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Minimizing N-nitrosodiethanolamine formation from nitrite and NO_2 in nonaqueous triethanolamine systems

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Synopsis

The N-nitrosation of diethanolamine, an impurity in triethanolamine systems, was studied under nonaqueous and slightly alkaline conditions. On addition of stearic acid, nitrite was shown to react with chloroform mixtures of triethanolamine/diethanolamine (TEAM/DEAM) at 37°C. The rates at which these TEAM-stearate mixtures nitrosated in various other solvents were also measured and were observed to be affected by the solvent type. In general, nonpolar solvents facilitated nitrosation at higher rates than polar solvents. In addition, the mixtures using 99% TEAM nitrosated more slowly than those with the 85% grade. All reaction rate constants were found to be pseudo-first-order with respect to nitrite, as DEAM was always present in excess.

Studies were also conducted to simulate the maximum amount of nitrosation that could occur from air during regular consumer use of a cosmetic. A method is described whereby a lotion containing TEAM-stearate was uniformly spread over a surface at 2 mg/cm^2 and exposed to concentrations of NO_2 from 100 ppb to 600 ppb for 24 hours at 20, 30, and 37°C. Under these relatively anhydrous conditions, the lotion was then measured for N-nitrosodiethanolamine (NDELA) in ng/cm^2 by high performance liquid chromatography/thermal energy analyzer (HPLC/TEA). This type of nitrosation, described as atmospheric nitrosation, was shown to be less in a TEAM-stearate lotion when 99% TEAM was substituted in place of the 85% grade.

INTRODUCTION

Several studies have documented the presence of trace levels of nitrosamines in certain cosmetics products (1, 2). Nitrosamines result from the nitrosation of secondary amines according to the following accepted and general reaction:

$$R_2NH + Y\text{-}NO \rightarrow R_2NNO + HY$$

The formation of these nitrosamines has reportedly occurred after manufacture, primarily due to nitrosating agents within the formulations. Recently, though, lower nitrosamine levels have been reported (3), and have likely resulted from companies emphasizing the use of purer raw materials and probably avoiding those nitrite-releasing compounds (4).

Cosmetics studies concerning N-nitrosation have largely dealt with aqueous, slightly acidic emulsions (5). However, nitrosation can be relatively faster and considerably

more difficult to inhibit under nonaqueous, slightly alkaline conditions (6). Cosmetics formulated with triethanolamine (TEAM), which itself is not nitrosatable, unfortunately contain significant amounts of the diethanolamine (DEAM), which is nitrosatable. In efforts to further understand and minimize this nitrosation, the following results are presented.

The first study involves nonaqueous solvent mixtures with triethanolamine/diethanolamine and stearic acid, using nitrite (NO_2^-) as the nitrosating agent.

The second study involves the effects low levels of NO_2 have on TEAM-stearate lotions under conditions simulating normal cosmetic usage.

When a lotion is spread thinly over a surface, an essentially nonaqueous matrix forms as the water evaporates. There has been speculation that N-nitrosations might also occur during actual product use (7). To determine the significance of this concern, product use of lotions is simulated by exposing thin films to atmospheric levels of nitrogen dioxide and subsequently analyzing for nitrosamines. Reactions leading up to this nitrosation and ways to further minimize its occurrence in cosmetic products are discussed. Additional evidence is given that increased purity of triethanolamine helps to minimize its occurrence (8). The ramifications of these studies to other nitrosamine studies are also considered.

MATERIALS AND METHODS

CHEMICALS

N-Nitrosodiethanolamine (NDELA) was purchased from Thermo Electron Corp. (Waltham, MA). Technical grade (85%) and 99% triethanolamine (TEAM) are grades commonly used in cosmetic products. Both were analyzed by high performance liquid chromatography/refractive index detection (HPLC/RID) to contain diethanolamine (DEAM) as the primary remaining ingredient. Technical grade stearic acid was used except where specified. All additional chemicals were reagent grade. The solvents were purchased from Burdick and Jackson, except for uninhibited Omnisolv chloroform of MCB (Cincinnati, OH). Nitrogen dioxide (100 ppm in air) was obtained from Union Carbide.

ANALYTICAL PROCEDURE FOR NDELA BY HPLC/TEA

A Beckman 114M liquid chromatograph was interfaced to a Model 502 thermal energy analyzer (TEA) of Thermo Electron. The TEA was operated at 500°C with an acetone/dry ice cold trap and a pressure of 0.3 Torr. A mobile phase of iso-octane, dichloromethane (DCM), methanol of approximately 60:30:10 composition was pumped at 1.5 ml/min and ambient temperature through a 3.9 mm (i.d.) × 30 cm u Bondapak NH_2 column (P/N 84040) of Waters Associates (Milford, MA). NDELA eluted at 8 ± 1 minutes.

