Processes for Producing Butanediol (BDO), Diaminobutane (DAB), From Fermentation Broths Containing Ammonium Succinate

Abstract: Processes that make nitrogen-containing compounds include converting succinic acid (SA) or monoammonium succinate (MAS) derived from a diammonium succinate (DAS)- or MAS-containing fermentation broth to produce such compounds including diamnobutane (DAB), succinic dinitrile (SDN), succinic amino nitrile (SAN), succinamide (DAM), and related polymers.
PROCESSES FOR PRODUCING BUTANEDIOL (BDO), DIAMINOBUTANE (DAB), SUCCINIC DINITRILE (SDN) AND SUCCINAMIDE (DAM)

Technical Field

Technical Field

This disclosure relates to processes for producing nitrogen containing compounds such as DAB, SDN and DAM from succinic acid (SA) and monoammonium succinate (MAS) produced by fermentation.

Background

Certain carbonaceous products of sugar fermentation are seen as replacements for petroleum-derived materials for use as feedstocks for the manufacture of carbon-containing chemicals. One such product is MAS.

A material related to MAS, namely SA, can be produced by microorganisms using fermentable carbon sources such as sugars as starting materials. However, most commercially viable, succinate producing, microorganisms described in the literature neutralize the fermentation broth to maintain an appropriate pH for maximum growth, conversion, and productivity. Typically, the pH of the fermentation broth is maintained at or near a pH of 7 by introduction of ammonium hydroxide into the broth, thereby converting the SA to diammonium succinate (DAS). The DAS may be converted to MAS to derive MAS from the fermentation broth.

Kushiki (Japanese Published Patent Application, Publication No. 2005-139156) discloses a method of obtaining MAS from an aqueous solution of DAS that could be obtained from a fermentation broth to which an ammonium salt is added as a counter ion. Obtained from a fermentation broth to which an ammonium salt is added as a counter ion. Specifically, MAS is crystallized from an aqueous solution of DAS by adding acetic acid to the solution to adjust the pH of the solution to a value between 4.6 and 6.3, causing impure MAS to crystallize from the solution.

Masuda (Japanese Unexamined Application Publication P2007-254354, Oct. 4, 2007) describes partial deammoniation of dilute aqueous solutions of "ammonium succinate" of the formula H,NOOCCH2CH2COONH4. From the molecular formula disclosed, it can be seen that "ammonium succinate" is diammonium succinate. Masuda removes water and ammonia by heating solutions of diammonium succinate to yield a solid SA-based composition containing, in addition to ammonium succinate, at least one of MAS, SA, monoamide succinate, succinimide, succinamide or ester succinate. Thus, it can be inferred...
that like Kushiki, Masuda discloses a process that results in production of impure MAS. The processes of both Kushiki and Masuda lead to materials that need to be subjected to various purification regimes to produce high purity MAS.

Bio-derived MAS and SA, such as that derived from MAS itself are platform molecules for synthesis of a number of commercially important chemicals and polymers. Therefore, it is highly desirable to provide a purification technology that offers flexibility to integrate clear, commercially viable paths to derivatives such as DAB, SDN and DAM. In response to the lack of an economical and technically viable process solution for converting fermentation-derived SA/MAS to DAB, SDN, succinic amino nitrile (SAN) and DAM, it could be helpful to provide methods for providing a cost effective SA/MAS stream of sufficient purity for direct hydrogenation.

We further provide a process for making nitrogen containing compounds, including indirect conversion of SA to DAB by hydrogenation of SA to 1,4-butanediol (BDO) and animation of DAB to DAB.

Summary

We provide a process for making nitrogen containing compounds of SA, including (a) providing a clarified DAS-containing fermentation broth; (b) distilling the broth to form an overhead that comprises water and ammonia, and a liquid bottoms that comprises MAS, at least some DAS, and at least about 20 wt% water; (c) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (d) separating at least part of the containing solid portion that is substantially free of DAS; (e) separating at least part of the solid portion from the liquid portion; and (f) (1) contacting the solid portion with hydrogen and optionally an ammonia source in the presence of at least one hydrogenation catalyst to produce DAB; or (2) dehydrating at least a part of the solid portion to produce SDN; or (3) dehydrating at least a part of the solid portion to produce DAM; and (f) recovering the DAB, SDN or DAM.

We also provide a process for making nitrogen containing compounds of SA, including (a) providing a clarified DAS-containing fermentation broth; (b) distilling the broth to form an overhead that comprises water and ammonia, and an overhead liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water; (c) cooling and/or evaporating the bottoms, sand; optionally adding an antisolvent to the bottoms, and (d) attaining a...
temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (d) separating the solid portion from the liquid portion; (e) recovering the solid portion; (f) dissolving the solid portion in water to produce an aqueous MAS solution; (g) distilling the aqueous MAS solution at a temperature and pressure sufficient to form a second overhead that includes water and ammonia, and a second bottoms that includes a major portion of SA, that includes water and ammonia, and a second bottoms that includes a major portion of SA, a minor portion of MAS, and water; (h) cooling and/or evaporating the second bottoms to a minor portion of MAS, and water; (h) cooling and/or evaporating the second bottoms to cause the second bottoms to separate into a second liquid portion in contact with a second liquid portion in contact with a second solid portion that preferably consists essentially of SA and is substantially free of MAS; (i) separating at least part of the second solid portion from the second liquid portion; and (j) contacting the second solid portion with hydrogen and an ammonia source in the presence of at least one hydrogenation catalyst to produce DAB; or (2) dehydrating at least a part of the second solid portion to produce SDN; or (3) dehydrating at least a part of the second solid portion to produce DAM; and (h) recovering the DAB, SDN or DAM.

[0010] We further provide a process for making nitrogen-containing compounds, including (a) providing a clarified MAS-containing fermentation broth; (b) optionally adding MAS, DAS, SA, NH₃, and/or NH₄⁺ to the broth to preferably maintain the pH of the broth below 6; (c) distilling the broth to form an overhead that includes water and optionally ammonia, and a liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water; (d) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (e) separating at least part of the solid portion from the liquid portion; (f) contacting the solid portion with hydrogen and optionally an ammonia source in the presence of at least one hydrogenation catalyst to produce DAB; or (2) dehydrating at least a part of the second solid portion to produce DAM; and (g) recovering the DAB, SDN or DAM.

[0011] We further yet provide a process for making nitrogen-containing compounds, including (a) providing a clarified MAS-containing fermentation broth; (b) optionally adding MAS, DAS, SA, NH₃ and/or NH₄⁺ to the broth to preferably maintain the pH of the broth below 6; (c) distilling the broth to form an overhead that includes water and optionally ammonia, and a liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water; (d) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (e) separating at least part of the solid portion from the liquid portion; (f) contacting the solid portion with hydrogen and optionally an ammonia source in the presence of at least one hydrogenation catalyst to produce DAB; or (2) dehydrating at least a part of the second solid portion to produce DAM; and (g) recovering the DAB, SDN or DAM.
ammonia, and a liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water; (d) cooling a n... illustrates selected reaction pathways from DAS to DAB, SDN and DAM and other selected downstream products.
Detailed Description

Detailed Description appreciated that at least a portion of the following description is intended
to represent the best mode of practice of the invention and may not reflect the actual description
of the specific embodiments of the invention. It will be appreciated that at least a portion of the following description is intended
to refer to representative examples of processes selected for illustration in the drawings and is
not intended to define or limit the disclosure, other than in the appended claims.

Our processes may be appreciated by reference to Fig. 1, which shows in flow
5 diagram form one representative example of our methods.

A growth vessel, typically an in-place steam sterilizable fermentor, may be used to
10 grow a microbial culture (not shown) that is subsequently utilized for the production of the grow a microbial culture (not shown) that is subsequently utilized for the production of the
dos, MAS, and/or SA-containing fermentation broth. Such growth vessels are known in
the art and are not further discussed.

