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## PYROLYSIS GAS-LIQUID CHROMATOGRAPHY OF N,N-DIMETHYL-ALKYLAMINE N-OXIDES AND THEIR MIXTURES

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### SUMMARY

A rapid quantitative and small scale method based on direct injection pyrolysis gas-liquid chromatography is described for the determination of N,N-dimethylalkylamine N-oxides. The method is suitable for determination of individual N-oxides as well as of their homologous compositions with or without the presence of parent tertiary amines in water or methanol solutions. The sensitivity of the method is 10–15 nmol of compounds injected. The unsymmetrical (1-methyldodecyl)dimethylamine N-oxide forms two isomeric alkenes 1-tridecene and *trans*-2-tridecene in a ratio of 1.68, in agreement with the predicted value.

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### INTRODUCTION

Non-aromatic amine oxide surfactants have wide technological and basic scientific applications in physical and biological systems<sup>1,2</sup>. A rapid and quantitative small scale analytical method is required for determination of these compounds not only as individual substrates but often in mixtures containing two or more members of homologous series and/or of the parent N,N-dimethylalkylamines.

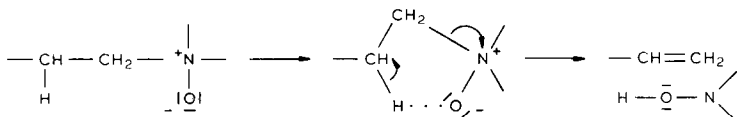
Such a method is essential for determining small amounts of amine oxides from an environmental point of view, as well as in studies of their biological activity or their biological formation, *e.g.*, in *in vitro* tests, as the results obtained are clearly dependent upon the purity of the substrates used. Since amine oxides are usually prepared by oxidation of the corresponding tertiary amines, they can contain them as impurities.

Analytical methods used to date for determination of individual amine oxides and their homologous mixtures are summarized in a recent review<sup>3</sup>. Some of these methods are tedious and ill suited to small scale analysis, because of low sensitivity (titration methods) or require relative large amounts of compound (IR, <sup>1</sup>H NMR) or

are unable to detect individual members in mixtures of homologues (reductometric methods and methods using  $^{18}\text{O}$ -labelling).

The heat sensitivity of non-aromatic amine oxides make them suitable for pyrolysis gas-liquid chromatography (GLC) which is a method sensitive enough to determine small amounts of compounds and at the same time separate the reaction products (alkenes) from the parent amines. This method is, however, limited to amine oxides possessing at least one  $\beta$ -hydrogen and is not suitable for N-methyl six-membered heterocycloalkylamine N-oxides<sup>4</sup>.

It is well known, *e.g.*, refs. 4 and 5 that non-aromatic tertiary amine oxides containing one or more  $\beta$ -hydrogens undergo cleavage upon heating to produce an alkene and N,N-dialkylhydroxylamine (Cope reaction). The reaction is a stereoselective *syn* process and a five-membered  $\text{E}_i$  mechanism operates:



The reaction requires mild conditions ( $100$ – $150^\circ\text{C}$ ), however the conversion of alkylamine N-oxide into alkene at these temperatures is usually not quantitative<sup>6</sup>. Solvents play a decisive rôle: with tetrahydrofuran or dimethyl sulphoxide the reaction can proceed even at room temperature<sup>7</sup>; hydroxylic solvents capable of hydrogen bonding, such as alcohols and water, stabilize the amine oxide.

To overcome these difficulties, different techniques have been devised, *e.g.*, use of a separate pyrolytic unit attached to the inlet port of a gas chromatograph and heated to  $650^\circ\text{C}$ <sup>8</sup> or direct injection with injector temperatures of  $220^\circ$ ,  $300^\circ$ <sup>10</sup> or  $150$ – $340^\circ\text{C}$ <sup>11</sup>, or use of ionic exchangers before GLC analysis<sup>12</sup>.

