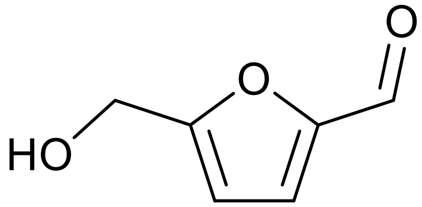
UK BioChem 10 – 4 HMF

Name	5-(hydroxymethyl)furfural
Synonyms	2,5-hydroxymethyl-2-furfuraldehyde, HMF
CAS Number	67-47-0
Molecular formula	$C_6H_6O_3$
MW	126.11 g mol^{-1}
Patents related to synthesis	134



Why is it of interest?

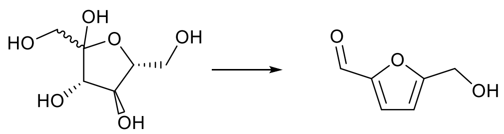
5-(hydroxymethyl)furfural (HMF) in itself is unlikely to be a commodity chemical, bought and sold on the market as it is too reactive. It is however easily obtained from a range of feedstocks and is a compound containing four key functionalities, a primary alcohol, an aldehyde, unsaturation (two double bonds) and a furan ring. This in turn means there are a diverse number of ways to immediately further react HMF, giving rise to a wide range of important products/intermediates with sufficient stability. In most cases the derivatisation of HMF has been achieved in , or almost in, quantitative yield, *i.e.* >99% conversion of HMF to the desired product.

Feedstocks for HMF

The simplest route to HMF is the dehydration of fructose (fruit sugar) as this is already a 5 membered ring, although this is a high cost, edible feedstock.[1] Fructose can however been also found in polymeric form as the non-digestible oligosaccharide inulin. This is also an excellent raw material for HMF synthesis but is not widely abundant, found in root crops and speciality vegetables such as chicory and artichokes at up to 18% by dry weight.[2] Glucose (6 membered ring) can be isomerised in an acidic environment to give fructose and in turn HMF, as too can its related polysaccharide, starch.[3,4] Sucrose, more commonly known as table sugar, a disaccharide of glucose and fructose, can also be easily utilised as a route to HMF.[5] The most abundant, cheap and none edible feedstock for HMF however is cellulose. (a polymer of glucose, present in many wastematerials).[6]