The microbial culture may comprise microorganisms capable of producing SAs
15 from fermentable carbon sources such as carbohydrate sugars. Representative examples of
microorganisms include, but are not limited to, Escherichia coli (E. coli), Aspergillus niger, Corynebacterium
glutamicum (also called Brevibacterium flavum), Enterococcus faecalis, Weilliella parvula,
Actinobacillus succinogenes, Mannheimia succiniciproducens, Anaerobiospirillum
suciniciproducens, Paecilomyces variotii, Saccharomyces cerevisiae, Bacteroides fragilis,
Bacteroides ruminicola, Bacteroides amylophilus, Alcaligenes eutrophus, Brevibacterium
ammoniagenes, Brevibacterium lactofermentum, Candida brumptii, Candida catenulate,
10 Candida mycoderma, Candida zeylanoides, Candida paludigena, Candida sonorensis,
Candida utilis, Candida zeylanoides, Debaryomyces hansenii, Fusarium oxysporum,
Humicola lanuginosa, Kloeckera apiculata, Kluyveromyces lactis, Kluyveromyces
tunicatum, Kluyveromyces lactis, Kluyveromyces wickerhamii, Penicillium simplicissimum, Pichia anomala, Pichia hesseyi, Pichia media,
Pichia guilliermondii, Pichia inositovora, Pichia stipitis, Saccharomyces bayanus,
Pichia guilliermondii, Pichia inositovora, Pichia stipitis, Saccharomyces bayanus,
Schizosaccharomyces pombe, Torulopsis Candida, Yarrowia lipolytica, mixtures thereof and
schizosaccharomyces pombe, Torulopsis Candida, Yarrowia lipolytica, mixtures thereof and
20 the like.

A preferred microorganism is an E. coli strain deposited at the ATCC under
accession number PTA-5132. More preferred is this strain with its three antibiotic resistance
genes (cat, ampH, tetA) removed. Removal of the antibiotic resistance genes cat (coding for
the enzyme phospho-ampH, tetA) removed. Removal of the antibiotic resistance genes are coding for
the resistance to chloramphenicol), and ampH (coding for the resistance to kanamycin) can be
25 performed by the so-called Lambda-red (λ-red) procedure as described in Datsenko and
of which is incorporated herein by reference. The tetracycline resistant gene tetA can be
of which is incorporated herein by reference. The tetracycline resistant gene tetA can be

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removed using the procedure originally described by Bochner et al., J Bacteriol. 1980 August; 143(2): 926-933, the subject matter of which is incorporated herein by reference. Glucose is a preferred fermentable carbon source for this microorganism.

A fermentable carbon source (e.g., carbohydrates and sugars), optionally a source of nitrogen and complex nutrients (e.g., corn steep liquor), additional media components such as vitamins, salts and other materials that can improve cellular growth and/or product formation, and water may be fed to the growth vessel for growth and sustenance of the microbial culture. Typically, the microbial culture is grown under aerobic conditions within a vessel. Typically, the microbial culture is grown under aerobic conditions provided by sparging an oxygen-rich gas (e.g., air or the like). Ammonium hydroxide is provided for pH control during the growth of the microbial culture.

In one example (not shown), the aerobic conditions in the growth vessel (provided by sparging an oxygen-rich gas) are switched to anaerobic conditions by changing the oxygen-rich gas to an oxygen-deficient gas (e.g., CO₂ or the like). The anaerobic environment triggers bioconversion of the fermentable carbon source to SA in situ in the growth vessel. Ammonium hydroxide is provided for pH control during bioconversion of the fermentable carbon source to SA. The SA that is produced is at least partially neutralized to DAS due to the presence of the ammonium hydroxide, leading to the production of a broth comprising DAS. The CO₂ provides an additional source of carbon for the production of SA.

In another example, the contents of the growth vessel may be transferred via a stream to a separate bioreactor vessel for bioconversion of a carbohydrate source to SA. An oxygen-deficient gas (e.g., CO₂ or the like) is sparged in the bioreactor vessel to provide anaerobic conditions that trigger production of SA. Ammonium hydroxide is provided anaerobic conditions that trigger production of SA. Ammonium hydroxide is provided for pH control during bioconversion of the carbohydrate source to SA. Due to the presence of the ammonium hydroxide, the SA produced is at least partially neutralized to DAS, leading to production of a broth that comprises DAS. The CO₂ provides an additional source of carbon for production of SA.

In another example, the bioconversion may be conducted at relatively low pH (e.g., 3-6). A base (ammonium hydroxide or ammonia) may be provided for pH control during bioconversion of the carbohydrate source to SA. Depending on the desired pH, due to the presence or lack of the ammonium hydroxide, either SA is produced or the SA produced is at least partially neutralized to MAS, DAS, or a mixture comprising SA, MAS, and/or DAS.
Thus, the SA produced during bioconversion can be subsequently neutralized, optionally in an additional step, by providing either ammonia or ammonium hydroxide leading to a broth comprising DAS. As a consequence, a "DAS-containing fermentation broth" generally means that the fermentation broth comprises DAS and possibly any number of other components such as MAS and/or SA, whether added and/or produced by bioconversion or otherwise. Similarly, a "MAS-containing fermentation broth" generally means that the fermentation broth comprises MAS and possibly any number of other components such as DAS and/or SA, whether added and/or produced by bioconversion or otherwise. DAS and/or SA, whether added and/or produced by bioconversion or otherwise.

The broth resulting from the bioconversion of the fermentable carbon source (in either the growth vessel or the bioconversion vessel depending on where the bioconversion takes place), typically contains insoluble solids such as cellular biomass and other suspended material, which are transferred via a stream to a clarification apparatus before distillation.

Removal of insoluble solids clarifies the broth. This reduces or prevents fouling of subsequent distillation equipment. The insoluble solids can be removed by any one of several solid-liquid separation techniques, alone or in combination, including but not limited to, centrifugation and filtration (including, but not limited to ultra-filtration, micro-filtration or depth-filtration). The choice of filtration can be made using techniques known in the art.

Soluble inorganic compounds can be removed by any number of known methods such as, but not limited to, ion-exchange, physical adsorption and the like.

An example of centrifugation is a continuous disc stack centrifuge. It may be useful to add a polishing filtration step following centrifugation such as dead-end or cross-flow filtration that may include the use of a filter aid such as diatomaceous earth or the like. Flow filtration that may include the use of a filter aid such as diatomaceous earth or the like, or more preferably ultra-filtration or micro-filtration. The ultra-filtration or micro-filtration can be ceramic or polymeric, for example. One example of a polymeric membrane can be ceramic or polymeric, for example. One example of a polymeric membrane is SelRO MPS-U20P (pH stable ultra-filtration membrane) manufactured by Koch Membrane Systems (850 Main Street, Wilmington, MA, USA). This is a commercially available polyethersulphone membrane with a 25,000 Dalton molecular weight cut-off which typically operates at pressures of 0.35 to 1.38 MPa (maximum pressure of 1.55 MPa) and at temperatures up to 50°C. Alternatively, a filtration step may be employed, such as ultra-filtration or micro-filtration alone.
The resulting clarified DAS-containing broth or MAS-containing broth, substantially free of the microbial culture and other solids, is transferred via a stream to a distillation apparatus.

The clarified distillation broth should contain DAS and/or MAS in an amount that is at least a majority by weight at least about 70 wt%, more preferably about 80 wt% and most preferably at least about 90 wt% of the total dicarboxylic acid salts in the broth. The concentration of DAS and/or MAS as a weight percent (wt%) of the total dicarboxylic acid salts in the fermentation broth can be easily determined by high pressure liquid chromatography (HPLC) or other known means.

Water and ammonia are removed from the distillation apparatus as an overhead. A more preferred amount of water is at least about 75 wt% and an even more preferred amount is at least about 80 wt% of the total dicarboxylic acid salts in the fermentation broth. The rate of ammonia removal from the distillation step increases with increasing temperature and also can be increased by injecting steam (not shown) during distillation. The rate of ammonia removal during distillation may also be increased by conducting distillation under a vacuum or by sparging the distillation apparatus with a non-reactive gas such as air, nitrogen or the like.