Prepared samples were injected via a Rheodyne 7105 valve. Exactly two minutes after a 10-50 µl sample injection, a 0.2 or 1.0 ppm NDELA standard was injected. An automatic switching value was used to change the LC stream from waste to the TEA after six minutes. As shown in Figure 1, the peak ratio of sample NDELA to standard NDELA,

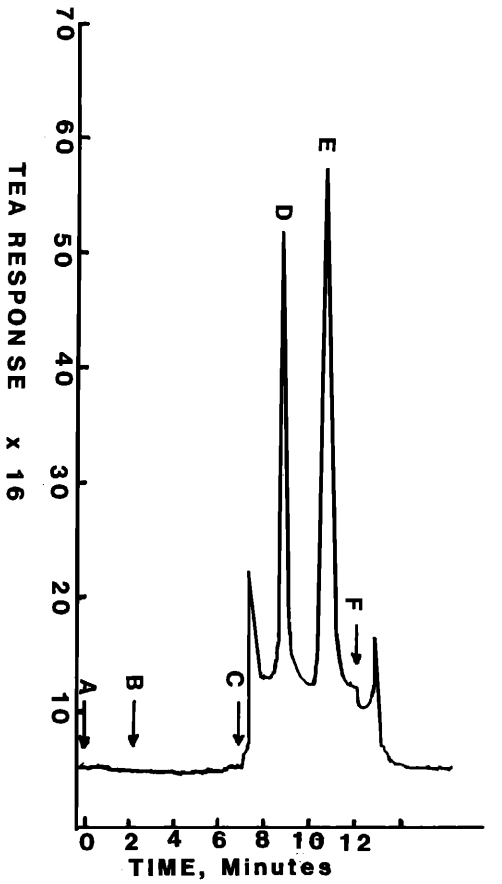


Figure 1. HPLC/TEA chromatogram of NDELA. A: 50 µl sample injection. B: 10 ng NDELA standard injection. C: Mobile phase diverted from waste to TEA. D: Sample NDELA response. E: Standard NDELA response. F: Mobile phase diverted from TEA to waste.

eluting exactly two minutes later, was used in the calculation to minimize variations of TEA detection.

EXPERIMENTAL SETUP FOR TEAM-STEARATE NITROSATION IN NON-AQUEOUS SOLVENTS

Equimolar amounts of TEAM and stearic acid were separately weighed in designated nonaqueous solvents. Five ml of each were added to a 10 ml reaction vial and capped with a Teflon mininert valve cap (Altech, Deerfield, IL). Vials were immersed in a regulated water bath that controlled temperature to within ± 0.5°C. Nitrite was added by injecting 2.5 µl of aqueous 0.1 molar sodium nitrite into the desired nonaqueous solvent with shaking. In order to measure the formation of NDELA, samples were withdrawn at specific times (kept near 15°C) and immediately injected directly into the HPLC/TEA. Scavenging the remaining nitrite was unnecessary.

EXPERIMENTAL SETUP TO SIMULATE ATMOSPHERIC NITROSATION OF LOTIONS

Normal skin coverage of a lotion and its exposure to atmospheric levels of NO_2 was

simulated in the following manner. Lotion (0.19 ± 0.01 g) was smeared as evenly as possible via a Wilshire foam applicator (Fisher Scientific # 14-900-2, Pittsburgh, PA) over the entire 95-cm^2 inner surface of a polyethylene drying tube (15 mm i.d. × 200 mm). The weight of the lotion on the tube was measured by weighing the tube before and after application. The lotion stayed in position in the tube and quickly resulted in a rather dry smear, providing the cosmetically accepted coverage of 2 mg/cm^2. Eight of these prepared tubes were then positioned with flexible tubing onto a circular aluminum manifold, as shown in Figure 2, for exposure to air.

The flow of air through each tube was calculated to be 0.26 liter/min, which resulted in laminar air flow velocities of 2.4 cm/sec or 5 linear feet/min. During the exposure tests, the manifold and sample tubes were housed in a low temperature incubator with temperature held to within ± 1°C. The air was first purified to remove any background nitrogen oxides by passing it first through charcoal and then through an adsorption tube (4 × 30 cm) of TEAM-impregnated silica gel. (Relative humidity was maintained at 50% throughout the studies by bubbling the appropriate amount of air through water.) The NO_2 from the cylinder tank was added to the purified air and diluted to the

