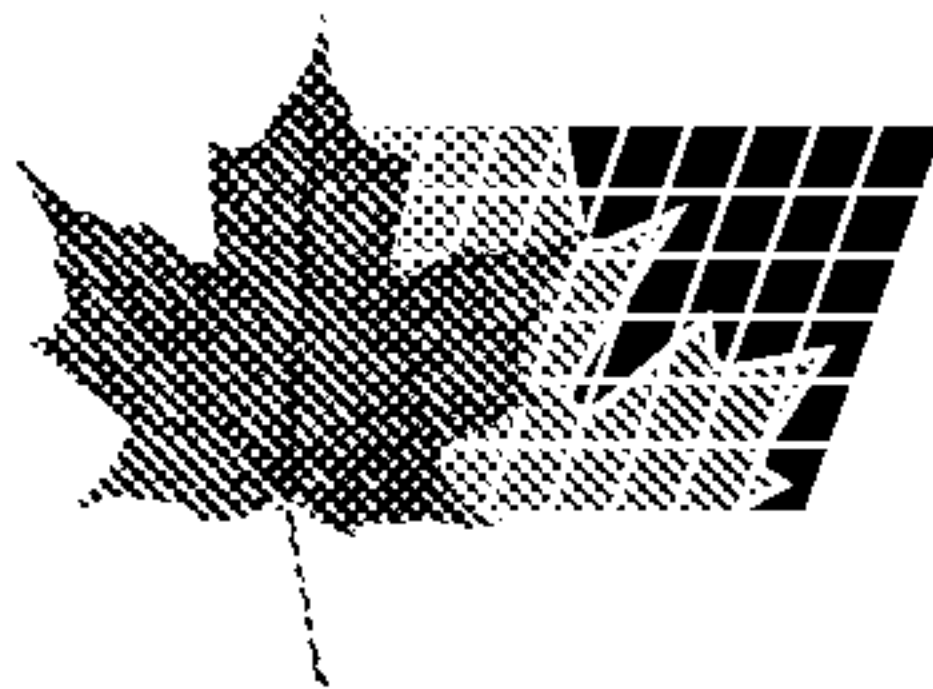




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(54) **PROCEDE D'OBTENTION DE 3-AMINOCROTONONITRILE**

(54) **PROCESS FOR THE PRODUCTION OF 3-  
AMINOCROTONONITRILE**

(57) A process is disclosed for the production of 3-aminocrotononitrile by dimerization of acetonitrile in which acetonitriles is deprotonated with sodium amide as a strong base in the presence of liquid ammonia.

ABSTRACT OF THE DISCLOSURE

A process is disclosed for the production of 3-aminocrotononitrile by dimerization of acetonitrile in which acetonitriles is deprotonated with sodium amide as a strong base in the presence of liquid ammonia.

This invention relates to a new process for the production of 3-aminocrotononitrile by dimerization of acetonitrile.

3-Aminocrotononitrile is an intermediate product with a very wide spectrum of use. Thus, it is used, e.g., for the production of pharmaceutical agents (Chemical Abstracts, 85, 177262) pesticides, (Chemical Abstracts, 79, 53185b) and azo dyes (Chemical Abstracts, 80, 122383).

Numerous processes are known for producing 3-aminocrotononitrile by dimerization of acetonitrile in the presence of strong bases. However, such dimerization is problematic in that acetonitrile, when mixed with a base such as an amide ion, can react in various ways. Namely, if the nitrile group is attacked, undesirable acetamidine is formed with the amide ion. Only the deprotonation of the acetonitrile to carbanion forms the prerequisite for the production of the desired 3-aminocrotononitrile.

Thus, according to Takeda et al., J. Pharm. Chem. Soc., Japan, 75, (1955), pages 957 to 959, a mixture of 3-aminocrotononitrile and acetamidine resulted after the reaction of acetonitrile with sodium amide at 100°C for 3 hours.

Subsequently, an attempt was made to foster the carbanion formation by specific performance of the reaction, i.e., by the use of sterically-demanding, strong bases.

Building upon the studies of Ziegler et al., Justus Liebigs Annalen, 504, (1933), 115, in which acetonitrile with lithium diethylamide as a base was reacted specifically to produce 3-aminocrotononitrile (iminonitrile) with 86 percent yield. Krueger, J. Organometal. Chem., 9, (1967), pages 125 to 134, synthesized 3-aminocrotononitrile with sodium-bis-trimethylsilylamide with 90 percent yield. Except for the very good yields, the above-mentioned syntheses have the drawback of high cost because the sterically-demanding bases had to be produced, in part, in a complicated and particularly expensive manner, thus constituting an economic obstacle to the application of

these processes in large-scale operations, as demonstrated through the comparison examples which follow.

