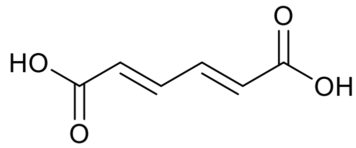
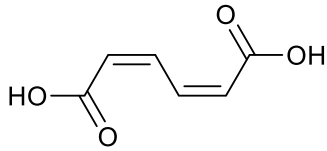
UK BioChem 10 – 5 Muconic acid

Name	Muconic Acid (trans-trans and cis-cis)
Synonyms	2,4-hexadienedioic acid
CAS Number	3588-17-8 (trans), 1119-72-8 (cis)
Molecular formula	$C_6H_6O_4$
MW	142.11 g mol^{-1}
Patents related to synthesis	22





Why is it of interest?

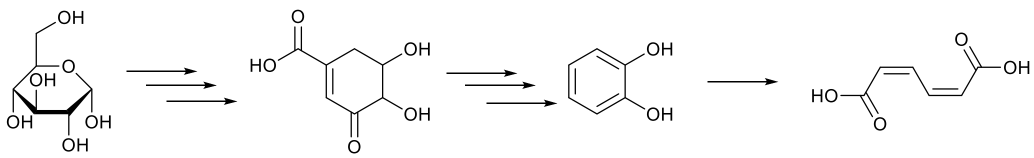
Muconic acid (MA) is both a diacid and a diene, giving many options for use as a building-block chemical. The current interest in MA is as a precursor to bio-derived adipic acid, used in the production of nylon 6,6 and other commodity chemicals. MA can be employed as a monomer in the formation of unsaturated polyesters and polyamides in its own right. The double bonds then allow for post polymerisation functionalisation. The dienes also allow for MA to be used in Diels-Alder reactions, most notably as a route to bio-derived terephthalate, used in the production of polyethylene terephthalate (PET).

Feedstocks for muconic acid

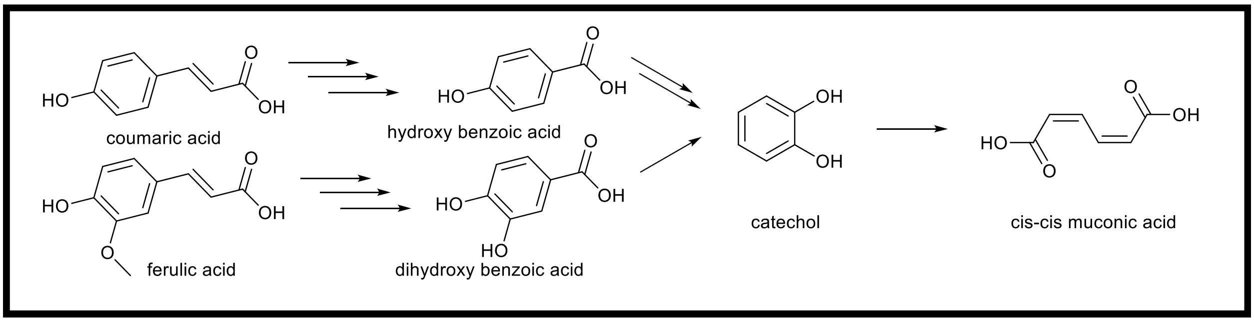
Like many other platform molecules, MA can be formed *via* fermentation of free sugars. Early published work showed a multi step process from glucose using engineered *Escherichia coli* (*E.coli*), although here MA was formed as an intermediates, with adipic acid the target compound of the reaserch.[1] The same metabolic pathways were later introduced into other strains of bacteria, but with MA now the desired product.[2,3] MA has also been produced in good yield from pectin, principally using sugar beet as feedstock.[4] As these pathways all entail the formation of aromatic before ring opening to give the product, other research has focused on utilising aromatic feedstocks in MA production. Initially this focused on model compounds such as benzoic acid, before moving to more complex feedstocks such as coumarates and ferulates, which can be obtained from both softwood and hardwood lignin.[3,5] This is significant as lignin is available in large quantities, is cheap and is underutilised (predominantly burnt as an energy source) in the production of bio-based products. In fact it would be a by-product of any 2nd generation sugar production facilty such as to give bio-ethanol in addition to numerous suggested fermentation routes to applicable UK BioChem 10 compounds.

Highlighted routes of production

As already stated, MA was fist synthesised to provide a bio-derived route to adipic acid. As there was no naturally existing pathway to yield MA from glucose, a 7 enzyme system had to be bio-engineered in *E.Coli*.[1] Producing MA bio-catalytically from glucose is surprisingly efficient in terms of AE, with a value of 66.9%. Yields in this early work gave 236 mg of MA per g of sugar, which corresponds to a yield of 30%

