

PROCESS FOR PREPARING DTEA HCl

BACKGROUND OF THE INVENTION

Field of the Invention

5 This invention generally concerns an improved process for preparing DTEA HCl from 1-decene and cysteamine HCl (CA HCl).

Background of the Invention

Industrial chemicals are most commonly manufactured using solvent-based reaction methodology, followed by isolation, purification, and packaging. Many such chemical products
10 are then formulated into a commercial product by blending the active ingredient (AI; see Glossary below for a full listing of abbreviations and acronyms) with other materials optimized for, and specific to, its end use. When formulated as an aqueous solution, often problems with solidification and or AI precipitation can become an issue when formulations are stored at (or in some cases, even briefly subjected to) below room temperature environments. Partial
15 precipitation and settling of solids result in variable AI concentration as well as inaccurate and inefficient transfers of the formulation from storage to end-use vessels. Solids may cause major difficulties with clogging filters and/or nozzles in applications requiring the formulation be pumped or sprayed. Thus, the ability to remain as a pumpable, homogeneous material that is free of solids is essential to avoid costly and inconvenient heating and agitation operations during
20 formulation operations and use.

Description of Related Art

Several patents disclosed use of additives in microbiocidal formulations to increase low temperature stability (to hinder AI precipitation or formulation solidification). A few of such patents are provided below. None of this next listed art uses GLTS agents (as defined in the
25 Glossary below) as a co-solvent for the reaction to make DTEA HCl.

US Pub Appln. 2008/0076803 (Beilfuss) describes addition of one or more aromatic alcohols to 1,2-benzisothiazolin-3-one formulations to increase low temperature stability. Specifically, the preferred additives are chosen from (i) aryloxyalkanols (glycol monoaryl

ethers), (ii) arylalkanols and (iii) oligoalkanol aryl ethers or mixtures thereof. This reference proscribes in Claim 13 a sequence for preparation of a formulation specifying the GLTS is the last component to be added, and is not taught or used in any GLTS-co-solvent process of this reference.

5 WO2001/041570 (Beilfuss) describes use of the same suite of additives as those in US 2008/0076803 above but they are used to improve the stability and lessen inhomogeneity of a different mixture of AIs.

US Pub Appln 2013/0217579 (Wacker) describes a new low temperature solvent for pesticide formulations and includes addition of GLTS propylene glycol (PG) and glycerol to said
10 formulations.

US 5,371,105 (Damo) describes novel aqueous formulations of agrochemical active substances which are sparingly soluble in water. These formulations are either water-in-oil or oil-in-water emulsions. One additive to the formulation is GLTS, preferably glycerol, but also mentions EG, PG, and polyglycols.

15 US 5,369,118 (Reizlein) teaches the use of GLTS auxiliaries to improve the stability of triazole fungicide formulations to retard solids formation in aqueous spray liquors to prevent clogging spray nozzles and in-line filters. PG and glycerol are preferred.

US 5,206,225 (Horstmann) teaches use of GLTS auxiliaries to improve the stability of triazole fungicide formulations to retard solids formation in aqueous spray liquors to prevent
20 clogging spray nozzles and in-line filters. PG and glycerol are preferred.

US 7,368,466 (Beilfuss) discloses a water-based formulation of the fungicide, a salt of carbedazim, containing certain GLTS exhibit long-lasting low temperature stability. Beilfuss, *et al.* cite benzyl alcohol (BA) as a preferred GLTS and 1-phenoxy-2-propanol (PP) as a particularly preferred GLTS; neither of these is a satisfactory LTS-co-solvent in the DTEA HCl
25 process described herein.

US 5,087,757 (Mariam) taught the use of various solvents in the reaction of decene and CA HCl (2-aminoethanethiol hydrochloride, also referred to as cysteamine HCl) to produce DTEA HCl using catalysts/initiators including hydrogen peroxide and azo initiators. These included glycols and glycol ethers, and their mixtures with water. Examples mentioned are:

ethylene glycol; propylene glycol; propylene glycol methyl ether; dipropylene glycol methyl ether; diethylene glycol; triethylene glycol; tetraethylene glycol; and dipropylene glycol, with propylene glycol and tetraethylene glycol preferred. Some of the disadvantages of using the Mariam reaction to produce DTEA HCl are: (1) achieving high conversion of reactants is
5 difficult and requires multiple additions of catalyst and extended reaction times to achieve high conversion of reactants to DTEA HCl; and (2) dilution with the preferred solvent (water) produces a formulation with serious solidification/solids formation problems at low temperatures (defined as about 32°F to about 60°F).

US H1265 Statutory Invention Registration (Brady) taught a variety of alcohol (hydroxyl
10 group-containing) additives that could be added to the DTEA HCl reaction product prepared by the Mariam process (using PG or tetraethylene glycol (TEG) as a reaction solvent). This Brady technique dilutes the reaction product mixture with BTS (as defined in the Glossary below) to provide low temperature stability. BTS solvents mentioned are butyl alcohol, cyclohexanol, hexyl alcohol, isobutyl alcohol, ethylene glycol phenyl ether (a synonym for 2-phenoxyethanol
15 (PE)) and propylene glycol phenyl ether (a synonym for 1-phenoxy-2-propanol (PP)) and mixtures thereof. Some of the disadvantages of using Brady's BTS with the products of these processes are: 1) addition of the BTS to the organic solvent-based reaction mixture results in higher overall product costs; and 2) adding additional organic chemicals to the formulation is problematic in the application of this product in industrial water treatment: organic solvents in
20 the formulation are nutrients for microbial growth and make its control more challenging and costlier. The amount of organic solvent in the formulation should be minimized to the extent possible. A major limitation to extrapolation of Brady to other solutions is that the screening for low temperature stabilization was done, specifically, on a solution of DTEA HCl consisting of (approximately) 45 wt% DTEA, 45 wt% PG, 7 wt% water, and 3 wt% impurities. Although PG
25 is not LTS for this formulation, PG is a better solvent for DTEA HCl than water. Brady's findings do not correlate well to other DTEA HCl formulations that do not contain PG.

