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Note

Direct determination of N-nitrosamines in amines using a gas chromatograph–thermal energy analyzer

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In recent years the nitrosyl selective thermal energy analyzer (TEA) interfaced to a gas chromatograph[1] or a high-performance liquid chromatograph[2] has become routinely used for the determination of trace levels of N-nitroso compounds. An increasing number of laboratories have used the TEA to analyze air[3–7] and water[4,8] samples, pesticides[9], foodstuffs[10] and other commercial products[11,12] for N-nitrosamine content.

Despite the role of amines as N-nitrosamine precursors only a few papers have described the analysis of amines for N-nitrosamines. Spiegelhalder *et al.*[13] published a brief study of several commercial amines in which a gas chromatograph–TEA was used. A similar gas chromatography (GC)–TEA method was reported for the analysis of several alkylamines by Tully and Kuryla[14]. In both studies, the N-nitrosamine was isolated from the amine, prior to GC–TEA analysis, by acidification followed by dichloromethane extraction.

To date only one study has been reported describing the direct analysis of neat amines for N-nitrosamine content by GC–TEA. Parees[15] showed that similar results could be obtained for the quantification of nitrosamines in amines by GC–TEA analysis and GC–nitrogen–phosphorus detector analysis. A silica gel isolation procedure was used to separate the N-nitrosamine from the amine in the latter method. However, a recent paper reported suppression of the TEA nitrosamine response in the presence of amines[16].

The purpose of this study was to investigate amine matrix effects on the TEA response for N-nitrosamines. A comparison of TEA responses produced by N-nitrosamine standards of equal concentrations in amines and dichloromethane will be reported. The effects of various TEA operating conditions on the instrumental response to N-nitrosamines in such matrices will also be discussed.

EXPERIMENTAL

Instrumention

Aliquots (2–3 μl) of neat amines were injected into one of two Perkin-Elmer 3920 gas chromatographs used in this study. One was equipped with a flame ionization detector (FID) and the other was interfaced to a thermal energy analyzer Model 502 (Thermo Electron Corporation). The interface between the gas chromatograph

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and the TEA was constructed from a 10-in. length of 0.0625-in. narrow-bore stainless-steel tubing. Complete details of its construction were published previously[15]. The interface temperature was maintained at 250°C.

The double cold trap used with the TEA was fabricated from a 5-ft. length of 0.25-in. O.D. stainless-steel tubing bent into a W shape. The first leg was kept at −78°C (solid carbon dioxide–isopropanol) and the second at −160°C (liquid nitrogen–2-methylbutane) or −127°C (liquid nitrogen–*n*-propanol). Trap temperatures were measured using an alcohol thermometer (Fisher Scientific, Pittsburgh, PA, U.S.A., Cat. No. 15-038). In some of the experiments, a 4 × 0.25 in. O.D. stainless-steel tube filled with 60–80 mesh Tenax GC resin was placed in line between the cold traps and the reaction chamber.

The TEA oxygen flow-rate was set at 15 ml/min and the detector cell pressure was 1.2 Torr (143 Pa) in the GC mode. The catalytic furnace temperature was set at 450°C except as noted. The recorder used has a 5-V span.

The GC injection ports were maintained at 200°C and the interface to the FID was maintained at 260°C.

Chemicals

N-Nitrosodimethylamine (NDMA), N-nitrosomorpholine (NMOR) and diethylamine (DEA) were obtained from Aldrich (Milwaukee, WI, U.S.A.). Dichloromethane (DCM) and *n*-propanol were distilled-in-glass high purity solvents from Burdick & Jackson Labs. (Muskegon, MI, U.S.A.). The DCM was tested for impurities by concentration to one part in 1000 parts. No interfering chromatographic species were found. The 2-methylbutane was obtained from Eastman Chemicals (Rochester, NY, U.S.A.). The morpholine was obtained from Jefferson Chemical Company.