It is also known from Swiss Patent No. 415,603 to condense acetonitrile to 3-aminocrotononitrile using sodium in an aliphatic hydrocarbon as solvent at 70° to 180°C with a yield of 90 percent. This dimerization has the drawback that, because of the reaction mechanism, 2 moles of sodium are required to react with 3 moles of acetonitrile instead of 1 mol of sodium or base to 2 moles of acetonitrile. While this process constitutes an operating method for producing 3-aminocrotononitrile it is uneconomical and also unecological due to the accumulation of sodium cyanide.

The main object of the invention is to provide a process for the production of 3-aminocrotononitrile ecologically and economically on a large scale which reduces or eliminates the drawbacks of the prior art.

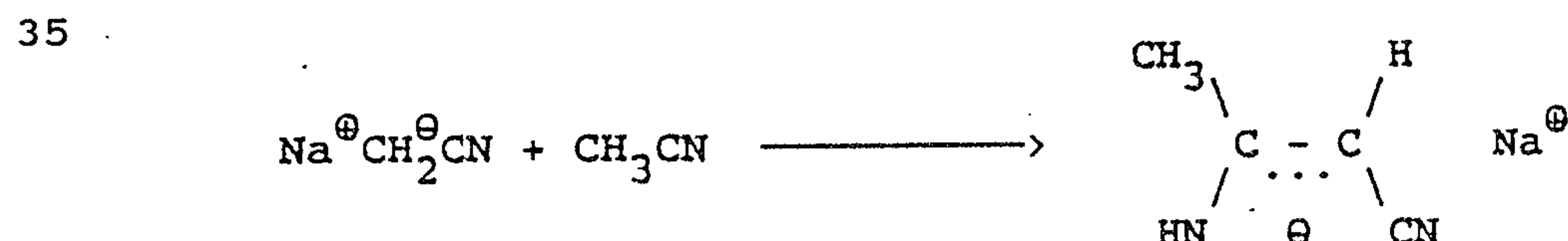
According to the invention there is provided a process for the production of 3-aminocrotononitrile by dimerization of acetonitrile, comprising the reaction steps of deprotonating acetonitrile with sodium amide as a strong base in the presence of liquid ammonia to effect formation of the sodium salt of 3-aminocrotononitrile and hydrolysing the salt.

The dimerization of acetonitrile, according to the process of the invention, takes place according to the following mechanism:

(a) deprotonation of acetonitrile in the presence of a strong base according to the formula:

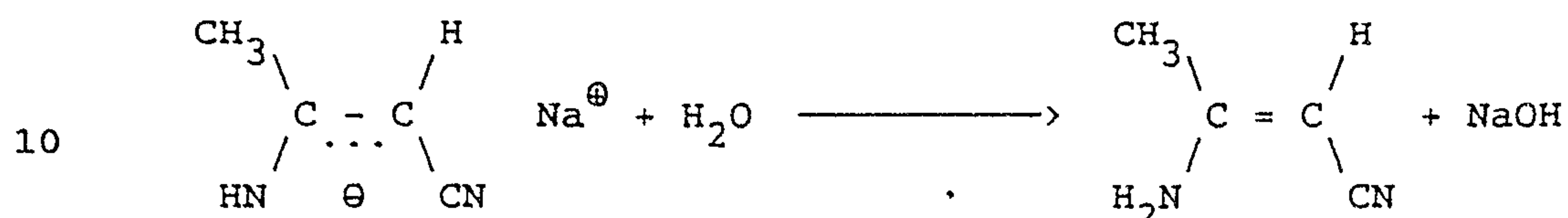


(b) formation of the sodium salt of 3-aminocrotononitrile by reaction of the acetonitrile carbanion with excess acetonitrile according to the formula:



and,

(c) hydrolysis of the sodium salt of 3-aminocrotononitrile with water according to the formula:



According to the invention, the deprotonation of acetonitrile with sodium amide as a strong base is performed in the presence of liquid ammonia. The sodium amide may be produced in situ suitably ahead of time and in a known way [F.W. Bergstroem and W.C. Frenelius, Chem. Rev., 12, (1933), 45 ff.] by the catalytic reaction of sodium with liquid ammonia. The deprotonation suitably takes place in the temperature range at which the ammonia is present at standard pressure in the liquid aggregation state, i.e. between  $-32^{\circ}$  and  $-75^{\circ}\text{C}$ . The deprotonation preferably takes place at a temperature between  $-32^{\circ}$  to  $-35^{\circ}\text{C}$ . The ammonia that is being freed in the deprotonation step and the excess ammonia used as solvent are suitably recycled and used for the production of the sodium amide.