US 5,025,038 (Relenyi) describes an ETOX process using PG as solvent to make DTEA HCl to afford low temperature stability; however, this process has similar solidification/solids formation problems as Mariam at low temperatures.

Clearly, there is still a need for a better process to make DTEA HCl in order to: obtain effective contact of the reactants in the reaction process to obtain high reactant conversion and yield; have a final homogeneous liquid product formed after the process with no solidification/solids formation occurring at lower temperatures such as 32°F; control microbial growth by limiting adding more organic components; have a more economical process by using a solvent serving as both a reaction co-solvent and LTS that eliminates a further step for the addition of LTS; and have ease of handling with low environmental impact by using a larger portion of an aqueous based system for the reaction.

The two methods for industrial-scale production (the EtOx and MEAH processes) result in formation of a solid product or a phase-separated mixture at above room temperature (*i.e.*, about 70 °F) as a reaction concentrate unless the reaction concentrate is sufficiently diluted with water or other diluents.

The EtOx process (Relenyi, et. al, WO 90/09983) involves a reaction of decenethiol with ethyl-2-oxazoline without solvent at about 140 °C to form an intermediate that is immediately, *in situ*, hydrolyzed with additional heat and conc. HCl to form DTEA HCl. This material is directly pumped into another, larger reaction vessel (to avoid solidification of the product in the reactor as it is cools and of sufficient size for product dilution). The second vessel contains water and PG to form a reaction concentrate medium similar to that obtained from the Marriam MEAH process.

The MEAH process involves a reaction of cysteamine HCl with decene in propylene glycol which then diluted with water or a water-PG mixture which is then further diluted with water (Mariam, U.S.Pat. 5087757A, Eur. Pat. Appl. (1989), EP 320783 A2 19890621).

The reaction concentrate from the EtOx is diluted before drumming and has a typical content of about 18 wt% DTEA HCl, 16 wt % PG, and 66 wt % water after dilution. The MEAH process reaction concentrate can be made readily at 45-50 wt% DTEA HCl or, as described in Mariam (Example 1), as a 15 wt% DTEA HCl solution in PG and water (~15 wt% DTEA HCl, ~16 wt % PG, and ~67 % water). Brady notes that a typical Marriam reaction concentrate consists of 45 wt% DTEA, 45 wt% PG, 7 wt% water, and 3 wt% impurities.

The undiluted reaction concentrate from the Marriam reaction process must be drummed while the reaction mixture is still hot because the mixture solidifies at around 60°F and can form

solids in the solution even around typical room temperature. Commercial formulations typically contain from about 5 to about 15 wt% DTEA HCl prepared by dilution of the reaction concentrate with the appropriate amount of water. From solubility data (see Figures 1 and 2), ~15 wt% DTEA HCl a PG/water mixture provides a solid-free solution of DTEA HCl at room

5 temperature, and this serves as a basis for the wt % DTEA HCl, PG and water in reaction mixture (Mariam, Example 1). The **solubility of DTEA HCl** in the MEAH reaction concentrate medium (Mariam, Example 1) and of the EtOx process reaction medium (Relenyi, Example 1) when each is diluted with water is about 15 wt% at about 68 °F, about 10 wt % at about 63 °F, and about 5 wt% at 55 °F.

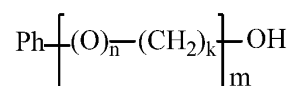
10 The drummed Mariam reaction concentrate is rock solid at typical room temperatures and must be heated to form a liquid in order to get it out of the drum for further dilution or other formulation uses.

BRIEF SUMMARY OF THE INVENTION

15 The present invention describes an improvement over known processes for the production of 2-(*n*-decylthio)ethylamine HCl (DTEA HCl) in which the reaction efficiency is improved and incorporates an Additive that is both a low temperature stabilizer (LTS) and a reaction Co-solvent to provide a commercial formulation with improved low temperature stability with minimal post reaction processing. Use of the claimed Additive in the reaction, as

20 well as the final formulation, eliminates the need of a separate reaction solvent and thereby reduces the production cost.

More specifically, the present invention concerns a process for preparing 2-(*n*-decylthio)ethylamine HCl (DTEA HCl) comprising reacting decene and cysteamine HCl, with (a) a catalyst, (b) water, and (c) an Additive of the Formula (A):



Formula (A)

wherein:

Ph is phenyl;

n is 0 or 1;

k is 2-4; and

m is 1-3;

that provides the 2-(*n*-decylthio)ethylamine HCl as a concentrated mixture in about >90% yield, wherein such concentrated reaction mixture is further diluted with water to provide a low
5 temperature stable (LTS) liquid product.

