Industrial biotechnology provides opportunities for commercial production of new long-chain dibasic acids

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"Oh, My: Such Good Apple Pie, Sweet As Sugar" is but one mnemonic used by desperate students in introductory chemistry classes to remember the common names of organic compounds. This particularly savory saying helps students remember the names of a common group of aliphatic dicarboxylic acids: oxalic, malonic, succinic, glutaric, adipic, pimelic, suberic, azelaic, and sebacic acids.

However, this compound class (known industrially by the terms "dibasic" or "dicarboxylic" acids) is far more important to the global chemical marketplace than this vestigial memory from college days might initially suggest.

Dibasic acids are used as reliable, well-characterized intermediates in a wide range of end- products. Historically, these versatile acids usually have been obtained from petrochemical raw materials by traditional chemical reaction pathways such as multistep butadiene oxidation (Figure 1).

Challenges in traditional synthesis pathways and limitations imposed by the physical properties of unsaturated starting materials have effectively limited dibasic acid production to a certain finite subset of possible dibasic acids. However, this compound class is currently attracting attention owing to the commercial availability of new, longerchained dicarboxylic acids that are now easily produced *via* microbial fermentations. Innovative biorenewable fermentation processes offer new sources for a far wider range of dibasic acids, enhancing the availability of these versatile building blocks. Long-chain dibasic acids that were previously unavailable can now be synthesized using these advances. In addition, long-chain dibasic acids with varying degrees of unsaturation can permit the addition of functional groups, and, as a result, formulators have fresh options for imparting novel qualities and physical characteristics to new as well as established products. Longer-term developments using heterogeneous catalysis of vegetable oils may also offer future promise.

Dibasic acid definitions

Dibasic acids may be better known by their more descriptive synonym "dicarboxylic acids." The name dibasic acid initially seems confusing for a compound with two carboxyl groups, but it also reflects industry emphasis on their robust capabilities and utility over rigorously accurate nomenclature.

With a chemical formula of HOOC $(CH_2)_nCOOH$ (where n = number of methylene groups), these important industrial chemicals are used in the production of numerous products and intermediates (Tables 1 and 2). Nylons and other polyamides, resins, hot melt adhesives, powder coatings, corrosion inhibitors, perfumes, lubricants, plasticizers, and greases are just some of the wide variety of products arising from dibasic acid intermediates.

The dibasic acid compound class should not be confused with "dimer acids," which are typically obtained from tall oil feedstocks or formulated from oleic acid dimerization. This branched, dimerized oleic acid product is technically a branched dibasic acid, but possesses different physical qualities from aliphatic long-chain dibasic acids. It is also important to distinguish between aliphatic long-chain dibasic acids and the mixture of shorter-chained aliphatic dibasic acids commonly known as DBA (a mixture typically composed of C_4-C_6 dibasic acids).

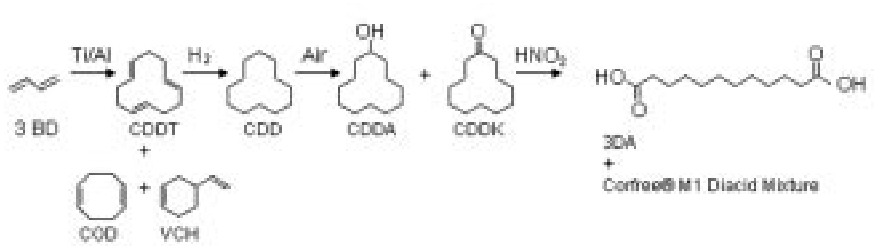
Sources of dibasic acids

Dibasic acids have been derived from petrochemical feedstocks *via* established industrial chemical processes, such as the multistage butadiene oxidation process that produces adipic acid. In addition, ozonolysis has been used for the production of adipic acid from petroselenic acid, azeleic acid from oleic acid, and brassylic acid from erucic acid, as well as other shorter-chain dibasic acids.

However, the suite of dibasic acids available as intermediates has proved historically to be constrained by the limitations inherent to the reactants used to create them. The specific position of the diene (two –C=C– double bonds) within the carbon skeleton of the reactant, coupled with the degree of steric accessibility of that diene for potential reaction, effectively can limit the variety of actual dibasic acids possible.