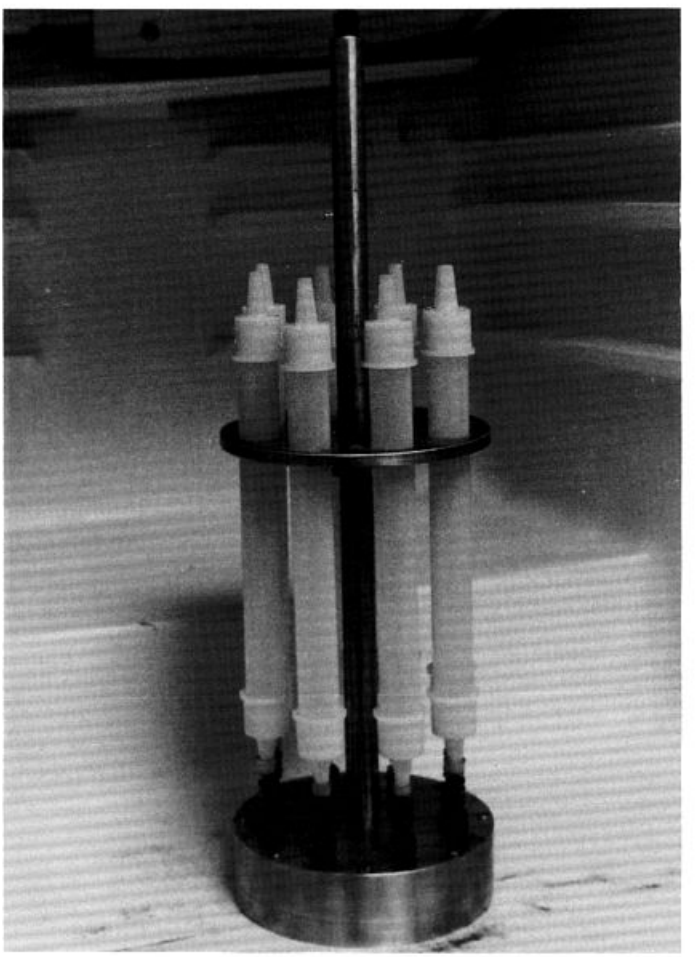


Figure 2. Aluminum manifold to simulate atmospheric nitrosation of cosmetics.

desired levels by carefully controlled flowmeters. Most experiments were designed for 24 hour exposures to NO_2, at 600 ppb to nondetectable levels.

MEASURING FOR ATMOSPHERIC LEVELS OF NO_2

To assure accuracy and since the concentration of NO_2 in cylinders often decreases with time, the final diluted stream was measured for NO_2 at the ppb level. In the assay, a constant-flow air sampling pump (Dupont Model P125A, Wilmington, DE) was operated at 200 ml/min. Collection of the NO_2 in a bubbler was made via a 10 ml aqueous solution of 1.5% triethanolamine, which contained 2 drops of butanol. Ten ml of 2% sulfanilamide in 5% H_3PO_4 and 1.4 ml of 0.1% N-(1-napthyl)ethylenediamine · 2HCl were then added to the above solution and diluted to 25 ml with water. After five minutes, the resulting color was measured at 540 nm with a spectrophotometer by the accepted US-EPA Method P & CAM 231 (9). However, to increase sensitivity and precision, the method was slightly modified by eliminating hydrogen peroxide. Calculations were based on the prevalent concept that 1 mole of NO_2 produces 0.63 mole of NO_2^-, an empirically determined value, yet one that is not universally held (10,11).

ANALYTICAL TECHNIQUES FOR NDELA EXTRACTION

After air exposure, the tubes were removed from the manifold and sealed on one end with 18-mm septa. NDELA was extracted by adding 10 ml of 2% methanol in dichloromethane (DCM) to each tube. The contents were then shaken, transferred to 13 ml centrifuge tubes, and evaporated with nitrogen to 1 ml, near 0°C. Samples were measured in triplicate for NDELA by direct injection into the HPLC/TEA. When needed, UV-photolysis was used for confirming it a nitrosamine.

Nitrite scavengers were not used. Thus, two types of blanks were examined to guard against artifact problems. The first blank consisted of exposing the prepared sample tubes to essentially NO_2-free air (indicated by <2 ppb NO_2). The second blank consisted of isolating the prepared sample tubes in a NO_2-free desiccator. The tubes were kept at the specified temperature for 24 hours and measured for NDELA as above.

RESULTS

NITROSATION VIA NITRITE

Effect of stearic acid on non-aqueous nitrosation of triethanolamine. When one mole of stearic acid was added to a chloroform solution containing one molar technical grade triethanolamine (85%) and 25 nM of nitrite, significant nitrosation occurred at 50°C. The formation of nitrosamine with time is depicted graphically in Figure 3. In contrast, a mixture of one molar TEAM and nitrite in $CHCl_3$ with no stearic acid, under the same conditions, provided no detectable NDELA.