Additional Additive can be added directly to the concentrated reaction mixture or as part of the dilution with water or after the dilution with water. The amount of Additive present after dilution with water in the final solution is from about 1 to about 30 wt% or from about 2 to about 20 wt%. The amount of Additive used in the reaction is from about 10 to about 49 wt%.

10 The low temperature stability of the resulting product means at temperatures from about 32°F to about 60°F. A stable liquid product means that the product has no solids formation or separation of any phases at the low temperatures.

The amount of product present in the final solution is from about 2 to about 25 wt%; or from about 5 to 15 wt%.

15 The reaction is run under an inert atmosphere, at a temperature from about 70°C to about 79°C.

The yield of the DTEA HCl product from the present reaction is >90%, often >95%, even when run on a commercial scale and can be further optimized.

The selection of the Additive and catalyst used in this process is not trivial and discussed
20 further below.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 graphically represents the water solubility of DTEA HCl in an unprocessed Mariam reaction mixture (*i.e.*, approximately 47-51% DTEA HCl, 18-21% PG, 21-27% water). There is no LTS used so the data is comparative.

25 **Figure 2** graphically represents the solubility of pure DTEA HCl when the only solvent is water. This shows the solubility of pure solid DTEA HCl in water with no LTS used. The data is comparative.

DETAILED DESCRIPTION OF THE INVENTION

It is understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting. As used in this specification, the singular forms “a”, “an”, and “the” include plural referents unless the content clearly indicates otherwise. The following terms in the Glossary as used in this application are to be defined as stated below and for these terms, the singular includes the plural.

Various headings are present to aid the reader, but are not the exclusive location of all aspects of that referenced subject matter and are not to be construed as limiting the location of such discussion.

Also, certain US patents and PCT published applications have been incorporated by reference. However, the text of such patents is only incorporated by reference to the extent that no conflict exists between such text and other statements set forth herein. In the event of such conflict, then any such conflicting text in such incorporated by reference US patent or PCT application is specifically not so incorporated in this patent.

Glossary

The following terms as used in this application are to be defined as stated below and for these terms, the singular includes the plural.

Additive means a compound that is both a Co-solvent (defined below) and LTS (defined below)

AI means active ingredient

azo catalyst means, preferably, one of the following:

2,2'-Azobis[N-(2-carboxyethyl)-2-methylpropionamidine];

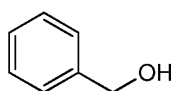
2,2'-Azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA 044);

2,2'-Azobis[2-methyl-N-(2-hydroxyethyl)propionamide];

4,4'-Azobis(4-cyanovaleric acid); or

2,2'-Azobis(2-methylpropionamidine) dihydrochloride (V-50)

BA means benzyl alcohol, as depicted by the following structure



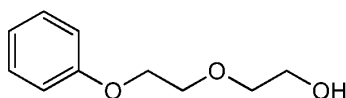
BTS means an GLTS subset as defined by Brady and applicable only to temperature stability of a specific formulation of DTEA HCl

CA means cysteamine or 2-aminoethanethiol or 2-mecaptoethylamine

Co-solvent means a solvent used with water in the reaction of this invention

5 **Decene** means 1-decene, C₁₀H₂₀

DiEPH means diethyleneglycol phenylether or 2-(2-phenoxyethoxy)ethanol, as depicted by the following structure



10 **DTEA** means *n*-decylthioethylamine or 1- decylthioethylamine or 2-(1-decylthio)ethylamine

g means grams

GLTS means generally well known, widely used low temperature stabilizers without defining the stabilization or temperature range of use but for specific applications

h means hour or hours

15 **HCl** means a hydrochloride salt

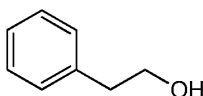
L means liter

LTS means a compound that acts as a low temperature stabilizer, in which a liquid solution remains homogeneous and does not become solid, or contain solids (precipitates), or undergo phase separation at low temperature (low temperature means from about 32°F to about 60°F) and low temperature stability is determined by instrument measurement or visually by the absence of solid particulates (crystalline or other solid forms) or by absence of any solidification of the liquid.

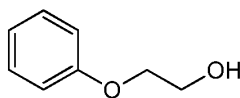
20 **min** means minute or minutes

25 **mL** means milliliter

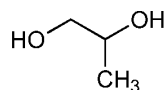
PA means 2-phenylethanol as depicted by the following structure



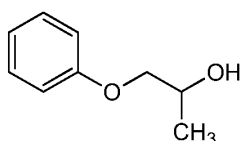
PE means 2-phenoxyethanol, as depicted by the following structure



PG means propylene glycol, as depicted by the following structure



PP means 1-phenoxy-2-propanol, as depicted by the following structure



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RT means room temperature or ambient temperature, from about 20°C to about 25°C or about 72°F

sec means second

Solids formation includes but is not limited to formation of a solid phase within the original liquid phase, which includes but is not limited to crystallization; if the amount of solid is substantial, the entire volume may appear solid

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Water means water purified by reverse osmosis (RO) as used in the present examples, but this is not critical

wt% means percent by weight

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Discussion

In aggregate, the above prior art establishes the utility of GLTS in formulations but provides no guidance for selection of LTS, let alone one that would be a suitable Co-solvent for a DTEA HCl manufacturing process.