In this communication we present the results of direct injection pyrolysis GLC of an homologous series of N,N-dimethylalkylamine N-oxides (alkyl: hexyl to hexadecyl); mixtures of amine oxides and in the presence of parent N,N-dimethylalkylamines.

## EXPERIMENTAL

### Materials

N,N-Dimethylalkylamines,  $\text{C}_n\text{H}_{2n+1}\text{N}(\text{CH}_3)_2$  ( $n = 6, 8, 10, 12, 14$  or  $16$ ) and  $\text{C}_{10}\text{H}_{21}\text{CH}[\text{N}(\text{CH}_3)_2]\text{CH}_3$  (2-ATD), were prepared from doubly distilled 1-alkylamines and (1-methyldodecyl) amine by reductive methylation using formic acid and formaldehyde<sup>13</sup>. The resulting tertiary amines were purified by double distillation from sodium wire under nitrogen using a 30-cm Vigreux column and stored in the dark in sealed ampoules under a nitrogen atmosphere.

The corresponding N-oxides were prepared by a method described earlier<sup>14</sup> using a 30% aqueous solution of hydrogen peroxide in 10% molar excess. After azeotropic drying, the hygroscopic compounds were crystallized four to six times from dry acetone until pure according to thin-layer chromatography<sup>15</sup> (TLC), dried and stored over  $\text{P}_4\text{O}_{10}$  *in vacuo*. 1-Dodecylpyrrolidine N-oxide, 1-dodecylpiperidine N-oxide, 4-dodecylmorpholine N-oxide and 1-dodecylperhydroazepine N-oxide were prepared in the same way.

1-Alkenes were obtained as follows: 1-hexene, 1-octene, 1-dodecene from Aldrich (U.K.); 1-decene, 1-tetradecene, 1-hexadecene from Lancaster Synthesis (U.K.); *trans*-2-octene from Sigma (U.K.). Organic solvents used were of high-performance liquid chromatographic (HPLC) purity (Fison's, U.K.).

### Methods

GLC was carried out on a Perkin-Elmer Model F33 gas chromatograph equipped with flame ionization detection. The precoiled glass column (1 m × 3 mm I.D.) was packed with 8% Apiezon L on Chromosorb G AW DMCS (80–100 mesh) and 10% potassium hydroxide, conditioned for 48 h before use. The part of the column inserted into the injection port (*ca.* 7 cm) was packed with non-treated support material. Gas pressures were set as follows (kN/m<sup>2</sup>): air 126, hydrogen 140, nitrogen (carrier gas) 175, except for 1-hexene (and consequently also for N,N-dimethylhexylamine N-oxide) which was 35 kN/m<sup>2</sup>. The injection port temperatures were 200, 250, 300, 375 or 450°C. For the final analysis it was maintained at 450°C. The column temperature was programmed from 50 to 220°C at 4°C/min with an initial hold of 10 min. The samples (1 ml of different concentrations in methanol or water) were directly injected into the gas chromatograph. The peak areas were determined by a standard integration method. Relative retention times (RRTs) were calculated according to ref. 8 and are based on a time of 100 for 1-decene and a time of zero for the injection of the sample.

### RESULTS AND DISCUSSION

The estimated lowest amounts required for quantitative analysis according to the sensitivity of the method (under the described experimental conditions) were 10–15 nmol of the injected compounds. The detectable amounts were about 5 nmol, however, these concentrations were useful only for qualitative purposes. For the lower members of the homologous series ( $n = 6$  and 8), *i.e.*, tertiary amines and 1-alkenes formed by pyrolysis of the parent amine oxides, the peaks were very close to the solvent front when using methanol. In the case of aqueous solutions there was no interaction with the solvent.

