N-Nitrosodimethylamine in Air

by DAVID H. FINE[1], DAVID P. ROUNBEHLER[1], EDO D. PELLIZZARI[2],
JOHN E. BUNCH[2], RICHARD W. BERKLEY[2], JOHN MCCRAE[2],
JOAN T. BURSEY[2], EUGENE SAWICKI[3], KEN KROST[3], and
GERARD A. DEMARRAIS[3]
[1]*Thermo Electron Corporation*
85 First Avenue, Waltham, Mass. 02154
[2]*Research Triangle Institute*
P.O. Box 12194, Research Triangle Park, N.C. 27709
[3]*Environmental Protection Agency, National Environmental Research Center*
Research Triangle Park, N.C. 27711

INTRODUCTION

Over the past twenty years there has been an increasing concern about the role that N-nitroso compounds may play in the etiology of human cancer.[1] The search for N-nitroso compounds in the environment has centered upon foodstuffs and liquors,[2] particularly from regions where reliable epidemiological studies suggest localized areas of high cancer incidence.[3]

In spite of extraordinary difficulties, analytical procedures have been developed for assaying the volatile N-nitrosamines in a variety of nitrate/nitrite preserved foodstuffs such as bologna, ham and bacon. Cooked bacon, for example, has been shown to contain N-nitrosodimethylamine (DMN) at the 1-10 μg/kg level and N-nitrosopyrrolidine (NPyrr) at the 20-50 μg/kg level. Formation of N-nitrosamines has been demonstrated under in vivo conditions from suitable precursors in the human stomach.[4]

The environmental distribution of N-nitroso compounds has been placed in a new perspective since DMN was found in the air in two U. S. cities.[5] Using a new sensitive and selective detection system for N-nitroso compounds,[6] Fine, et al. found DMN at the 3.0 to 320 ng/m^3 level in the air in Baltimore, Maryland and at the 5.0 to 170 ng/m^3 level in the air in Belle, West Virginia. The same authors have also reported DMN in nearby Curtis Bay and in the Kanawha River in Belle.[7] Because N-nitrosamines have been thought to be

Bulletin of Environmental Contamination & Toxicology,
Vol. 15, No. 6

absent in aquatic and atmospheric environments, the possibility that a compound as carcinogenic as DMN may be an air pollutant had not been considered previously.

Using two entirely different collection and analysis techniques, we report here on further extensive experiments in Baltimore and Belle. The possibility of DMN being detected as an artifact in the collection and analysis technique is also discussed.

APPARATUS AND TECHNIQUES

Parallel analyses were carried out using different collection and analysis procedures. The two techniques were as follows:

One analytical team (TECO) collected samples cryogenically and analyzed the samples on a Thermal Energy Analyzer (Thermo Electron, Model 502). Air was drawn through two successive cold traps at a flow rate of between 1 and 3 L/min; the temperature of the traps was -78° C. The sample time varied from 20 to 60 minutes. The contents of the traps and the washings were extracted with dichloromethane (DCM) and concentrated to about 0. 5 ml on a Kuderna-Danish evaporator. Between 1 and 10 μl of the final DCM concentrate was introduced into the TEA-gas chromatograph (GC) and the TEA-high pressure liquid chromatograph (HPLC). The TEA-GC instrumentation was mounted inside a mobile vehicle and analyses were carried out on site.

The second analytical team (RTI) concentrated organic vapors on preconditioned Tenax GC (35/60 mesh) cartridges. In general, a sampling rate of 1 L/min was used for a period 120 minutes. The Tenax GC cartridge was transported to the laboratory where it was desorbed and resolved by capillary gas-liquid chromatography, and mass cracking patterns were continuously and automatically obtained throughout the GLC run with a Varian-MAT CH-7 GC-MS-comp system. Identification of DMN was achieved by comparing the mass cracking pattern to an eight major peak index,[8, 9] as well as by comparison with authentic compounds on two different chromatographic capillaries.[10] For quantitative analysis of DMN, a 55-meter glass SCOT capillary column coated with DEGS was used, with the mass spectrometer set on the 74 m/e ratio.