The philosophy that emerges in these prior teachings is that low temperature stabilizers are thought of as an interchangeable, generic class such that one may simply choose any one of a myriad of known GLTS agents. These GLTS agents are generally the last component of the formulation to be described and commonly include the phrase 'as needed'. As such, post-reaction GLTS selection provides no guidance for selection of a suitable reaction solvent, especially free radical reaction where solvent selection is especially critical to reaction success (see, for example, Litwinienko, G.; Beckwith, A. L. J.; Ingold, K. U. "The frequently overlooked

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importance of solvent in free radical syntheses” *Chem. Soc. Rev.* **2011**, 40 (5), 2157-2163. DOI: 10.1039/C1CS15007C).

There is no overlap in the BTS taught by Brady, and the co-solvents taught by Mariam. Indeed, it has now been found by this invention that most BTS are not generally good reaction
5 Co-solvents and also that good co-solvents are not generally good as LTS. It is also important to note that the Brady BTS data were generated using a DTEA HCl formulation containing mainly PG (45 wt%) and only 7 wt% water. These data are not applicable for identification of LTS, even as a post reaction additive, for a solution of DTEA HCl product that does not contain PG.

Present Process

10 An improved process is needed to avoid the increased processing time and costs, to improve the conversion of reactants, and to improve the yield DTEA HCl. It would also be advantageous to use only water for dilution of the DTEA HCl reaction mixture to provide a commercial formulation. Replacing currently used DTEA HCl reaction co-solvents with LTS as a Co-solvent avoids the solidification/solids formation issue of such formulations. Using
15 traditional GLTS co-solvents (such as PG), then adding LTS in the post production formulation process, requires additional equipment and complicates formulation. The presence of GLTS co-solvent in the commercial formulation (as done in the prior art processes) dilutes the AI, adds unnecessary cost to production, and essentially serves only as food for microorganisms in a water treatment environment. Another factor when considering an organic material for use as a
20 Co-solvent concerns flammability. Solvents with higher flash points are preferred over low flash point solvents whenever possible. For example, considering two of Brady’s mentioned BTS, namely PE and 1-butanol, if both actually worked as a Co-solvent in the DTEA HCl process, PE (flash point 250°F) would be the preferred solvent over 1-butanol (flash point 96°F) on this basis.

25 A preferred form of DTEA HCl for sale is a liquid in various concentrations, for example about 5 to about 15 wt% DTEA HCl, whereas the DTEA HCl is produced most efficiently at a higher concentration in the reaction. Thus, the reaction mixture must be diluted to yield the final formulation for sale. Water is the preferred dilution solvent due to its low toxicity and low cost and environmental preference. Also, water is not a nutrient for microbial growth during product
30 application, so lowering organic solvent content by increasing the water content provides benefit

in applications. Unfortunately, even at these low concentrations of DTEA HCl, aqueous mixtures prepared by dilution of the reaction product produced by the Mariam process (above) begin to solidify at temperatures that are commonly used in storage and handling (32°F to 60°F). Concentrations as low as 1-5 wt% showed problematic solids formation. It should also be noted
5 that dilution of the crude product with additional propylene glycol, both a preferred reaction co-solvent taught by Mariam and a commonly used low temperature stabilizer in many applications, is NOT effective for this present process. That is, PG is not an effective LTS in this application. It would be of great value to be able to use a different co-solvent that BOTH afforded a high reaction yield of DTEA HCl and functioned as an effective low temperature stabilizer (LTS) in
10 the diluted, end-use product.

The reactants for this present process are decene (which is soluble in several organic solvents and relatively insoluble in water), and CA HCl (which is soluble in aqueous systems). The present process requires a water solvent with an organic co-solvent that serves multiple functions (including improving homogeneity of the reaction process and also providing LTS for
15 the product formulation), and a catalyst. When these two reactants are mixed with the solvents and catalyst, the reaction occurs. An Additive is needed as a Co-solvent to ensure effective contact and reaction of the reactants in the initial two-phase mixture in a high reaction yield, which also serves as LTS for the final product that is needed for handling and storage. Finding an Additive that will work as both a Co-solvent and LTS in this specific reaction has proven
20 difficult. The formulation of DTEA HCl (product) from the reaction must remain as a homogenous liquid to provide accurate and simple transfer of the product without solidification, phase separation such as solids formation by crystallization (which is a problem in prior systems). Aqueous solutions with minimal organic content are preferred in this process and its ultimate formulation as they are inexpensive, relatively non-hazardous, and especially, provide
25 minimal organic nutrients for microbial growth in end use applications.

Water and LTS used as a Co-solvent

Prior teachings suggest that aqueous propylene glycol (PG) is the reaction solvent of choice. However, the product obtained from a PG-based process when diluted with water unfortunately forms solids at low temperatures (as defined above) and requires addition of LTS
30 to achieve a homogeneous liquid at 32°F to 60°F.

Brady taught the use of BTS such as 2-phenoxyethanol (PE) and 1-phenoxy-2-propanol (PP) with the DTEA HCl product to provide stable, homogeneous liquids at low temperature. These BTS were not used in the reaction but added after the product was formed. None of the BTS agents that were found successful by Brady were used or taught as a co-solvent for the reaction and, as noted above, have limited application; their use pertains only to low-water, high-PG solvent mixtures in DTEA HCl formulations. It would be more cost effective and efficient when LTS is also used as a Co-solvent in the reaction as it eliminates the need for and cost of any other co-solvent used strictly for the reaction step, such as propylene glycol (PG). Thus, in a streamlined process the formulated product can maintain its low temperature stability without the usual operation steps of separating the co-solvent from the reaction mixture to isolate the AI to which the LTS is added in a separate formulation step.