Uses for dibasic acids

As such, the dibasic acid palette has been traditionally dominated by just a few well-characterized key players. Ensuing industrial process developments have then been optimized for reactants such as adipic (hexanedioic) acid—$HOOC(CH_2)_4COOH$—and its C_{12} analog, dodecanedioic acid—$HOOC(CH_2)_{10}COOH$.



BD–Butadiene
CDDT–Cyclododecatriene
CDD–Cyclodecane
CDDA–Cyclododecanol
CDDK–Cyclododecanone
3DA/DDDA–Dodecanedioic Acid
COD–Cyclooctadiene
VCH–Vinylcyclohexene
Dorfree® M1 Diacid mixture–mixture of C_{10}-C_{12} dioic aids

Figure 1. *Dibasic acid industrial production process (C_{12} process)*
Courtesy: INVISTA (http://c12.invista.com/e-trolley/page_25/index.html)

Dodecanedioic acid is more commonly known by the industry as 3DA or DDDA.

Adipic acid is synonymous with nylon-6, 6 production (see sidebar). DDDA is used in nylon-6, 12 production, and in the powder coating industry as a cross-linker for acrylic powder coating production, acting as a curing agent and storage stabilizer to enhance coating characteristics. Both adipic acid and DDDA are also key production intermediates for a range of varied applications, demonstrating the enormous versatility inherent to the compound class (Table 2).

New sources of dibasic acids via biotechnology

Given the demonstrated versatility of these available dibasic acids, additional sources and variants of dibasic acids would be a welcome addition to manufacturers and formulators.

Biotechnology is permitting the creation of new and established dibasic acids courtesy of a novel fermentation process now in commercial use by Cathay Biotechnology of Shanghai, China, and Cognis Group, headquartered at Düsseldorf, Germany.

This yeast fermentation process features the use of either long-chain *n*-alkanes (from paraffin sources) or fatty acids (from natural products) in reaction with a specific strain of *Candida tropicalis* to produce the dibasic acids. Long-chain alkenes and unsaturated fatty acids can also participate as fermentation reactants.

Candida tropicalis is more commonly recognized as a common medical yeast pathogen, existing as part of the normal human flora. Commercial dibasic acid production by fermentation involves ω-oxidation of the terminal CH_3 group of long-chain *n*-alkanes or fatty acids, a capability possessed by this yeast. Further adaptation of the yeast, primarily by the Cognis Biotechnology Group in Cincinnati, Ohio, utilizes a specific mutation that selectively blocks the normal β-oxidation pathway for fatty acid metabolism, which otherwise would consume the dibasic acids produced in the fermentation process. This mutant strain of *Candida tropicalis* also effects desirable emulsification during the reaction that enhances fermentation efficiency.

Both Cathay and Cognis manufacture dibasic acids from both fatty acid and long-chain *n*-alkane precursors *via* fermentation. Cathay's offerings are primarily (though not exclusively) derived from high-purity long-chain *n*-alkanes, whereas Cognis derives their acids from vegetable oil fatty acids.

Commercially familiar dibasic acids such as adipic acid and DDDA can both be manufactured *via* fermentation, and can be used in established manufacturing processes for desired product formations. Targeted marketing and production of such familiar dibasic acids permits an easy introduction of these new commodities to existing dibasic acid commercial processes and infrastructure.

Acceptance of these dibasic acids produced *via* microbial fermentation methods will pave the way for the acceptance of new longer chain dibasic acids previously unavailable by other synthesis methods. New dibasic acids (and by extension, new polyamides, polyamines, polyesters, and anhydrides) are now available that can be used to update long-established processes, as well as permit the manufacture of new end-products not possible with the previously limited suite of dibasic acids. The palette of precursor possibilities available to the formulator is expanded, making new and improved products possible.

