production**	**Scheme #**	**Remarks & References**
High Polarity						
Cyrene	+++	+++	+	+	11	h, 159
Isohexide derivatives	++	+++	++	++	3	h, 28,29
Isosorbide dimethyl ether	++	+++	++	+++	3	h, 35
Levulinic acid derivatives	++	+++	+	+	4 & 8	h
Methyl levulinate	++	+++	+	+/-	4	75,77
Ethyl levulinate	+	+++	+	+/-	4	75
GVL	++	+++	+/-	+/-	4	-
Levulinic ketals	++	+++	+	+	4	75
Lactic acid derivatives	++	+++	++	++	2	17
THfurfuryl alcohol ethers	++	++	+	+/-	5	102
Succinic acid amides	++	++	-	-	2	h
1,2,3-TMP	++	++	-	-	7	-
HMF derivatives	+	+++	+	+	4	h
3-HPA derivatives	+	+++	+	+	2	-
1,3-PDO derivatives	+	+++	++	++	3	-
Itaconic acid derivatives	+	++	+	+	2	h, 8
1,4-PDO derivatives	+	++	+/-	-	4	-
BHMTHF derivatives	+	+++	-	-	4	h, 102
THFDCA esters	+	++	-	-	4	h

Substance[b]	PAS substitute[c]	(potential) Availability[d]	Industrial scale[e]	Commercial production	Scheme #	Remarks & References
Medium Polarity						
Succinic acid esters	+/-	+++	++	++	2	[21,22]
Isobutanol derivatives	+/-	+++	+	+/-	3	-
2-MethylTHF	+/-	++	++	+	5	[102]
FDCA esters[f]	+/-	+++	+	+	4 & 5	[h]
Limonene derivatives	+/-	+	+	+	10	-
(iso) Amyl alcohol derivatives	+/-	++	+/-	+/-	3	-
Methylsuccinic acid esters	+/-	++	+/-	-	2	[h]
Difuran derivatives	+/-	++	+/-	-	5	-
Muconic acid derivatives	+/-	+++	-	-	2 & 6 & 9	-
2,3-BDO derivatives	+/-	++	-	-	3	-
2,5-HDO derivatives	+/-	++	-	-	4	-
Hexaric acid derivatives	+/-	+	-	-	6	[h, 121]
Hexuronic acid derivatives	+/-	+	-	-	6	[121]
Aldaric ketals	+/-	+/-	-	-	6	[121]
Guaicols and syringols	+/-	+	-	-	9	-
Low Polarity						
Farnesene	-	++	+++	+	10	[158]
DMTHF	-	++	+/-	+/-	4	-
2-Methylfuran[g]	-	++	+/-	+/-	5	-
1,5-PDO derivatives	-	+	+/-	-	5	-
2,5-DMF[g]	-	++	-	-	4	-
Near drop-in bio aromatics	-	+	-	-	9	-

[a] +++ = good fit with criterion, ++ = fits with criterion, + = potential fit with criterion, +/- unclear fit with criterion, - = no fit with criterion.
[b] Specific representatives for substance classes in italics.
[c] Based on criteria described in Methods section.
[d] Based on feedstock availability and process feasibility; see Methods section.
[e] Demo scale and higher, > TRL 7.
[f] Most polar FDCA derivatives are solids, while liquid diesters are relatively apolar.
[g] High toxicity.[91]
[h] Also covered in BBI project Resolve.

Of the 19 different polar biobased substances and substance classes listed in table 1, many will require toxicity assessment. This falls outside of the scope of the current study, but will be part of a separate report by the RIVM.

- Note 1: In June 2017 the EU BBI project Resolve (REnewable SOLVEnts with high performance in application and improved toxicity profile) started, which aims to replace toluene and NMP with safer alternatives derived from non-food carbohydrates.[164] This three year project is a collaboration of 11 partners from five European countries, including the academic partners University of York (Coordinator) and Wageningen University & Research. Some of the substances listed in table 1 are also the subject of research and development in project Resolve, as indicated in table 1. The developments in project RESOLVE are expected to form a stepping stone towards further development of new polar aprotic biobased solvents. Since only one of the various development lines in project RESOLVE is at a demo stage (Cyrene), most 'new' solvent candidates that are chemical derivatives of existing biobased chemicals, will require further development after the project.
- Note 2: Solvents in general are a product group with widely differing applications and users. This also applies to PAS, which makes it difficult to predict which of the biobased substances listed in table 1 will be a successful PAS replacement. A one-size-fits-all approach is not very likely given the widely differing property requirements (e.g. boiling point, vapour pressure, solvency power, thermal-, hydrolytic, acid-, base-, photo- and thermal stability, flammability, etc.) for the wide range of applications (e.g. industrial cleaning solutions, water borne coating dispersion technology, paint stripping solutions, butadiene recovery in petroleum refining, and even *lithium ion battery electrode manufacturing* [165-167]). Furthermore, for many of the substances listed in table 1 only limited data on environmental and health effects is available, especially compared to existing PAS like NMP. Hence, for the moment no reliable estimations can be given on which biobased alternatives can replace the currently disputed PAS in specific applications and markets, and at which volumes.