The present process uses an Additive that is both a Co-solvent and LTS. This has the advantages given below. Determining what Co-solvent that works well for the present reaction and is also LTS was neither appreciated nor attempted by the prior art.

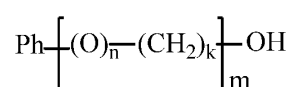
However, choice of LTS that is also a good reaction Co-solvent is not a trivial exercise. A commonly used and widely preferred GLTS (such as propylene glycol (PP), glycerol, or ethylene glycol) are not good as LTS for DTEA HCl. These prior art GLTS do not function well or at all in the present process. Neither is an aromatic ring functional group a sufficient criterion for selection of LTS as a Co-solvent, *e.g.*, neither benzyl alcohol (BA) nor 1-phenoxy-2-propanol (PP) is an effective Co-solvent for the present DTEA HCl reaction using H₂O₂ or azo catalysts in the present invention, although both are known as excellent GLTS.

The present Additives that are Co-solvents used in the present reaction and used as LTS, can be optionally further added to the aqueous DTEA HCl product solution to provide a stable liquid at temperatures down to at least 32°F.

A formulation that forms solids at low temperatures such as these which are commonly encountered in storage and use of this product is not practical and is problematic. When solids form in a formulation, it is often difficult to regain homogeneity. Storage in specially heated storage areas to prevent lower temperatures or using heat and agitation to melt and re-blend the mixture is time-consuming, expensive and inconvenient. Heterogeneous mixtures are difficult to

pump, can clog nozzles and filters, do not meter well, and cannot be used to provide consistent or accurate dosing.

Suitable Co-solvents of the present invention are phenyl containing alcohols, such as 2-phenoxyethanol (PE) and 2-phenylethanol (PA), preferably those having a significant water
 5 solubility of about 1 to about 10 wt%. The amount of Additive (LTS/Co-solvent) used in the reaction is from about 10 to about 49 wt%, and preferably from about 15 to about 35 wt%. The effective Additives are represented by the following Formula A:



10 Formula (A)

wherein:

Ph is phenyl;

n is 0 or 1;

k is 2-4; and

15 m is 1-3.

Representative examples of such Additives of Formula A are PA, PE, and DiEPh. Some examples of GLTS found ineffective as Co-solvents are BA, PP and PG. Thus, it is not apparent to one skilled in this art what will work as an Additive in the process based on prior known reactions.

20 When carrying out the current reaction, the mixture initially has two liquid phases; namely, an organic phase containing decene and an aqueous phase containing cysteamine HCl (CA HCl). The latter aqueous phase also contains the catalyst. While not wishing to be bound by theory, it is believed that for reaction to occur efficiently, decene must have sufficient solubility in or contact with the aqueous phase. The present phenyl alcohol Co-solvents have a
 25 suitable balance of polar and nonpolar character which facilitates the required mixing and solubilization in the reaction. These Co-solvents also possess suitable properties to solubilize the final product at low temperatures from about 32°F to about 60°F to avoid solidification, solids formation and/or phase separation as LTS agents. These present LTS are present in the final

product solution from about 1 to about 30 wt%, preferably from about 2 to about 20 wt%. Many of the prior used solvents do not have such properties and do not provide these desired results.

Catalyst/Initiator

The present process requires that a free radical initiator is used. When the Co-solvent is used with various catalysts/initiators there is the issue of solubility and which ones will work in the system. For example, hydrogen peroxide and the azo initiator (including non-water soluble azo initiators) are taught by Mariam (discussed above). However, the preferred azo initiators that Mariam taught were azobisnitriles which are not water soluble. Mariam also provided no data for the azo initiators, which have been found in this present testing that even water soluble azo initiators are not effective with PG as the solvent. However, surprisingly, an azo catalyst with PE or PA solvent in the present reaction alone resulted in the desired LTS product.

The present preferred catalysts are azo catalysts that are water soluble such as:

- 2,2'-Azobis(2-methylpropionamidine) dihydrochloride (V-50);
- 2,2'-Azobis[N-(2-carboxyethyl)-2-methylpropionamidine];
- 2,2'-Azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA-044);
- 2,2'-Azobis[2-methyl-N-(2-hydroxyethyl)propionamide]; and
- 4,4'-Azobis(4-cyanovaleric acid).

Selection of these various reaction parameters is not simple to obtain the desired results. Even though Brady's results showed 2-phenoxyethanol (PE) and PP to be good BTS for the diluted reaction product (added after the reaction was run), and Mariam teaches that good reaction solvents are specific glycols and glycol ethers, Mariam did not teach any of Brady's claimed BTS as reaction solvents and did not teach any phenyl-substituted alcohols of Formula (A). The present results show that good BTS and GLTS are not necessarily good reaction solvents (*e.g.*, BA and PP) and, *vice versa*, good reaction solvents are not good LTS [*e.g.*, PG (present data and Brady), Dowanol DPM (dipropylene glycol methyl ether, Brady)]. Thus, it is not apparent to a skilled person how to identify a solvent that is successful for both purposes, *i.e.*, an Additive. Indeed, it was surprising that two structurally similar compounds taught by Brady as a good BTS (2-phenoxyethanol (PE) and PP) gave greatly different results as reaction solvent, good and poor, respectively. Another solvent which now is identified as an excellent BTS was BA; however, it proved to be a poor reaction solvent. Another good Co-solvent diethylene

glycol phenyl ether (Dowanol DiEPH) has been found to also be a good LTS for DTEA HCl. The present data and observations indicate that successful reaction results not only depend on the solvent but also the catalyst. Comparison of data in Tables 1 and 2 show good results with H₂O₂ but poor results with V-50.