Nitrosation rates of TEAM-stearate in non-aqueous solvents. Similar measurements at 37°C were made of 6% equimolar TEAM-stearate mixtures using other nonaqueous solvents. The pH of these equimolar mixtures were near 8.5, and nitrite was added to obtain 25 nM/ml. Using those conditions described above, aliquots were taken at specific time periods for each of the 11 solvents listed in Table I. The first order rate constants, k, were calculated in hr^{-1}, as well as the time required for ½ of the available nitrite, $t_{½}$,

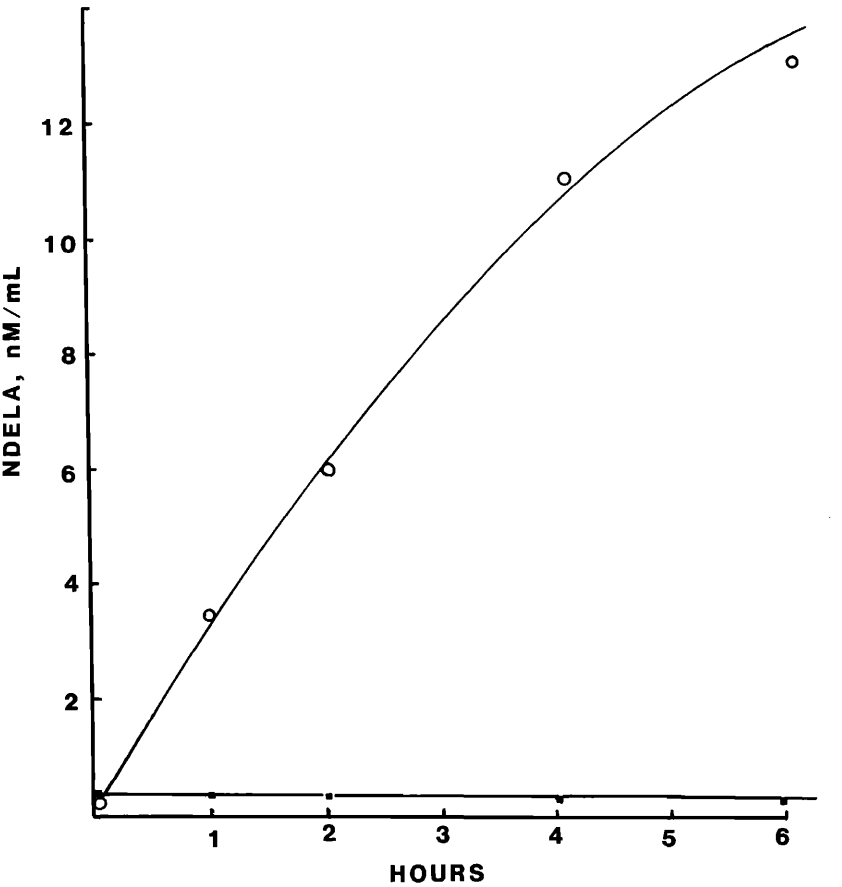


Figure 3. N-nitrosation of diethanolamine in chloroform using 1 molar TEAM, with and without stearic acid at 50°C (nitrite, 25 nM/ml). ○: TEAM-stearate (1:1 molar ratio). ■: TEAM only.

to react in each solvent. As may be observed in the table, the nitrosation rates were significantly different for most solvents, in part due to the increased polarities and other inherent solvent characteristics.

Effects of triethanolamine purity on nitrosation. The rates at which different concentrations of diethanolamine (DEAM) in 0.1 M TEAM-stearate mixtures nitrosated at 37°C were also determined and are shown in Table II. While the ratio of DEAM to TEAM was varied, both the total ethanolamine and stearic acid were kept constant. The procedure was similar to the preceding ones, except, having established a first order rate equation, aliquots were simply analyzed for NDELA in nM/ml after 24 hr or eight days. Isopropanol was used in these studies because the solvent more approximated the matrices of a cosmetic base.

Notably, since each experimental test contained a great excess of DEAM, the reaction rates were pseudo-first-order with respect to the added nitrite. The reaction rate was considerably faster with the 85% technical grade of triethanolamine.

NITROSATION VIA NO_2

Simulated atmospheric nitrosation of applied cosmetics. Two somewhat typical cosmetic lo-

Table I
Nitrosation Rates of 6% TEAM-Stearate in Non-Aqueous Solvents at 37°C

Solvent	k ($\times 10^{-3}$ hr^{-1})	$t_{1/2}$ (hr)
Chloroform	240	2.9
Dichloromethane	120	5.8
Ethyl acetate	59	12
Toluene	35	20
Isopropanol	31	22
1-Butanol	18	39
Acetone	16	43
1-Propanol	13	53
Ethanol	7.1	98
Isopropyl myristate	5.5	130
Methanol	4.1	170

tions (Lotions I and II), were formulated in the laboratory to contain between 0.7–0.9% TEAM and a molar equivalent of stearic acid, giving a pH of 8.1. Each lotion was prepared in duplicate (A and B), using either 85% technical grade or 99% triethanolamine. After application and exposure to NO_2 for 24 hr, the resulting smears were measured for the amount of nitrosation. This nitrosation was calculated in terms of applied surface area, i.e., nanograms of NDELA per cm^2.