Chromatography

The GC–FID work was done using a 10-ft. × 0.125 in. O.D. stainless-steel (premium grade; Supelco, Bellefonte, PA, U.S.A.) column packed with 10% Carbowax 20M on 2% KOH-treated Chromosorb W HP (100–120 mesh). Helium was used as the carrier gas at a flow-rate of 27 ml/min.

The GC–TEA work was done using an 11-ft. column identical in all other respects to the column described above. Argon was used as the carrier gas at a flow-rate of 30 ml/min. The column temperature was 160°C for all work except the morpholine experiments, in which 210°C was used.

RESULTS AND DISCUSSION

The response of nitrosamines in the presence of amines was studied to show that under typical operating conditions the simultaneous presence of amines and the nitrosamines in the catalyst chamber does not affect the TEA response. It had been postulated that the nitrosyl radical cleaved from the nitrosamine in the catalyst chamber could, in the presence of an amine, react to form another nitrosamine upon leaving the chamber[16]. Depending upon the degree of this recombination, either a diminished or lack of TEA response for the nitrosamine would be observed.

Initially the TEA response of NDMA in the presence of DEA was studied.

NDMA was chosen instead of N-nitrosodiethylamine (NDEA) for spiking into DEA so that no correction for the background concentration of NDEA was required. Examination of the DEA, by injection of 8.0 μl of the neat amine, indicated that no NDMA was present (less than 5.3 ppb) and the concentration of NDEA was 46 $\pm$ 5 ppb*. Identification and quantification of the N-nitrosamines were carried out by a comparison with the retention times and responses of known standards. NDMA elutes relatively early in the DEA peak tail, with considerable component overlap (Fig. 1).

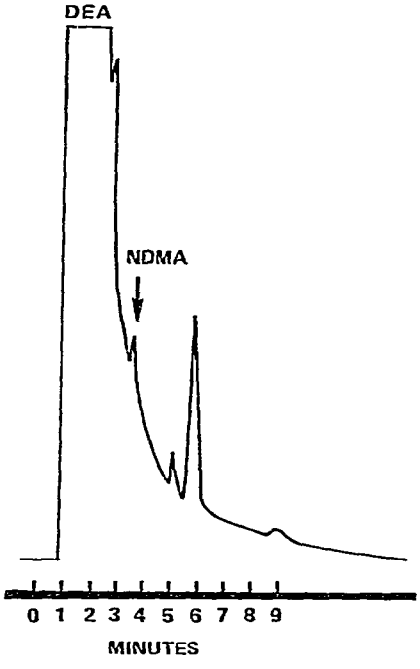

Fig. 1. GC–FID chromatogram of 1.9 μl of 1.17 ng/μl NDMA/DEA.

As a result, the amount of DEA co-eluting with NDMA under these conditions is many times greater than the spiked level of NDMA. Table I lists the results of several analyses with the TEA detector comparing equal levels of NDMA in both DCM and DEA measured using various operating conditions. There was no difference in the detector response to the nitrosamine contained in DEA as compared with DCM (Fig. 2). The cold-trap temperature, the presence or absence of a Tenax trap in line with the detector, and the catalytic furnace temperature were all investigated, as listed in Table I. No significant differences in response were noted for the two nitrosamine solutions. Fiddlet *et al.*[17] studied the effects of various cold-trap temperatures (0 to −196°C) on TEA selectivity for complex matrices They found that different matrices required different optimal cold-trap temperatures, although no difference in TEA response was observed in this work. Lowering the catalyst furnace temperature (from

* The American part per billion (10^9) is meant.