Table I summarizes the retention times and relative retention times for 1-alkenes formed by pyrolysis of the parent amine oxides and N,N-dimethylalkylamines. Included are also the results for the *trans*-2-octene standard and the 1- and *trans*-2-tridecene pyrolysis products. The tridecenes were formed from (1-methyldodecyl) dimethylamine oxide in 62.7% (1-tridecene,  $t_R = 71$  min) and 37.3% (*trans*-2-tridecene,  $t_R = 64$  min) yield, respectively, and were well separated at 95°C. At 150°C the two peaks collapse to one symmetrical peak with a retention time of 8.0 min.

Thermal degradation of N,N-dimethylalkylamine oxides with a straight chain alkyl substituent gives 1-alkenes and N,N-dimethylhydroxylamine. Though it is generally believed that this reaction requires mild conditions (100–150°C), it has been previously shown<sup>6</sup> that at 100°C the pyrolysis of N,N-dimethyldodecylamine oxide yields only 11–21% of 1-dodecene and 52–53% of deoxygenated product (N,N-dimethyldodecylamine). Increasing the temperature to 120°C improved the yield of 1-dodecene to 86.5%, however, still *ca.* 12% of tertiary amine was formed. Our results (Table II) shows that the quantitative pyrolysis of N,N-dimethylalkylamine

TABLE I

RETENTION TIMES,  $t_R$ , AND RELATIVE RETENTION TIMES (RRT) OF 1-ALKENES  $C_mH_{2m}$  (A), FORMED BY PYROLYSIS OF N,N-DIMETHYLALKYLAMINE N-OXIDES AND OF N,N-DIMETHYLALKYLAMINES  $C_nH_{2n+1}N(CH_3)_2$  (B)<sup>a</sup>

| A               |                |     | B                  |                |     |
|-----------------|----------------|-----|--------------------|----------------|-----|
| <i>m</i>        | $t_R$<br>(min) | RRT | <i>n</i>           | $t_R$<br>(min) | RRT |
| 6 <sup>b</sup>  | 2.8            | 11  | 6                  | 9.1            | 34  |
| 8 <sup>b</sup>  | 16.0           | 60  | 8                  | 21.4           | 81  |
| 8 <sup>c</sup>  | 21.0           | —   | —                  | —              | —   |
| 10              | 26.6           | 100 | 10                 | 30.8           | 116 |
| 12              | 35.4           | 133 | 12                 | 38.8           | 146 |
| 14              | 42.6           | 160 | 14                 | 45.9           | 173 |
| 16              | 49.3           | 185 | 16                 | 58.5           | 221 |
| 13 <sup>d</sup> | 64.0           | —   | 2-ATD <sup>e</sup> | 5.8            | —   |
|                 | (62.7%)        |     |                    |                |     |
| 13 <sup>f</sup> | 71.0           | —   | —                  | —              | —   |
|                 | (37.3%)        |     |                    |                |     |

<sup>a</sup> Injection port temperature 450°C, column temperature programmed from 50 to 220°C at 4°C/min with an initial hold of 10 min.

<sup>b</sup> Nitrogen pressure = 35 kN/m<sup>2</sup>.

<sup>c</sup> *trans*-2-Octene standard; conditions same as in footnote *b*.

<sup>d</sup> 1-Tridecene (oven temperature 95°C).

<sup>e</sup> (1-Methyldodecyl)dimethylamine (oven temperature 210°C).

<sup>f</sup> *trans*-2-Tridecene (oven temperature 95°C).

oxides to 1-alkenes requires temperatures well above 250°C. This finding is not surprising in the light of the high sensitivity of aliphatic amine oxides to some metal ions which catalyse their deoxygenation to tertiary amines. In contact with the metal surface of the injection port at relatively low temperatures, the amine oxides can easily be reduced to their parent tertiary amines.