Removal of water during the distillation step can be enhanced by the use of an organic azeotroping agent such as toluene, xylene, cyclohexane, methyl cyclohexane, methyl isobutyl ketone, heptane or the like, provided that the bottoms contains at least about 30 wt% of the azeotrope. The distillation is carried out in the presence of an organic agent capable of forming an azeotrope consisting of the water and the agent, distillation produces a biphase bottoms.

A preferred temperature for the distillation step is in the range of about 50°C to about 300°C, depending on the pressure. A more preferred temperature range is about 60°C to about 150°C, depending on the pressure. A distillation temperature of about 110°C to about 150°C, depending on the pressure. A distillation temperature of about 110°C to
about 140°C is preferred. “Distillation temperature” refers to the temperature of the bottoms (for batch distillations, this may be the temperature at the time when the last desired amount of overhead is taken).

A water miscible organic solvent or an ammonia separating solvent

Adding a water miscible organic solvent or an ammonia separating solvent

facilitates deammoniation over a variety of distillation temperatures and pressures as discussed above. Such solvents include aprotic, bipolar, oxygen-containing solvents as may be able to form passive hydrogen bonds. Examples include, but are not limited to, diglyme, triglyme, tetruglyme, propylene glycol, sulfoxides such as dimethylsulfoxide (DMSO), triglyme, tetraglyme, propylene glycol, sulfides such as dimethylsulfoxide (DMSO), lactones such as gamma-butyrolactone (GBL), amides such as dimethylformamide (DMF), lactones such as gamma-butyrolactone (GBL), amides such as dimethylformamide (DMF), propylene glycol (PEG), butoxytriglyme, N-methylpyrrolidone (NMP), ethers such as dioxane, 'methyl ethyl ketone (MEK) and the like. Such solvents aid in the removal of ammonia from the DAS of the clarified broth. Regardless of the distillation technique, it is important that the distillation be carried out in a way that ensures that at least some DAS and at least about 20% water remain in the bottoms and even more advantageously at least about 30%.

The distillation can be performed at atmospheric, sub-atmospheric or super-atmospheric pressures. The distillation can be a one-stage flash, a multistage distillation (i.e., a multistage column, distillation), or the like. The one-stage flash can be conducted in any type of flasher (e.g., a wiped film evaporator, thin film evaporator, thermosiphon flasher, forced circulation flasher, and the like). The number of the distillation column can be achieved by using trays, packing, or the like. The packing can be random packing (e.g., Raschig rings, Pall rings, Berl saddles and the like) or structured packing (e.g., Koch-Sulzer packing, Intalox packing, Mellapak and the like). The trays can be of any design (e.g., sieve packing, Intalox packing, Mellapak and the like). The trays can be of any design (e.g., sieve trays, valve trays, bubble-cap trays and the like). The distillation can be performed with any number of theoretical stages.

If the distillation apparatus is a column, the configuration is not particularly critical, and the column can be designed using well-known criteria. The column can be operated in either stripping mode, rectifying mode or fractionation mode. Distillation can be conducted in either batch or continuous mode. In the continuous mode, the broth is fed continuously into the distillation apparatus, and the overhead and bottoms are continuously removed from the apparatus as they are formed. The distillate from distillation is an aqueous ammonia/water solution, and the distillation bottoms is a liquid, aqueous solution of MAS ammonia/water solution, and the distillation bottoms is a liquid, aqueous solution of MAS
and DAS, which may also contain other fermentation by-product salts (i.e., ammonium and DAS, which may also contain other fermentation by-product salts (i.e., ammonium acetate, ammonium formate, ammonium lactate and the like) and color bodies. The distillation bottoms can be transferred via a stream to a cooling apparatus and cooled by conventional techniques. Cooling technique is not critical. A heat-exchanger (with heat recovery) can be used. A flash evaporation cooler can be used to cool the bottoms to about 10°C. Cooling to ≤15°C typically employs a refrigerated coolant such as, for example, glycol solution or, less preferably, brine. A concentration step can be included prior to glycol solution or, less preferably, brine. A concentration step can be included prior to cooling to help increase product yield. Further, both concentration and cooling can be used to help increase product yield. Further, both concentration and cooling can be combined using methods known such as vacuum evaporation and heat removal using integrated cooling jackets and/or external heat exchangers.

We found that the presence of some DAS in the liquid bottoms facilitates cooling-induced separation of the bottoms into a liquid portion in contact with a solid portion that at least "consists essentially" of MAS (meaning that the solid portion is at least substantially pure crystalline MAS) by reducing the solubility of MAS in the liquid, aqueous, DAS-containing bottoms. Fig. 4 illustrates the reduced solubility of MAS in an aqueous 350 wt% DAS solution at various temperatures ranging from 0°C to 60°C. The upper curve shows that even at 0°C, MAS; remains; significantly soluble in water (i.e., about 20 wt% in aqueous solution). The lower curve, shows that at 0°C MAS is essentially insoluble in a 350 wt% aqueous DAS solution. We discovered, therefore, that MAS can be more completely crystallized out of an aqueous solution if some DAS is also present in that solution. A preferred concentration of DAS in such a solution is in the ppm to about 3 wt% range. This preferred concentration of DAS in such a solution is in the ppm to about 3 wt% range. This allows crystallization of MAS (i.e., formation of the solid portion of the distillation bottoms) at temperatures higher than those that would be required in the absence of DAS.

When about 50% of the ammonia is removed from DAS contained in an aqueous medium the succinate species establish an equilibrium molar distribution that is about 0.1:0.8:0.1 in DAS:MAS:SA within a pH range of 4.8 to 5.4, depending on the operating temperature and pressure. When this composition is concentrated and cooled, MAS exceeds its solubility limit in water and crystallizes. When MAS undergoes a phase change to the solid phase, the liquid phase equilibrium resets thereby producing more MAS (DAS donates an ammonium ion to SA). This allows more MAS to crystallize from solution and continues until appreciable quantities of SA are exhausted and the pH tends to rise. As the pH rises, the liquid phase distribution favors DAS. However, since DAS is highly soluble in water, MAS liquid phase distribution favors MAS. However, since DAS is highly soluble in water, MAS
continues to crystallize as its solubility is lower than DAS. In effect, the liquid phase continues to crystallize as its solubility is lower than DAS. In effect, the liquid phase equilibrium and the liquid-solid equilibria of succinate species act as a "pump" for MAS crystallization, thereby enabling MAS crystallization in high yield.

[0039] In addition to cooling, evaporation, or evaporative cooling described above, crystallization of MAS can be enhanced and/or facilitated by addition of an antisolvent. In this context, antisolvents may be solvents typically miscible with water, but cause crystallization of a water soluble salt such as MAS due to lower solubility of the salt in the solvent.

[0040] The distillation bottoms, after cooling in the cooling unit, is fed via a stream to a separator for separation of the solid portion from the liquid portion. Separation can be accomplished via pressure filtration (e.g., using Nutsche or Rosendorn type pressure filters), centrifugation and/or like. The resulting solid product can be recovered as a product and dried, if desired, by standard methods.

[0041] After separation, it may be desirable to treat the solid portion to ensure that no liquid portion remains on the surface(s) of the solid portion. One way to minimize the amount of liquid portion that remains on the surface of the solid portion is to wash the separated solid portion with water and dry the resulting washed solid portion. A convenient way to wash the solid portion is to use a so-called "basket centrifuge." Suitable basket centrifuges are available from The Western States Machine Company (Hamilton, OH, USA).

