

FIELD OF THE INVENTION

The present invention pertains to the field of chemical technology. More specifically it pertains to the preparation of a pure Sodium 2-ethylhexanoate salt useful as Chemical/Pharmaceutical intermediate, especially in the preparation of synthetic medicines.

BACKGROUND OF THE INVENTION

Sodium 2-ethylhexanoate (Fig. 1) belongs to category of API i.e. active pharmaceutical intermediates. It is a white to off white hygroscopic crystalline powder and highly soluble in water; having a molecular formula of $C_8H_{15}NaO_2$ and a molecular weight of 166.19.

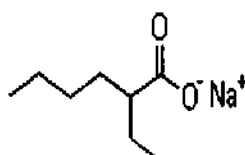


Fig. 1 Chemical Structure of Sodium 2-ethylhexanoate

Uses of Sodium 2-ethylhexanoate as chemical and pharmaceutical intermediate

Sodium 2-ethylhexanoate is a strong reducing agent; used as a **chemical intermediate** for the synthesis of metallic salts (for paint and varnish driers), polyester coating additives and esters (for plasticizers and stabilizers). It is also utilized as a mild acid scavenger which is useful in acylation of amines with acid chlorides as the base. It is highly soluble in common organic solvents such as methanol, ethanol, acetone, and the like, so it is used in the conversion of higher molecular weight organic acids to the corresponding salt of such acid by metathesis.

It is widely used as **pharmaceutical intermediate** in the preparation of sodium ampicillin, crystalline salts of amoxicillin which are useful for preparing potent antibiotic solutions. It is also used as salifiable agent in semi-synthetic cephalosporin.

Methods of preparation of Sodium 2-ethylhexanoate in prior art and their limitations

It is important that Sodium 2-ethylhexanoate should be of a high purity and easy to handle for its effective utilization as a chemical and pharmaceutical intermediate. Various methods have been reported in the literature for preparation of such alkali metal salts but suffer from one limitation or the other which are described as below:

Organic anti-solvent method

The preparation of Sodium 2-ethylhexanoate has been accomplished by **simply titrating** an aqueous solution of the alkanolic acid with the appropriate alkali metal hydroxide and then adding to the aqueous solution a suitable **organic anti-solvent** in order to force the alkanolic acid salt out of solution and into a solid form.

Such process suffers from **various drawbacks** viz.

1. **High cost** due to the use of organic anti-solvents.
2. **Safety hazards** resulting from working with large volumes of such solvents.
3. **Poor quality** of the sodium 2-ethylhexanoate so formed which is impure, in the form of precipitated solid of undesirable crystalline characteristics, hard to dry and generally difficult to manage especially on a commercial scale due to its extreme hygroscopic properties.

Spray drying method

Patent No. US4142059 discloses a process for preparing Sodium 2-ethylhexanoate having improved purity and crystalline character, in addition to having improved handleability by **spray drying** method. In this patent, a solution of sodium hydroxide in water was stirred and cooled in an ice-water bath to 20° C. The 2-ethylhexanoic acid was added drop wise to the reaction mixture over a time period of thirty minutes. The whole reaction temperature was maintained at or below 70° C by cooling in an ice water bath.

After stirring for one hour, the aqueous solution obtained was of 63.5 % by weight of Sodium 2-ethylhexanoate and was atomized through a spray nozzle into a spray drying apparatus (Spray drying typically is a process which involves the rapid dehydration of moist particles which contain solids in either the soluble or insoluble form or both) having an inlet air temperature of about 118° to about 138° C and the

outlet temperature was recorded at about 107° C. Finally, the Sodium 2-ethylhexanoate was collected from the bottom of the spray dryer.

But the above patent suffers from **various drawbacks** viz.

1. **Special reaction conditions** such as high viscosity of the solution being atomized and operational temperature are required for achieving successful drying and formation of a crystalline product.
2. **High cost** of spray drying apparatus makes the method difficult to apply for routine processes especially when automated instrumentation is not available.