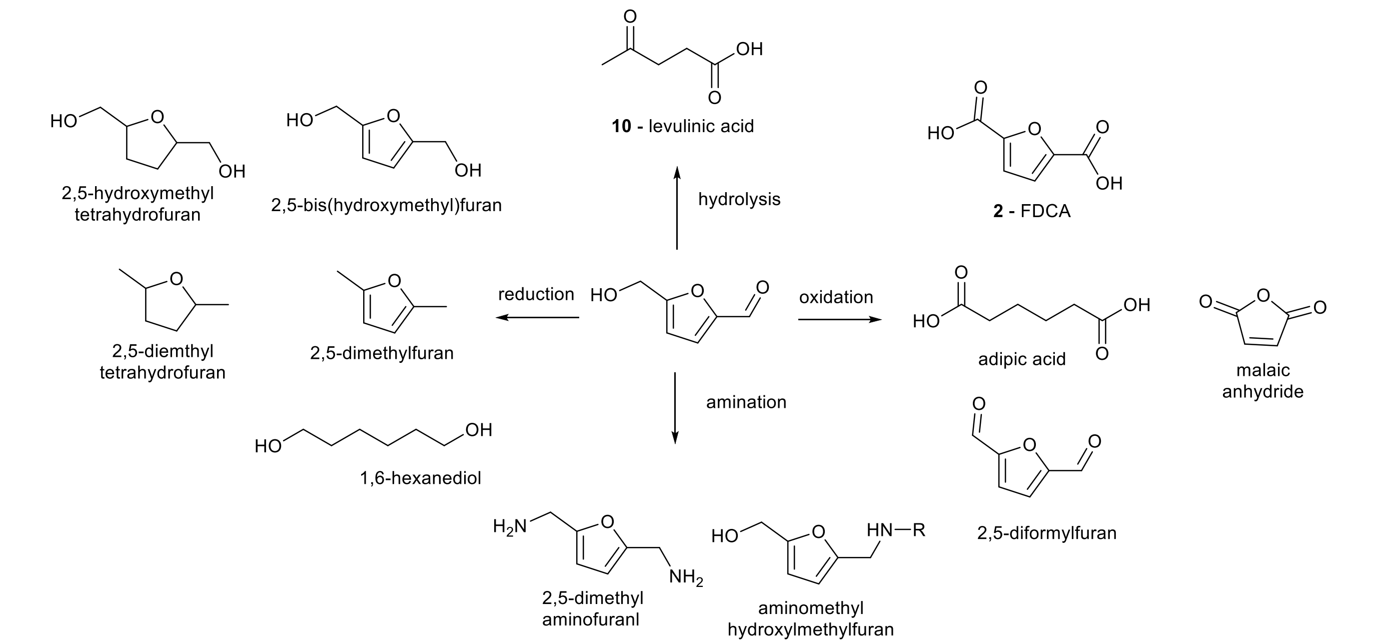
Highlighted routes of production

Route 1— Fructose to HMF



Fructose HMF

All early work for the production of HMF focused on fructose as a feedstock as only simple dehydration is required to give the final product. There are numerous publications detailing this route using Lewis acid, Brønsted acid, base and heterogeneous catalysed routes, giving yields of >98% in papers and patents.[1] This gives an AE of 70% and an RME of 68.8%, these values are low due to the loss of 3 moles of water per mole of HMF. Direct conversion from inulin has been reported with yields of 87% in a water/butanol by-phasic system, giving an AE of 77.8% and an RME of 67.7%. AE is higher as the polymeric form is less oxygen rich. As stated, 6 membered ring sugars can be readily isomerised in the presence of acid catalysts to give fructose in high selectivity and moderate yield or if pushed, directly form HMF in yields of > 90%.[3] This gives AE of 70% and an RME of 63.7%. Using either starch or cellulose as feedstocks, best yields would be obtained by carrying out a two step synthesis, first hydrolysing to glucose and then synthesising HMF. Best yields for glucose from starch are quantitative and from cellulose are 93%.[7] One pot conversion is lower at 73% and 53% respectively.[4,7]



As can be seen from the above figure, the importance of HMF is the wide range of bio-derived compounds that can be easily accessed from this platform molecule. This list is by no means exhaustive, but highlights some of the most significant products. Of particular note is that HMF is the intermediate for two other **UKBioChem10** compounds, furandicarboxylic acid (**2**) and levulinic acid (**10**).

Applications of some HMF derived compounds

2,5-bishydroxymethyl furan has potential in the production of various polymers (foams, fibres, resins) as well as an intermediate in the synthesis of active pharmaceutical ingredients and crown ethers. Further hydrogenation gives 2,5-hydroxymethyl-THF which can be applied as a solvent and has also been used in the production of polyols and as the diol in a range of polyesters. Hexanediol has similar applications. Dimethyl furan has shown potential for use as bio-fuel due to it's high energy density (40% greater than that of ethanol), non-miscibility with water and reasonable boiling point. Dimethyl-THF has similar potential for use as a transport fuel, in addition to use as a solvent. Diformylfuran has found application in the production of polymers, adhesives, binders, foams, in furan urea resins, pharmaceuticals, antifungal agents and as ligands in catalyst production. Adipic acid has numerous applications, but the vast majority currently produced is used in the synthesis of nylon 66. Maleic anhydride similarly has a variety of applications, but of most note is in the production of commodity polyesters and as cross-linking (curing) agents in adhesives and resins. Diamines have application in the production of polyamides and polyureas while aminomethyl hydroxylmethyl furans have seen extensive use in the pharmaceutical sector.

References: **1.** a) DOI: 10.1002/ange.200803207, b) DOI: 10.1002/c ssc.201200236, c) JP2015209411 (A), d) JP2012149008, e) DOI: 10.1016/j.catcom.2009.06.012 **2.** a) DOI: 10.1039/C0CC05138A, b) DOI: 10.1111/1541-4337.12119 **3.** a DOI: 10.1016/j.tetlet.2009.07.053 b) JP2015209411 (A), **4.** DOI 10.1002/star.201000012 , 5. DOI: 10.1002/cssc.201500395, 6. 7. a) DOI: 10.1002/(SICI)1521-379X(199808)50:83.0.CO;2-W, b) 10.1039/C2EE03373A

Additional feedstocks

Three sets of feedstocks have been investigated to determine how much of each would be required to supply a 40 kton HMF plant. First generation biomass, energy crops and second generation biomass.

First generation biomass

The crops presented are those that are most intensively farmed in the UK, principally as food crops, although a small percentage of wheat, maize and sugar beet are also utilised in industrial applications. Sugar cane figures are from Brazil.*

crop	ktons needed to supply a 40 kton HMF plant	ktons produced per annum (UK)	% required
wheat	64.5	14837	0.43
barley	64.5	7169	0.90
maize	63.6	3054	2.08
sugar beet	277.0	8325	3.33
potatoes	269.1	5075	5.30
field beans	261.6	965	27.11
oats	71.4	875	8.16
sugar cane*	471.0	666925	0.07

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.

crop	ktons needed supply make 50 kton PEF plant	ktons produced per annum (UK)	% required
forestry waste	357.4	1340.9	26.66
miscanthus	126.6	87.5	144.69
short rotation coppice	117.7	28.2	417.

Second generation biomass

This is byproducts of food production which contain an appreciable quantity of cellulose that can be depolymerised to give sugars for use in the synthesis of platform molecules. Additionally included is the steam autoclaving of municipal solid waste (the Wilson process), the organic fraction of which is converted into a fibre, rich in free sugars.

feedstock	ktons needed to supply a 50 kton PEF plant	ktons produced per annum (UK)	% required
wheat straw	196.2	3828	5.13
barley straw	235.5	1850	12.73
maize stover	159.1	916	17.37
oilseed rape straw	184.0	379	48.51
oat straw	218.0	247	88.36
MSW	392.5	15734	2.49