[0042] The liquid portion of the distillation bottoms (i.e., the mother liquor) may contain remaining dissolved MAS, any unconverted DAS, any fermentation byproducts such as ammonium acetate, lactate, or formate, and other minor impurities. This liquid portion can be fed via a stream to a downstream apparatus. In one instance, the downstream apparatus may be a means for making a de-icer by treating in the mixture with an appropriate amount of potassium hydroxide, for example, to convert 'the' ammonium salts to potassium salts. Ammonia generated in this reaction can be recovered for reuse in the byconversion vessel (or the growth vessel operating in the anaerobic mode). The resulting mixture of potassium salts is valuable as a de-icer and anti-icer.
The mother liquor from the solids separation step, can be recycled (or partially recycled) to the distillation apparatus via a stream to further enhance recovery of MAS, as well as further convert DAS to MAS.

The solid portion of the cooling-induced crystallization is substantially pure MAS and is, therefore, useful for the known utilities of MAS. HPLC can be used to detect the presence of nitrogen-containing impurities such as succinamide and succinimide. The purity of MAS can be determined by elemental carbon and nitrogen analysis. An ammonia electrode can be used to determine a crude approximation of MAS purity.

Depending on the circumstances and various operating inputs, there are instances when the fermentation broth may be a clarified MAS-containing fermentation broth or a clarified SA-containing fermentation broth. In those circumstances, it can be advantageous to add MAS, DAS, SA, ammonia and/or ammonium hydroxide to those fermentation broths to facilitate the production of substantially pure MAS. For example, the operating pH of the fermentation broth may be oriented such that the broth is a MAS-containing broth or a SA-containing broth. MAS, DAS, SA, ammonia and/or ammonium hydroxide may be optionally added to those broths to facilitate production of the above-mentioned substantially pure MAS. In one particular form, it is especially advantageous to recycle DAS, SA, ammonia and/or ammonium hydroxide to those broths to attain a broth pH preferably below 6 to facilitate production of the above-mentioned substantially pure MAS. Also, it is possible that MAS, DAS and/or SA from other sources may be added as desired. In one particular form, it is especially advantageous to recycle DAS, SA, ammonia and/or ammonium hydroxide to those broths and may be optionally added to those broths to facilitate production of the above-mentioned substantially pure MAS.

The solid portion can be converted into SA by removing ammonia. This can be carried out as follows. The solid portion (consisting essentially of MAS) obtained from any of the above-described conversion processes can be dissolved in water to produce an aqueous MAS solution. This solution can then be distilled at a temperature and pressure sufficient to distill the water from the aqueous MAS solution, thereby producing a substantially pure MAS.
form an overhead that comprises water and ammonia, and a bottoms that comprises a major portion of SA, a minor portion of MAS and water. The bottoms can be cooled to cause it to separate into a liquid portion in contact with a solid portion that consists essentially of SA and is substantially free of MAS. The solid portion can be separated from the second liquid portion and recovered as substantially pure SA as determined by HPLC. Streams comprising SA, MAS and/or DAS as described above may be converted to selected downstream products such as nitrogen containing compounds including but not limited to DAB, SDN, DAM and the like as disclosed below and illustrated in Fig. 2 and Fig. 3. In initiating those processes, typically the SA, MAS and/or DAS may be dissolved in water to form an aqueous solution thereof which can be directly fed to the downstream reactor. The SA, MAS or DAS may be converted to SDN directly or indirectly through the intermediate DAM by dehydration. Such dehydrations may be achieved thermally, enzymatically or in the presence of catalysts. Thus, appropriate temperatures, pressures and catalysts are selected to achieve the appropriate level of dehydration, depending on whether the conversion to SDN occurs directly or indirectly.

For example, the conversion can employ an appropriate dehydrating catalyst such as acidic or basic catalysts, including phosphates as disclosed in US 4,237,067; and supported catalysts utilizing Ti, V, Hf or Zr on clays or alumina as disclosed in US 5,587,498. Such catalysts are typically employed at temperatures of 220°C to 350°C and pressures of 1,000 psig, for example.

Alternatively, dehydration can be achieved thermally as disclosed in US 3,296,303. Alternatively, dehydration can be achieved thermally as disclosed in US 2,270,253, wherein acids plus an ammonia source are thermally dehydrated in the presence of glycol wherein acids plus an ammonia source are thermally dehydrated in the presence of glycol solvents at temperatures of 100°C to 130°C and at pressures of 150 to 200 psig.

As a consequence, SA, MAS or DAS may be dehydrated directly to SDN or to the intermediate DAM. Then, once SDN is produced, it is possible to convert SDN directly to an amine such as DAB or to indirectly convert SDN to DAB through the intermediate of DAM.

For example, direct conversion from SDN to DAB can be achieved in any number of ways such as disclosed in US 6,376,714, wherein dinitriles are converted utilizing catalysts such as Fe, Co, Ni, Rh or Pd and an ammonia source are converted utilizing catalysts such as Fe, Co, Ni, Rh or Pd...
promoted with Ru, Cr or W at temperatures of 50°C to 150°C at 300 to 1500 psig. The result
is high yields of the diamine, in this case DAB.

Similarly, US 4,003,933, converts nitriles to amines with hydrogen over a Co/ZrO

2 catalyst at 120°C to 130°C and at 1500 psig. Other catalysts may include Fe, Al or Mo

as catalysts at 250°C to 300°C and at pressures of 0.1 to 40 MPa. Suitable catalysts and reaction conditions for this pathway are also disclosed in

US 4,935,546. Further, US 4,935,546 discloses the conversion of acids to amines with hydrogen

and an ammonia source at temperatures of 200°C to 300°C at pressures of 10 to 300 ATM. Similarly, US 3,579,583 discloses the conversion of dicarboxylic acids to amines, particularly alkylamines,

utilizing hydrogen and an ammonia source at temperatures of 200°C to 300°C at pressures of

100 to 300 ATM in the presence of a Zn-Al2O3 or Zn-Cr catalyst. Further, US 4,935,546 discloses the conversion of acids to amines with hydrogen

and an ammonia source in the presence of a Co, Cu or Cr catalyst on a TiO2 or Al2O3 support at temperatures of 250°C to 350°C and at pressures of 20 to 150 bar.

Indirect conversion of SA to DAB may also be achieved by hydrogenation of SA

to 1,4-butanediol (BDO), as shown in Fig. 3. Amination of BDO to DAB can be conducted by the use of a suitable catalyst and an ammonia source. For example, suitable catalysts and reaction conditions for amination of BDO include zirconium, copper and nickel catalysts disclosed in US 6,057,442 and suitable conditions include 80 to 300°C and pressures of 0.1 to 40 MPa. Suitable catalysts and reaction conditions for this pathway are also disclosed in

US 6,057,442.
WO 2012/158180

WO97/35834 and include contacting BDO and ammonia in the presence of a catalyst, that may include platinum, rhenium, cobalt, molybdenum, nickel, tungsten or palladium.

[0060] Once the conversions to DAB and SAN have been completed, it is also possible to convert those compounds into polyamide-type compounds in any number of ways known in the art. Representative examples include the following conversions. Polyamides may be produced from monoamines such as SAN. One example of conversions of this type may be found in US 5,109,104 which converts an omega amino nitrile in the presence of an oxygenated phosphorus catalyst with water. This is generally achieved in a several-step oxygenated phosphorus catalyst with water. This is generally achieved in a several-step conversion at temperatures of 200°C to 330°C and at pressures ranging from 250 to 350 psig.

[0061] An alternative methodology is disclosed in US 6,958,381 wherein a starting monomer such as SAN may be polymerized into a polyamide in the presence of a chain regulator containing a nitrile group and a functional group capable of forming a carboxamide group.

[0062] Polyamides may also be formed from the diamines such as DAB, wherein the dicarboxylic acid have a chain length of C4 to C12. The dicarboxylic acid or ester may be an aromatic dicarboxylic acid or ester or it may be an alkyl dicarboxylic acid.