Figure 4 demonstrates the nitrosation differences of Lotions IA and IB after exposure to the higher level of NO_2 at 600 ppb, from 20°C to 37°C. Figure 5 presents the nitrosation at 37°C, but as a function of NO_2 concentration. As expected, significantly less nitrosation occurred at the lower, 100 ppb level. Both figures demonstrate lower nitrosations when purer 99% TEAM formulations were used.

The data obtained at different levels and temperatures is more completely shown in

Table II
Nitrosation Rates in Isopropanol With Varying Concentrations of DEAM in TEAM-Stearate Mixtures @ 37°C (25 nM/ml $NaNO_2$)

	Concentrations					
Exp. #	DEAM Molar	TEAM Molar	Stearic Acid Molar	NDELA nM/ml @ 24 hrs	k ($\times 10^{-3}$ hr^{-1})	$t_{1/2}$ (days)
1	0.100	0.000	0.100	1.0*	1.9	14
2	0.075	0.025	0.100	2.9	5.1	5.7
3	0.050	0.050	0.100	4.8	8.9	3.2
4	0.025	0.075	0.100	7.5	15	1.9
5**	0.015	0.085	0.100	8.6	18	1.6
6	0.010	0.090	0.100	6.3	12	2.4
7	0.005	0.095	0.100	4.9	9.1	3.2
8	0.003	0.097	0.100	3.4	6.1	4.7
9	0.001	0.099	0.100	2.0	3.5	8.3
10	<0.001	0.100	0.100	1.0*	2.0	14

* NDELA concentration measured after 8 days.
** Approximate composition of technical grade TEAM.

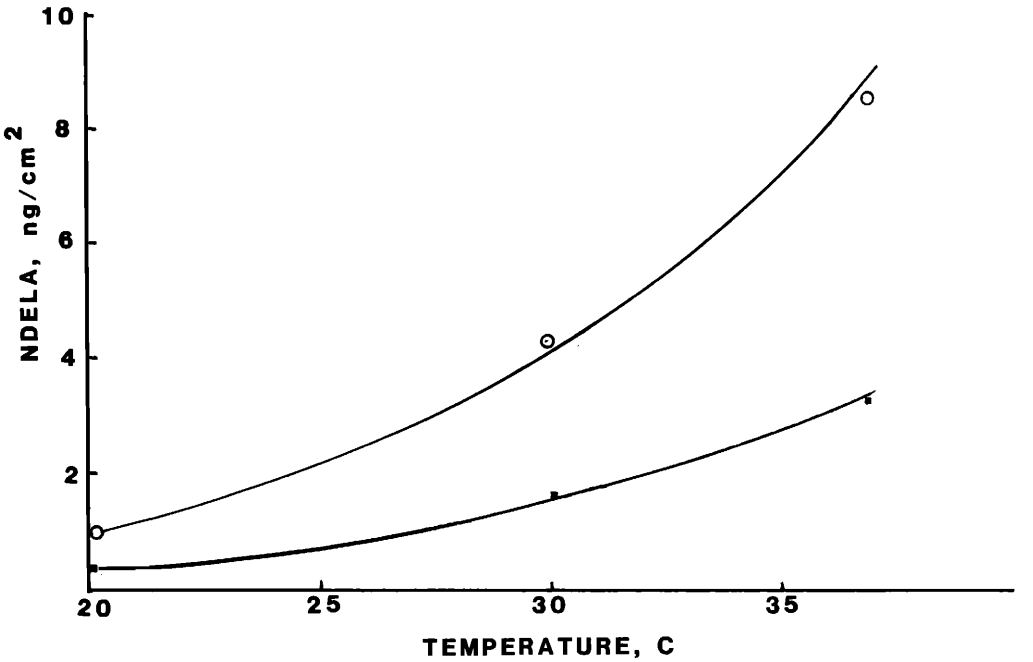


Figure 4. N-Nitrosation of Lotion I after 24-hr exposure to 600 ppb NO_2. ⊙: Lotion IA (85% TEAM). ■: Lotion IB (99% TEAM).

Table III. It should be noted that when the products were exposed to higher levels of NO_2 at the relatively low temperature of 20°C, NDELA did not form. This was further demonstration that artifacts did not occur within the methodology. There was also no significant difference between the two types of blanks. Consequently, it could be assumed the NO_2 scrubber was adequate. The trace nitrosation detected with the blanks at 37°C was due to trace nitrosating agents originally present in the formulation.

