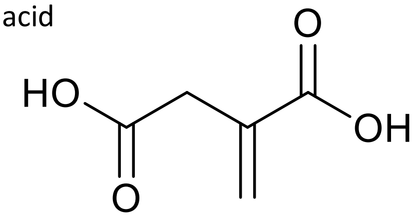
UK BioChem 10 – 6 IA

Name	Itaconic acid
Synonyms	Methylenesuccinic acid, 2-methylene butanedioic acid
CAS Number	97-65-4
Molecular formula	$C_5H_6O_4$
MW	130.10 g mol^{-1}
Patents related to synthesis	27



Why is it of interest?

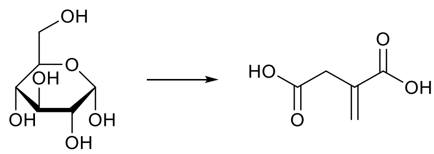
Itaconic acid (IA) is a bio-derived platform molecule with a long history, first being synthesised from citric acid in 1837. It is already being produced at scale industrially , with global production of 41 kton (capacity to produce 80 kton) in 2011, none of which is petro-chemically derived.[1] The two carboxylic acid groups can easily be functionalised to give esters and amides, or if reacted with diols or diamines to give polyesters and polyamides. The presence of the alkene allows post polymerisation modification. Additionally the alkene can itself be functionalised or due to activation by the adjacent carboxylic acid, be polymerised *via* radical initiation similar to petro-chemically derived acrylates and methacrylates.

Feedstocks for IA

All early work regarding IA synthesis utilised citric acid as feedsock to chemocatalytically give the desired product *via* decarboxylation. This route gives IA in poor yield and selectivity, and the methodology is energy intensive, requiring high pressure and temperature.[2] Other synthetic routes have also been reported and patented although none are economically viable other than biosynthesis. Microbial biosynthetic production of IA utilises the most abundant sugar, glucose, as feedstock. Free sugars xylose, sucrose, mannose and arabinose have successfully been used to produce IA, in addition to starch, sugar beet/sugar cane molasses, jatropha seed cake, olive waste and waste fruit (banana and apple).[3] More complex lignocellulosic feedstocks have been hydrolysed to give sugars for use in IA production (corn cobs, hydrolysed hemicellulose, beech wood hydrolysate) although yields reported have been poor at best, through to nothing if lignin is still present in the system.

Highlighted routes of production

Route — Glucose to IA



Glucose IA

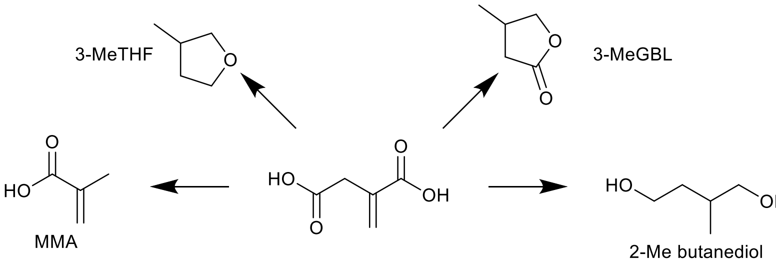
As stated, early work focused on decarboxylation of citric acid to give IA to which can be found numerous papers and patents. Yields here are low, with 6% being the highest and IA being one of many products, of which methyl methacrylate was the most abundant,[4] although this has been an area of focus as citric acid is easily produced *via* fermentation in good yield (70%) and high concentration (140-220 g L^{-1}).[5] The cumulative AE is low at 65% as the sugar is first hydrolysed then decarboxylated, while low yield gives an RME of 2.9%. This clearly isn't viable at scale, industrial production of IA utilises a glucose feed and the fungus *Aspergillus terreus*. Best yields recorded are 72-87% at pilot scale although to achieve such a conversion, the glucose concentration applied is low (4%), resulting in only 20-25 g L^{-1} IA production in 3 days which results in greater waste and more intensive work-up.[6] AE here is 72.2% while RME is 63%, indicating a significantly better process than the chemo-catalysed alternative. More recent work utilising an isolated strain of *Aspergillus terreus* has given yields of 86% while producing IA at a concentration of 86.2 g L^{-1} after 7 days fermentation time.[7] A large number of other fungal, bacterial and yeast strains have been investigated for IA production, including genetic engineering, but none have bettered yields and concentrations of *A. terreus*.

Current Applications of IA

As IA is already produced at scale, there are a number of existing markets where it is employed, the largest of which is as a co-monomer styrene butadiene rubber (SBR) where it increases tack/adhesion in certain applications, such as in coatings. Similarly, itacoinc acid has been employed in emulsion polymerisation for paints and coatings to improve adhesion and wear of the final product. The homopolymer polyitaconic acid, or polyacrylates with a high itaconic acid co-monomer content, have a very high water absorbency leading to applications as super absorbent materials. The other major field of application is as a chelating (metal capture) agent in home and personal care markets. Additionally there are a number of niche applications, including drug delivery in vaccine loaded hydrogels and replacement surfactants.

Future markets and applications

One potential market for IA derivatives is that of methyl methacrylate (MMA), due to the large market that already exists with global demand currently at 3,200 kton pa. Current research has shown that IA can be converted directly to MMA with a 67%,[8] which is currently not economically viable, but is in the same order of magnitude as MMA cost per ton is similar to that of current IA production costs.[1] Selective hydrogenation of IA has been shown to give either 3-methly THF, 3-methyl γ-butyrolactone or 2-methyl butanediol in yields of 97, 93 and 93% respectively. The first compound is analgous to 2-methyl THF, which is already employed as a solvents, while the latter two are useful platform molecules.[9] All three of these compounds can also be considered as fuels, although at high cost. The area of greatest flexibility is that of polymer production where IA has been applied in the formation of epoxy resins, hydrogels, shape memory polymers, elastomers, composites and plasticisers.



References: **1.** https://www.cbp.fraunhofer.de/content/dam/cbp/en/documents/BioConSepT_Market-potential-for-selected-platform-chemicals_report1.pdf **2.** DOI 10.1007/s002530100685 **3.** a) DOI 10.1111/lam.12810, b) DOI 10.1016/S0960-8524(02)00075-5 , c) **4.**a)WO2018065475 (A1), b) doi.org/10.1002/cssc.201402117 **5.** DOI 10.1016/j.biotechadv.2007.01.002 **6.** DOI 10.1021/ie50516a055, **7.** DOI 10.1007/s00253-012-4221-y **8.** 10.1002/c ssc.201402117 **9.**DOI 10.1002/anie.201002060

Additional feedstocks

Suitable feedstocks have been investigated to determine how much of each would be required to supply a 10 kton IA plant (increasing current global production by 25%). Here only First generation biomass has been considered due to the inability to successfully ferment IA from lignocellulosic feedstocks. As such, energy crops and second generation biomass can not currently be considered in routes to IA production, though these alternative feedstocks may become viable for IA in the future following further development.

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 10 kton IA plant	ktons produced per annum (UK)	% required
wheat	20.66	14837	0.14
barley	20.66	7169	0.29
maize	20.38	3054	0.67
sugar beet	88.73	8325	1.07
potatoes	86.19	5075	1.70
field beans	83.80	965	8.68
oats	22.85	875	2.61
sugar cane*	150.83	666925	0.02