In contrast, the present invention has developed an easy, cost effective procedure which does not require any water bath to maintain the temperature of the reaction and costly apparatus for drying. A brief comparison of process of synthesis of Sodium 2-ethylhexanoate of the above patent in prior art and that of present invention is given below in **Table 1**.

Table1 Comparison between prior art patent and present invention

S.No	Steps used	Prior art patent (US4142059)	Present invention
1.	Synthesis of Sodium 2-ethylhexanoate	<p>The synthesis of Sodium 2-ethylhexanoate is done by adding 2-ethylhexanoic acid drop wise to the solution of sodium hydroxide.</p> <ul style="list-style-type: none"> • The whole reaction temperature was maintained at or below 70° C by cooling in an ice water bath. So it is more energy consuming. • The aqueous solution obtained was of 63.5% by weight of Sodium 2-ethylhexanoate. 	<p>The synthesis of Sodium 2-ethylhexanoate is done by adding solution of sodium hydroxide under constant stirring to 2-ethylhexanoic acid.</p> <ul style="list-style-type: none"> • No water bath is used to maintain the temperature of the reaction below 70° C. So it is less energy consuming. • The aqueous solution obtained was of 70% by weight of Sodium 2-ethyl hexanoate.
2.	Drying method/Equipment requirement	<p>Spray drying method used</p> <ul style="list-style-type: none"> • Skilled manpower required to operate the apparatus. • Very costly. 	<p>Pan drying method used</p> <ul style="list-style-type: none"> • Skilled manpower not required to supervise the reaction. • Highly cost effective.
3.	Special reaction conditions during drying of Sodium 2-ethylhexanoate	<p>It requires high viscosity of the solution being atomized and operational temperature during drying.</p>	<p>It is not required in the present process of the invention.</p>
4.	Moisture content	<p>Sodium 2-ethylhexanoate which is thus formed is having a moisture content of 0.5-5.0%.</p>	<p>Sodium 2-ethylhexanoate is having a moisture content as desired even below 2.0%.</p>

Other processes for preparing the sodium salt of 2-ethylhexanoic acid include **freeze drying** an aqueous solution of such salt. However, this method is commercially unfeasible since an aqueous solution containing about fifty percent by weight of Sodium 2-ethylhexanoate fails to remain frozen under normal freeze-drying conditions. **Simple tray-drying** of such aqueous solutions is commercially unfeasible

due to the extreme length of time required to effect dehydration and more importantly because such process fails to provide a product of acceptable crystalline quality.

Thus, in all the methods of synthesis reported in prior art, the major limitation was the requirement of special chemicals and equipments. Some processes in the prior art require a very long time for the synthesis of Sodium 2-ethylhexanoate which is commercially unfeasible and they could not be performed when automated instrumentation is not available. Even Sodium 2-ethylhexanoate formed by such processes is of very poor quality. The process of the present invention has been able to overcome all these limitations as it permits the synthesis of pure Sodium 2-ethylhexanoate at the commercial level by the use of easily available chemicals and equipments.

OBJECTS OF THE INVENTION

The invention has the following objects:

1. To disclose a novel process for synthesis of pure Sodium 2-ethylhexanoate which is less energy consuming, more cost effective, faster and easier than the processes existing in prior art.
2. To disclose a novel process for synthesis of pure Sodium 2-ethylhexanoate in which the equipment used for subsequent drying of aqueous solutions of Sodium 2-ethylhexanoate to get fine powdered form is readily available in most of the chemical and pharmaceutical industries.
3. To disclose a novel process for synthesis of pure Sodium 2-ethylhexanoate which does not require special reaction conditions during drying of aqueous solutions of Sodium 2-ethylhexanoate.

