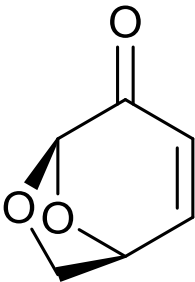


# UK BioChem 10 – 3 LGO

<b>Name</b>	levoglucosenone	
<b>Synonyms</b>	1,6-dehydro-3,4-dideoxy-β-D-pyranose-2-one	
<b>CAS Number</b>	37112-31-5	
<b>Molecular formula</b>	C <sub>6</sub> H <sub>6</sub> O <sub>3</sub>	
<b>MW</b>	126.11 g mol <sup>-1</sup>	
<b>Patents related to synthesis</b>	3	

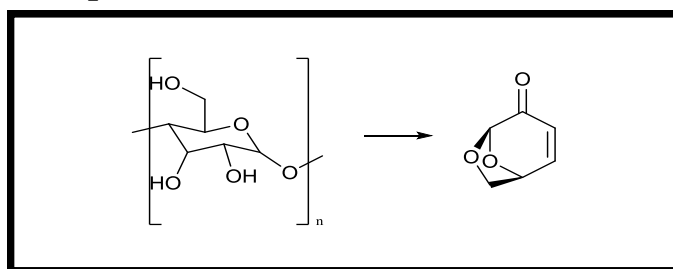
## Why is it of interest?

Levoglucosenone (LGO) has been known in scientific literature for some time although a route to obtain it at scale has only recently been demonstrated. It is of high interest as it can be produced directly from cellulose, the most abundant constituent of biomass and therefore a low cost feedstock. There are a number of points of chemical functionality with which to further react, the alkene, ketone and the acetal bridge as well as being produced in a single stereoisomer. This results in LGO having potential applications in the area of pharmaceuticals as well as a general platform molecule. Of most current interest is the ability to form the polar aprotic solvent dihydrolevoglucosenone, more formally known as Cyrene, *via* hydrogenation of the double bond.

## Feedstocks for LGO

Although there is some work looking at free sugars and reduced sugars in the synthesis of LGO, these show little enhanced benefit as compared to cheaper and more readily available feedstocks. The majority of papers and patents over the last 40 years have all used various lignocellulosic feedstocks, predominantly wood pulp or sawdust, as well as other cellulose-rich materials such as straws and grasses and also pure cellulose.<sup>1,2</sup> A more recent and potentially very promising route to LGO utilises the “carbohydrate contaminated” lignin produced *via* second generation fermentation, in its self a significant and growing sector of the bio-economy producing predominantly ethanol, butanol and acetone without being part of the food versus fuel debate. Here the lignin byproduct still contains a significant portion of unfermented polysaccharides, which can be readily converted to LGO at a high yield and purity.<sup>3</sup> This would be implemented in a bio-refinery concept, making a high value product from a low value side stream, while also producing a cleaner lignin by-product.

## Highlighted routes of production



Pyrolysis is the heating of a material in the absence of air, which in biomass utilisation results in the production of a high energy char (suitable for combustion), a liquid bio-oil rich in volatile small molecules and

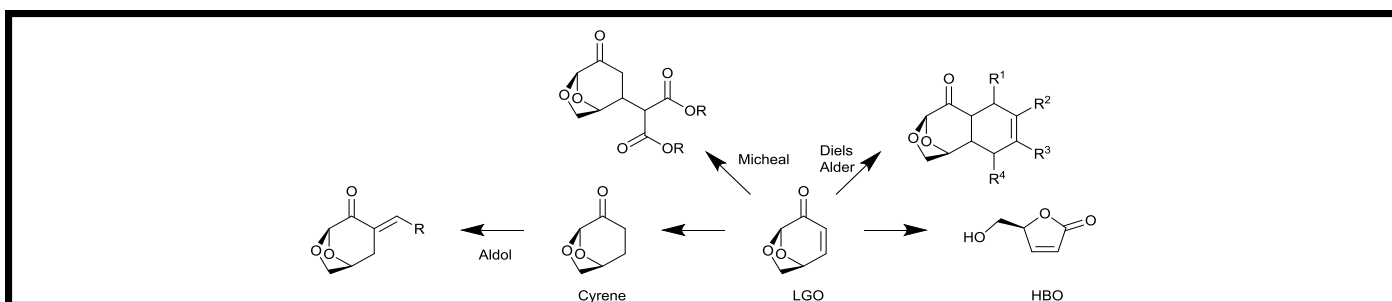
non-condensable gases such as carbon dioxide, carbon monoxide, hydrogen and methane. As such it is an area of much potential in the bio-economy but has not been more widely taken up at scale due to the complex mixtures of organic molecules produced which then require lengthy and costly separation. Direct pyrolysis of lignocellulosic material gives LGO yields over a 0.1 to 0.5% range.<sup>4</sup> With the application of an acid catalyst however, LGO can be obtained at a minimum of 3% when first published and up to 15% by weight of the feedstock and easily purified by distillation.<sup>1,5</sup> This phosphoric acid catalyst route has been implemented at pilot plant scale, capable of producing 50 ton *p.a.*<sup>6</sup> Commercial LGO production from cellulose has an AE of 78% and an RME of 26%. The use of 2<sup>nd</sup> generation fermentation lignin gives an 8% by mass yield of LGO, accounting for 40% of the total residual carbohydrates present.<sup>3</sup> LGO has been also been produced from pure cellulose, which first has to be isolated from biomass, here acid catalysis gives yields of over 50%.<sup>7</sup>