The macrocyclic fragrance market has already seen positive impact from biosynthesized dibasic acids. Fragrances such as synthetic musks already have been produced from macrocyclic ketones and lactones derived from Cathay's biosynthesized C_{12} and C_{13} dibasic acids. Ready availability of the acids from microbial fermentations over limited natural

Table 1
Common saturated dibasic acids

Total Carbons		Common Name	CAS Number	Notes
2	$HOOC(CH_2)_0COOH$	Oxalic	144-62-7	Methanedioic acid
3	$HOOC(CH_2)_1COOH$	Malonic	141-82-2	Ethanedioic acid
4	$HOOC(CH_2)_2COOH$	Succinic	110-15-6	Butanedioic acid
5	$HOOC(CH_2)_3COOH$	Glutaric	110-94-1	Pentanedioic acid
6	$HOOC(CH_2)_4COOH$	Adipic	124-04-9	Hexanedioic acid
7	$HOOC(CH_2)_5COOH$	Pimelic	111-16-0	Heptanedioic acid
9	$HOOC(CH_2)_7COOH$	Azelaic	123-99-9	Nonanedioic acid
10	$HOOC(CH_2)_8COOH$	Sebacic	111-20-6	Decanedioic acid
11	$HOOC(CH_2)_9COOH$	Undecanedioic	1852-04-6	
12	$HOOC(CH_2)_{10}COOH$	Dodecanedioic	693-23-2	DDDA or 3DA
13	$HOOC(CH_2)_{11}COOH$	Brassylic	505-52-2	Tridecanedioic acid
14	$HOOC(CH_2)_{12}COOH$	Tetradecanedioic	821-38-5	
15	$HOOC(CH_2)_{13}COOH$	Pentadecanedioic	1460-18-0	
16	$HOOC(CH_2)_{14}COOH$	Hexadecanedioic	505-54-4	
17	$HOOC(CH_2)_{15}COOH$	Heptadecanedioic	N/A	
18	$HOOC(CH_2)_{16}COOH$	Octadecanedioic	871-70-5	

CAS– Chemical Abstracts Service Registry

Table 2
Representative Applications of Adipic Acid and DDDA

Adipic Acid Applications	DDDA Applications
Nylon-6,6	Nylon-6,12
Adhesives	Polyamides
Coatings	Powder Coatings
(alkyd, urethane, gel coat, polyester)	(stabilizer and curing agent)
Hydraulic Fluids	Hot Melt Adhesives
Flue Gas Desulfurization Scrubber Additive	Corrosion Inhibitors
Food Additives	Lubricants
Unsaturated Polyester Resins	Greases
Cleaning Additive	Synthetic Resins
Soil Conditioners	Polyesters
Glass Protection Agents	Polyurethanes
Lubricants	Dyestuffs
Solvents	Cleaning Agents
Epoxy Curing	Agents Detergents
Polymer/Plasticizer Additives	Fertilizers
Leather Tanning	Flame Retardants
Personal Care Emollients	Plasticizing Agents
Chemical Intermediates	Fragrances

Courtesy: www.invista.com

raw material sources will likely result in increased synthetic musk production.

New variants of established products

Other new dibasic acids may well shed new vigor into previously established technologies in nylon manufacturing. Cathay has demonstrated the commercial feasibility of nylon 6, x and nylon 10, x production. (The numerical nomenclature for nylon is based on the number of carbon atoms in the diamine, first number, and dibasic acid, second number, monomers used in the product's manufacture. The ratio of carbon atoms is the basis for the characteristic properties associated with each particular nylon type). Using tetradecanedioic acid—$HOOC(CH_2)_{12}COOH$—as an example, Cathay reports that this C_{14} acid offers increased hydrophobic behavior and physical properties compared with other available dibasic acids, and Cathay has demonstrated that nylon 6, 14 offers increased hydrophobicity (water resistance) over nylon 6,12.

Commercial application of this dibasic acid for use in the coatings industry also will be realized with a current agreement with BMW in the production of clear acrylic coatings for the luxury car manufacturer.

An example of another new dibasic acid now available is octadecanedioic acid—$HOOC(CH_2)_{16}COOH$. This C_{18} dioic acid can be synthesized using Cognis' biofermentation process, and subsequently manufactured to yield products such as nylon, polyamides, polyesters, macroglycols, polyacrylate esters, and polyurethane (netlink: www.aocs.org/meetings/ia/techprog.asp).

