

## DETERMINATION OF ALKIMIDE GROUPS BY MODIFIED HERZIG-MEYER METHOD USING VAPOUR-PHASE INFRARED SPECTROSCOPY

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Vapour-phase infrared spectroscopy has been used for the quantitative determination of the alkimide groups (N-CH<sub>3</sub>) by the modified Herzig-Meyer method. The main features of this method are that the reaction is carried out in a sealed tube at comparatively low temperatures and the amount of hydriodic acid used is very small. For most of the compounds under study a reaction period of about two hours is suitable. The modified method is simple, economical, accurate and much more rapid than those previously described.

### Introduction

The determination of alkimide groups is based on the formation of the corresponding quaternary alkyl-ammonium iodide when treated with hydriodic acid.

The gravimetric or the iodometric method<sup>1</sup> of estimating alkimide groups is useful and works quite well for many substances, such as atropine, cocaine hydrochloride and theobromine,<sup>2</sup> but a survey of the literature indicates that the determination of alkimide groups by the Herzig-Meyer method is a difficult operation and requires 6-8 hours for a single determination.<sup>3,4</sup> Other investigators report a rapid sub-micro method of determining the tertiary nitrogen content of certain organic compounds.<sup>5</sup> It was observed, however, that some compounds did not give quantitative results due to the non-splitting off, quantitatively, of the alkyl iodide.<sup>1,5</sup>

Considerable attention has been devoted in recent years to the development of new methods of analysis, including the ion exchange resin method.<sup>5</sup> Vapour-phase infrared spectroscopy offers a rapid and accurate method for the quantitative estimation of alkimide groups (N-CH<sub>3</sub>).

### Experimental

#### REAGENTS

|                |                    |
|----------------|--------------------|
| Hydriodic acid | M.A.R. Sp. gr. 1.7 |
| Anhydron       | M.A.R. 14-22 mesh  |
| Soda-asbestos  | M.A.R.             |

Methyl iodide

Spectroscopically pure  
for calibration purposes.

#### GAS CELLS:

A 10 cm gas-cell supplied by Leitz Co.

#### APPARATUS

The apparatus was assembled as shown in Fig. 1, and consisted of:

- (a) A glass tube of 20 cm long and a diameter of 3 cm with a B<sub>14</sub> cone.
- (b) A delivery tube, which is packed with anhydron and soda-asbestos. Ground-glass joints are coated with silicone grease.
- (c) A trap made with Vigreux type indentations in the inner absorption tube,<sup>6</sup> as shown in Fig. 1.

#### SPECTROMETER

A Leitz automatic recording double-beam spectrometer was used in the present investigations. This spectrograph has space for gas cells upto 20 cm. With the normal slit programme and a sodium chloride prism the spectrograph gives resolutions of about 20 cm<sup>-1</sup>, which is sufficient for our studies in the region of the observed alkyl iodide peaks.

#### CALIBRATION CURVES

The required amount of methyl iodide was weighed in a micro-weighing bottle (10 × 5 mm) fitted with a leak-proof ground-glass stopper.

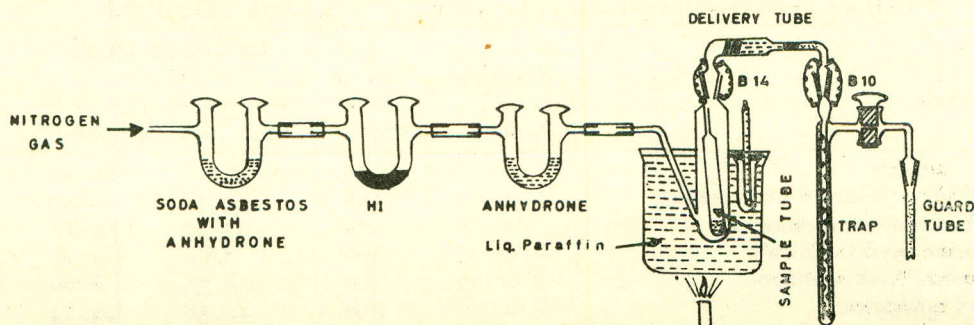


Fig. 1.—Assembled apparatus.

The bottle was placed through the position A in the trap as shown in Fig. 2, the limb of the trap was immersed in liquid nitrogen. The evacuated gas-cell was kept at A and the trap was evacuated by

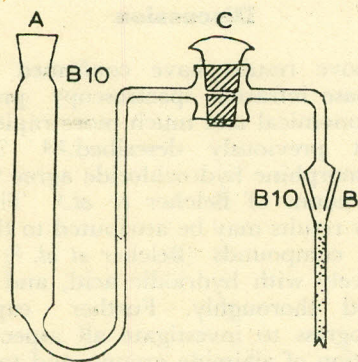


Fig. 2.—Calibration curve for the determination of methyl iodide.

connecting B to a vacuum line. The trap was warmed to vaporise the methyl iodide into the gas-cell. The stopper C was opened to the atmosphere (The air would rush through an anhydron guard tube and the trap into the gas cell making the total pressure equal to that of the atmosphere. The particular absorption peak selected for calibration ( $1265\text{ cm}^{-1}$ ) was recorded three times, and the mean peak height was then calculated. Fig. 3. shows a typical calibration curve of methyl iodide, using a 10 cm gas-cell.

#### FLOW OF CARRIER GAS

Nitrogen (pure 99.9%) was passed through soda-asbestos anhydron and pure hydriodic acid (which was used for controlling the flow rate) and then again through an anhydron tube in order to absorb the vapours of hydriodic acid.