RESULTS

Artifact experiments were conducted to demonstrate that DMN was not formed either during collection or analysis. For the cryogenic procedure, DMN was not detected when dimethylamine (DMA) and NO_x (as sodium nitrite) was added to the trap at levels in excess of those found in polluted factory environments. In the field, enhancement of DMN above background levels was not observed, even when a one-thousandfold excess of DMA was added. In Baltimore, some air samples were analyzed directly on the TEA-GC without solvent extraction or concentration and found to contain DMN. The possibility of formation of DMN on the TENAX cartridge was investigated both in the laboratory and in the field. Enhancement of DMN was not observed above the background when DMA was either pre-loaded into the TENAX cartridge or when field air (in the laboratory moist air containing $NO + NO_2$, 1:1, was used) was drawn across a permeation tube containing DMA and then into the cartridge. On the basis of the results from both of these analytical procedures it was concluded that DMN was not formed at detectable levels during collection or analysis.

Figure 1 is the mass spectrum of a compound found near the FMC property in Baltimore; compared to an authentic DMN standard, the mass spectra as well as the gas chromatographic retention times were virtually identical. Most of the results reported here were confirmed in this manner.[10] Using TEA-GC and TEA-HPLC only one major peak was observed, which corresponded in retention time to DMN in either the GC or the HPLC modes.

In Baltimore, much of the sampling was concentrated near the Food Manufacturing Corporation (FMC) facility which manufactured unsymmetrical dimethyl hydrazine (UDMH) for which DMN is an intermediate. Table 1 lists the comparison of the parallel data collected by both analytical techniques. The two techniques are seen to compare quantitatively to within the limits of experimental error. The high value of 32, 000 - 36, 000 ng/m^3 was measured on the FMC property adjacent to the UDMH facility. Independent coldtrap GC-MS experiments conducted by an FMC analytical team also confirm the presence of DMN in the air on the FMC property.[11]

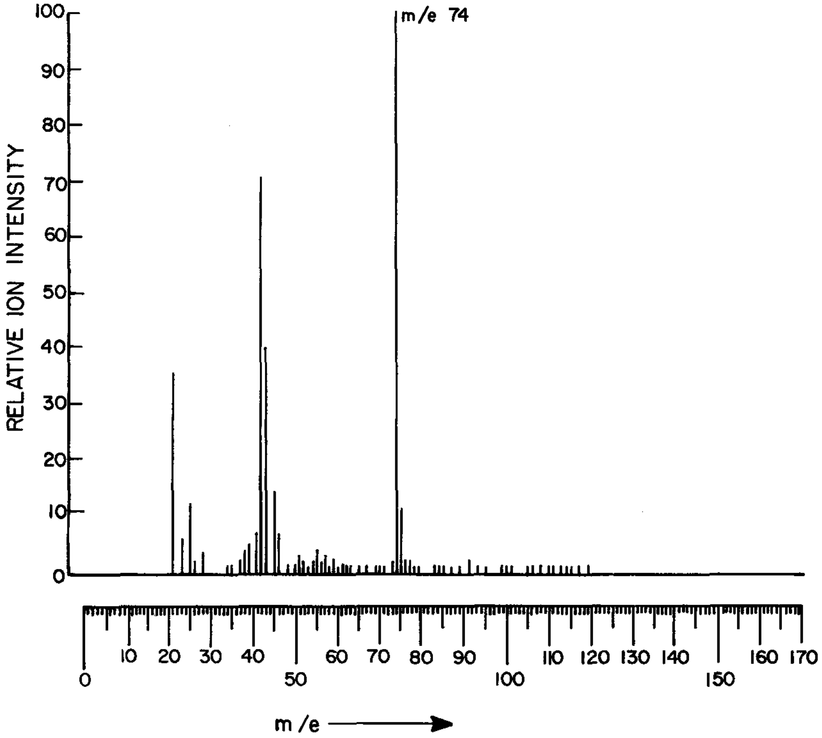

Figure 1. Mass spectrum of N-nitrosodimethylamine. A 55 m DEGS glass SCOT capillary was used; programmed from 70 - 205° C at 40/min. Spectrum was taken of the chromatographic peak occurring at 27 min. Ambient air sample was collected on 10/14/75 from 3:00 p. m. - 6:50 p. m.