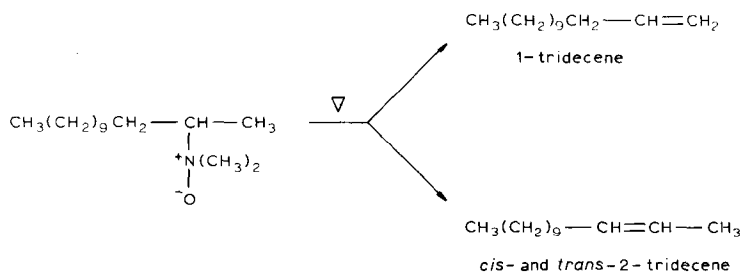
TABLE II

INJECTION PORT TEMPERATURE DEPENDENT DEOXYGENATION OF N,N-DIMETHYLALKYLAMINE N-OXIDES,  $C_mH_{2m+1}N(O)(CH_3)_2$ , TO N,N-DIMETHYLALKYLAMINES

For conditions see Experimental. Values are percentages.

| <i>m</i> | Temperature (°C) |     |     |                |     |
|----------|------------------|-----|-----|----------------|-----|
|          | 200              | 250 | 300 | 375            | 450 |
| 6        | 1.2              | 0.2 | 0.1 | 0 <sup>a</sup> | 0   |
| 8        | 1.2              | 0.4 | 0.1 | 0              | 0   |
| 10       | 1.0              | 0.6 | 0.2 | 0              | 0   |
| 12       | 1.6              | 0.5 | 0.2 | 0.02           | 0   |
| 14       | 1.8              | 0.7 | 0.4 | 0              | 0   |
| 16       | 1.3              | 0.4 | 0.2 | 0              | 0   |
| 2-ATDNO  | 1.5              | 0.5 | 0.3 | 0.02           | 0   |

<sup>a</sup> 0 represents less than 0.02% conversion to the amine.



We included in our experiments an unsymmetrical long chain amine oxide (1-methyldodecyl)dimethylamine oxide (2-ATDNO) to study the formation of different isomeric alkenes. Using high column temperatures (210°C) for rapid analysis of mixtures containing this compound, we observed a sharp and symmetrical peak of non-resolved alkenes. Because of the possibility that this amine oxide forms different reaction products we carried out a more detailed analysis of the pyrolysis of 2-ATDNO.

The reaction theoretically follows Hofmann's rule and the main product is expected to be a 1-alkene. In reality this is the case; 1-tridecene was formed in 62.7% yield, other isomers giving an total yield of 37.3%. From the generally accepted mechanism of amine oxide pyrolysis (five-centre *cis* intramolecular elimination) the *cis* isomer is more likely to occur. The orientation of the double bond is statistical and is determined by the number of  $\beta$ -hydrogens available. However, steric effects in long chain molecules play an important rôle and can influence the direction of elimination by the need to minimize steric interactions in the transition state or to relieve steric interactions in the ground state. In this case the Zaitsev product (2-alkene) should be formed. Our results (Table I) show that the orientation in pyrolytic elimination of 2-ATDNO is statistically, as well as sterically, dependent. The ratio of 1-alkene and 2-alkene formed (1.68) is very close to the 3:2 distribution predicted statistically using the number of  $\beta$ -hydrogens available.

The transition state requires that eclipsing of the 1,2-alkyl group be at a maximum in order to obtain the *cis*-olefin, while production of the *trans* isomer would involve only hydrogen-alkyl eclipsing. This effect may influence the course of the reaction and suggests that the effect is greater when one of the eclipsed groups is ethyl or larger<sup>16</sup>. In our case the eclipsing group is dodecyl which would indicate that the formation of *trans*-2-tridecene is preferred. In fact we did not detect any *cis*-olefin. These results are in agreement with the findings of Cope *et al.*<sup>16</sup> for N,N-dimethylisobutylamine N-oxide which upon pyrolysis yielded 67.3% 1-butene, 11.7% *cis*- and 21% *trans*-2-butene, and for (1-ethylpropyl)dimethylamine oxide which yielded 29% of *cis*- and 71% of *trans*-2-pentene, respectively.