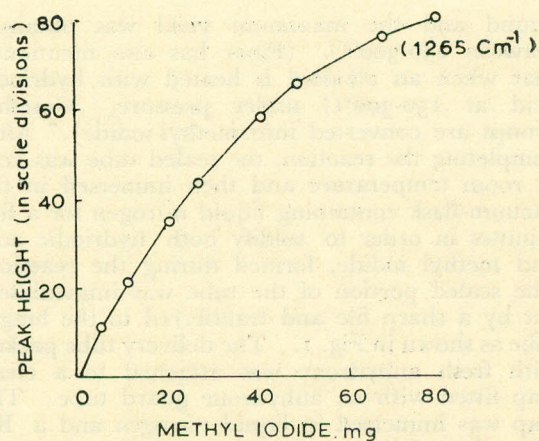


Fig. 3.—Calibration trap.

#### COMPOUNDS

The majority of the compounds investigated were analytically pure. Ajmaline was kindly provided by Mr. Vaqar-uddin Ahmed of Chemistry Division, for which satisfactory elemental analysis existed.

#### PROCEDURE

Samples (60-90 mg) of each compound listed in Table I was weighed directly in a thick walled Pyrex test tube, and 1.5 ml of constant boiling hydriodic acid was added to it. The tube was sealed from the top and put in a guard iron or copper tube containing high-boiling paraffin liquid or wax. This guard tube was further placed in a metal bath. Extreme care was necessary when volatile samples were used and while carrying out the reaction at higher temperature.

By preliminary experiments it was found that two-hour reaction time is enough for each com-

TABLE I.—DETERMINATION OF N-CH<sub>3</sub> GROUPS IN KNOWN COMPOUNDS.

| Compounds                                     | Reaction period (hours) | Metal bath temp. °C. | Alkimide content N(CH <sub>3</sub> ) <sub>n</sub> |         | Dif. ference % |
|---|-------------------------|----------------------|---|---------|----------------|
|   |                         |                      | theoretical %                                     | Found % |                |
| 1. Methyl aniline                             | 2                       | 250                  | 27.10   | 26.93   | -0.17          |
| 2. <i>N</i> -methyl-3-ethyloro-6 nitroaniline | 2                       | 300                  | 15.58   | 15.40   | 0.18           |
| 3. Ephedrinium hydrochloride                  | 2                       | 250                  | 14.42   | 14.22   | -0.20          |
| 4. Morphine hydrochloride                     | 2                       | 300                  | 7.69  | 7.07    | -0.62          |
| 5. Cocainium hydrochloride                    | 2                       | 300                  | 8.55  | 8.60    | +0.05          |
| 6. Methyl ephidrine                           | 2                       | 300                  | 24.58   | 24.74   | +0.16          |
| 7. Atropine                                   | 2                       | 250                  | 9.98  | 9.82    | -0.16          |
| 8. Dimethyl aniline                           | 2                       | 275                  | 36.36   | 36.31   | -0.05          |
| 9. Ajmaline                                   | 2                       | 300                  | 8.10  | 7.93    | -0.17          |

pound and the maximum yield was obtained between 250-300°C. (Finar has also mentioned that when an alkaloid is heated with hydriodic acid at 150-300°C under pressure, *N*-methyl groups are converted into methyl iodide).<sup>7</sup> After completing the reaction, the sealed tube was kept at room temperature and then immersed in the vacuum-flask containing liquid nitrogen for a few minutes in order to solidify both hydriodic acid and methyl iodide, formed during the reaction. The sealed portion of the tube was immediately cut by a sharp file and transferred to the longer tube as shown in Fig. 1. The delivery tube packed with fresh anhydrous was attached to a clean trap fitted with an anhydrous guard tube. The trap was immersed in liquid nitrogen and a B<sub>14</sub> cone of the delivery tube was attached to the outer reaction tube which was immersed in a bath filled with liquid paraffin. The nitrogen flow rate of 15-20 bubbles/min was adjusted through hydriodic acid. After 30-minute refluxing of the contents of the reaction tube, the delivery tube was removed and the trap was closed, keeping it immersed in the liquid nitrogen. The evacuated gas-cell was placed on the trap and the whole system evacuated. The system was removed from the vacuum line and then the trap from the liquid nitrogen. The trapped reaction products were volatilised into the gas-cell. The whole spectrum of the products on infrared spectrograph was taken. The characteristic peak was drawn thrice (ensuring that the correct base line was given) on which calibration of methyl iodide was based. The average height for methyl iodide was referred to the appropriate calibration curve, and the weight of the methyl iodide liberated was thus determined. In order to check the retention of methyl iodide in the reaction tube, another evacuated gas-cell was immediately replaced on the B<sub>14</sub> cone of the reaction tube in order to collect the remaining product in the sample tube. On running the spectrum, no methyl iodide was found, which

confirmed the total recovery of methyl iodide in the trap. Table I shows the results obtained from standard compounds containing alkimide groups after two-hours reaction period.

### Discussion

The above results have confirmed that the vapour-phase infrared spectroscopy provides a simple, economical and much more rapid method than that previously described.<sup>3,4</sup> The low results of morphine hydrochloride agree well with the observations of Belcher *et al.*<sup>5</sup> The reason for the low results may be attributed to the failure of certain compounds (Belcher *et al.*<sup>5</sup>) to react quantitatively with hydriodic acid, and must be investigated thoroughly. Further experiments are in progress to investigate all aspects of the determination of alkimide groups, and to improve the sensitivity, reproducibility and accuracy of the modified Herzig-Meyer method. The results will be published in due course.

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