SUMMARY OF THE INVENTION

The invention relates to a novel process for synthesis of pure sodium 2-ethyl hexanoate using batch process which is less energy consuming, more cost effective, faster and easier. Here, subsequent drying of aqueous solutions of Sodium 2-ethylhexanoate is done in a pan to obtain purified sodium 2-ethylhexanoate in fine powdered form.

BRIEF DESCRIPTION OF THE DRAWINGS

NIL – No drawings attached.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to a novel process for synthesis of pure Sodium 2-ethyl hexanoate using batch process which can obviate the drawbacks of existing processes.

NOVELTY ASPECT OF THE INVENTION

The present invention describes a novel process for synthesis of pure Sodium 2-ethyl hexanoate which consume less energy, easy, faster and more cost-effective to obtain concentrated form of aqueous solutions of Sodium 2-ethylhexanoate.

INVENTIVE STEP

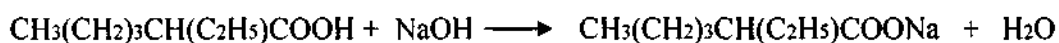
The inventive step of the present invention lies in obtaining concentrated form of aqueous solutions of Sodium 2-ethylhexanoate at the very first stage of production cycle wherein the heat generated during the reaction itself is used in dehydrating the aqueous solution of salt, thus significantly reducing energy and equipment requirements, drastically reducing the cost of production. Subsequent drying of this concentrated form is done in a pan to obtain purified Sodium 2-ethylhexanoate in fine powdered form which meets all the quality parameters of final product.

INDUSTRIAL APPLICATION

The present method is simple, fast, cost effective and efficient in obtaining pure Sodium 2-ethylhexanoate salt. The chemicals and equipments required for the synthesis of Sodium 2-ethylhexanoate are easily available commercially at low cost. The present process of invention does not require high energy consumption machinery like spray dryer and skilled manpower to supervise the reaction. Owing to all the above advantages, the present invention has a good industrial application for the chemical and pharmaceutical manufacturers as it allows the commercial scale production of Sodium 2-ethylhexanoate salt at the economical rate.

NOVEL PROCESS FOR THE SYNTHESIS OF PURE SODIUM 2-ETHYLHEXANOATE

In this batch processing method 950 kg of ethylhexanoic acid (Octoic acid) is charged in the reactor and aqueous solution of sodium hydroxide (caustic solution) is added continuously to the reactor under constant stirring till the desired pH of 7.2-7.6 is achieved. Here, caustic solution is made by dissolving 265 kg of sodium hydroxide in 275-300 liters of water and almost all solution is consumed during the reaction to achieve desired pH. The reaction is as follows:



2 EthylHexanoic Acid Sodium Hydroxide Sodium 2 Ethyl Hexanoate water

Since the reaction between 2-ethylhexanoic acid and sodium hydroxide is exothermic in nature, most of the water content is evaporated by the use of heat generated during the reaction. The whole process occurs at atmospheric or reduced pressure and is completed in time duration of about 6-8 hrs.

When the mixture becomes concentrated, it is unloaded and transferred to open pan for drying with stirring in between, using suitable heating media like steam, hot oil etc. The pH of solution, moisture content and clarity of the product solution is monitored all the time during the process of pan drying. Clarity of solution is 10.0% w/v in water and ethyl acetate in the present process of invention. As acidic pH is hazardous during pan drying so continuous monitoring is required in between the process. When moisture content reaches below 2.0 % (about 1.5%), the material is unloaded, allowed to cool and results in formation of lumps of sodium 2-ethyl hexanoate salt. It is then subjected to operation of multi milling where it is grinded to obtain fine powdered form. Finally, the powdered material undergoes quality testing and yield is found to be about 98% and this final product is packed in the containers and sealed. .

In the above detailed description of the invention, method of preparation of a pure Sodium 2-ethylhexanoate salt has been disclosed. It is to be understood that this invention is not limited to particular embodiments described as such and these may of course vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting, since the scope of the present invention will be limited only by the appended claims.