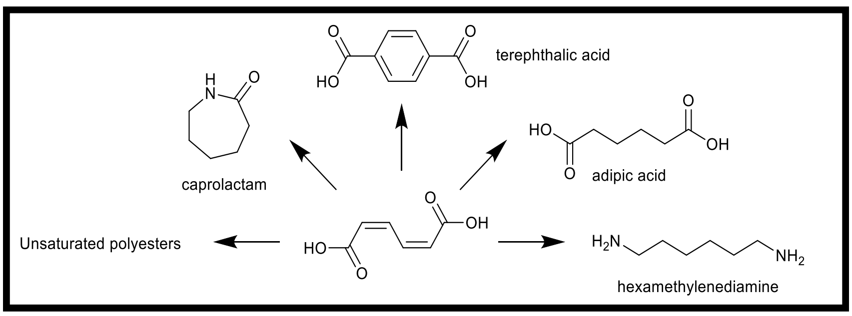


glucose 3-dehydroshikimate catechol cis-cis muconic acid and an RME of 22.4%. Other research has been conducted on sugar feedstocks, such as developing numerous novel pathways,[6] or utilising more complex organisms such as yeast lines.[7] However even in patented routs,[8] a yield above 30% has yet to be reported. Biocatalytic routes utilising aromatic feedstocks however have shown much greater yields of MA. Both catechol and benzoate give 100% yield, the former being the final step in the glucose pathway, the latter being the most simple aromatic acid.[9,10] The most abundant natural source of aromatic compounds is lignin, which constitutes 15-40 % of wood, being more prevalent in softwood than hardwood, as well as being present in most secondary biomass. Lignin however is difficult to break down and does not give a single product but rather a complex mixture of aromatics. As such the initial focus was on coumaric acid and ferulic acid as these are the major constituents of lignin depolymerisation. Using a pure feed of either aromatic gives quantitative conversion of MA, with an AE of 72.4% for coumaric acid and 62.8% for ferulic acid.[11] Excellent results were observed from depolymeised lignin from pine with total conversion of the acids to MA.[10] Maize (corn) stover depolymerisation gave yields so high that additional aromatic compounds had to be being consumed as feedstock, giving 150 mg of MA per g of lignin, which corresponds to 30 mg of MA per g of maize stover.[11]



Future markets and applications

There is no current large-scale usage of MA as it is still relatively novel and early in its exploitation, as stated, all early work focused on a route to adipic acid as this is a substantial commodity chemical, principally used alongside hexamethylenediamine (which can also be obtained from MA) in the production of Nylon 6,6. Additionally MA can be readily converted to caprolactam,[12] of which the major use is polymerisation to Nylon 6, of which 4.6 million tons (petrochemical) was produced in 2016.[13] Another significant commodity plastic is polyethylene terephthalate (PET), the major monomer of which can be obtained *via* a cascade Diels-Alder reaction between trans-trans-MA (easily obtained *via* isomerisation), ethanol and ethane.[14] Perhaps of greater future interest is direct co-polymerisation to give a range of unsaturated polyesters which can then be further functionalised, such as cross linking to give thermoset plastics.[15]



References: **1.** DOI.org/10.1021/ja00080a057, **2.** DOI.org/10.1016/j.ymben.2012.10.003, **3.** DOI.org/10.1016/j.meteno.2016.04.002, **4.** DOI.org/10.1002/cctc.201600069, **5.** DOI.org/10.1039/C4EE03230F, DOI.org/10.1021/acssuschemeng.7b03597, **6.** DOI.org/10.1021/acssynbio.7b00331, **7.** DOI.org/10.1128/AEM.01095-18, **8.** US20130030215, **9.** DOI.org/10.1246/cl.2011.381, **10.** DOI.10.1186/s12934-018-0963-2 , **11.** DOI.org/10.1039/C8GC02519C , **12.** US9073867B2, **13.** https://www.plasticsinsight.com/resin-intelligence/resin-prices/polyamide/, **14.** DOI.org/10.1002/anie.201509149, **15.** DOI.org/10.1021/acssuschemeng.6b01820

Additional feedstocks

Three sets of feedstocks have been investigated to determine how much of each would be required to supply a 5 kton muconic acid plant. The volume of first generation crops has been calculated based on the sugar route, energy and second generation crops are based on the lignin route.

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 5 kton muconic acid plant	ktons produced per annum (UK)	% required
wheat	27.5	14837	0.19
barley	27.5	7169	0.38
maize	27.1	3054	0.89
sugar beet	118.1	8325	1.42
potatoes	114.7	5075	2.26
field beans	111.5	965	11.55
oats	30.4	875	3.48
sugar cane*	200.7	666925	0.03

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. Best figures for lignin utilisation have been applied.[11]

crop	ktons needed to supply a 5 kton muconic acid plant	ktons produced per annum (UK)	% required
forestry waste	148.8	1340.88	11.10
miscanthus	239.7	87.50	273.91
short rotation coppice	128.2	28.20	454.63

Second generation biomass

This is by-product of food production which contain an appreciable quantity of lignin that can be depolymerised to give aromatics for use in the synthesis of platform molecules.

feedstock	ktons needed to supply a 5 kton muconic acid plant	ktons produced per annum (UK)	% required
wheat straw	137.7	3828	3.60
barley straw	154.3	1850	8.34
maize stover	166.7	916	18.19
oilseed rape straw	144.9	379	38.22
oat straw	140.6	247	57.00