Interestingly, when a 1% aqueous solution of TEAM (w/o stearic acid and at pH 10) was smeared in polyethylene tubes and exposed to 600 ppb NO_2, 5 to 8 ng/cm^2 of NDELA formed, even at relatively low temperatures (30°C). In additional tests, where *concentrated* TEAM smears were used, a certain ease toward surface nitrosation occurred when the tubes were exposed to approximately 1000 ppb NO_2. This nitrosation was shown to be relatively independent of temperature. (The amount of NO_2 absorbed to that nitrosated was measured colorimetrically and found to be on the order of 250 nm NO_2 to 1 nm of NDELA.) These results showing triethanolamine reactivity with nitrosyl gases were in contrast to the nitrite (NO_2^-) additions where stearic acid was necessary for nitrosation, but were in agreement with the studies of Challis (12,13).

Various procedures were used to eliminate nitrosation on simple addition of solvent. The most extreme treatment included scavenging the sample initially with sodium bisulfite in aqueous H_3PO_4 and subsequently percolating it through sodium sulfate. After correction for recovery, no differences were noted between the regular analysis and the nitrite-scavenged one. The accepted procedures of Krull *et al.* were also used to ascertain that the NDELA detected by the TEA was neither a nitrite/nitrate ester nor a nitramine (14,15).

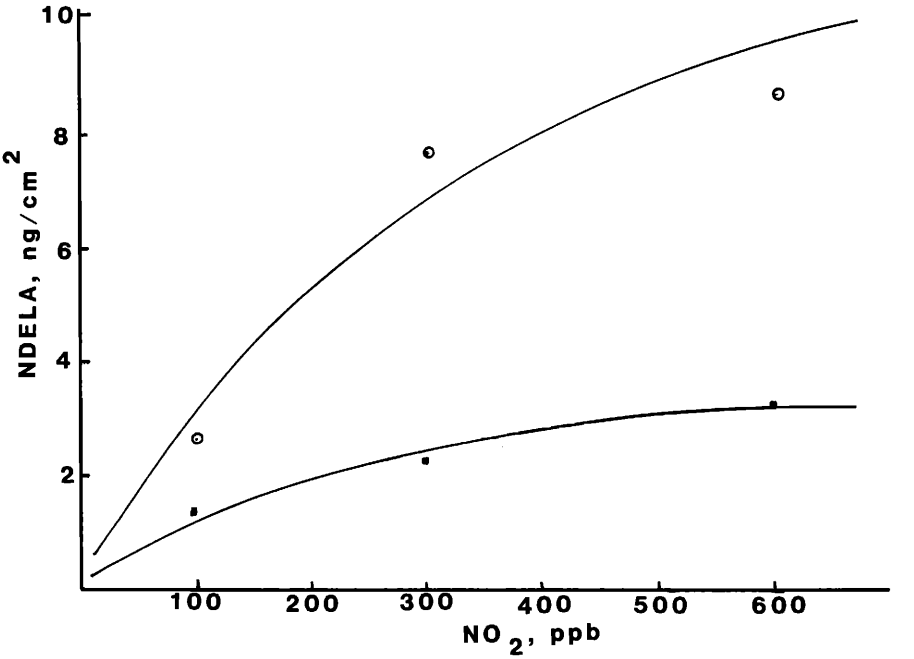


Figure 5. N-nitrosation of Lotion I after 24-hr exposure at 37°C. ⊙: Lotion IA (85% TEAM). ■: Lotion IB (99% TEAM).

DISCUSSION

NON-AQUEOUS NITROSATION BY NITRITE

Nitrite ion, by itself, is generally accepted to be an ineffective nitrosating agent for secondary amines (16). Thus nitrosation was not detected when nitrite was added to a

Table III
Surface Nitrosation of Lotions After 24-Hr Exposure to NO_2-Contaminated Air

NO_2 ppb	Temp. °C	Concentration of NDELA (ng/cm²)			
		Lotion IA w/85% TEAM	Lotion IB w/99% TEAM	Lotion IIA w/85% TEAM	Lotion IIB w/99% TEAM
0*	37	1.1	0.19	0.39	0.18
<2**	37	1.0	0.83	0.81	0.84
100	37	2.6	1.3	2.6	1.1
300	37	7.6	2.2	5.6	1.5
600	37	8.5	3.2	9.3	2.4
100	30	1.4	0.46	1.0	0.37
300	30	3.5	0.89	3.4	0.81
600	30	4.4	1.6	3.6	1.0
100	20	0.66	0.27	0.32	0.18
300	20	0.89	0.23	0.83	0.18
600	20	1.0	0.41	0.63	0.20

* Tubes enclosed in desiccator for 24 hr at 37°C and free of NO_2 for 24 hr.
** Tubes exposed as normal to NO_2-free air (<2 ppb NO_2).

chloroform solution of diethanolamanine/triethanolamine (DEAM/TEAM), as shown in the first study (Figure 3) (Eq. 1).