5 Conclusions

The goal of this desk study was to identify new biobased alternatives to the currently disputed polar aprotic solvents NMP, DMAc and DMF.

A comprehensive overview has been compiled of both emerging and existing biobased chemicals (and materials), including potential (side) streams of 'new' biobased chemicals that will (need to) be valorised in the near future. For most of the existing and emerging biobased product streams 'new' substances have been identified, which has resulted in a list of substances (or classes of substances) that are likely to reach a significant production volume in the coming decades. This list has been prioritised according to criteria like feedstock availability, level of (industrial) development, whether or not a substance is already commercially produced, and their potential as alternative biobased polar aprotic solvents. The result is a list of 19 polar biobased substances (and classes of substances) that are potential (precursors for) new polar aprotic solvents.

Toxicological analysis should give more insight into the feasibility of these substances as safe (non-regrettable) alternatives for the currently disputed polar aprotic solvents. Next, the technical and economic feasibility should be determined for these substances in various key applications by the relevant stakeholders (industry, knowledge institutes, government). This also implies that synthesis and production of substances that are not yet readily available should be developed further in R&D programs, as well as process development, application development, and formulation technology.

Due to the rather diffuse nature of the solvents market, with both many (potential) producers and end-users, as well as a myriad of applications, a proactive role of the government in stimulating and facilitating the development of these new biobased solvents and chemicals is strongly advised. Next to e.g. matchmaking events and 'green deals', a specific R&D program involving a broad number of stakeholders, (potential) solvent producers and users, and knowledge institutes (comparable to e.g. the Biobased Performance Materials program) is recommended in order to accelerate the introduction and acceptance of new, safe biobased solvents.

6 Results of external survey

As final part of this study a survey has been held among a limited number of stakeholders in the area of biobased chemicals and solvents. The goal of the survey was to serve as external validation of the report, as well as to retrieve additional essential information.

The survey has been distributed by e-mail to 14 representatives of agro raw materials producers, biobased chemicals producers, and biobased solvent producers. After a second round of emails 6 people responded, of which 1 indicated that no response would be given, as the requested information was considered confidential. The remaining 5 respondents were positive with regard to supplying information and have been interviewed over the telephone for 30 min. The anonymised results are summarised in table 2.

Table 2: Anonymised results of the stakeholder interviews.

	Resp. 1	Resp. 2	Resp. 3	Resp. 4	Resp. 5
Location of company	EU	EU	US	US	EU
Type of company	Large	SME	Large	Large	SME
Type of business	Agro producer	R&D	Agro producer	Agro producer	Chemical producer
Type(s) of technology	Biorefinery, Chemical conversion, Biotech-fermentation	Chemical conversion	Biorefinery, Chemical conversion, Biotech-fermentation	Biorefinery, Chemical conversion, Biotech-fermentation	Chemical conversion
Type of biobased feedstocks	Sugar beet, potato, chicory, fruit, vegetables	All types of ligno-cellulosic and other biobased materials	Corn, wheat, soy, oilseeds	Oilseeds (+ others, but outside expertise of respondent)	Wood, sawdust
Main types of biobased products	Sucrose, ethanol, starch and inulin derivatives	Glucose, lignin, ethylene glycol, oxalic acid	Sorbitol, ethanol, citric acid, glycerol, 1,2-propylene glycol, vegetable	Vegetable oils, biodiesel	Bio solvents

	Resp. 1	Resp. 2	Resp. 3	Resp. 4	Resp. 5
			oils, biodiesel		
Expected 'new' biobased chemicals	Not disclosed	Ethylene glycol, oxalic acid	FDCA and DMFDCA	Not disclosed	Cyrene derivatives
Biobased products in current or future portfolio	Cheap sucrose, ethanol	Not disclosed	FDCA, citric acid, ethanol, propylene glycol, fatty acid methyl esters, fusel oils, triacetin	Fatty acids and methyl esters	Cyrene
Biobased chemicals that can be used as (feedstocks for) PAS	Not a focus area	Levulinic acid esters	FDCA, levulinic acid, itaconic acid, isohexides,	Not a focus area	Cyrene
Need for (biobased) solvents	If they are cheap and easily recyclable solubilise carbohydrates	No	If they are cheap and easily recyclable, and reduce overall LCA	If they are cheap and easily recyclable	Not yet

- Although the total number of respondents was low, the spread in types of business and geography helps to get a balanced view. In general, no major additions were suggested to the substances listed in table 1, except for oxalic acid, which is already an established chemical from petrochemical feedstsocks.
- Only one of the respondents (SME) is an actual producer of a biobased polar solvent.
- Two of the large agro producers have a number of products and technologies in their portfolio to produce biobased polar solvents if sufficient demand presents itself.
- Of those respondents that indicated that biobased solvents could play a (future) role in their processes, functionality, low costs and recyclability were specifically mentioned as prerequisites.

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