COMPARISON OF TEA-GC AND GC-MS
BALTIMORE

DATE	PLACE	DMN LEVEL ng/m^3	
		TEA-GC	GC-MS
10-15	FMC PARKING LOT	13,000 15,000 11,000 8,700	32,200 13,400
10-16	SEWAGE TREATMENT FACILITY	ND	TRACE
10-17	CHESSIE COAL PIER	1,800 1,200 130	920 84
11-19	FMC PROPERTY	36,000 11,000	32,000
11-20	CNR FAIRFIELD AND CHESAPEAKE	340 1,800	1,950
	MINERAC CORPORATION	170 330	1,360

COMPARISON OF TEA-GC AND GC-MS
WEST VIRGINIA

DATE	PLACE	DMN LEVEL ng/m^3	
		TEA-GC	GC-MS
12-1-75	DUPONT	38 18 90	10.1 4.2 3.9 38.0
12-2-75	DUPONT	460	103.0
12-3-75	UNION CARBIDE	22 30 16	1.0 ND 0.0 ND 14.0 56 12.0 ND 40.0 ND
12-4-75	FIKE	Trace	ND ND

Sixteen samples were collected by the cryogenic technique upwind and far removed from the FMC property. Data in Arundel county showed a decreasing DMN level in the early hours of the morning, starting with 110 ng/m^3 at 3:45 a. m. to 36, 31, 23, 21 and 16 ng/m^3 at 12:35 p. m. In downtown Baltimore, the opposite trend was observed with the DMN level increasing from 26 ng/m^3 at 6:42 - 7:55 a. m., to 88 ng/m^3 at 8:25 - 9:25 a. m. and 110 ng/m^3 at 9:25 - 10:25 a. m.

In Belle, as in Baltimore, DMN was found by both techniques. Although the DMN levels were less than found in Baltimore, the two techniques gave essentially the same results (see Table 2). The highest DMN level that was found was 980 ng/m^3, with the sample being collected during a temporary weather inversion. In Belle, both DuPont and Union Carbide use or manufacture DMA. Airborne DMN may result either from atmospheric reaction of DMA with NO_x, or from a DMN impurity (usually less than 5 ppm) generally found in DMA. Independent cold trap GC-MS experiments were carried out by a DuPont analytical team, and their results agreed with those reported here to within an order of magnitude.[12] Using TEA-GC and TEA-HPLC, wastewater from DuPont and Fike Chemical Company was found to contain DMN at the 2000-4000 ng/l concentration level. Using GC-MS, DuPont scientists confirmed the presence of DMN in their wastewater.

DISCUSSION AND CONCLUSIONS

The presence of DMN in the air of two U. S. cities has been confirmed. In Baltimore, DMN levels between 1000 and 36,000 ng/m^3 were found in the immediate vicinity of a chemical factory which used DMN as an intermediate, and this must be considered as the most likely local DMN source. However, the DMN found several miles upwind of the chemical factory may come from another source. Potential sources included industrial users of amines, and combustion products from stationary and non-stationary sources. In Belle, the source of the DMN may be the amine chemical plants in the area, with air nitrosation being a possible mechanism. It should be noted that the studies reported here make no distinction between gas phase DMN, aerosol DMN or DMN adsorbed on the particulate. Air nitrosation could therefore have occurred in the gas, the liquid (aerosol droplet), or in the solid phase.

N-nitrosodimethylamine has been shown to be carcinogenic in a wide variety of laboratory animals. In mink fed DMN twice a week, a dose level of 50,000 ng/kg b. w. /day has been shown to be clearly carcinogenic.[13] DMN has also been shown to be carcinogenic if inhaled.[14] For inhalation studies the lowest level tested and shown to be carcinogenic was 200,000 ng/m^3 for rats and mice.[14] It is instructive to compare the DMN load from air with that from other known sources. Eating four slices of bacon per day would result in an uptake of about 500 ng DMN from most U. S. produced bacon products. The DMN intake from a pack of 20 cigarettes is about 1000 ng.[15] By comparison, an adult breathing air containing 1000 ng/m^3 of DMN for 24 hours would inhale about 10,000 to 14,000 ng of DMN per day.