[0063] The subject matter and contents of the above mentioned US Patent Nos. 4,237,067; 5,587,498; 3,296,303; 6,376,714; 4,003,933; 5,151,543; 7,132,562; 2,223,303; 3,579,583; 4,935,546; 5,109,104; and 6,958,381 are incorporated herein by reference.

Examples

[0064] Our processes are illustrated by the following non-limiting representative examples. In a number of the examples, a synthetic, aqueous DAS solution was used in place of an actual clarified DAS-containing fermentation broth. Other examples use an actual clarified DAS-containing fermentation broth. Other examples use an actual clarified DAS-containing fermentation broth.

[0065] The use of a synthetic DAS solution is believed to be a good model for the behavior of an actual broth in our processes because of the solubility of the typical fermentation by-products found in actual broth. The major by-products produced during fermentation are ammonium acetate, ammonium lactate and ammonium formate. If these impurities are present during the distillation step, one would not expect them to form ammonia and formic acid in significant quantities until all of the DAS had been converted to MAS. This is because acetic acid, lactic acid and formic acid are stronger acids than the second acid.

This is because acetic acid, lactic acid and formic acid are stronger acids than the second acid.
group of SA (pKa = 5.48). In other words, acetate, lactate, formate and even monohydrogen succinate are weaker bases than the dianion succinate. Furthermore, ammonium acetate, ammonium lactate and ammonium formate are significantly more soluble in water than MAS, and each is typically present in the broth at less than 10% of the DAS concentration. In and each is typically present in the broth at less than 10% of the DAS concentration. In

Example 1

This example demonstrates conversion of a portion of DAS into MAS via distillation and recovery of MAS solids from distillation bottoms liquid via cooling-induced crystallization. A three-neck 500mL round bottom flask was fitted with a thermometer and Dean Stark trap topped with a reflux condenser. The vent from the reflux condenser went to a scrubbing bottle which contained 100g of a 1.4M acetic acid solution. The flask was charged with 400g of 10% DAS aqueous solution (pH 8.5). The contents of the flask were stirred with a magnetic stirrer and heated with a heating mantle to distill off 320.6g of distillate (an aqueous ammonia solution) which was removed via the Dean Stark trap. Analysis of the distillate indicated that about 20% of the contained ammonia had been removed from the charged DAS during distillation (i.e., the salts in the bottoms liquid were about 40% MAS and about 60% DAS). Only traces of ammonia were found in the scrubbing bottle. The final and about 60% DAS) only traces of ammonia were found in the scrubbing bottle. The final

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Example 2
This example demonstrates mother liquor recycle.

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This example demonstrates mother liquor recycle. 300 g of a synthetic 4.5% DAS solution, and then a distillation head was attached to the flask. The contents of the flask were solution, and then a distillation head was attached to the flask. The contents of the flask were distilled at atmospheric pressure leaving 67 g of residue (bottoms liquid) in the flask. The bottoms liquid contained approximately 45% water. Ammonia analyses of the distillates indicate that the first distillation cycle removed about 29% of the ammonia, making a 42/58 mol/mol mixture of DAS and MAS. The residue (bottoms liquid) was then removed from the vacuum, and allowed to stir for 30 minutes. The temperature of the bath was then lowered to 15°C and held for 30 minutes. The temperature was then lowered to 10°C and held for 30 minutes. The temperature was then cooled to 5°C and held for 30 minutes and finally to 0°C where it was held for 30 minutes. The slurry (consisting of solid and liquid portions) was then quickly filtered using a pre-cooled sintered glass filter funnel and vacuum flask. The solids were dried in a vacuum oven yielding 13.9 g of dry MAS solids. The mother liquor (liquid portion, 47.2 g) was then combined with 800 g of synthetic 4.5% DAS solution and distilled, leaving 86.6 g of residue (bottoms liquid). In the second distillation (i.e., mother liquor recycle run) about 28% of the ammonia from the total amount of DAS present was removed. The residue (bottoms liquid) was then cooled (crystallized) in a similar manner. However, the solution became cloudy at 46°C, so it was seeded at 46°C and allowed to slowly cool to room temperature overnight while stirring. The next day the temperature was slowly ramped down by 5°C increments to 0°C. The slurry (solid and liquid portions) was filtered as before, and the solids dried, yielding 23.5 g of MAS solids. This is equal to about a 75% recovery of the solids dried, yielding 23.5 g of MAS solids. This is equal to about 75% recovery of the SA equivalents in the 800 g of fresh DAS solution distilled. The recovered solids from the first cycle were 95% MAS (about 5% water). In the second cycle, the solids were 97% MAS (about 3% water). The mother liquor from the second cycle contained 28.8% SA equivalents (i.e., as SA salts).

Example 3
This example demonstrates the absence of amide and imide species in the solid portion of cooled distillation bottoms, the absence of amide and imide species in the solid portion of cooled distillation bottoms.
A 1-L round bottom flask was charged with 800g of a synthetic 4.5% DAS solution. The flask was fitted with a five tray 1" Oldershaw section which was capped with a distillation head. The distillate was collected in an ice-cooled receiver. The contents of the flask were heated with a heating mantel and stirred with a magnetic stirrer. The contents of the flask were distilled giving 721.1g of an overhead distillate and 152.8g of a liquid residue in the flask. The distillate was distilled giving 721.1g of an overhead distillate and 72.2g of a liquid residue in the flask (i.e., distillation bottoms). The aqueous ammonia distillate was titrated revealing a 0.34% ammonia content (i.e., about 55% conversion of DAS to MAS). The hot distillation bottoms (approximately 47% salt solution of DAS and MAS) were placed in a 125 mL (approximately 47% salt solution of DAS and MAS) were then placed in a 15 mL Erlenmeyer flask and allowed to cool slowly to room temperature while stirring overnight. Erlenmeyer flask and allowed to cool slowly to room temperature while stirring. The next morning the cloudy solution was cooled to 15°C and held for 60 minutes, then cooled to 10°C and held for 60 minutes and finally cooled to 5°C and held for 60 minutes while stirring. The resulting white slurry was filtered yielding 12.9g of wet crystals and 55.8g of mother liquor. The crystals were dissolved in 35.8g of distilled water. HPLC analysis of the mother liquor revealed no detectable amounts of amide or imide species. However, HPLC analysis of the mother liquor revealed a trace of succinic acid, but no detectable succinamide or succinimide.

Example 44

This example produces a solid portion of a cooled distillation bottoms that consists essentially of MAS and is substantially free of DAS.

A three neck 1-L round bottom flask was fitted with an addition funnel and a 1" five tray Oldershaw column which was capped with a distillation head. An ice cooled five tray Oldershaw column which was capped with a distillation head. An ice cooled receiver was used to collect the distillate. The flask was charged with 800g of a synthetic receiver was used to collect the distillate. The flask was charged with 800g of a synthetic 4.5% DAS solution. The contents of the flask were heated with a heating mantel and stirred with a magnetic stirrer. Distillation was started. While the distillation occurred an additional 1600g of the 4.5% DAS solution was slowly added to the flask at the same rate as distillate. 25 1600g of the 4.5% DAS solution was slowly added to the flask at the same rate as distillate. The distillate was taken. A total of 2135g of distillate was taken overhead. Titrations of the distillate revealed the overhead was a 0.33% ammonia solution. The hot aqueous distillation bottoms (253.8g) was removed from the flask and placed in an Erlenmeyer flask. The distillation bottoms were allowed to cool to room temperature while stirring overnight. The contents of the flask were seeded and allowed to stir for 30 minutes. The slurry was then cooled to 15°C and held for 60 minutes, then to 10°C and held for 60 minutes and finally to 5°C and held for 60 minutes all while stirring. The slurry was filtered cold and the solids (i.e., the
solid portion) washed three times with about 20g portions of a cold (about 5°C) 20% sodium chloride solution to displace the mother liquor (i.e., the liquid portion). Air was sucked through the cake for several minutes to remove as much liquid as possible. The solids were then dried in a vacuum oven at 75°C for one hour yielding 7.2g of white crystals. Carbon and nitrogen analyses of the solids revealed a 4.06 atomic ratio of carbon to nitrogen (i.e., a 1.01 ratio of ammonia to SA or about 99% MAS). That a ratio of 1.00 was not obtained is believed to be attributable to incomplete washing of the solids.