5 If a skilled person were to randomly screen a list of solvents taught by Brady and other solvents of similar structure (such as alcohols) with both H₂O₂ and V-50 (and possibly other commercially available free radical initiators), as well as at varying solvent concentrations and with varying amounts of water, the number of combinations to test would be very large and require undo experimentation and an impractical amount of time to test, making the ultimate
10 selection of successful reaction solvent for this present process not practical. A method to just find them by testing is daunting as the list to test would be very large with multiple conditions and the reaction actually run to determine what was effective for the desired results. Thus, this is not a simple substitution of a few items to see what would work; rather it requires multiple variables and undue experimentation to find what is now claimed.

15 Clearly, previous attempts to make DTEA HCl have had difficulties obtaining high reactant conversion and yields, to have no phase separation, solidification, or solids formation at lower temperatures such as 32°F without LTS; to control microbial growth by limiting organic components; to not require separation steps of the solvent or product; and to have ease of handling with low environmental impact by using a larger portion of an aqueous based system.
20 The present process provides these advantages.

 This process provides a final product which is formed from the present reaction as a solution containing: a) from about 2 to 25 wt% of DTEA HCl, preferably from about 5 to about 15 wt%, b) additional water and Additive added after the reaction if needed in an amount from about 1 to about 30 wt% of Additive, preferably from about 2 to about 20 wt%. The final
25 product provides a low temperature stability of at least from 32°F to about 60°F. The invention will be further clarified by a consideration of the following examples, which are intended to be purely exemplary of the invention.

 The letter examples are comparative examples. The numbered examples are directed to the compounds of the present invention.

Materials

Decene was purchased from Shell.

DiEPH was obtained from DowDupont.

PE was obtained from Nexeo.

5 Benzyl alcohol and PA were purchased from Sigma-Aldrich.

PP was obtained from GNS Technologies LLC.

CA HCl was purchased from Hangzhou Qianjin Technology Ltd.

Water is prepared by reverse osmosis (RO).

V-50 was purchased from Wako.

10 VA-044 was obtained from Sigma-Aldrich.

H₂O₂ was purchased from GFS Chemicals, Inc., as a 50% aqueous solution and then diluted to 1.5-1.8% solution with water.

Pure, solid DTEA HCl was made by the method described in US 5087757 and isolated by dilution and crystallization with acetonitrile.

15 General Reaction conditions

The general present reaction conditions are:

Temperatures from about 25°C to about 120°C (preferably from about 74°C to 77°C preferred);

Atmosphere is air, nitrogen or argon;

20 Catalyst concentration from about 0.01 to about 5 wt%, preferably from about 0.1 to about 1 wt%;

Decene concentration from about 1 to about 40 wt%, preferably from about 15 to about 30 wt%;

25 Cysteamine HCl concentration from about 1 to about 40 wt%, preferably from about 15 to about 30 wt%;

Water concentration from about 10 to about 49 wt%, preferably from about 15 to about 35 wt%;

Additive concentration from about 10 to about 49 wt%, preferably from about 15 to about 35 wt%; and

Optionally are: 36 wt% HCl added from about 0.01 to about 1 wt%; DTEA HCl added from about 1 to about 5 wt%, preferably from about 0.5 to about 2 wt%.

Preparation of DTEA HCl and Comparatives

5 Example 1: General Procedure for H₂O₂ as the catalyst

Using 72 g of decene, 62 g of CA HCl, 50-75 g of Co-solvent, 44 g of water, 2.75 g of DTEA HCl, 26-30 mL of H₂O₂, 0.1 mL of concentrated HCl, the following general process was run with the various Co-solvents indicated.

10 To a three necked flask equipped with mechanical stirrer, thermocouple, addition funnel and nitrogen inlet, cysteamine HCl, Co-solvent, water and DTEA HCl were added. The system was flushed with nitrogen and the reaction was carried out under the atmosphere of nitrogen. The mixture was stirred and heated to 65°C using a water bath. To this mixture 0.1 mL of concentrated HCl was added followed by 10 mL of decene. The addition of hydrogen peroxide solution was then started along with the remaining decene, maintaining the reaction temperature
15 below 80°C (about 74°C to 77°C is preferred). Hydrogen peroxide solution was added over a period of 40 min. and decene was added over a period of 20 min. The reaction mixture was stirred for another h after completion of the addition of hydrogen peroxide while maintaining the reaction temperature below about 80°C (about 74°C to about 77°C temperature is preferred). The mixture was cooled and analyzed. The results are shown in the following Table 1.

