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CONTINUOUS PROCESS FOR THE MANUFACTURE OF
SODIUM C₄-C₈ALKOXIDE

Sodium C₄-C₈alkoxides are important, versatile chemicals useful in a wide variety of synthetic reactions and manufacturing procedures wherein a strong organic base is desired. Although the formation of a sodium C₄-C₈alkoxide by the reaction of sodium metal and a C₄-C₈ alkanol is well-known, in actual practice, the reaction on a large scale may be hazardous and costly. In many
5 processes, the addition of a catalyst is required or energy-intensive reaction conditions, such as high temperature (>160°C) and high pressure, are required.

Therefore, it is an object of this invention to provide a safe, efficient process for the production of
10 sodium C₄-C₈alkoxide.

It is another object of this invention to provide a continuous, integrated source of sodium C₄-C₈alkoxide, suitable for use in a manufacturing process wherein a strong organic base is required.

15 It is a further object of this invention to provide a ready and convenient source of essentially pure crystalline sodium C₄-C₈alkoxide suitable for storage and shipping.

It is a feature of this invention that essentially
20 quantitative conversion of the C₄-C₈alkanol is obtained.

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It is an advantage of this invention that by continuous recycle and essentially complete conversion of the reactants, the process is effective with little or no negative environmental impact.

5 Further objects and features of the invention will become apparent by the detailed description set forth hereinbelow.

10 The present invention provides a safe, efficient and essentially quantitative process for the manufacture of sodium C₄-C₈alkoxide which comprises treating a stirred dispersion of sodium metal in a solvent optionally under an inert atmosphere with a less than stoichiometric
15 amount of a C₄-C₈alkanol at a temperature of about 110°-140°C to form a two phase mixture and separating the top phase to obtain the product sodium C₄-C₈alkoxide as a solvent solution, optionally continuously recycling the remaining phase mixture.

20 The sodium C₄-C₈alkoxide solution, thus obtained, may be used as a manufacturing intermediate and directly integrated into an existing manufacturing process stream or, alternatively, the solution may be cooled and filtered to give a pure crystalline sodium C₄-C₈alkoxide
25 product suitable for storage and shipping.

The production and handling of sodium C₄-C₈alkoxides are frequently costly and hazardous, particularly sodium
30 tertiary-alkoxides, such as sodium t-butoxide. Even so, such strong organic bases are commonly used in synthetic reactions and manufacturing processes.

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It has now been found that sodium C₄-C₈alkoxide may be prepared safely and effectively on a large manufacturing scale with essentially quantitative conversion of the C₄-C₈ alkanol and optionally the continuous recycle of the

5 unreacted sodium metal. Accordingly, sodium metal is dispersed in a solvent, preferably an aromatic hydrocarbon or mixture thereof having a boiling point greater than 100°C, optionally under an inert atmosphere, at about 100° to 140°C, preferably about 120° to 130°C. A less than

10 stoichiometric amount of a C₄-C₈alkanol, preferably about 0.1 to 0.9 molar equivalents, more preferably about 0.4 to 0.6 molar equivalents, alone or in combination with a solvent, preferably an aromatic hydrocarbon or mixture thereof, is added to the heated dispersion with rapid

15 stirring to form a two phase reaction mixture. Said reaction mixture is held without stirring at about 100° to 140°C, preferably at about 120° to 130°C, until the phase separation is complete. The top phase is removed by decantation to give a solvent solution of the product

20 sodium C₄-C₈alkoxide. Optionally, the remaining phase mixture may be cooled to room temperature, treated with additional sodium metal and solvent, heated to about 100° to 140°, preferably 120° to 130°C, optionally under an inert atmosphere with rapid stirring to form a dispersion

25 and treated with a less than stoichiometric amount of a C₄-C₈ alkanol as described hereinabove to produce a solvent solution of the product sodium C₄-C₈alkoxide and a phase mixture containing unreacted sodium metal. Said solvent solution of sodium C₄-C₈alkoxide may be removed by

30 decantation and said phase mixture containing unreacted sodium may be continuously recycled in the above manner. The inventive process is illustrated in Flow Diagram I

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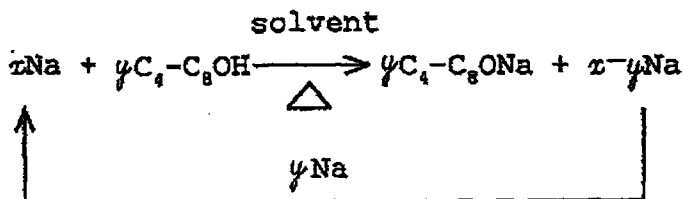
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wherein χ and ψ are molar equivalents of Na and C_4-C_8 alcohol, respectively, and $\psi < \chi$.

Flow Diagram I

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Since ψ is always less than χ , i.e. less than a stoichiometric amount, the starting C_4-C_8 alkanol is essentially quantitatively converted to the product sodium C_4-C_8 alkoxide. Further, since the unreacted sodium is continuously recycled, the inventive process is essentially waste free and, therefore, highly environmentally desirable. Moreover, the inventive process allows for relatively mild reaction conditions, atmospheric pressure, lower reaction temperatures and shorter reaction times which result in high throughput and high productivity without the loss of safety or the burden of hazardous or toxic waste.

