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A method to determine N-nitrosoalkanolamines in alkanolamines

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Synopsis

A method to determine N-nitrosoalkanolamines in alkanolamines is described. Removal of the amine by adsorbing it onto a cation exchange resin avoids artifact nitrosamine formation during subsequent work-up. Analysis of commercial grade samples showed various degrees of contamination. Analysis of high purity diethanolamine by this method showed no detectable contamination by N-nitrosodiethanolamine (< 5 ppb). This confirms that even with highly reactive secondary alkanolamines, artifact formation during analysis can be avoided.

INTRODUCTION

Alkanolamines, such as mono-, bis-, tris(2-hydroxyethyl)amine (ethanolamine, MEA, diethanolamine, DEA, triethanolamine, TEA) and bis(2-hydroxypropyl)amine (diisopropanolamine, BHPA) are widely used as formulation aids for cosmetics because they form stable emulsions in creams, lotions, and shampoos. They are utilized also for production of other cosmetic ingredients, such as amides of cocoa fatty acids, so-called "foam boosters." The high reactivity of secondary amines towards nitrosating agents represents a potential health hazard because the resulting nitrosamines such as N-nitroso-bis(2-hydroxyethyl)amine (N-nitrosodiethanolamine, NDELA) and N-nitroso-bis(2-hydroxypropyl)amine (N-nitrosodiisopropanolamine, NBHPA) are potent carcinogens (1-6).

Analytical studies have demonstrated that NDELA can be present at sometimes rather high concentrations in a wide spectrum of cosmetics and toiletries (7-10). In order to reduce NDELA contamination already in the constituents used for production of cosmetics, the German "Industrieverband Körperpflege und Waschmittel" issued a specification for TEA in 1983 that defined tolerable contents of <1% each for DEA and

MEA and a maximum tolerable level of 50 ppb for NDELA (11). It appears logical that analogous specifications for other cosmetic ingredients that are based on alkanolamines should be established.

Another step to decrease the risk of nitrosamine formation has been taken by a recommendation of the German Federal Health Office (Bundesgesundheitsamt) to stop using secondary amines for production of cosmetics and toiletries (12).

EXPERIMENTAL

REAGENTS

- Analytical grade, unless specified otherwise.
- Amberlite Ion Exchange Resin IR 120, 20-50 mesh, counter ion: Na.
- Silica gel 40 (0.063-0.200 mm) from Merck, Darmstadt.
- Methanol, chloroform, hydrochloric acid, acetone, i-octane.
- Ethylformate, redistilled twice.
- Sodium sulfate.
- Nitrogen (>99.99 vol.%).
- N-methyl-N-trimethylsilylheptafluorobutyramide (MSHFBA).
- Internal (i.st.) and external (e.st.) standards: NEHPA (i.st.) and NDELA (e.st.), 1 μg/ml each in ethylformate.
- indicator solution (methyl red in methanol).

APPARATUS

Chromatography columns 30 × 200 mm, teflon stop cock, frits P3 (pore size 16–40 μm), receiver (13).
Gas chromatography: a Hewlett-Packard Gas Chromatograph (5880 A Series) connected to a Thermal Energy Analyzer (Thermo Electron Corporation, Waltham, MA, Mod. 502) was used.

ION EXCHANGE RESIN

Pour 200 ml, presoaked in water, into appropriate column and prepare H^+-form by treatment with hydrochloric acid (2n, 1000 ml). Wash with water (800 ml) and displace the solvent by methanol/water (1:1, 200 ml).

CLEAN-UP COLUMN

Bottom layer of sodium sulfate (6 g), wetted with methanol/acetone (1:1), upper layer of silica gel (10 g) suspended in the same solvent (40 ml); displace solvent by chloroform/acetone (5:1).

METHOD

Dissolve the amine (1 g) in methanol/water (1:1, 10 ml), add internal standard NEHPA (50 μl) and three drops of indicator solution. Add ion exchange resin in small portions to the stirred mixture until the solution, after first turning red, becomes colorless. Transfer the suspension quantitatively into glass column and elute with methanol/water (1:1, 100 ml). Take down in a vacuum rotary evaporator (40°C) and take up residue in chloroform/acetone (5:1, 10 ml). Transfer quantitatively to clean-up column, wash the column with the same solvent (40 ml). Elute nitrosamines with acetone (50 ml). Rotate down (5 ml), transfer quantitatively into a receiver, and remove solvent by nitrogen stream.