Example 5

This example demonstrates the effect of solvents on ammonia evolution from aqueous DAS. Run 5 is the control experiment where no solvent is present.

The outer necks of a three neck 1-L round bottom flask were fitted with a thermometer and a stopper. The center neck was fitted with a five tray 11" Oldershaw section. The Oldershaw section was topped with a distillation head. An ice cooled 500mL round bottom flask was used as the receiver for the distillation head. The 1-L round bottom flask was charged with distilled water, the solvent being tested, SA and concentrated ammonium hydroxide solution. The contents were stirred with a magnetic stirrer to dissolve all the solids. After the solids dissolved, the contents were heated with the heating mantle to distill 350g of distillate. The distillate was collected in the ice cooled 500 mL round bottom flask.

The pot temperature was recorded as the last drop of distillate was collected. The pot contents were allowed to cool to room temperature and the weight of the residue and weight of the distillate were recorded. The ammonia content of the distillate was then determined via titration. The results were recorded in Table 1.

<table>
<thead>
<tr>
<th>Run #</th>
<th>Name of Acid charged</th>
<th>Wt Acid Charged (g)</th>
<th>Moles Acid Charged</th>
<th>Wt 28% NH3 Solution Charged (g)</th>
<th>Moles NH3 Charged</th>
<th>Name of Solvent</th>
<th>Wt Solvent Charged (g)</th>
<th>Wt Water Charged (g)</th>
<th>Wt Distillate (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Succinic</td>
<td>11.81</td>
<td>0.1</td>
<td>12.11</td>
<td>0.2</td>
<td>Diglyme</td>
<td>400</td>
<td>400</td>
<td>350.5</td>
</tr>
<tr>
<td>2</td>
<td>Succinic</td>
<td>11.79</td>
<td>0.1</td>
<td>12.09</td>
<td>0.2</td>
<td>PG*</td>
<td>400.1</td>
<td>400</td>
<td>351.6</td>
</tr>
<tr>
<td>3</td>
<td>Succinic</td>
<td>11.8</td>
<td>0.1</td>
<td>12.1</td>
<td>0.2</td>
<td>GBL**</td>
<td>400</td>
<td>400</td>
<td>350.1</td>
</tr>
<tr>
<td>4</td>
<td>Succinic</td>
<td>11.79</td>
<td>0.1</td>
<td>12.11</td>
<td>0.2</td>
<td>butoxy triglycol</td>
<td>400</td>
<td>400</td>
<td>350.7</td>
</tr>
<tr>
<td>5</td>
<td>Succinic</td>
<td>11.8</td>
<td>0.1</td>
<td>12.1</td>
<td>0.2</td>
<td>none</td>
<td>0</td>
<td>800</td>
<td>351</td>
</tr>
</tbody>
</table>
Example 6

This example produced a solid portion from a cooled distillation bottoms that consists essentially of SA and is substantially free of MAS.

A 300 L Parr autoclave was charged with 80g of synthetic MAS and 120g of water. The autoclave was sealed, and the contents stirred and heated to about 200°C at an autogenic pressure of about 100 psig. Once the contents reached temperature, water was fed to the autoclave at a rate of about 2g/min and vapor removed from the autoclave at a rate of about 2g/min with a back pressure regulator. Vapor exiting the autoclave was condensed and collected in a receiver. The autoclave was run under these conditions until a total of 1020g of water had been fed and a total of 1019g of distillate collected. The distillate was titrated for ammonia content (0.29% ammonia by weight). This translates into an about 29% conversion of MAS to SA. The contents of the autoclave (194.6g) were partially cooled and discharged from the reactor. The slurry was allowed to stand under stirring at room temperature overnight in an Erlenmeyer flask. The slurry was then filtered and the solids rinsed with 25g of water. The moist solids were dried in a vacuum oven at 75°C for 1 hr yielding 9.5g of SA product. HPLC analysis revealed the solids were SA with 0.8% succinic acid impurity.

Example 7

This example used DAS-containing clarified fermentation broth derived from a fermentation broth containing E. coli strain ATCC PTA-5132. This example produced a solid portion of the cooled distillation bottoms that consists essentially of MAS and is substantially free of DAS. and is substantially free of DAS.

Wt Residue (g) 466.3 461.7 464.3 460.9 466
% Mass Accountability 99.1 98.7 98.9 98.5 99.2
Wt% NH₃ in distillate (titration) 0.48 0.4 0.27 0.47 0.13
Moles NH₃ in distillate 0.099 0.083 0.056 0.097 0.027
% NH₃ removed in Distillate 49.5 42 28 49 13.4
% First NH₃ removed in Distillate 99 84 56 98 27
% Second NH₃ removed in Distillate 0 0 0 0 0
Final Pot Temp (°C) 101 120 110 107 100

* PG is propylene glycol
** GBL is gamma butyrolactone
[0079] A three neck 1-L round bottom flask was fitted with an addition funnel and a 1" five-tray Oldershaw column which was capped with a distillation head. A 1-L cooled receiver was used to collect the distillate. The flask was charged with 800g of clarified DAS-containing fermentation broth which contained 4.4% DAS, 1% ammonium acetate, 0.05% succinamic acid, and 0.03% ammonium lactate. The contents of the flask were heated to 75°C and held for 30 minutes, allowing the broth to be added to the flask at the same rate as distillate was removed. A total of 2703g of distillate was taken as overhead, same rate as distillate was removed. A total of 2703g of distillate was taken as overhead.

Titration of the distillate revealed the overhead was a 0.28% ammonia solution. The hot aqueous distillation bottoms solution (269.7g) was removed from the flask and placed in an aqeous distillation bottoms solution (269.7g) was removed from the flask and placed in an Erlenmeyer flask. The distillation bottoms were allowed to slowly cool to room temperature while stirring overnight. The next day, the contents of the flask were seeded and allowed to stand at 10°C for 30 minutes. The slurry was then cooled to 15°C and held for 30 minutes, then to 10°C and held for 30 minutes, and finally to 5°C and held for 30 minutes, all while stirring. The slurry was filtered cold and air was sucked through the cake for several minutes to remove as much liquid as possible. Light brown solids (72.5g) and dark brown mother liquor ((188.4g with a pH of 6.4) were obtained. The solids were recrystallized to remove the mother liquor by dissolution in 72g of water at 50°C. The solution was then allowed to slowly cool to room temperature while stirring overnight. The next day, the contents of the flask were seeded and stirred for 30 minutes. The slurry was then cooled to 15°C and held for 30 minutes, then to 10°C and held for 30 minutes, and finally to 5°C and held for 30 minutes, all while stirring. The slurry was filtered cold and air was sucked through the cake for several minutes to remove as much liquid as possible, yielding 110g of brown mother liquor (pH 5.0). The remove was more liquid than possible, yielding 110g of brown mother liquor (pH 5.0). The solids were then dried in a vacuum oven at 75°C for one hour yielding 24g of off-white solids were then dried in a vacuum oven at 75°C for one hour yielding 24g of off-white crystals. Carbon and nitrogen analyses of the solids revealed a 4.04 molar ratio of carbon to nitrogen (i.e., a 1.01 ratio of ammonia to SA or about 99% MAS). HPLC analysis revealed that the MAS contained 0.07% succinamic acid but no detectable succinamide, succinimide, or the MAS contained 0.07% succinamic acid but no detectable succinimide, succinimide, or acetate species. In other words, the MAS was free of DAS and other substantially pure. In other words, the MAS was free of DAS and otherwise substantially pure. Example 8