## Current Applications of LGO

The 50 ton *p.a.* plant currently in operation is not primarily being used to supply LGO to market, but instead hydrogenates the platform molecule to give dihydrolevoglucosenone, more commonly known as Cyrene.<sup>6</sup> Cyrene has generated interest as initial work on this molecule suggests that as a solvent it has similar properties to the key industrial polar aprotic NMP.<sup>8</sup> This is significant as NMP has an annual production of 150,000 tons but has also recently been restricted by REACH and may move to full authorisation, meaning alternatives will be needed.<sup>9</sup> However currently there are very limited alternatives, meaning a significant opportunity for Cyrene. To date Cyrene has been successfully applied in; exfoliation of graphene,<sup>10</sup> pharmaceutically relevant carbon-carbon coupling reactions<sup>11</sup> and the polymerisation and application of polyamide imides,<sup>12</sup> all of which are currently conducted in NMP. Most importantly, Cyrene has received Annex VIII REACH approval and so can currently be manufactured or imported into the EU at up to 100 tons per annum.

## Future markets and applications

Currently the number of products and compounds accessible from LGO is relatively small as for the previous 40 years, this has only been a compound available in small quantities and thus not thought of as significant. The reaction of LGO with an oxidising agent results in the formation of a 5 membered lactone (HBO), which in turn can be easily further reacted to give high value flavour and fragrance compounds.<sup>13</sup> In addition various transformations towards chiral auxiliaries, ligands and organocatalysts have been reported via Diels Alder cyclo additions<sup>14</sup> as well as Michael additions to generate diesters.<sup>15</sup> Cyrene has also been applied as a platform molecule as under base conditions enol chemistry occurs. This has led to the production of a series of scaffolds which appear likely to be pharmaceutically active.<sup>16</sup>



References: **1.**WO 2011/000030 A1, **2.**WO 2016/039996 A1, **3.**WO 2016/170329 A; DOI.org/10.1039/C6EE01352J, **4.**DOI.org/10.1039/C1EE02743C, **5.**DOI.org/10.1021/jo00942a005, **6.**Appita J., **2016**, **4**, 344, **7.**DOI.org/10.1002/cssc.201801420, **8.**DOI.org/10.1039/c4cc04133j, **9.**DOI.org/10.1016/j.chempr.2018.08.035, **10.** DOI.org/10.1039/C7GC00112F, **11.**DOI.org/10.3762/bjoc.12.187; DOI.org/10.1055/s-0036-1589143, **12.**WO 2017/050541 A1, **13.**DOI.org/10.1002/ejoc.201801780; WO 2015/165957 A1, **14.** doi.org/10.1002/ejoc.201701227, **15.**doi.org/10.1016/S0008-6215(00)88064-7, **16.**DOI.org/10.1039/C8GC01227J

## Additional feedstocks

Two sets of feedstocks have been investigated to determine how much of each would be required to supply a 5 kton LGO plant. 1st generation have been omitted as they are not necessary as LGO is derived from cellulose and therefore 2nd generation and energy crops would likely supersede 1st generation to avoid the food versus fuel/chemical debate.

## Energy crops

Both Miscanthus and short rotation coppice are primarily grown for energy generation in biomass boilers. Data here for the latter has been generated using Willow as this is the crop most commonly used. Forestry waste is material left in woodland post harvesting and generally is 10-15% by mass compared to the lumber harvested. The average value has been used here and only softwood has been considered. All yields have been calculated based on the %cellulose available in each crop.

crop	ktons needed supply make 5 5 kton LGO plant	ktons produced per annum (UK)	% required
forestry waste	118.3	1340.88	8.82
miscanthus	41.9	87.50	47.88
short rotation coppice	39.0	28.20	138.16

## Second generation biomass

This is by-product of food production which contain an appreciable quantity of cellulose. Assumptions have been made that a similar portion of cellulose is able to be converted to LGO as for that of sawdust. Carbohydrate rich lignin from secondary fermentation has not been included as the UK currently does not have any commercial operations producing this, but an opportunity would arise for LGO production if such a feedstock was available.

feedstock	ktons needed to supply a 5 kton LGO plant	ktons produced per annum (UK)	% required
wheat straw	64.9	3828	1.70
barley straw	77.9	1850	4.21
maize stover	52.7	916	5.75
oilseed rape straw	60.9	379	16.05
oat straw	72.2	247	29.24