The process according to the invention is advantageously performed such that the acetonitrile is added to the sodium amide produced in situ, in the presence of an excess of liquid ammonia.

By employing such process, it is possible to maintain a molar ratio of acetonitrile to sodium amide of 2 to 1.

The acetonitrile already in the inert solvent (preferably toluene) and necessary for the subsequent salt formation is suitably added to the sodium amide solution.

Instead of toluene, other aromatic hydrocarbons, such as xylene or benzene, ethers, such as tetrahydrofuran or dimethoxyethane, or amines, such as aliphatic di- or trialkylamines, can be used as the inert solvent.

5           The deprotonation takes place quickly, so suitably directly after the addition step the reaction mixture can be heated to the temperature necessary for the formation of the sodium salt of 3-aminocrotononitrile, namely a temperature in the range of  $-5^{\circ}$  to  $+35^{\circ}\text{C}$ , preferably to room temperature.

10           In this case, the volatilizing ammonia is collected and recycled.

          The salt formation is completed usually after about 0.5 to 2 hours. Then, the sodium salt of the 3-aminocrotononitrile can be hydrolysed by slow feeding of  
15   water to the reaction mixture in a known way, e.g. according to Swiss Patent No. 415,603, and converted to 3-aminocrotononitrile.

          The 3-aminocrotononitrile can be suitably obtained from the reaction mixture in yields of over 90 percent and  
20   purities of over 99.5 percent in a manner known to one skilled in the art, and preferably by distillation.

          The following Examples illustrate the process according to the invention:

#### Example 1

25           In a double-jacketed stirrer flushed with dry nitrogen, sodium amide was produced with 250 ml of liquid ammonia under catalysis of 0.2 g of iron(III) nitrate from 13.8 g of sodium (0.6 mol). A solution of 49.3 g of acetonitrile (1.2 mol) in 200 ml of toluene was instilled at  
30   the temperature of the liquid ammonia ( $-33^{\circ}$ ) over 25 minutes. When the addition was completed, excess ammonia was evaporated. After the suspension had reached a temperature of  $20^{\circ}\text{C}$  by heating, it was allowed to react for a further hour at this temperature. The reaction mixture was then  
35   subjected to a slow hydrolysis by instilling 75 ml of water. After a further 15 minutes of reaction with stirring, the mixture was transferred into a separating funnel for phase separation, and three phases were formed. After separation

of the lower aqueous phase, which was extracted for further purification twice, each with 25 ml of solvent, the combined organic phases were first freed from toluene on the rotary evaporator in a water jet vacuum and then subjected to vacuum distillation. 99.7 to 99.8 percent pure 3-aminocrotononitrile was distilled over in a vacuum of 20 mbars and at a temperature of 134° to 140°C. The yield was 46.4 g (94.1 percent). The solvent toluene and the ammonia were recycled into the process.

10                    Examples 2 to 7

In these Examples, other inert solvents were used instead of toluene, but the amounts of the other feedstocks were kept constant.

| 15 | <u>Ex.</u> | <u>Inert Solvent</u>               | <u>Yield</u><br><u>%</u> | <u>Purity</u><br><u>%</u> |
|----|------------|------------------------------------|--------------------------|---------------------------|
|    | 2          | xylene, 225 ml<br>(isomer mixture) | 87.0                     | 99.6                      |
| 20 | 3          | benzene, 225 ml                    | 85.8                     | 99.7                      |
|    | 4          | dimethoxyethane<br>(1, 2), 200 ml  | 78.3                     | 99.6                      |
| 25 | 5          | tetrahydrofuran<br>200 ml          | 87.6                     | 99.5                      |
|    | 6          | diethylamine, 225 ml               | 88.2                     | 99.5                      |
| 30 | 7          | triethylamine, 225 ml              | 88.2                     | 99.4                      |

In all other aspects, the embodiments of Examples 2 to 7 correspond to those as described in Example 1.