Fig. 1 illustrates the separation of 1-alkenes (formed by pyrolysis of mixtures of N,N-dimethylalkylamine oxides) and different N,N-dimethylalkylamines. Samples (1  $\mu$ l) containing equal amounts of N,N-dimethylalkylamine N-oxides and N,N-dimethylalkylamines in water were injected at an injection port temperature of 450°C. The samples were prepared by dissolving homologous amine oxides in water and adding tertiary amines to this solution so that the concentration of each compound in the final mixture injected was  $1 \cdot 10^{-5}$  g. After sonication, clear solutions were obtained.

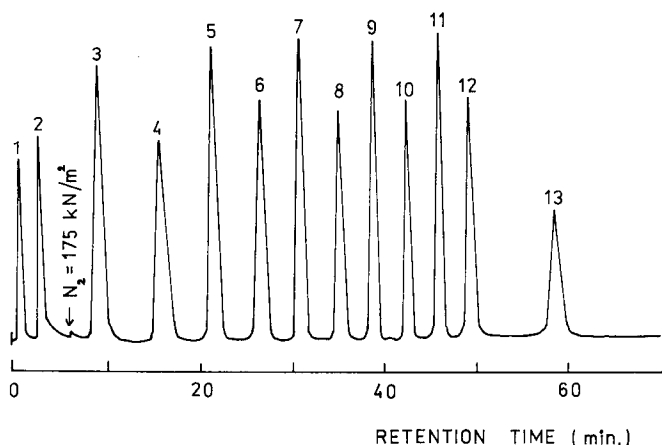


Fig. 1. Separation of pyrolysis products of *N,N*-dimethylalkylamine *N*-oxides (1-alkenes and *N,N*-dimethylhydroxylamine) and appropriate *N,N*-dimethylalkylamine standards. Conditions: injection port temperature 450°C; column temperature programmed from 50 to 220°C at 4°C/min with a 10-min initial hold; carrier gas, 175 kN/m<sup>2</sup> nitrogen; 1  $\mu$ l of an aqueous solution containing a  $1 \cdot 10^{-5}$  g of *N,N*-dimethylalkylamine *N*-oxides and *N,N*-dimethylalkylamines, respectively. Peak identities: 1 = *N,N*-dimethylhydroxylamine; 2 = 1-hexene; 3 = C<sub>6</sub>dimethylamine; 4 = 1-octene; 5 = C<sub>8</sub>dimethylamine; 6 = 1-decene; 7 = C<sub>10</sub>dimethylamine; 8 = 1-dodecene; 9 = C<sub>12</sub>dimethylamine; 10 = 1-tetradecene; 11 = C<sub>14</sub>dimethylamine; 12 = 1-hexadecene; 13 = C<sub>16</sub>dimethylamine.

2-ATD and 2-ATDNO were not included in this mixture. The retention times of the 1-alkenes formed were identical with those of standard compounds. The same results were obtained irrespective of whether aqueous or methanolic solutions were used.

The peak with  $t_R = 1$  min was obtained for the product of pyrolysis of respective *N*-oxides and was comparable to that for standard *N,N*-dimethylhydroxylamine.

In the case of *N*-dodecylheterocycloalkylamine oxides (pyrrolidine, piperidine, morpholine, perhydroazepine), 1-dodecene was formed exclusively, clearly as the result of the stereochemistry of the pyrolyzed compounds.

## CONCLUSIONS

The results indicate that pyrolysis GLC can be used for qualitative as well as quantitative determination of nanomolar quantities of individual as well as mixtures of homologous *N,N*-dimethylalkylamine oxides and in the presence of the parent tertiary amines. The method does not require, *e.g.*, a separate pyrolysis unit and is sensitive enough even for a complex mixture containing six amine oxides and six parent tertiary amines with an alkyl chain length variation from C<sub>6</sub> to C<sub>16</sub>. Under the given experimental conditions no deoxygenation of amine oxides to tertiary amines occurs and 1-alkenes are formed quantitatively.

## ACKNOWLEDGEMENTS

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