ISSN 1070-4272, Russian Journal of Applied Chemistry, 2013, Vol. 86, No. 6, pp. 845−847. © Pleiades Publishing, Ltd., 2013.
Original Russian Text © A.J. Markosyan, G.A. Baghdasaryan, G.P. Hovhannisyan, H.S. Attaryan, G.V. Hasratyan, 2013, published in Zhurnal Prikladnoi Khimii, 2013, Vol. 86, No. 6, pp. 902−905.

ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

Waste-Free Technology for *N*-Methylmorpholine Synthesis

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Received November 19, 2012

DOI: 10.1134/S1070427213060104

Morpholine and its derivatives, (*N*-formylmorpholine, *N*-acetylmorpholine, *N*-methylmorpholine-*N*-oxide, etc.) due to their high solvency are widely used for extracting aromatic hydrocarbons [1] and also as solvents of natural polymers. Thus, in manufacturing cellulosic fibers *N*-oxides of tertiary amines, often *N*-methylmorpholine-*N*-oxide, are widely used as solvents for cellulose [2, 3].

Besides of cellulose *N*-methylmorpholine-*N*-oxide dissolves fibroin, natural polymer more than by 80% consisting of simplest amino acids: glycine, alanine, and serine [4]. Fibroin is the main component of natural fibers such as a web and natural silk.

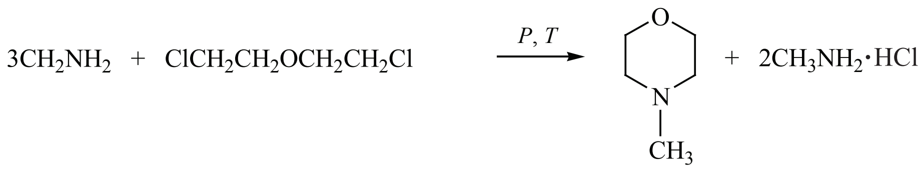
Application of *N*-methylmorpholine-*N*-oxide is enlarged both as solvent and reagent in fine organic synthesis [5].

In the study the sunthesis of *N*-methylmorpholine, the basic starting material for the synthesis of *N*-methylmorpholine-*N*-oxide was descibed.

In preparative practice *N*-methylmorpholine is generally prepared by *N*-methylation of morpholine by classical methylating agents, methyl halide (usually methyl iodide), dimethyl sulfate, a mixture of formic acid with formalin, etc. [6–8].

These reagents are usually quite expensive, and some of them are very toxic and aggressive (dimethyl sulfate, formic acid).

The way of the direct synthesis of *N*-methylmorpholine (**IV**) from methylamine (**I**) and 2,2'-dichlorodiethyl ether (**II**) was suggested according the scheme [9]:



By this way the reaction is carried out at 100–200°C for 5 hours. Hardware design of the process requires an autoclave that increases the technology cost and makes it unsafe. Furthermore, recovery of methylamine from the resulting hydrochloride should be carried out that implies the use of additional reaction equipment.

We have modified the process of preparation of *N*-methylmorpholine (**IV**) from methylamine (**I**) and 2,2'-dichlorodiethyl ether (**II**). For simplification the synthesis was carried out in a dilute aqueous solution of methylamine at 90–95°C in the presence of sodium hydroxide solution with simultaneous removal of the

Results of alkylation of methylamine by 2,2'-dichloroethyl ether. Alkylation time 4 h

Mole ratio of 2,2'-dichlorodiethyl ether : methylamine (25% aqueous solution)	V_{H_2O}, ml	Amount of NaOH, g	Output of *N*-methylmorpholine, %	Output of byproducts, %		
				V	**VI**	**VII**
1 : 1 (125)[a]	–	100	25.0	12	7	20
1 : 1 (125)	300	100	50.0	3	4	10
1 : 3 (360)	400	100	70.0	–	–	–
1 : 4 (500)	400	100	75.0	–	–	–
1 : 4 (500)	500	100	80.0	–	–	–

[a] In parentheses the amount of methylamine was given in mL.

end product. An output of *N*-methylmorpholine reaches 75–80%. The method does not require the use of elevated pressure: methylamine is recovered directly from the hydrochloride in the synthesis: it is directed to the absorption and returned in the process.

Process for producing *N*-methylmorpholine is based on the monoalkylation of methylamine by 2,2'-dichlorodiethyl ether, followed by intramolecular dehydrohalogenation of resulting monoalkylated product **III**.

Since there is high probability of formation of other byproducts in the presence of alkali [10], it is very important to establish conditions, under which only the monoalkylation product is formed (Scheme 1).

In the case of an equimolar ratio of methylamine (**I**) and 2,2'-dichlorodiethyl ether (**II**) methylamine is quickly removed from the reaction medium, whereby an excess of 2,2'-dichlorodiethyl ether (**II**) subsequently undergoes a series of transformations to form byproducts **V–VII** (Scheme 2).

In three fold dilution of the reaction medium without changing the molar ratio of methylamine (**I**) and 2,2'-dichlorodiethyl ether (**II**) the output of *N*-methylmorpholine (**IV**) rises by 2 times (see the table).