Example 8

[0080] This example used fermentation derived MAS from a fermentation broth containing E. coli strain ATCC PTA-5132. This example produced a solid portion from a cooled distillation bottoms that consists essentially of SA, and is substantially free of MAS.
A 300 mL Parr autoclave was charged with 80 g of broth derived MAS and 120 g of water. The autoclave was sealed and the contents stirred and heated to about 202°C at an autogenic pressure of about 205 psig. Once the contents reached temperature, water was fed to the autoclave at a rate of about 2 g/min and vapor was removed until the autoclave at a rate to the autoclave at a rate of about 2 g/min and vapor was removed from the autoclave at a rate of about 2 g/min with a back pressure regulator. Vapor exiting the autoclave was condensed and collected in a receiver. The autoclave was run under these conditions until a total of 905 g of water had been fed and a total of 905 g of distillate collected. The distillate was titrated for ammonia content (0.28% ammonia by weight). This translates into an about 34% titrated for ammonia content (0.38% ammonia by weight). This translates into an about 34% conversion of MAS to SA. The contents of the autoclave (178.2 g) were partially cooled and conversion of MAS to SA. The contents of the autoclave (178.2 g) were partially cooled and discharged from the reactor. The slurry was allowed to stand under stirring at room temperature overnight in an Erlenmeyer flask. The slurry was then filtered and the solids cooled with 25 g of water. The moist solids were dried in a vacuum oven at 75°C for 1 hr yielding 88.5 g of SA product. Analysis via an ammonium ion electrode revealed 0.027 mmol of solid. HPLC analysis revealed solids were SA with 0.4% succinamic acid and 0.01% succinamide impurities.

Example 99

This example used an ammonia releasing solvent to aid deamination. This example produced a solid portion from a cooled distillation bottoms that consists essentially of SA and is substantially free of MAS.

A 500 mL round-bottom flask was charged with 29 g of MAS solids, 51 g of water and 80 g of triglyme. The flask was fitted with a 5 tray 1.5 glass column section and 4/17 glass. The flask was cooled with a distillation head. An addition funnel containing 2500 g of water was which was stirred with a distillation head. An addition funnel containing 2500 g of water was also connected to the flask. The flask was filled with a magnetic stirrer and heated with a heating mantle. The distillate was collected in an ice cooled receiver. When the distillate was being taken. A total of 249 g of water was taken. The distillate contained 2.3 g of ammonia, as determined by titration. This means about 63% of the MAS was converted to SA. The residue in the flask was then placed in an Erlenmeyer flask and cooled to 45°C while stirring. After stirring for 30 minutes the slurry was filtered while cold yielding 15.3 g of solids. The solids were dissolved in 15.3 g of hot water and then cooled in an ice bath while stirring. The cold slurry was filtered and the solids dried in a vacuum oven.
at 100°C for 2 hrs yielding 6.5g of succinic acid. HPLC analysis indicated that the solids at 100°C for 12 hrs yielding 6.5g of succinic acid. HPLC analysis indicated that the solids were SA with 0.18% succinamic acid present.

Example 10

Example 10

This example used an ammonia releasing solvent to aid deammoniation. This example produced a solid portion of a cooled distillation bottoms that consists essentially of MAS and is substantially free of DAS.

A 500 mL round bottom flask was charged with 80g of an aqueous 36% DAS solution and 80g of triglyme. The flask was fitted with a 5 tray 1" glass Oldershaw column section which was topped with a distillation head. An addition funnel containing 700g of water was also connected to the flask. The flask was stirred with a magnetic stirrer and heated with a heating mantle. The distillate was collected in an ice cooled receiver. When the distillate started coming over the water in the addition funnel was added to the flask at the same rate as the distillate was being taken. A total of 747g of distillate was taken. The distillate contained 13.7g of ammonia, as determined by titration. This means about 57% of the ammonia was removed. In other words, all of the DAS was converted into MAS and about 14% of the MAS was further converted into SA. The residue in the flask was then placed in an Erlenmeyer flask and cooled to 5°C while stirring. After stirring for 30 minutes the slurry was filtered while cold and the solids dried in a vacuum oven at 100°C for 2 hrs yielding 10.3g of MAS. Analysis indicated that the solids were MAS with 0.77% succinamic acid and 0.14% succinimide present.

Example 11

This example demonstrates the use of an azeotropyng solvent, particularly separation of MAS from other by-products in the broth.

A three neck 500 mL round bottom flask was fitted with a thermometer, a 250 mL addition funnel and a Dean Stark trap topped with a reflux condenser. The flask was charged with 100g of toluene and 100g of an about 9% DAS broth solution (which also contained 1% ammonium acetate and ammonium formate combined). The addition funnel was charged with 250g of the 9% ammonium succinate broth solution. The contents of the flask were stirred with a magnetic stirrer and heated with a heating mantle bringing the contents to boil. The contents of the addition funnel were added slowly to the flask allowing the toluene-water azeotrope to distill into the Dean-Stark trap with return of the toluene to the flask.
all the contents of the addition funnel had been added (at a rate substantially equal to the distillate) the contents were allowed to further reflux until a total of 277.5 g of aqueous phase had been collected from the Dean-Stark trap. The contents of the flask were removed while hot and the two phases separated in a warm separatory funnel. The aqueous phase was cooled in an ice bath while being stirred. The resulting solids were recovered via filtration using a sintered glass funnel. The mother liquor was dark brown and the filtered solids were off-white. The solids were dried in a vacuum oven and analyzed via HPLC. The dried solids were off-white. The solids were dried in a vacuum oven and analyzed via HPLC. The dried solids (5.7 g) were about 96% monoammonium succinate and about 1% ammonium acetate with the rest being water.

Example 12

A pressure distillation column was constructed using an 8 ft long 1.5" 316 SS Schedule 40 pipe packed with 316 SS Propak packing. The base of the column was equipped with an immersion heater to serve as the reboiler. Nitrogen was injected into the reboiler via a needle valve to pressure. The overhead of the column had a total take-off line which went to the condenser with a receiver. The receiver was equipped with a pressure gauge and a back pressure regulator. Material was removed from the overhead receiver via blow casing through a needle valve. Preheated feed was injected into the column at the top of the packing via a pump. Preheated water was also injected into the reboiler via a pump. The distillation column was operated at 30 psig pressure which gave a column temperature of 137°C. The top of the column was fed a synthetic 10% DAS solution at a rate of 5 mL/min and water was fed to the reboiler at a rate of 5 mL/min. The overhead distillate rate was 10 mL/min and the residue rate was 2 mL/min. Titration of the distillate for ammonia indicated 10% DAS solution at 15 mEq/mL. The bottom of the column was fed a synthetic 10% DAS solution at a rate of 5 mL/min and the residue rate was 2 mL/min. Titration of the distillate for ammonia indicated that the about 47% of the ammonia had been removed in the distillate (i.e. the conversion to about 47% of the ammonia had been removed in the distillate (i.e. the conversion to MAS was about 94%). The residue liquid was about 20% MAS and HPLC analysis of the residue indicated an about 3% inefficiency to succinamic acid.

Residue indicated an about 3% inefficiency to succinamic acid.

Example 13

A portion of the residue (800 g) from Example 12 was concentrated via a batch distillation to about 59% MAS solution (i.e. 530 g of water was distilled off). The residue was then cooled to 95°C while stirring. The resulting slurry was filtered and the solids dried in a vacuum oven at 75°C for 1 hour yielding 52.5 g of MAS solids (i.e. about 32% recovery).
HPLC analysis indicated that the solids contained 0.49% succinamic acid and no succinimide. Example 14
Example 14 A second portion of the pressure column residue (3200g) from Example 12 was placed in the evaporative crystallizer and concentrated to about 1200g MAS by distilling off the mother liquor from the crystallizing step was allowed to cool to room temperature forming a second crop of crystals. This slurry was filtered and the recovered solids were dried at 75°C under vacuum yielding 114.8g of MAS solids. Based on the succinate concentration of the feed to the crystallizer, 20% and 18% recovery was realized for the first and second crops, respectively (i.e. a 38% overall recovery). HPLC analysis of the two crops indicated that the first crop had no detectable succinamic acid and succinimide while the second crop had 0.96% succinamic acid and 0.28% succinimide.