In cosmetic formulations, amines are generally neutralized by organic acids, such as stearic acid, and it is under these conditions that diethanolamine was observed to readily nitrosate. The nucleophilic stearic acid anion (Y^-) evidently acts as a carrier for the nitrosonium ion (NO^+) (Eq. 2), which in turn, reacts with the amine to form the nitrosamine (Eq. 3) (17,18). This occurs even under neutral-to-basic conditions.

$$R_2NH + HNO_2 \rightarrow R_2NH_2^+, NO_2^- \quad (1)$$

$$YH + NO_2^- \rightarrow NOY + OH^- \quad (2)$$

$$NOY + R_2NH \rightarrow R_2NNO + HY \quad (3)$$

$$\text{rate} = k(R_2NH)(NOY)$$

Nitrosation rates are dependent on a number of parameters; these include the pH, the amount and basicity of the amine, the type of catalytic anions present, as well as the nitrite concentration (16). However, as all parameters essentially remain constant in a particular cosmetic system, the resulting rate of the above reactions (Eq. 3) actually becomes pseudo-first-order with respect to the nitrosonium ion alone.

In all of the above studies, the pH was kept above 8, and the results show that in addition to the importance of stearic acid, the reaction rate is also greatly influenced by the matrix of both solvent and solute. This is shown in Table I, where the rate constants generally decrease with increasing polarity. However, it is likely that other solvent parameters, such as their protophylic characteristics and electron rich environments, also play significant roles. Apparently, solvents do not interact mechanistically in TEAM-stearate mixtures, as may have occurred in other nitrosamine studies with dichloromethane (19). Instead, this solvent, as well as other similar ones, are shown to simply facilitate nucleophilic nitrosation due to the solvents' own innate characteristics. At the other extreme are the relatively polar alcohols and aqueous emulsions. Both provide for significant hydrogen-bonding effects and thus nitrosate quite slowly. Since most cosmetics which contain TEAM are formulated as an emulsion, the nitrosations occur very slowly in finished products (5).

In Table II, where DEAM was varied in relation to TEAM, the solute's innate characteristics were observed to influence it as well. Nucleophilic nitrosation reactions were shown to occur most readily in stearate mixtures of 85% TEAM and 15% DEAM. In fact, higher concentrations of DEAM did not increase the nitrosation rate over what occurred at 15%. This was further evidence that the final nucleophilic environment of the matrix plays a dominating role in influencing the rate of DEAM nitrosation. Thus NDELA formation was significantly slowed in slightly alkaline mixtures of this type, merely by increasing the purity level of the TEAM.

This increased understanding of DEAM nitrosation has had impact, both in laboratory practice and in formulation. For example, during analysis, preventing artifacts is particularly difficult in nitosamine research. Even if aqueous nitrite scavenging is initially used, trace nitrite contamination from the air, glassware, etc., may easily enter the solvents and cause difficulties. It was observed that the moderately high temperatures often used during different phases of nitrosamine analysis actually should not be used at all if one is to be assured of total artifact prevention. In addition, scavenging nitrite is unnecessary and not recommended, due to the dangers of artifact formation during the

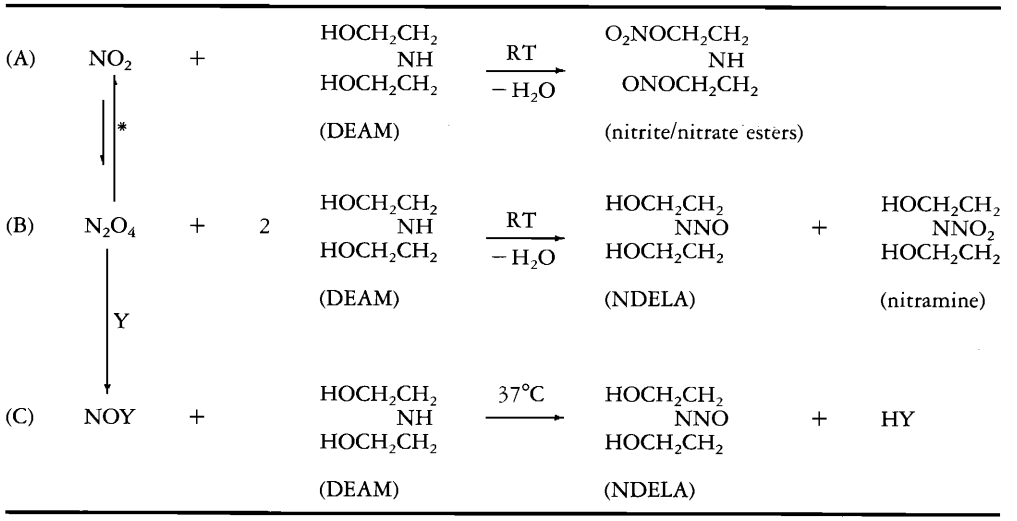
process. These solvent studies with NDELA also show that by using appropriate solvents, such as alcohol or combinations with alcohol, NDELA will be less likely to form during analysis. In addition, it would appear that these techniques would minimize nitrosation in similar procedures as well.