Emerox 118® is the brand name for Cognis' C_{18} dibasic acid. Both saturated (Emerox 118®) and partially unsaturated (Emerox 118U®) C_{18} dibasic acids are commercially available.

The availability of a partially unsaturated C_{18} long-chain dibasic acid (octadecenedioic acid) offers significant potential for future uses, as the availability for further selective functional group incorporation into resultant backbones permits development of new intermediates and endproducts with enhanced physical properties.

Industry leaders

At present time two major industrial groups are associated with the microbial production of dibasic acids, Cathay Biotechnology and the Cognis Group.

Cathay Biotechnology began production of C_{11}–C_{18} long-chain dibasic acids at its fermentation facility in Jining, Shandong, China, early in 2003. All dibasic acids are currently available from two production lines under the Cathay DC brand name. According to Cathay, the production plant has production volume capacity capabilities for dibasic acids second only to those plants already established by Invista, headquartered at Wichita, Kansas (netlink: www.cathaybiotech.com).

Cathay also has several strategic alliances in place for marketing long-chain dibasic acids. Dibasic acid corrosion inhibitors will be marketed by CIBA Specialty Chemicals of Basel, Switzerland, under the Irgacor® brand name (netlink: www.cibasc.com), with Cognis providing marketing inroads with the Emerox® brand of long chain dibasic acids.

The Cognis Group (netlink: www.cognis.com) is also a major producer of oleochemicals from vegetable and animal raw materials for the nonfood sector. Cognis markets both Cathay's dibasic acid products under Cognis' Emerox ® brand, along with their own suite of shorter-chain dibasic acids produced by other synthesic strategies. The commercial availability of a long-chain (C_{18}) dibasic acid with unsaturation (Emerox® 118U: octadecenedioic acid) is especially interesting and holds promise for future product developments and current product enhancements.

A former major supplier of dibasic acids was DuPont Textiles and Interiors division (DTI), now named Invista (netlink: www.invista.com), which was purchased from DuPont of Wilmington, Delaware, by Koch Industries of Wichita, Kansas (netlink: www.kochind.com) in April 2004. Koch then reorganized Invista to include the capabilities of polyester manufacturer KoSa (netlink: www.kosa.com) with the strengths of Invista's nylon and lycra capabilities, combining both companies under the Invista brand umbrella.

Invista's main focus is in the adipic acid (brand name Adi-*pure*®), C_{12} (DDDA and Corfree® products), and DBA arenas. DBA is seeing increased usage as a pH buffer additive to decrease operational and maintenance costs for wet limestone scrubbers used in flue gas desulfurization for SO_2 emissions control.

Future developments

Several developments seem possible with the new availability of a wider range of long-chain dibasic acids:

- Though long-chain alkanes from paraffin sources are somewhat highlighted in current developments, fatty acids from biorenewable vegetable oil sources can be and are being used to produce this new set of intermediates. Future developments will likely increasingly utilize vegetable oil-based fatty acids as precursors over paraffin or animal-based long-chain *n*-alkanes.
- The introduction of new starter materials now available can result in a fresh injection into established markets that might be considered flat. New advances in high-performance nylon and the powder coatings sector could well be expected as a result of the availability of these new starting materials.
- Dibasic acids with some degree of unsaturation in the parent long-chain that permits alternative chemistry enhancements to the basic chemical backbone will become increasingly available and important. Cross-linking or additions of different functional groups to the structure may well bring enhancements or innovations to end-products produced.

A May 2004 press release by Invista indicates potential movement in this direction. A strategic alliance between Invista and International Flavors and Fragrances, Inc. (IFF) of New York has been formed for consumer textile enhancement.

Additional mechanistic pathways in addition to fermentation also may be available in the future. By using recent advances in material science and synthesis techniques, heterogeneous catalysis can be more rationally designed to mechanistic specifics and reaction requirements, according to Brent Shanks at Iowa State University at Ames. Researchers in his group are extending this concept to dibasic acid production from vegetable oil-based fatty acid oxidation in their work with inorganic heterogeneous catalysis from solid substrates. Potential commercial production of azelaic and suberic acids by this methodology offers an alternative production modality for adipic acid production. (netlink: www.energy.iastate.edu/renewable/biomass/cs-catalyst_systems.html).

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