Comparative Example 2
This example demonstrates that an atmospheric distillation of an aqueous MAS solution removes very little ammonia when triglyme is not present. A 500-mL round bottom flask was charged with 30g of MAS solids and 120g of water. The flask was fitted with a 5 tray 1" glass Oldershaw column section which was topped with a distillation head. An addition funnel containing 600g of water was also connected to the flask. The flask was stirred with a magnetic stirrer and heated with a heating mantle. The distillate was collected in an ice cooled receiver. When the distillate started coming over the water in the addition funnel was added to the flask at the same rate as the condensate over the water in the addition funnel was added to the flask at the same rate as the distillate was being taken. A total of 606g of distillate was taken. The distillate contained 0.15g of ammonia, as determined by titration. This means ~4% of the MAS was converted to SA.

Comparative Example 2
This example demonstrates the decrease in ammonia removal for DAS when triglyme is not present. A 500mL round bottom flask was charged with 80g of an aqueous 36% DAS solution and 80g of water. The flask was fitted with a 5 tray 1" glass Oldershaw column and 80g of water. The flask was heated to 75°C for 1 hour yielding 130.7g of MAS solids. The mother liquor from the centrifuging step was allowed to cool to room temperature forming a second crop of crystals. This slurry was filtered and the recovered solids were dried at 75°C under vacuum yielding 114.8g of MAS solids. Based on the succinate concentration of the feed to the crystallizer, a 20% and 18% recovery was realized for the first and second crops, respectively (i.e. a 38% overall recovery). HPLC analysis of the two crops indicated that the first crop had no detectable succinamic acid and succinimide while the second crop had 0.96% succinamic acid and 0.28% succinimide.
section which was topped with a distillation head. An addition funnel containing 1200g of water was also connected to the flask. The flask was stirred with a magnetic stirrer and heated with a heating mantel. The distillate was collected in an ice cooled receiver. When the distillate started coming over the water in the addition funnel was added to the flask at the same rate as the distillate was being taken. A total of 1290g of distillate was taken. The distillate contained 2.2g of ammonia, as determined by titration. This means about 44% of the DAS was converted to MAS. Although our processes have been described in connection with specific steps and forms thereof, it will be appreciated that a wide variety of equivalents may be substituted for the specified elements and steps described herein without departing from the spirit and scope of this disclosure as described in the appended claims.
Claims

1. A process for making nitrogen containing compounds, comprising:
   (a) providing a clarified DAS-containing fermentation broth;
   (b) distilling the broth to form an overhead that comprises water and ammonia, and a liquid bottoms that comprises MAS, at least some DAS, and at least about 20 wt% water;
   (c) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS;
   (d) separating at least part of the solid portion from the liquid portion;
   (e) contacting the solid portion with at least one hydrogenation catalyst to produce BDO;
   (f) aminating the BDO to produce DAB; and
   (g) recovering the DAB.

2. A process for making nitrogen containing compounds, comprising:
   (a) providing a clarified DAS-containing fermentation broth;
   (b) distilling the broth to form a first overhead that includes water and ammonia, and a first liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water;
   (c) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS;
   (d) separating at least part of the solid portion from the liquid portion;
   (e) contacting the solid portion with at least one hydrogenation catalyst to produce BDO;
   (f) aminating the BDO to produce DAB; and
   (g) recovering the DAB.

   (h) cooling and/or evaporating the second bottoms to cause the second bottoms to separate into a second liquid portion in contact with a second solid portion that preferably consists essentially of SA and is substantially free of MAS; and
   (i) recovering the second solid portion that preferably consists essentially of SA and is substantially free of MAS;
separating at least part of the second solid portion from the second liquid portion; (j) contacting the second solid portion with at least one hydrogenation catalyst to produce BDO; (k) aminating BDO to produce DAB; and (l) recovering the DAB.

3. A process for making nitrogen containing compounds, comprising:
(a) providing a clarified MAS-containing fermentation broth;
(b) optionally, adding MAS, DAS, SA, NH₃, and/or NH₄⁺ to the broth to preferably maintain the pH of the broth below 6; (c) distilling the broth to form an overhead that includes water and optionally ammonia and a liquid bottoms that includes MAS, at least some DAS, and at least about 70 wt% water; (d) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (e) separating at least part of the solid portion from the liquid portion; (f) contacting the solid portion with hydrogen and optionally an ammonia source in the presence of at least one hydrogenation catalyst to produce BDO; (g) aminating the BDO to produce DAB; and (h) recovering the DAB.

4. A process for making nitrogen containing compounds, comprising:
(a) providing a clarified MAS-containing fermentation broth;
(b) optionally, adding MAS, DAS, SA, NH₃, and/or NH₄⁺ to the broth to preferably maintain the pH of the broth below 6; (c) distilling the broth to form an overhead that includes water and optionally ammonia and a liquid bottoms that includes MAS, at least some DAS, and at least about 20 wt% water; (d) cooling and/or evaporating the bottoms, and optionally adding an antisolvent to the bottoms, to attain a temperature and composition sufficient to cause the bottoms to separate into a DAS-containing liquid portion and a MAS-containing solid portion that is substantially free of DAS; (e) separating the solid portion from the liquid portion; and
(f) recovering the solid portion;

(g) dissolving the solid portion in water to produce an aqueous MAS solution; 

(h) distilling the aqueous MAS solution at a temperature and pressure sufficient to form a second overhead that includes water and ammonia, and a second bottoms that includes a major portion of SA, a minor portion of MAS, and water;

(i) cooling and/or evaporating the second bottoms to cause the second bottoms to separate into a second liquid portion in contact with a second solid portion that preferably consists essentially of SA and is substantially free of MAS;

(j) separating at least part of the second solid portion from the second liquid portion;

(k) contacting the solid portion with hydrogen and an ammonia source in the presence of at least one hydrogenation catalyst to produce BDO;

(l) animating BDO to produce DAB; and

(m) recovering the DAB.

55. The processes of any of claims 1-4, further comprising polymerizing the DAB with a dicarboxylic acidester to form a polyamide.

66. The processes of any of claims 1-4, wherein the distillations are carried out in the presence of an ammonia separating solvent which is at least one selected from the group consisting of diglyme, triglyme, tetraglyme, sulfoxides, amides, sulfones, polyethylene glycol (PEG), butoxy triglyme, N-methylpyrrolidone (NMP), ethers, and methyl ethyl ketone (MEK) or in the presence of a water azetroping solvent which is at least one selected from the group consisting of toluene, xylene, methylcyclohexane, methyl isobutyl ketone, hexane, cyclohexane and heptane.
MAS SOLUBILITY CURVE

TEMPERATURE DEGREES CENTIGRADE

PERCENT MAS

- IN WATER
- IN AQUEOUS 30% DAS

FIG. 4
**INTERNATIONAL SEARCH REPORT**

**International application No**
PCT/US2011/049682

### A. CLASSIFICATION OF SUBJECT MATTER

- INV. C07C51/02
- C07C55/10
- C07C51/41
- C07C51/43
- C07C51/44
- C07C29/149
- C07C31/20
- C07C209/16
- C07C211/09

### B. FIELDS SEARCHED

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

- EPO-Internal
- CHEM ABS Data
- WPI Data

### C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<th>Relevant to claim No.</th>
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<td>JP 2007 254354 A (NAT INST OF ADV IND &amp; TECHNOL; SHOWA HIGHPOLYMER) 4 October 2007 (2007-10-04) cited in the application on paragraphs [0021] - [0029], [0044]; example 1 -----</td>
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Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:
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Date of the actual completion of the international search

10 February 2012

Date of mailing of the international search report

24/02/2012

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Authorized officer

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