Secondly, it may not always be possible to totally eliminate nitrosating agents during the manufacture of cosmetics. Thus, simply slowing the reaction rate becomes very important. Using a more pure form of triethanolamine is at least one effective way to reduce DEAM nitrosation which might conceivably occur over a long time span, should endogenous nitrites be present in a formulation. These results are very much in agreement with those acidic studies of Ong and Rutherford (8).

NITROSATION BY NO_2 EXPOSURE

Alkanolamines, it should be noted, have enormous capacities for holding NO_2. This affinity is probably based on the alkaline properties the amines exhibit. But the actual retention of NO_2 is postulated to occur because the hydroxyl groups of the alkanolamine form esters with nitrite/nitrate (20). Figure 6 and the following are presented to better understand the nitrosations that occur with TEAM mixtures.

Reaction A. Most of the moisture in a typical TEAM-stearate lotion will evaporate quickly during product use and the NO_2 present in the air will be readily adsorbed by the alkanolamine. NO_2 itself is known *not* to be a particularly good nitrosating agent, and, under anhydrous conditions, may instead form nitrite/nitrate esters with the alkanolamines (TEAM/DEAM). If water is still present in an applied mixture, the adsorbed NO_2 is likely to be converted to the inactive NO_2^- and NO_3^- ions (16, 17).



(A) = Primary reaction with TEAM only, or with mixtures containing TEAM-stearate.
(B) = Secondary reaction with TEAM only.
(C) = Secondary reaction with mixtures containing TEAM-stearate.
* k_{eq} = 0.15 Atm. for $N_2O_4 \rightleftharpoons 2NO_2$ @25°C & ambient pressure.
k_{eq} = 1.91 Atm. for $N_2O_3 \rightleftharpoons NO + NO_2$ @25°C & ambient pressure (23).

Figure 6. Scheme for atmospheric nitrosation of diethanolamine.

Reaction B. Although NO_2 may not react, the trace amounts of N_2O_3/N_2O_4 which would be available are highly reactive with secondary amines, themselves, i.e., without a catalyst (6). As shown in the equilibrium expression, only a minute amount of these oxides co-exist with NO_2 in air. However, the nitrosation rates can be very rapid in simple organic matrices, as the equilibrium shifts sharply, making even more N_2O_3/N_2O_4 available (12). For these reasons, thin films of TEAM (containing, of course, a small fraction of diethanolamine) easily nitrosate under normal ambient conditions to the nitrosamine, and the nitramine as well. This reaction is particularly important in the metal-cutting fluid industry, due to the abundance of free amines in the fluids (21, 22).

Reaction C. Fortunately, when thin films of cosmetic products containing TEAM-stearate are exposed to nitrogen oxides, the reactions are less spontaneous. This is because those trace amounts of available N_2O_3/N_2O_4 gases (probably parts per trillion) first form the intermediate nitrosonium carrier, NOY, due to the presence of the stearate catalyst Y^-. This carrier will remain as such, unless the temperature and media are conducive to forming a nitrosamine, as shown above.

Adsorption of nitrogen oxides on smears of TEAM-stearate products or TEAM itself is strictly a surface phenomenon. It may be the amount of DEAM available for atmospheric nitrosation on a surface plays a more significant role than occurred with the nitrite studies of table II. That is, the lower atmospheric nitrosation rates observed in the above 99% TEAM formulations are likely due to *both* a decrease of available DEAM and the resulting matrix. Nevertheless, formulations prepared with a purer form of TEAM showed significantly lower nitrosation, normally at least ⅓ or less at all NO_2 levels. Even at the more extreme conditions of 600 ppb NO_2 at 37°C, the 99% formulations aquired levels of less than 3 ng/cm^2 NDELA.

As an aside, it appears that triethanolamine may tie up nitrogen oxides. Somewhat paradoxically, if it is necessary to formulate a product with tertiary amines, for its emulsive properties or other reasons, adding a pure grade of triethanolamine may prevent nitrosation reactions that might inadvertently occur from normal exposure to the atmosphere during usage. In this way, any susceptibility a product might have toward forming other nitrosamines may be lowered.

SUMMARY AND CONCLUSIONS

The NDELA found in certain cosmetic products is not from the nitrosation of triethanolamine itself, but from the nitrosation of its usual contaminate, diethanolamine. The rate and extent of this nitrosation was shown to be highly dependent on the media composition. However, even when these cosmetics were exposed to relatively high levels of nitrite or NO_2, products formulated with the more pure triethanolamine formed considerably less NDELA.

Aside from the direct information obtained with NDELA, these experimental procedures could be helpful in determining the susceptibility amine products might have toward forming nitrosamines other than NDELA. For example, products might easily be challenged for their nitrosating potential with the above atmospheric simulation procedures and subsequently measured for nitrosamines by whatever technique is avail-

able. Likewise, the effectiveness that nitrite scavengers might have in products could easily be examined.

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