SILYLATION

Add MSHFBA (150 μl) to residue and allow to stand 45 min at room temperature. Make up to 0.5 ml with i-octane. Treatment of standard (50 ng NDELA and 50 ng NEHPA): remove solvent under nitrogen and derivatize in the same way.

GC CONDITIONS

Column: 6% OV 275 on Volaspher A2 (80–100 mesh ASTM) (2 mm × 3 m) silanized glass. Carrier gas: He (20 ml/min). Injector: 200°C. Temperature programme: initial temperature, 1 min, 150°C, at 2°/min to 170°C and then at 10°/min to 220°C. Pyrolyzer temperature: 400-500°C. Volume injected: 5 μl.

RESULTS AND DISCUSSION

Artifact formation represents a great problem when analyzing alkanolamines, especially secondary amines. Inorganic (Kieselguhr) or organic (ion exchange resin XAD2) mate-

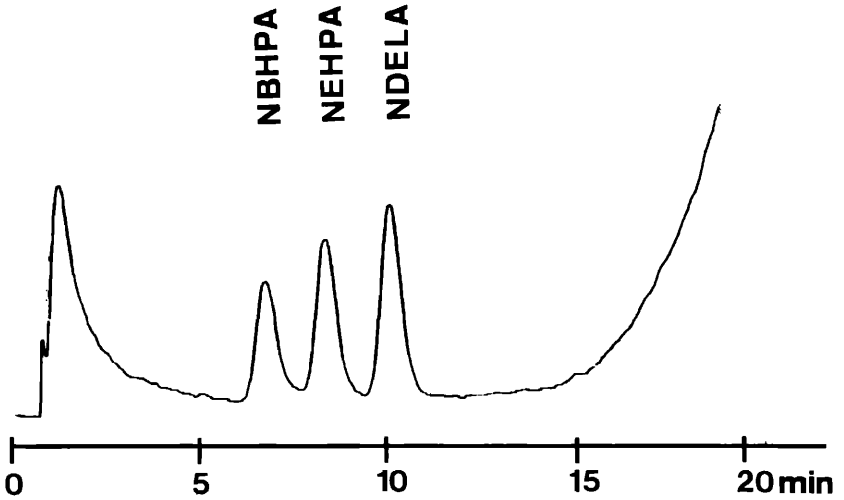

Figure 1. Gas chromatogram with contaminants NBHPA and NDELA and internal standard NEHPA.

rials are especially critical because traces of NO_x adsorbed to these sorbents lead to nitrosamine formation. Removal of the amine by adsorption to a cation exchange resin prevents artifact formation. Subsequent clean-up on a silica gel 40-column represents an efficient further purification step. Analysis of high purity DEA by this method did not show detectable NDELA contamination (<5 ppb), which proves that artifact formation is inhibited.

For trimethylsilylation, the conditions described were found to be appropriate; heating in a closed system to 80°C did not improve the yields. A gas chromatogram as obtained from a typical diethanolamine sample is illustrated in Figure 1. Baseline separation of internal standard (NEHPA-TMS) and contaminating nitrosamine (NDELA-TMS) is obtained.

To test the reproducibility of the analytical procedure, a sample of DEA was analyzed ten times. An average NDELA content of 279 μg/kg ± 11 μg/kg (SD = standard deviation) was found. The average recovery of the internal standard was 89 ± 8% (SD). The determination limit was 5 μg/kg in our hands. Preliminary results of a first collaborative study indicate that this limit might not be reached in all instances, depending on analytical experience and sensitivity of the Thermal Energy Analyzer. Therefore, a range of 5–15 μg/kg is given.

As can be seen from Table I, most of the alkanolamines analyzed are contaminated with the corresponding nitrosamines. This is in agreement with results obtained earlier with a series of secondary alkylamines (14). The finding that specific samples showed no detectable contaminations demonstrates that nitrosamine formation obviously can be reduced or prevented by maintaining appropriate conditions for production and/or storage of the corresponding amines. To examine possibilities for removal of nitrosamine contamination, DEA contaminated with 280 ppb NDELA was treated overnight with Ni/Al alloy (0.5 g of the amine, diluted in 10 ml water, 150 mg of alloy). This treatment resulted in a 90% reduction of the NDELA content.

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Table I
Contamination of Alkanolamines With NDELA and NBHPA

	NDELA (μg/kg)	NBHPA (μg/kg)
DEA 1	91	
DEA 2	1460	
DEA 3	279	
DEA 4	<5	
TEA	<5	
MEA 1	41	
BHPA 1		465
BHPA 2		36
BHPA 3		13

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