Among solvents suitable for use in the process of the invention are aromatic hydrocarbons or mixtures thereof having a boiling point greater than about 100°C, such as xylene, toluene, xylidene, cumene or the like, either alone or in combination.

All C_4-C_8 alkanols are suitable for use in the process of the invention, particularly branched alkanols such as *t*-butanol or *t*-amyl alcohol, more particularly *t*-butanol.

Although the inventive process may be carried out in the presence of air, the introduction of an inert atmosphere

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such as nitrogen, helium, argon or the like, preferably nitrogen, greatly enhances the safe handling of the hydrogen gas which is produced during the reaction.

In one embodiment of the invention, the product
5 sodium C₄-C₈alkoxide solvent solution may be integrated directly into an existing manufacturing process stream, such that a continuous production of a solvent solution of a strong organic base is supplied to a manufacturing scale reaction such as a base condensation or Knoevenagel
10 reaction.

In another embodiment of the invention, the product sodium C₄-C₈alkoxide solvent solution may be cooled and filtered to give an essentially pure crystalline sodium C₄-C₈alkoxide product suitable for storage and shipping
15 and as a resource for a high quality, reagent grade, organic base.

For a more clear understanding of the invention, specific examples are set forth below. These examples are merely illustrative and are not to be understood as
20 limiting the scope and underlying principles of the invention in any way. Indeed, various modifications of the invention, in addition to those shown and described herein, will become apparent to those skilled in the art. Such modifications are also intended to fall within the
25 scope of the appended claims.

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EXAMPLE 1

Continuous Production Of Sodium t-Butoxide As A 17%
wt/wt Solution

5 A mixture of sodium metal (87.6 g, 3.81 mole) in
752g of CYCLOSOL®53, a solvent consisting of a mixture of
aromatic hydrocarbons manufactured by Shell Oil Company,
Houston, Texas, in a 1.5L double wall reactor with four
baffles and a double 4-bladed skew propeller is blanketed
10 with nitrogen and heated to 125°C. At 125°-130°C, the
mixture is stirred rapidly to disperse the molten sodium
metal and 5g of a 1:1 mixture of t-butanol and
CYCLOSOL®53 (2.5g, 0.03 mole t-butanol) is added to
initiate the reaction. The remaining t-butanol is added
15 over a 3 hour period as a 1:1 mixture with CYCLOSOL®53
(277.3g, 1.87 mole t-butanol) at 130°C. The resultant
mixture is held at 130°C with no stirring for 0.25 hours
to separate the phases. A portion of the top phase
(670.9g) is separated by decantation to give a 17% wt/wt
20 solution of sodium t-butoxide in CYCLOSOL®53. The
remaining phase mixture consisting of a sodium t-butoxide
solution in CYCLOSOL®53 (415.7g) and molten sodium metal
(44g, 1.91 mole) is cooled to room temperature.

This cooled phase mixture is treated with a second
25 mixture of fresh sodium metal (26.3g, 1.14 mole) and 452g of
CYCLOSOL®53, blanketed with nitrogen and heated to 125°C. At
125-130°C, the reaction mixture is stirred rapidly to disperse
the molten sodium metal. The heated, stirred reaction
mixture is treated with 169.6g of a 1:1 mixture of t-butanol
30 and CYCLOSOL®53 (1.14 mole t-butanol) over a 1.5 hour period
at 125°-130°C. The resultant two phase mixture is held with
no stirring at 130°C for 0.25 hours. A 640.2g portion of the
top phase is separated by decantation to give a 17% wt/wt

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solution of sodium t-butoxide (1.13 mole sodium t-butoxide) in CYCLOSOL®53. The remaining phase mixture of 411.7g of a solution of sodium t-butoxide in CYCLOSOL®53 and 44g of molten sodium (1.91 mole) is cooled to room temperature.

- 5 The above procedure is then repeated to give a continuous production of sodium t-butoxide as a 17% wt/wt solution in CYCLOSOL®53.

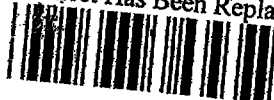
EXAMPLE 2

10 Continuous Production Of Sodium t-Butoxide As A Solid

- A mixture of sodium metal (77.3kg, 3.36 kmole) in 668kg of CYCLOSOL®53 in a reactor fitted with baffles and a propeller is blanketed with nitrogen and heated to 120°-
15 130°C. The heated mixture is rapidly stirred to finely disperse the molten sodium metal and a 1:1 mixture of t-butanol and CYCLOSOL®53 (3.9kg, 0.026 kmole of t-butanol) is added to initiate reaction. The remaining t-butanol is added as a 1:1 mixture with CYCLOSOL®53 (245.1kg, 1.65
20 kmole of t-butanol) at 130°C over a 1.5 hour period. The resultant two phase reaction mixture is held at 130°C with no stirring for about 1 hour. A portion of the top phase (570kg) is removed and cooled to about 20°C. The resultant white crystalline precipitate is filtered. The
25 filtercake is washed with about 10L of isohexane and dried at 30°C/400mBar to give the title product as a white solid, 96kg (1.0 kmole), 99-100% purity.