Comparison Example 1

35                    In a thermostatically controllable double-jacketed stirrer, 24.3 g of diisopropylamine was dissolved in 100 ml of absolute tetrahydrofuran and 150 ml of a 0.16 molar solution of n-butyllithium in hexane was instilled with stirring at a maximum temperature of 20°C. After the  
40 reaction was completed, the reaction mixture was added to a solution of 19.7 g (0.48 mol) of acetonitrile in 60 ml of tetrahydrofuran at a maximum temperature of -20°C. After completion of the addition, the mixture was allowed to react

for a further 30 minutes at this temperature with stirring and was heated over 1 hour to 20°C, and a white mass was precipitated onto the vessel walls. After standing overnight, the reaction mixture was hydrolysed at a temperature of 5° to 7°C with a solution of 14.5 g of acetic acid in 50 ml of water. After phase separation, the aqueous phase was extracted twice further with 25 ml of ether each time. The combined organic phases were freed of the solvent and of amine by distillation in a water jet vacuum. Distillation under the same conditions as in Example 1 produced 17.0 g of 3-aminocrotononitrile (86.3 percent yield) with a purity of 98.9 percent.

#### Comparison Examples 2 to 4

As was shown in Examples 2 to 4, it was possible to expand the process to other secondary and silylated amines, which were used as auxiliary base in lithiated form. As a metallization reagent, a solution of n-butyllithium (0.16 mol in hexane) equivalent to the amount of amine was used.

| Comp.<br>Ex. | Secondary<br>Amine                                  | Amount of<br>Solvent (ml)        | Reaction**<br>Temperature<br>(°C) | Yield/<br>Purity<br>(%)       |
|--------------|-----------------------------------------------------|----------------------------------|-----------------------------------|-------------------------------|
| 2            | N-methyl-<br>aniline<br>0.24 mol                    | tetrahydro-<br>furan<br>(160 ml) | -24°                              | 60/92.6<br>(crude<br>product) |
| 3            | diethyl-<br>amine<br>0.3 mol                        | diethyl<br>ether<br>(160 ml)     | -23°                              | 56.9/99.0                     |
| 4            | H-<br>N(SiMe <sub>3</sub> ) <sub>2</sub><br>0.6 mol | tetrahydro-<br>furan<br>75 ml    | 0°                                | 90.5/99.6                     |

Note:

\*\* temperature for deprotonation

#### Comparison Example 5

3.0 g (0.13 mol) of sodium metal in 115.5 g of hexamethyldisilazane (excess) was emulsified by a dispersing stirrer at a temperature of 124°C. Under the catalysis of 0.5 g of iron(III) stearate, the sodium salt was formed from hexamethyldisilazane over 5 hours and 30 minutes. Acetonitrile (10.7 g = 0.26 mol) was instilled at a

temperature of 80° to 92°C and the reaction mixture was cooled to 20°C, then filtered. The filter cake was washed with 30 ml of tert-butyl methyl ether mixed with 100 ml of water. After phase separation, the aqueous phase was  
5 extracted twice with 50 ml of ether and once further with 25 ml of ether. After the solvent was removed on the rotary evaporator and the residue distilled under vacuum, 5.7 g of 99.5 percent pure 3-aminocrotononitrile with a yield of 53.3 percent was obtained. From the filtrates,  
10 hexamethyldisilazane with a yield of up to 95 percent was recycled by fractional distillation.

THE EMBODIMENTS OF THE INVENTION IN WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A process for the production of 3-aminocrotononitrile by dimerization of acetonitrile, comprising the reaction steps of deprotonating acetonitrile with sodium amide as a strong base in the presence of liquid ammonia to effect formation of the sodium salt of 3-aminocrotononitrile and hydrolyzing the salt.

2. A process according to claim 1, wherein the deprotonation takes place at standard pressure and at a temperature of the liquid ammonia of between  $-32^{\circ}$  and  $-75^{\circ}\text{C}$ .

3. A process according to claim 1, wherein a molar ratio of acetonitrile to sodium amide of 2 to 1 is maintained for the dimerization.

4. A process according to claim 1, 2 or 3, wherein the formation of the salt of 3-aminocrotononitrile is conducted between  $-5^{\circ}$  and  $+35^{\circ}\text{C}$  in the presence of an inert solvent.

5. A process according to claim 1, 2 or 3, wherein the formation of the salt of 3-aminocrotononitrile is conducted between  $-5^{\circ}$  and  $+35^{\circ}\text{C}$  in the presence of toluene as the inert solvent.

6. A process according to claim 1, 2 or 3, wherein the hydrolysis is conducted by adding water.

7. A process according to claim 1, 2 or 3, wherein the sodium amide is produced in situ before the dimerization by catalytic reaction of sodium with liquid ammonia.

8. A process according to claim 1, 2 or 3, wherein the reaction steps comprising the dimerization are

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performed without isolation between the intermediate stages.