TABLE I

COMPARISON OF GC–TEA RESPONSE OF N-NITROSAMINE IN DICHLOROMETHANE *VS.* DIETHYLAMINE

*Sample**,***	*N-Nitroso-dimethylamine (mm peak height/μl)****,§	*Cold-trap temperatures (°C)*	*Tenax trap present*	*Furnace temperature (°C)*
NDMA/DCM	46.0 ± 0.9	−78/−160	yes	450
NDMA/DEA	44.7 ± 1.3	−78/−160	yes	450
NDMA/DCM	47.2 ± 1.0	−78/−160	no	450
NDMA/DEA	48.2 ± 0.7	−78/−160	no	450
NDMA/DCM§§	62.5 ± 1.3	−78/−160	yes	350
NDMA/DEA§§	62.4 ± 0.3	−78/−160	yes	350
NDMA/DCM	48.1 ± 0.6	−78/−127	yes	450
NDMA/DEA	47.1 ± 0.4	−78/−127	yes	450

* All samples were prepared at a concentration of 1.17 ng/μl regardless of the solvent.

** The injection volumes were 2–3 μl.

*** Arbitrary units for comparison.

§ ± standard deviation of 3–4 injections in each case.

§§ Attenuation of the detector output was ×4 for these analyses. It was ×32 for all other work in this table.

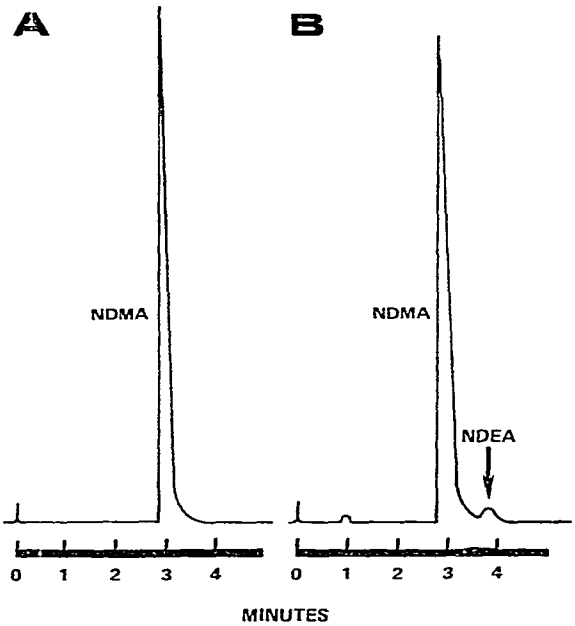

Fig. 2. (A) GC–TEA chromatogram of 2.45 μl of 1.17 ng/μl NDMA/DCM; response = 47.4 mm/μl; (B) GC–TEA chromatogram of 2.30 μl of 1.17 ng/μl NDMA/DEA; response = 47.8 mm/μl. Furnace temperature, 450°C; cold-trap temperature −78 and −160°C; the Tenax trap was in line.

450 to 350°C) decreased the nitrosamine response, but the diminished response was equal for both solutions. Hansen *et al.*[18] have reported response–temperature profiles for several N-nitrosamines and C-nitro compounds. The Tenax trap is sometimes useful for removing large "solvent front" interfering peaks sometimes present in TEA

chromatograms. The interfering components are believed to be volatile molecules such as olefins and ketenes, which may be pyrolysis products from the amines or solvents. Compounds volatile enough to pass through the cold trap are held up on the Tenax resin.

To investigate if other amines might be more subject to anomalous suppression of TEA response, morpholine was chosen for a similar study. GC–TEA analysis confirmed co-elution of N-nitrosomorpholine (NMOR) and the morpholine peak tail, similar to the case of NDMA in DEA. Analysis of the morpholine indicated a background level of 21 $\pm$ 2 ppb NMOR. The comparative NMOR studies in DCM *vs.* morpholine were corrected by this amount. The results again showed no suppression effect.

This study shows that amines can be analyzed for nitrosamine content without prior clean-up or isolation steps using a GC–TEA instrument. Detection limits of 30–40 pg NDMA and 70–80 pg NMOR were achieved with the present chromatographic system. Precision of $\pm$ 5% at ten times the detection limit was routinely obtained using external standards, and day-to-day intrumental stability is good.

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