At the present time, it is impossible to assess properly the carcinogenic risk to man when exposed to DMN levels of 50 - 30,000 ng/m^3, as reported here. However, the amount of DMN is relatively large when compared to the amount of other airborne carcinogens such as benzo (a) pyrene, which is found in urban atmospheres at the 2 ng/m^3 level.[16]

ACKNOWLEDGEMENTS

The work described here was carried out pursuant to U. S. Environmental Protection Agency Contract Nos 68-02-231214 (TECO) and 68-02-1228 (RTI). We thank E. I. DuPont DeNemours and Company, Inc., the Food Machinery Corporation, Union Carbide Corporation and Fike Chemical Company for permission to collect samples on their property. We also thank numerous city, state and regional EPA officials for assisting in every way possible with the collection of the data.

REFERENCES

1. Lijinsky, W. and Espstein, S. S., Nature (London) 225 21 (1970).

2. International Agency for Research on Cancer, Second and Third Meeting on the Analysis and Formation of N-nitroso Compounds, Lyon, France. IARC publications no. 3 and 9 (1974).

3. Anon., Chinese Medical Journal, (3), 167 (1975); International Agency for Research on Cancer, Annual Report for 1972-1973. Lyon, France (1973).

4. Mirvish, S. S., Toxicology and Applied Pharmacology 31, 325 (1975).

5. Fine, D. H., Rounbehler, D. P., Belcher, N. M., and Epstein, S. S. International Conference on Environmental Sensing and Assessment, Las Vegas (Oct. 1975). In the press; Fine, D. H., Rounbehler, D. P., Belcher, N. M., and Epstein, S. S. Science Magazine (In press).

6. Fine, D. H., Rufeh, F., and Lieb, D., Nature (London), 247, 309 (1974); Fine, D. H., and Rounbehler, D. P., J. Chromatog., 109, 271 (1975); Oettinger, P. E., Huffman, F., Fine, D. H., and Lieb, D., Anal. Letters 8, 411 (1975).

7. Fine, D. H., and Rounbehler, D. P., Presented at the First Chemical Congress of the North American Continent, Mexico City (Dec. 1975). Chapter 17 in "Identification and Analysis of Organic Pollutants in Water," American Chemical Soc. (In the press).

8. Pellizzari, E. D., Development of Method for Carcinogenic Vapor Analysis in Ambient Atmospheres. Publication No. EPA-650/2-74-121, Contract No. 68-02-1228, 148p (July 1974).

9. Pellizzari, E. D., Development of Analytical Techniques for Measuring Ambient Atmospheric Carcinogenic Vapors. Publication No. EPA-600/2-75-076, Contract No. 68-02-1288, 185p (Nov. 1975).

10. Pellizzari, E. D., Bunch, J. E., Berkley, R. E., and Bursey, J. T., Biomedical Mass Spectra. (In press).

11. Wade, W. A., Report of Study of N-nitrosodimethylamine, FMC Corporation, Industrial Chemicals Division, Baltimore, Maryland. The Research Corporation of New England Report No. 31555, (Nov. 1975).

12. Lasaske, B. Dimethylnitrosamine (DMN) Sampling Program Belle, W. VA Dec. 1-5, 1975, E. I. DuPont DeNemours and Company, Inc., Presented to EPA, Jan. 6 (1976); personal communication Lasaski, B.

13. Koppang. N., and Rimeslatten, H., Fourth Meeting on the Analysis and Formation of N-Nitroso Compounds, International Agency for Research on Cancer. Meeting held in Tallinn, USSR on October 1, 2; (1975) (In the press).

14. Moiseev, G. E., and Benemonskii, V. V., Vopresy Onkologii, 21, 107 (1975).

15. Rhoades, J. W., and Johnson, D. E., J. Nat. Cancer Inst. 48, 1841 (1972).

16. Faoro, R. B., J. Air Poll. Control Assoc., 25, 638 (1975).