Table 1: DTEA HCl Process Using Hydrogen Peroxide and Various Co-solvents

Example	Co-solvent (g)	Aqueous H ₂ O ₂	DTEA HCl Yield %	Unreacted decene %	Unreacted cysteamine HCl %	Comments
1	Propylene glycol (PG) (50.5 g)	30 mL (1.5% solution)	84.4	4	3.5	Reaction worked well in PG
2	2-Phenoxyethanol (PE) (75 g)	27 mL (1.85% solution)	83	Not available	3.9	Reaction worked well in PE
A	Benzyl alcohol (BA) (50.5 g)	27 mL (1.5% solution)	10	-----	-----	Not a good Co-solvent for the reaction. Three layers were formed
B	1-Phenoxy-2-propanol (PP) (75 g)	30 mL (3.1% solution)	Not analyzed	17.8	Not analyzed	Not a good Co-solvent for the reaction. Two layers were formed
3	2-Phenylethanol (PA) (75 g)	30 mL (3.1% solution)	Not analyzed	1.63	Not analyzed	Reaction worked well in PA

The presence of two or three layers is evidence of low conversion and yield. These results show that PG, PE and PA are effective Co-solvents with H₂O₂ catalyst. BA and PP were not effective and only produced a low product yield.

5 Example 2: General Procedure for V-50 as the catalyst

Using 72 g of decene, 62 g of CA HCl, 75 g of Co-solvent, 75 g of water, 2.75 g of DTEA HCl, 0.39-0.78 g of V-50 [2,2'-Azobis(2-methylpropionamidine) dihydrochloride] in 10 mL of RO water, 0.1 mL of concentrated HCl, the following general process was run with the various Co-solvents indicated.

To a three necked flask equipped with mechanical stirrer, thermocouple, addition funnel and nitrogen inlet, cysteamine HCl, Co-solvent, water and DTEA HCl were added. The system was flushed with nitrogen and the reaction was carried out under an atmosphere of nitrogen. The mixture was stirred and heated using a water bath to 65°C. To this mixture 0.1 mL of concentrated HCl was added, followed by 10-15 mL of decene. About 5 mL of V-50 solution was then added and continued the stirring. The remaining decene was added dropwise to the reaction mixture over a period of 30-35 min. maintaining the reaction temperature below 80°C (74°C to 77°C is preferred). Another portion of V-50 (5 mL) was added after the addition of about 50 mL of decene, and continued the stirring. Stirring was continued for another 1.5-2 h after completion of the addition of decene while maintaining the reaction temperature below 80°C (about 74°C to 77°C is preferred). The mixture was cooled and analyzed. The results are shown in the following Table 2.

Table 2: DTEA HCl Process Using V-50 and Various Co-solvents

Example	Co-solvent (g)	V-50 (g)	DTEA HCl Yield %	Unreacted decene %	Unreacted cysteamine HCl %	Comments
C	Propylene glycol (PG) (75 g)	0.78 g in 10 mL water	--	-----	-----	PG is not a good solvent with V-50 catalyst
4	2-Phenoxyethanol (PE) (75 g)	0.39 g in 10 mL water	95	1.5	1.4	Good solvent. Reaction worked well.
D	Benzyl alcohol (BA) (75 g)	0.5 g in 10 mL water	10	-----	-----	BA is not a good Co-solvent. Three layers were formed
E	1-Phenoxy-2-propanol (PP) (75 g)	0.78 g in 10 mL water	NA	24	NA	PP is not a good Co-solvent. Two layers were formed
5	2-Phenylethanol (PA) (75 g)	0.78 g in 10 mL water	NA	3.01	NA	PA worked a good as PE based on decene consumption.

NA = Not Analyzed

These results show that PE and PA were effective as Co-solvents. PG, PP and BA were not effective.

Example 3: Comparison of PE and PG

Addition of PE in the range of about 5 wt% to about 10 wt% to a 15 wt% DTEA solution (prepared from commercial DTEA HCl concentrate by diluting with water) produces homogeneous solutions at both RT and upon prolonged storage – several days- at 32°F. The weight percent DTEA HCl in the solutions after addition of PE ranges from about 6.5 wt% to about 7 wt%.

Similarly, addition of PE in the range of about 13 wt% to about 16 wt% to a 15 wt% DTEA solution (prepared from commercial DTEA HCl concentrate by diluting with water) produces homogeneous solutions at both RT and upon prolonged storage - several days- at 32°F. Below approximately 13 wt% PE the solution is homogeneous at RT, but solid at 32°F. The weight percent DTEA HCl in the solutions after addition of PE ranges from about 12.5 wt% to about 13 wt%.

It should be noted that like the reaction to manufacture DTEA HCl, these formulations require a delicate balance between water and organic Additive in order to maintain homogeneity. Addition of too much or too little of either can affect the low temperature stability to solidification and can also affect homogeneity of the mixture at higher temperatures due to phase separation. These studies contain only results in which the solutions remain homogeneous throughout the temperature range studied. Only solutions at the lower end of Additive concentrations effective as LTS of a given solution were studied. The goal is to add approximately the smallest amount of organic LTS that is effective since this is both economically and microbially prudent.

In a direct comparison of the effectiveness of PE relative to PG, a 16.7 wt% DTEA solution (prepared as described above for 7.5 and 15 wt% solutions) was diluted with either PE or PG to provide solutions that contain 13.9 wt% of DTEA HCl and 16.6 wt% of either PG or PE.

Both solutions were homogeneous at RT. The DTEA HCl formulation containing PE remained homogenous at 32°F while the DTEA HCl/PG formulation rapidly solidified and remained solid.