- The mother liquor and isohexane washings containing sodium t-butoxide (0.65 kmole) in CYCLOSOL®53 are combined
30 recycled to the original reactor containing the remaining reaction phase mixture and heated to 135°C to remove the isohexane. The resultant remaining reaction phase mixture is then included in a subsequent 1.0 kmolar reaction process as described hereinabove.

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The invention also provides a process for the
5 preparation of an organic compound by reaction of a
nucleophile with a substrate, which comprises:

- (a) preparing a sodium C₄-C₈ alkoxide by a process of the
invention;
- (b) converting an organic compound into a sodium salt
10 thereof by reaction with the sodium C₄-C₈ alkoxide; and
- (c) using the sodium salt as nucleophile for reaction with
the substrate.

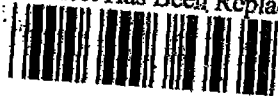
The above process is based upon the utility of the
15 sodium C₄-C₈ alkoxides for promoting aliphatic nucleophilic
substitution reactions. For example, compounds containing
active methylene groups can be converted into their sodium
salts for reaction with alkyl halides for the purpose of
alkylation. Another example is where an N-unsubstituted
20 sulfonamide is converted into its sodium salt for reaction
with alkyl halides for the purpose of N-alkylation.

The invention also provides a process for the preparation
of a condensation product, which comprises

- 25 (a) preparing a sodium C₄-C₈ alkoxide by a process of the
invention; and
- (b) .subjecting one or more condensable organic compounds
to base-catalysed condensation in the presence of, as
catalyst, sodium C₄-C₈ alkoxide prepared according to step
30 (a).

Condensation reactions for this purpose include, for
example, the Michael reaction, Cannizzaro reaction and
aldol condensations. One example is the process disclosed
35 in EP 0 329 256 B.

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CLAIMS:

1. A process for the manufacture of sodium C₄-C₈ alkoxide which comprises treating a stirred dispersion of sodium metal in a solvent optionally under an inert atmosphere with a less than stoichiometric amount of C₄-C₈ alkanol at a temperature of about 100° to 140°C to form a mixture comprising a first phase and a second phase, wherein the first phase comprises a solution of the sodium C₄-C₈ alkoxide in the solvent and the second phase comprises the sodium metal, separating the first phase to obtain the product sodium C₄-C₈ alkoxide as the solution, and optionally continuously recycling the remaining mixture.

2. The process according to claim 1 wherein the solvent is an aromatic hydrocarbon or a mixture of aromatic hydrocarbons.

3. The process according to claim 1 or 2 wherein the process is carried out under inert atmosphere.

4. The process according to claim 3 wherein the inert atmosphere is nitrogen.

5. The process according to any of claims 1 to 4 wherein the amount of C₄-C₈ alkanol is about 0.10 to 0.90 molar equivalents.

6. The process according to claim 5 wherein the amount of C₄-C₈ alkanol is about 0.4 to 0.6 molar.

7. The process according to any one of claims 1 to 6 wherein the remaining the remaining phase mixture is continuously recycled.

8. The process according to any one of claims 1 to 7 wherein the temperature is about 120° to 130° C.

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9. The process according to any one of claims 1 to 8 wherein the C₄-C₈ alkanol is a tertiary C₄-C₈ alkanol.

10. The process according to claim 9 wherein the tertiary C₄-C₈ alkanol is t-butanol or t-amyl alcohol.

11. The process according to claim 10 wherein the tertiary C₄-C₈ alkanol is t-butanol.

12. The process according to claim 6 wherein the C₄-C₈ alkanol is t-butanol and the temperature is 120° - 130° C.

13. The process according to any one of claims 1 to 12 wherein the first phase is cooled after separation and filtered to yield the sodium C₄-C₈ alkoxide as a solid.

14. The process according to claim 1 whenever carried out substantially as hereinbefore described with reference to Example 1 or 2.

15. Sodium C₄-C₈ alkoxide whenever prepared by a process according to any one of claims 1 to 14.

16. A process for the preparation of an organic compound by reaction of a nucleophile with a substrate, which comprises:

(a) preparing a sodium C₄-C₈ alkoxide by a process as claimed in any one of claims 1 to 15;

(b) converting an organic compound into a sodium salt thereof by reaction with sodium C₄-C₈ alkoxide;

(c) using the sodium salt as nucleophile for reaction with the substrate.

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17. A process of preparation of a condensation product, which comprises:

(a) preparing a sodium C₄-C₈ alkoxide by a process as claimed in any one of claims 1 to 15; and

(b) subjecting one or more condensable organic compounds to base-catalysed condensation in the presence of, as catalyst, sodium C₄-C₈ alkoxide prepared according to step (a).

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