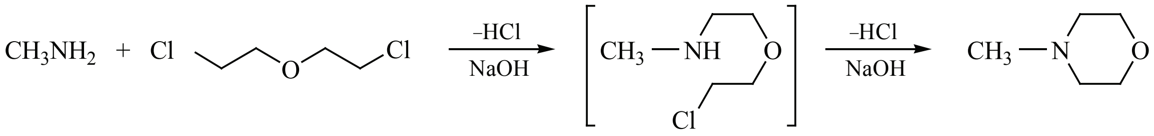
Positive results were obtained upon dilution of the reaction medium to 4–5 times at the molar ratio of 2,2'-dichlorodiethyl ether (**II**) and methylamine (**I**) 1 : 4.

Thus, dilution of the reaction medium increases the output of *N*-methylmorpholine (**IV**) (75–80%) as well as suppresses the formation of byproducts.

Technological scheme of *N*-methylmorpholine (**IV**) production is shown in the figure.

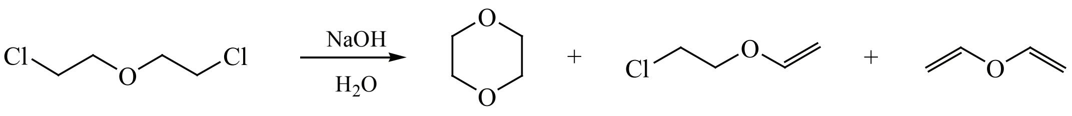
In the lower part of the reactor *1* a calculated amount of water from the measuring device *2*, 2,2'-dichlorodiethyl ether (**II**) from the measuring device *3*, and methylamine (**I**) from the measuring device *4* were charged. To maintain the desired temperature in the jacket of the reactor bottoms steam was fed with bringing the water in the bottom to boiling. In this mode, the reactor was operated for 1 hour, afterwards, a solution of sodium hydroxide was delivered to the upper part of the reactor

Scheme 1.

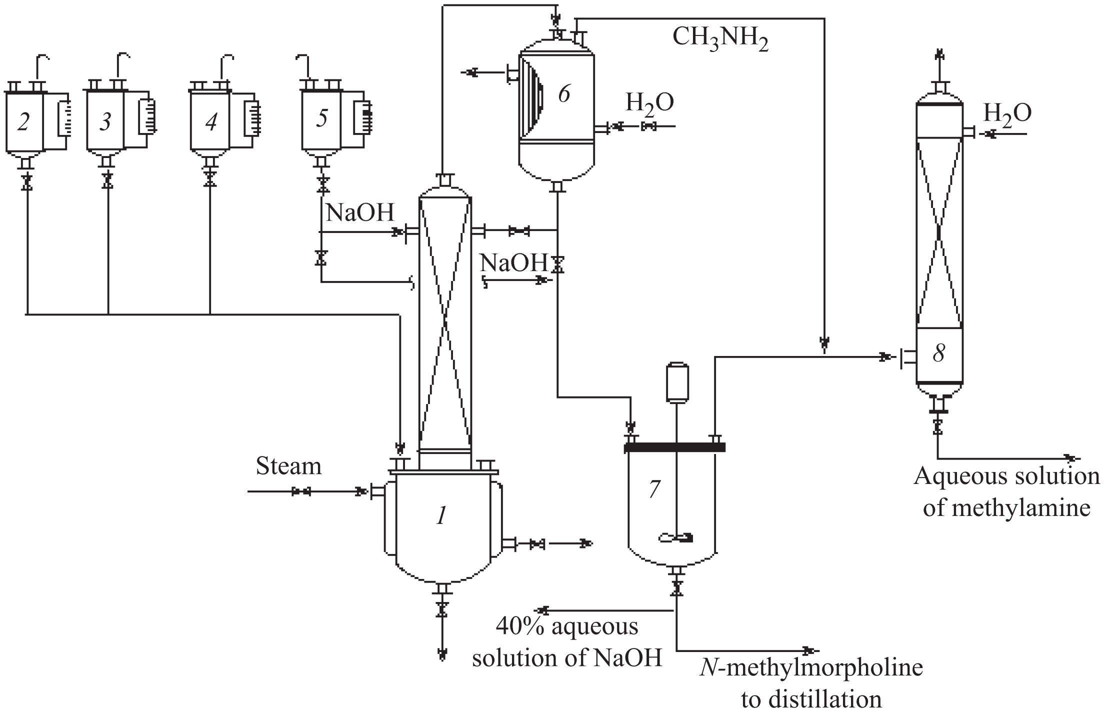


I **II** **III** **IV**

Scheme 2.



II **V** **VI** **VII**



Technological scheme of *N*-methylmorpholine synthesis. (*1*) Reactor; (*2*) water measuring device; (*3*) 2,2'-dichlorodiethyl ether measuring device; (*4*) methylamine measuring device; (*5*) measuring device of 40% aqueous solution of NaOH; (*6*) distillator; (*7*) separator; (*8*) methylamine scrubber.

from measuring device *5*. Therewith distilling off the resulting *N*-methylmorpholne (**IV**) started. The aqueous *N*-methylmorpholine (**IV**) (azeotropic mixture) is fed to the separator *7* (equipped with stirrer) through a condenser *6*. For the separation of *N*-methylmorpholine (**IV**) from the water in the separator a calculated amount of 40% solution of NaOH was added. The aqueous layer containing a small amount of *N*-methylmorpholine (**IV**) was fed to the collector of NaOH solution for further use. Top layer, technical *N*-methylmorpholine (**IV**) was further dried over NaOH and directed to distillation. The non-condensable gases, mainly, methylamine (**I**), enters the scrubber *8*, wherein they are absorbed by water. When the concentration of methylamine (**I**) in the scrubber reaches 25% the solution was fed to the methylamine collector.

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