For further comparison, see Figure 1, the solubility of DTEA HCl as an unprocessed DTEA HCl Mariam reaction mixture and pure DTEA HCl solid was determined in water at

different temperatures. The Mariam reaction mixture was produced using hydrogen peroxide catalyst and PG co-solvent. The mixture contained approximately 50 wt% of DTEA HCl, 20 wt% of PG, and 30 wt% of water), The pure DTEA HCl was isolated from a Mariam reaction mixture by addition of acetonitrile, cooling the mixture on ice, and collecting the white DTEA HCl solid, which was dried prior to use.

Solids form at 71°F when in the Mariam DTEA HCl reaction mixture to 20 wt% DTEA HCl by dilution with water. Further dilution with water of the Mariam reaction mixture to 5 wt% of DTEA HCl gives a solution forming solids at an even lower temperature (55°F), see Figure 1. By comparison, the solubility of pure DTEA HCl in water is 11 wt% at 67°F and less than 1 wt% at 56°F (see Figure 2). PG is a better for solvent than water for DTEA HCl, but PG does not provide low-temperature stability (LTS) to the mixtures containing it.

Example 4: Procedure for 2,2'-Azobis[2-(2-imidazolin-2-yl)propane] dihydrochloride (VA 044) as the catalyst

The general procedure outlined in Example 2 was followed using 72 g of decene, 62 g of CA HCl, 75 g of Co-solvent, 75 g of water, 2.75 g of DTEA HCl, 0.6 wt% of VA-044 in 10 mL of RO water. No solid DTEA HCl was added to this reaction. Analysis showed DTEA HCl was produced in 77.4% with 81% conversion in 2 h.

Example 5: Dilution Procedure

Part A: Propylene glycol/Hydrogen peroxide process – dilution with water and 2-phenoxyethanol (PE)

DTEA HCl product mixture (200 g, 50 wt% DTEA HCl) was mixed at RT with 380 g of water and 86.6 g of 2-phenoxyethanol (PE) to obtain 666.6 g of 15% DTEA HCl as a clear solution containing 13% of 2-phenoxyethanol (PE). Further 1:1 dilution at RT with water provided a 7.5% DTEA HCl as a clear solution containing 6.5% of 2-phenoxyethanol (PE).

Part B: 2-Phenoxyethanol/V-50 Process – dilution with water and 2-phenoxyethanol (PE)

DTEA HCl product mixture (270 g, 47.4 wt% DTEA HCl) was mixed at RT with 544 g of water and 39 g of 2-phenoxyethanol (PE) to obtain 853 g of 15% DTEA HCl as a clear solution containing 13% 2-phenoxyethanol (PE) (270 g of the product mixture had already 72 g of PE). Further 1:1 dilution at RT with water provided a 7.5% DTEA HCl as a clear solution containing 6.5% of 2-phenoxyethanol (PE).

Example 6: Crystallization behaviorPart A: Mariam reaction (propylene glycol/hydrogen peroxide process diluted with water and 2-phenoxyethanol (PE))

5 A 15% DTEA HCl solution containing 13% 2-phenoxyethanol and a 7.5% DTEA HCl containing 6.5% of 2-phenoxyethanol prepared from the crude product mixture obtained from propylene glycol/hydrogen peroxide process (Example 5A above) remained homogeneous liquids when the temperature was reduced to 32°F.

Also, a 16.4% solution of DEA HCl containing 10.34% of PE upon storing in a refrigerator for two days did not result in any solids precipitation or crystallization.

10 As a comparison, this result with may be contrasted with Figure 1 in which phenoxyethanol was not present and solids formation occurred at 32°F.

Part B: Reaction product from 2-phenoxyethanol/V-50 Process diluted with water and 2-phenoxyethanol (PE)

1) A 15% DTEA HCl solution containing 13% 2-phenoxyethanol prepared from the 15 crude product mixture obtained from 2-phenoxyethanol/V-50 process (Example 5B above) was a slightly cloudy solution at 32°F. However, no filterable solids were formed at this temperature.

As a comparison, this result with may be contrasted with Figure 1 in which phenoxyethanol was not present and solids formation occurred at 32°F.

2) A 7.5% DTEA HCl solution containing 6.5% 2-phenoxyethanol prepared from 20 the crude product mixture obtained from 2-phenoxyethanol/V-50 process (Example 5B above) was a homogeneous liquid at 32°F.

As a comparison, this result with may be contrasted with Figure 1 in which phenoxyethanol was not present and solids formation occurred at 32°F.

Part C: Purified DTEA HCl diluted with water and 2-phenoxyethanol (PE)

25 A first 15% DTEA HCl solution containing 13% 2-phenoxyethanol and a second 7.5% of DTEA HCl containing 6.5% of 2-phenoxyethanol prepared from DTEA HCl (isolated by crystallization of the crude product mixture using acetonitrile) were both homogeneous liquids at 32°F.

In contrast, DTEA HCl is essentially insoluble in water at 32°F and a 15 wt% DTEA HCl solution in water forms solids well above RT. (See Figure 2).

Methods of Use of DTEA HCl

5 The product formed from the present process, DTEA HCl, is used in industrial water treatment systems for control of biofouling and corrosion.

10 Although the invention has been described with reference to its preferred embodiments, those of ordinary skill in the art may, upon reading and understanding this disclosure, appreciate changes and modifications which may be made which do not depart from the scope and spirit of the invention as described above or claimed hereafter. Accordingly, this description is to be construed as illustrative only and is for the purpose of teaching those skilled in the art the general manner of carrying out the invention.